Electronic Supplementary Information

Residue dependent hydrogen bonding preferences in orthanilic acid-based short peptide β-turn motifs

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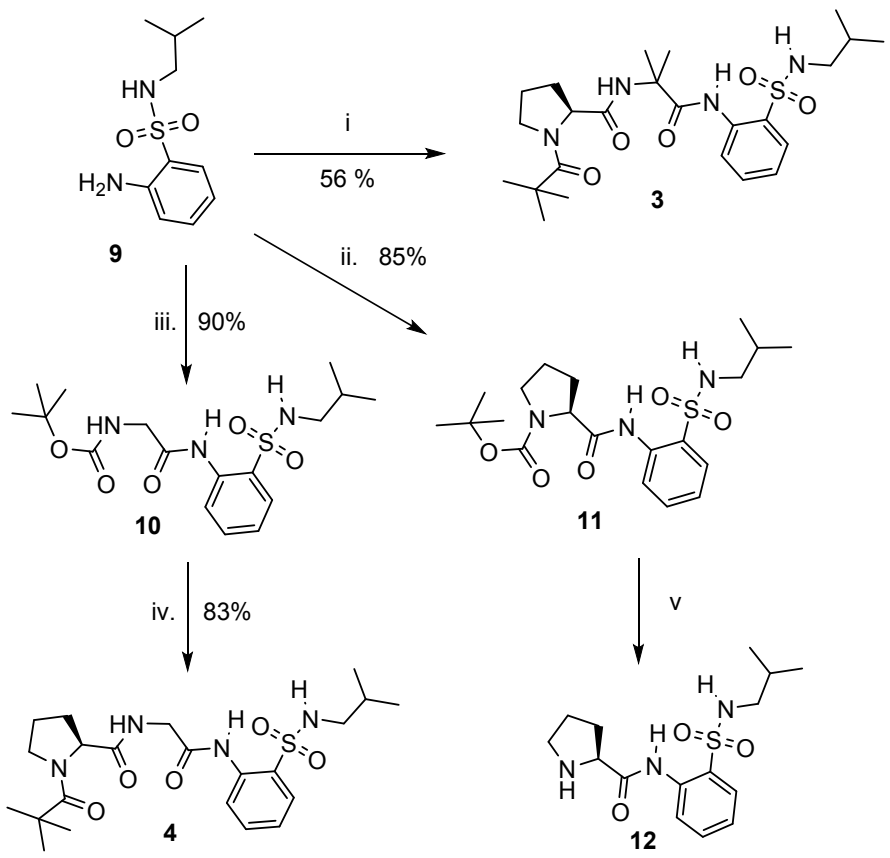
General Methods.

Unless otherwise stated, all the chemicals and reagents were obtained commercially. Dry solvents were prepared by the standard procedures. Analytical Thin Layer Chromatography was done on pre-coated silica gel plates (Kieselgel $60F_{254}$, Merck). Unless otherwise stated, column chromatographic purifications were done with 100-200 or 240-400 mesh silica gel. NMR spectra were recorded in $CDCl_3$ on Bruker spectrometers. All chemical shifts are reported in δ ppm downfield to TMS and peak multiplicities as singlet (s), doublet (d), quartet (q), broad singlet (bs), and multiplet (m) etc. The titration studies were done in $CDCl_3$. IR spectra were recorded in $CHCl_3$ using Shimadzu FTIR-8400 spectrophotometer. Melting points were determined on a Buchi Melting Point B-540 and are uncorrected.

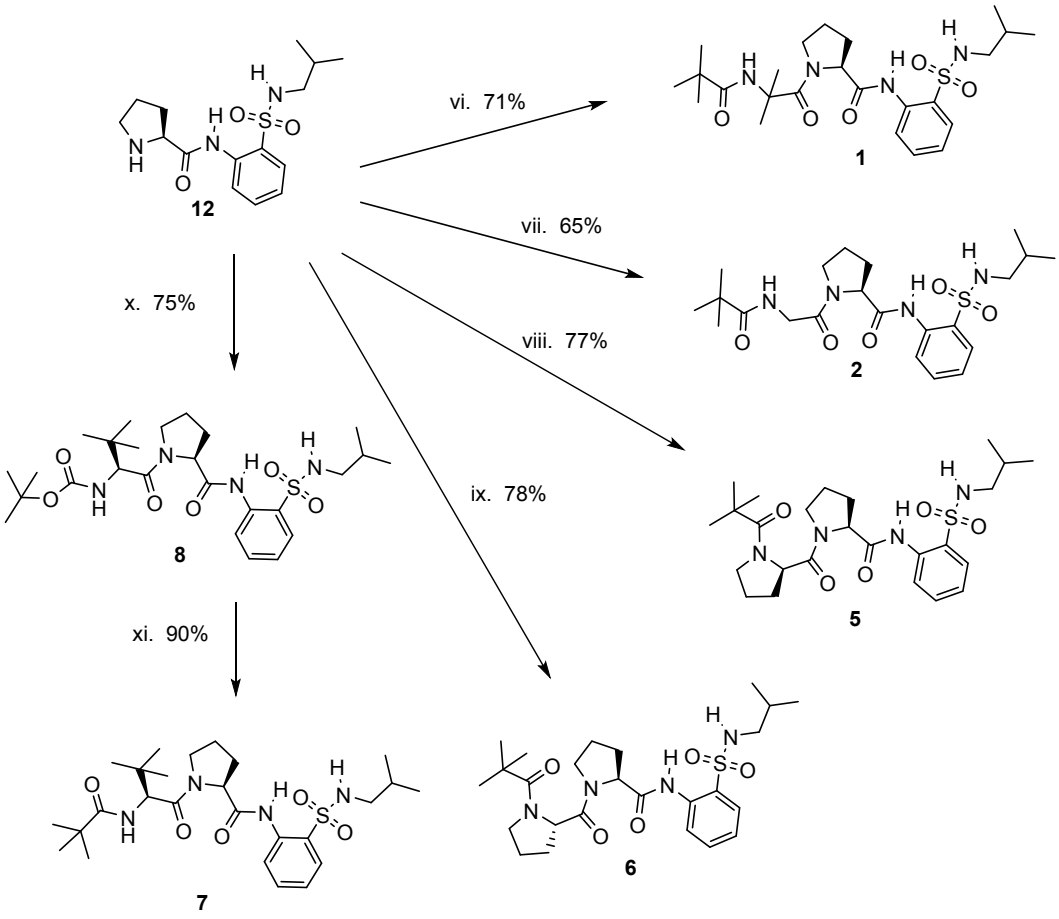
Synthetic Schemes

Scheme 1



Reagents and conditions: i. a. Bromoisobutrylbromide, Et_3N, DCM, rt, 6 h.; b. NaN_3, DMF, 60 °C 12h.; c. 10% Pd/C, H_2. 60 psi, EtOAc, rt, 3 h.; d. Piv-^{L}Pro-OH, TBTU, DIPEA, MeCN, rt, 8 h. ii. a. Piv-^{L}Pro-OH, EtOCOCl, Et_3N, THF, 0 ^{o}C to rt, 1h.; b. **9**, THF, reflux, 48 h. iii. a. Boc-Gly-OH, EtOCOCl, Et_3N, THF, 0 ^{o}C to rt, 1h.; b. **9**, THF, reflux, 48 h. iv. a. TFA, DCM, rt, 30 min.; b. Piv-^{L}Pro-OH, TBTU, DIPEA, MeCN, rt, 8 h. v. TFA, DCM, rt. 30 min.

Scheme 2



Reagents and conditions: vi. Piv-Aib-OH, TBTU, DIPEA, MeCN, rt, 8 h. vii. Piv-Gly-OH, TBTU, DIPEA, MeCN, rt, 8 h. viii. Piv-^{L}Pro-OH, TBTU, DIPEA, MeCN, rt, 8 h. ix. Piv-^{D}Pro-OH, TBTU, DIPEA, MeCN, rt, 8 h. x. Boc^{L}*tert*-LeuOH, TBTU, DIPEA, MeCN, rt, 8 h. xi. a. TFA, DCM, rt, 30 min.; b. Piv-Cl, DIPEA, DCM, rt, 3 h.

Experimental Procedures

(*S*)-N-(2-(N-isobutylsulfamoyl)phenyl)-1-(2-methyl-2-pivalamidopropanoyl)pyrrolidine-2-carboxamide 1

Compound **11** was synthesized using the literature procedure.[1] Compound **11** (0.2 g, 0.470 mmol) was subjected for *t*-Boc deprotection using TFA and DCM. The reaction mixture was evaporated and the residue was neutralized with $NaHCO_3$ solution, followed by extraction using DCM (3 x 5mL) and evaporation to yield the free amine **12**. To a solution of Piv-Aib-OH (0.088g, 0.470mmol) in MeCN (5mL), amine **12** (0.143g, 0.8312mmol) was added followed by the addition of TBTU (0.166g, 0.517mmol), and DIPEA (0.204mL, 1.175 mmols). After 8 hours, the reaction mixture was evaporated on rota vapor and residue was diluted with DCM (5mL) and the organic layer was washed with saturated solutions of sodium bicarbonate (5mL), potassium bisulphate (5mL) and water (5mL), sequentially. The organic layer was dried over anhydrous Na_2SO_4 solution and evaporated under reduced pressure to get crude product which was purified by column chromatography, (75:25 ethyl acetate/pet. ether, R_f: 0.5) to afford **1** as a white solid which was later crystallized from a solution of ethylacetate and pet-ether (0.167g, 71% yield).; white crystalline solid (95%). mp: 203-205^oC; $[\alpha]^{24}_D$: -24.32° (*c* = 0.001, MeCN); IR ($CHCl_3$, ν (cm^{-1}): 3324, 3020, 2400, 1648, 1618, 1618, 1482, 1425, 1341, 1215; ^1H NMR (500MHz, $CDCl_3$) δ: 9.17 (br. s., 1H), 8.00 (d, *J* = 7.9 Hz, 1H), 7.89 (d, *J* = 7.9 Hz, 1H), 7.55 (t, *J* = 7.6 Hz, 1H), 7.23 (t, *J* = 7.6 Hz, 1H), 6.64 (m, 1H), 6.16 (br. s., 1H), 4.57 (dd, *J* = 8.2, 5.2 Hz, 1H), 3.78 - 3.88 (m, 1H), 3.61 - 3.70 (m, 1H), 2.68 (ddd, *J* = 12.7, 6.7, 6.5 Hz, 1H), 2.55 (ddd, *J* = 12.7, 6.3, 6.1 Hz, 2H), 2.21 - 2.30 (m, 1H), 2.09 - 2.19 (m, 2H), 1.93 (dt, *J* = 12.4, 6.3x(2) Hz, 1H), 1.67 (dt, *J* = 13.4, 6.7x(2) Hz, 1H), 1.62 (s, 6H), 1.20 (s, 9H), 0.83 (dd, *J* = 6.3, 3.5 Hz, 6H); ^{13}C NMR (126 MHz, $CDCl_3$) δ: 177.6, 174.5, 170.7, 134.4, 133.2, 130, 129.3, 125.1, 124.4, 64.1, 57.5, 50.5, 48.5, 39.0, 28.7, 28.3, 27.5, 25.9, 25.0, 24.8, 19.9, 19.9. HRMS $C_{24}H_{39}O_5N_4S$ $[M+H]^+$ calculated mass 495.2636, observed mass 495.2621; $C_{40}H_{58}O_{11}N_{12}Na$ $[M+Na]^+$ calculated mass 517.2455, observed mass 517.2440.

(*S*)-N-(2-(N-isobutylsulfamoyl)phenyl)-1-(pivaloylglycyl)pyrrolidine-2-carboxamide 2

To a solution of Piv-Gly-OH (0.5mmol) in MeCN (5mL), amine **12** (0.5mmol) was added followed by the addition of TBTU (0.166g, 0.517mmol), and DIPEA (0.204mL, 1.175

mmols). After 8 hours, the reaction mixture was evaporated on rota vapor and the residue was diluted with DCM (5mL) and the organic layer was washed with saturated solutions of sodium bicarbonate (5mL), potassium bisulphate (5mL) and water (5mL), sequentially. The organic layer was dried over anhydrous Na_2SO_4 solution and evaporated under reduced pressure to get crude product which was purified using column chromatography (30:70 acetone/pet. ether, R_f: 0.4) to afford **1** as white solid (65 % yield). mp: 127-128 ^oC; $[\alpha]^{24}_D$: -154.2° (*c* = 0.001, MeCN); IR ($CHCl_3$, ν (cm^{-1}): 3432, 3348, 3191, 2965, 2879, 1640, 1588, 1525, 1438, 1324, 1155, 1073, 760; ^1H NMR (700 MHz, $CDCl_3$) δ: 9.27 (s, 1H), 8.12 (d, *J* = 8.2 Hz, 1H), 7.88 (d, *J* = 7.9 Hz, 1H), 7.57 (t, *J* = 7.7x(2) Hz, 1H), 7.24 (t, *J* = 7.6x(2) Hz, 1H), 6.57 (br. s, 1H), 6.35 (t, *J* = 5.8x(2) Hz, 1H), 4.61 (dd, *J* = 8.3, 3.1 Hz, 1H), 4.34 (dd, *J* = 17.4, 5.6 Hz, 1H), 4.34 (dd, *J* = 17.4, 3.4 Hz, 1H), 3.7 (m, 1H), 3.59 (m, 1H), 2.71 (m, 1H), 2.47 (dd, *J* = 12.4, 6.1x(2) Hz, 1H), 2.35(m, 1H), 2.28 (m, 1H), 2.09 (m, 2H), 1.88 (m, 1H), 7.61 (dt, *J* = 13.3, 6.6x(2) Hz, 1H), 1.25 (d, *J* = 0.6 Hz, 9H), 0.82 (t, *J* = 5.6x(2) Hz, 6H); ^{13}C NMR (176 MHz, $CDCl_3$) δ 178.7, 171.0, 169.3, 134.2, 133.6, 129.6, 128.8, 124.4, 124.2, 76.8, 62.1, 50.3, 46.9, 42.4, 38.7, 29.5, 28.2, 27.4, 27.4, 24.7, 19.8, 19.8. HRMS $C_{22}H_{35}O_5N_4S$ $[M+H]^+$ calculated mass 467.2323, observed mass 467.2308; $C_{22}H_{34}O_5N_4NaS$ $[M+Na]^+$ calculated mass 489.2142, observed mass 489.2124.

(*S*)-N-(1-((2-(N-isobutylsulfamoyl)phenyl)amino)-27 -methyl-1-oxopropan-2-yl)-1-pivaloylpyrrolidine-2-carboxamide 3

To a solution of amine **9** (0.7 mmol) in dry DCM at 0 ^oC, α-bromoisobutyrlbromide (0.09 mL, 0.7 mmol) was added followed by the addition of Et_3N (0.12 mL, 0.8 mmol) and the reaction mixture was stirred for 6 h after attaining room temperature. Later, the reaction mixture was washed sequentially with sat. $NaHCO_3$ and brine solutions. The organic layer was dried over anhydrous Na2SO4 and evaporated under reduced pressure to get the crude product and used without further purification. This crude bromo compound and NaN_3 (0.18g, 2.9 mmol) were dissolved in dry DMF and heated at 60 ^oC for 12h. Later, the reaction mixture was dissolved in ethyl acetate and washed with water and brine solutions sequentially to remove DMF. The organic layer was then dried over anhydrous Na_2SO_4 and evaporated under reduced pressure to get the crude product. This crude product was subjected for catalytic-hydrogenation using 10%Pd/C in ethylacetate at 60

psi for 3h. Catalyst was filtered over celite and filtrate was concentrated under reduced pressure to obtain crude amine. This crude amine was coupled with Piv-^{L}Pro-OH as described in procedure for the preparation of compound **2** to obtain target compound **3** (35:65 acetone/pet.ether, R_f: 0.5) as a white solid (overall 56 % yield). mp: 168-170 ^{o}C; $[\alpha]^{25}_{D}$: -47.08° (*c* = 0.001, MeCN); IR ($CHCl_3$, ν (cm^{-1}): 3189, 3000, 1670, 1629, 1594, 1543, 1407, 1327, 1220, 1157, 1044, 759, 663; ^{1}H NMR (500 MHz, $CDCl_3$) δ: 9.37 (s, 1H), 8.23 (br. s., 1H), 7.96 (d, *J* = 8.2 Hz, 1H), 7.84 (dd, *J* = 7.9 Hz, 1.5, 1H), 7.59 - 7.49 (m, 1H), 7.24 - 7.15 (m, 1H), 6.39 (t, *J* = 6x(2) Hz, 1H), 4.85 (dd, *J* = 8.1, 2.9 Hz, 1H), 3.75 - 3.65 (m, 2H), 2.67 - 2.57 (m, 1H), 2.55 - 2.45 (m, 2H), 2.23 - 2.13 (m, 1H), 1.96 - 1.89 (m, 1H), 1.88 - 1.81 (m, 1H), 1.65 (dt, *J* = 13.4, 6.7(x)2 Hz, 1H), 1.55 (s, 3H), 1.52 (s, 3H), 1.27 (s, 9H), 0.84 (t, *J* = 6.6x(2) Hz, 6H);^{13}C NMR (126 MHz, $CDCl_3$) δ: 178.9, 173.4, 172.5, 134.8, 133.1, 129.5, 129.2, 125.0, 124.0, 61.5, 57.7, 50.3, 48.4, 39.4, 28.2, 27.5, 26.4, 25.8, 24.8, 24.2, 19.8; HRMS $C_{24}H_{39}O_5N_4S$ $[M+H]^+$ calculated mass 495.2636, observed mass 495.2622; $C_{40}H_{58}O_{11}N_{12}Na$ $[M+Na]^+$ calculated mass 517.2455, observed mass 517.2437.

(*S*)-N-(2-((2-(N-isobutylsulfamoyl)phenyl)amino)-2-oxoethyl)-1-pivaloylpyrrolidine-2-carboxamide 4

Compound **10** was synthesized by the literature procedure.[1] Compound **4** was synthesized from compound **10**, following the synthetic procedure as described for compound **1** (75:25 ethyl acetate/pet. ether, R_f: 0.5), white viscous liquid (83%); $[\alpha]^{25}_{D}$: -53.2° (*c* = 0.001, MeCN); IR ($CHCl_3$, ν (cm^{-1}): 3189, 2973, 1676, 1598, 1522, 1419, 1374, 1325, 1221, 1155, 1069, 1041, 764, 664; ^{1}H NMR (700MHz, $CDCl_3$) δ: 9.34 (br. s, 1H), 8.32 (t, *J* = 6.0 Hz, 1H), 8.12 (d, *J* = 8 Hz, 1H), 7.85 (dd, *J* = 7.9, 1.4 Hz, 1H), 7.53 (m, 1H), 7.2(m, 1H), 6.27 (t, *J* = 6.0 x(2) Hz, 1H), 4.82 (dd, *J* = 8.2, 3 Hz, 1H), 4.98 (m, 2H), 3.72 (m, 2H), 2.63 - 2.56 (m, 2H), 2.45 - 2.38 (m, 1H), 2.16 (m, 1H), 1.93 (m, 1H), 1.88 (m, 1H), 1.61 (dt, *J* = 13.4, 6.7x(2) Hz, 1H), 1.24 (s, 9H), 0.8 (t, *J* = 6.7x(2) Hz, 6H); ^{13}C NMR (176MHz, $CDCl_3$) δ: 178.7, 174.9, 167.6, 134.3, 133.3, 129.3, 129.2, 124.3, 61.6, 50.1, 48.5, 44.7, 39.2, 28.2, 27.4, 27.4, 25.7, 25.7, 19.7. HRMS $C_{22}H_{35}O_5N_4S$ $[M+H]^+$ calculated mass 467.2323, observed mass 467.2309; $C_{22}H_{34}O_5N_4NaS$ $[M+Na]^+$ calculated mass 489.2142, observed mass 489.2125.

(*S*)-N-(2-(N-isobutylsulfamoyl)phenyl)-1-(pivaloyl-L-prolyl)pyrrolidine-2-carboxamide 5

Compound **5** was synthesized from amine **12** and Piv-^{L}Pro-OH by the procedure described for compound **2** (30:70, acetone/pet. ether, R_f: 0.5) to obtain **5** as a colorless viscous liquid in 75 % yield. $[\alpha]^{25}_{D}$: -74.12° (*c* = 0.001, MeCN); IR ($CHCl_3$, ν (cm^{-1}): 3348, 3190, 2980, 2883, 1695, 1633, 1520, 1424, 1375, 1327, 1220, 1159, 1070, 1045, 759, 663; ^{1}H NMR (700MHz, $CDCl_3$) δ: 9.10 (s, 1H), 7.94 (d, *J* = 8.2 Hz, 1H), 7.86 (d, *J* = 8.0 Hz, 1H), 7.51 (t, *J* = 7.7x(2) Hz, 1H), 7.2 (t, *J* = 7.6x(2) Hz, 1H), 6.64 (t, *J* = 6x(2) Hz, 1H), 4.67 (dd, *J* = 8.3, 5.1 Hz, 1H), 4.49 (dd, *J* = 7.7, 4.7 Hz, 1H), 3.9 (q, *J* = 8.2x(4) Hz, 1H), 3.75 - 3.68 (m, 2H), 3.66 - 3.59 (m, 1H), 2.56 (dt, *J* = 12.6, 6.5x(2) Hz, 1H), 2.48 (dt, *J* = 12.7, 6.4x(2) Hz, 1H), 2.28 - 2.21 (m, 2H), 2.20 - 2.14 (m, 1H), 2.11 - 2.04 (m, 4H), 1.9 (dt, *J* = 12.3, 6.4x(2) Hz, 1H), 1.67 (dt, *J* = 13.5, 6.7x(2) Hz, 1H), 1.23 (s, 9H), 0.83 - 0.76 (m, 6H); ^{13}C NMR (176MHz, $CDCl_3$) δ: 176.6, 173.9, 170.6, 134.2, 133.0, 130.1, 129.1, 125.0, 124.4, 62.3, 59.6, 50.3, 48.4, 47.6, 38.5, 29.3, 28.3, 27.1, 26.7, 26.1, 25.2, 19.8, 19.7. HRMS $C_{25}H_{39}O_5N_4S$ $[M+H]^+$ calculated mass 507.2636, observed mass 507.2624; $C_{25}H_{39}O_5N_4NaS$ $[M+Na]^+$ calculated mass 529.2455, observed mass 529.2438.

(*S*)-N-(2-(N-isobutylsulfamoyl)phenyl)-1-(pivaloyl-D-prolyl)pyrrolidine-2-carboxamide 6

Compound **6** was synthesized from amine **12** and Piv-^{D}Pro-OH by the procedure described for compound **2** (25:75 ethyl acetate/pet. ether, R_f: 0.5) to afford **5** as a white crystalline solid (78%), mp: 160 ^{o}C; $[\alpha]^{25}_{D}$: -68.84° (*c* = 0.001, MeCN); IR ($CHCl_3$, ν (cm^{-1}): 3189, 2994, 1628, 1598, 1538, 1420, 1312, 1218, 1156, 1044, 759, 664; ^{1}H NMR (700MHz, $CDCl_3$) δ: 9.61 (br. s., 1H), 8.30 (d, *J* = 8.2 Hz, 1H), 7.84 (dd, *J* = 8, 0.9 Hz, 1H), 7.49 (m, 1H), 7.36 (t, *J* = 5.6x(2) Hz, 1H), 7.18 (t, *J* = 7.6x(2) Hz, 1H), 4.79 (dd, *J* = 7.9, 5.3 Hz, 1H), 4.6 (d, *J* = 7.3 Hz, 1H), 4.14 (t, *J* = 7.3x(2) Hz, 1H), 3.80 - 3.73 (m, 2H), 3.49 (q, *J* = 8.5x(2) Hz, 1H), 2.75 - 2.68 (m, 1H), 2.62 (ddd, *J* = 13.1, 6.5, 6.2 Hz, 1H), 2.28 - 2.24 (m, 1H), 2.23- 2.12 (m, 4H), 2.12 - 2.07 (m, 1H), 2.01 - 1.97 (m, 1H), 1.96 - 1.91 (m, 1H), 1.85 - 1.78 (m, 1H), 1.68 (dquin, *J* = 13.6, 6.8x(4) Hz, 1H), 1.18 (s, 9H), 0.85 (d, *J* = 6.7 Hz, 4H), 0.85 (d, *J* = 6.7 Hz, 3H), 0.79 (d, *J* = 6.7 Hz, 3H); ^{13}C NMR (176MHz , $CDCl_3$) δ: 176.8, 172.1, 170.8, 134.9, 133.0, 129.4, 129.3, 123.9, 123.9,

62.0, 60.3, 50.5, 48.5, 47.1, 38.6, 29.8, 28.8, 27.2, 26.9, 25.8, 24.4, 19.9, 19.8. HRMS $C_{25}H_{39}O_5N_4S$ $[M+H]^+$ calculated mass 507.2636, observed mass 507.2622.

tert-butyl ((*S*)-1-((*S*)-2-((2-(N-isobutylsulfamoyl)phenyl)carbamoyl)pyrrolidin-1-yl)-3,3-dimethyl-1-oxobutan-2-yl)carbamate 8

Compound **8** was synthesized from amine **12** and Boc-^{L}*tert*-Leu-OH by the procedure described for compound **2** (25:75 ethyl acetate/pet. ether, R_f: 0.5) to obtain compound 8 as a white solid in 75 % yield, mp: 138 ^{o}C; $[\alpha]^{25}_{D}$: -57.76° (*c* = 0.001, MeCN); IR ($CHCl_3$, ν (cm^{-1}): 3452, 3356, 3249, 3192, 3018, 2967, 2880, 1705, 1626, 1513, 1442, 1373, 1328, 1217, 1161, 1072, 929, 763, 667; ^{1}H NMR (400MHz, $CDCl_3$) δ: 9.27 (s, 1H), 7.88 (d, *J* = 7.8 Hz, 1H), 7.81 (d, *J* =7.8 Hz, 1H), 7.52 (t, *J* = 7.6x(2) Hz, 1H), 7.23 (t, *J* = 7.6x(2) Hz, 1H), 6.95 (br. s, 1H), 5.05 (d, *J* = 9.8 Hz, 1H), 4.28 (m, 2H), 3.92 (br.s. 1H), 3.69 (m, 1H), 2.61 (m, 1H), 2.41 (m, 1H), 2.31 (m, 1H), 2.19 (m, 2H), 1.99 (m, 1H), 1.76 (dt, *J* = 13.3, 6.8x(2), 1H), 1.43 (s, 9H), 0.9 (m, 12H), 0.81 (d, *J* = 6.4 Hz). ^{13}C NMR (101MHz, $CDCl_3$) δ: 171.1, 170.1, 155.5, 134.1, 133.1, 130.6, 129.0, 125.1, 124.5, 79.7, 62.6, 58.4, 50.4, 48.9, 35.8, 29.6, 28.9, 28.3, 26.2, 25.5, 19.8, 19.7. HRMS $C_{26}H_{43}O_6N_4S$ $[M+H]^+$ calculated mass 539.2898, observed mass 539.2885; $C_{26}H_{42}O_6N_4NaS$ $[M+Na]^+$ calculated mass 561.2717, observed mass 561.2701.

(*S*)-1-((*S*)-3,3-dimethyl-2-pivalamidobutanoyl)-N-(2-(N-isobutylsulfamoyl)phenyl)pyrrolidine-2-carboxamide 7

Compound **8** (0.5mmol) was subjected to ^{t}Boc deprotection using TFA (2mL) in DCM (2mL). The reaction mixture was evaporated and the residue was neutralized with $NaHCO_3$ solution, followed by extraction using DCM (5 x 2mL) and evaporation to yield the free amine. The free amine was then subjected to amidation using pivaloyl chloride, in DCM using DIPEA as a base. The reaction mixture was evaporated and purified by column chromatography, (35:75 pet. ether/ethyl acetate, R_f: 0.5) to afford **7** as a white solid in 90 % yield. mp: 178 ^{o}C; $[\alpha]^{25}_{D}$: -74.48° (*c* = 0.001, MeCN). IR ($CHCl_3$, ν (cm^{-1}): 3440, 3347, 3189, 2971, 1705, 1627, 1510, 1441, 1375, 1327, 1227, 1163, 1049, 759; ^{1}H NMR ($CDCl_3$/200MHz): ^{1}H NMR (400MHz, $CDCl_3$) δ: 9.21 (s, 1H), 7.89 (d, *J* = 7.8 Hz, 1H), 7.81 (d, *J* = 8.1 Hz, 1H), 7.53 (t, *J* = 7.7x(2) Hz, 1H), 7.24 (t, *J* = 7.7x(2) Hz, 1H), 6.96 (dd, *J* = 7.1, 4.9 Hz, 1H), 6.18 (d, *J* = 9.3 Hz, 1H), 4.65 (d, *J* = 9.3 Hz, 1H), 4.25 (t, *J* = 7.5x(2)Hz, 1H), 3.98 (m, 1H), 3.7 (m, 1H), 2.62 (m, 1H), 2.41 - 2.29 (m, 1H), 2.25 -

2.12 (m, 2H), 2.04 - 1.92 (m, 1H), 1.79 (td, J = 13.7, 6.8 Hz, 1H), 1.19 (s, 9H), 0.93 (s, 9H), 0.87 (m, 6H); ^{13}C NMR (101MHz, $CDCl_3$) δ: 177.9, 170.6, 170.1, 134.0, 133.2, 130.5, 129.0, 125.3, 124.6, 62.6, 56.5, 50.3, 49.1, 38.7, 36.1, 29.7, 29.2, 27.4, 26.4, 25.6, 19.9, 19.8. HRMS $C_{26}H_{43}O_5N_4S$ $[M+H]^+$ calculated mass 523.2949, observed mass 523.2935; $C_{26}H_{42}O_5N_4NaS$ $[M+Na]^+$ calculated mass 545.2768, observed mass 545.2751.

Crystal data:

X-ray intensity data were collected on a Bruker SMART APEX II CCD diffractometer with graphite-monochromatized (Mo Kα=0.71073 Å) radiation at room temperature 296(2) K. The X-ray generator was operated at 50 kV and 30 mA. Diffraction data were collected with a ω scan width of 0.5° and at different settings of φ and 2θ. The sample-to-detector distance was fixed at 5.00 cm. The X-ray data acquisition was monitored by APEX II program suite.[2] All the data were corrected for Lorentz-polarization and absorption effects using SAINT and SADABS programs integrated in APEX II program package.[2] The structure was solved by direct method and refined by full matrix least squares, based on F^2, using SHELX-97.[3] ORTEPs were generated using Mercury program.[4] All the H-atoms were located in the difference Fourier and refined isotropically.

Compound 1: Single crystals of **1** were grown by slow evaporation of the solution mixture of ethyl acetate and pet. ether. Colorless block crystal of size 0.23 x 0.21 x 0.18 mm^3, was used for data collection, Temperature = 90(2) K, Wave length = 0.71073 Å Quadrant data acquisition, F(000) = 1064, θ range = 2.25° to 28.30°, completeness to θ is 90 %, Goodness-of-fit on F2 = 1.039, $C_{24}H_{38}N_4O_5S$, M = 494.64. Crystals belong to Orthorhombic, space group P212121, a = 8.6678(13), b = 16.756(3), c = 18.108(3) Å, α = β = γ = 90, V = 2629.9(7) $Å^3$, Z = 4, Dc = 1.249 g/cc, μ (Mo–Kα) = 0.163 mm-1, 5915 total reflections, 4381 unique reflections, R value 0.0656, wR2 = 0.1699.

Compound 2: Single crystals of **2** were grown by slow evaporation of the solution mixture of acetone and petroleum ether. Colorless needle crystal of size 0.420 x 0.250 x 0.170 mm3, was used for data collection, Temperature = 200(2) K, Wave length = 0.71073 Å Quadrant data acquisition, F(000) = 500, θ range = 1.929° to 25.996°, completeness to θ is 100 %, Goodness-of-fit on F^2 = 1.062, $C_{22}H_{34}N_4O_5S$, M = 466.59.

Crystals belong to monoclinic, space group P21, a = 11.074(3), b = 9.322(2), c = 12.530(3) Å, α = γ = 90°, β = 107.562(14) °, V = 1233.2(6) Å^3, Z = 2, Dc = 1.257 g/cc, μ (Mo–Kα) = 0.170 mm^{-1}, 20454 total reflections, 4853 unique reflections, R value 0.0387, wR2 = 0.0828.

Compound 6: Single crystals of **6** were grown by slow evaporation of the solution mixture of ethylacetate petether. Colorless needle crystal of size 0.437 x 0.285 x 0.109 mm3, was used for data collection, Temperature = 200(2) K, Wave length = 0.71073 Å Quadrant data acquisition, F(000) = 544, θ range = 1.850° to 24.995°, completeness to θ = 24.995° is 91.4 %, Goodness-of-fit on F^2 = 1.053, $C_{25}H_{38}N_4O_5S$, M = 506.65. Crystals belong to monoclinic, space group P21, a = 10.3453(4), b = 11.3579(4), c = 11.0517(4) Å, α = γ = 90°, β = 95.026(2) °, V = 1293.59(8) Å^3, Z = 2, Dc = 1.301 g/cc, μ (Mo–Kα) = 0.168 mm^{-1}, 7915 total reflections, 3883 unique reflections, R value 0.0306, wR2 = 0.0679.

Compound 7: Single crystals of **7** were grown by slow evaporation of the solution mixture of ethylacetate and petroleum ether. Colorless needle crystal of size 0.487 x 0.363 x 0.249 mm3, was used for data collection, Temperature = 200(2) K, Wave length = 0.71073 Å Quadrant data acquisition, F(000) = 1128, θ range = 2.005° to 27.000°, completeness to θ = 25.242° is 100 %, Goodness-of-fit on F^2 = 1.084, $C_{26}H_{42}N_4O_5S$, M = 522.69. Crystals belong to orthorhombic, space group P21 21 21, a = 11.0729(4), b = 11.2306(4), c = 23.8209(9) Å, α = β = γ = 90°, V = 2962.26(19) Å^3, Z = 4, Dc = 1.172 g/cc, μ (Mo–Kα) = 0.148 mm^{-1}, 27955 total reflections, 6478 unique reflections, R value 0.0489, wR2 = 0.1111.

Compound 8: Single crystals of **8** were grown by slow evaporation of the solution mixture of ethylacetate and petroleum ether. Colorless needle crystal of size 0.468 x 0.409 x 0.171 mm3, was used for data collection, Temperature = 200(2) K, Wave length = 0.71073 Å Quadrant data acquisition, F(000) = 1160, θ range = 1.786° to 27°, completeness to θ is 100 %, Goodness-of-fit on F^2 = 1.070, $C_{26}H_{42}N_4O_6S$, M = 538.69. Crystals belong to monoclinic, space group P21, a = 9.9914(2), b = 21.9595(4), c = 14.1883(3) Å, α = γ = 90°, β = 109.928(10) °, V = 2926.6(10) Å^3, Z = 4, Dc = 1.223 g/cc,

μ (Mo–Kα) = 0.155 mm^{-1}, 20842 total reflections, 10509 unique reflections, R value 0.0467, wR2 = 0.0759.

References:

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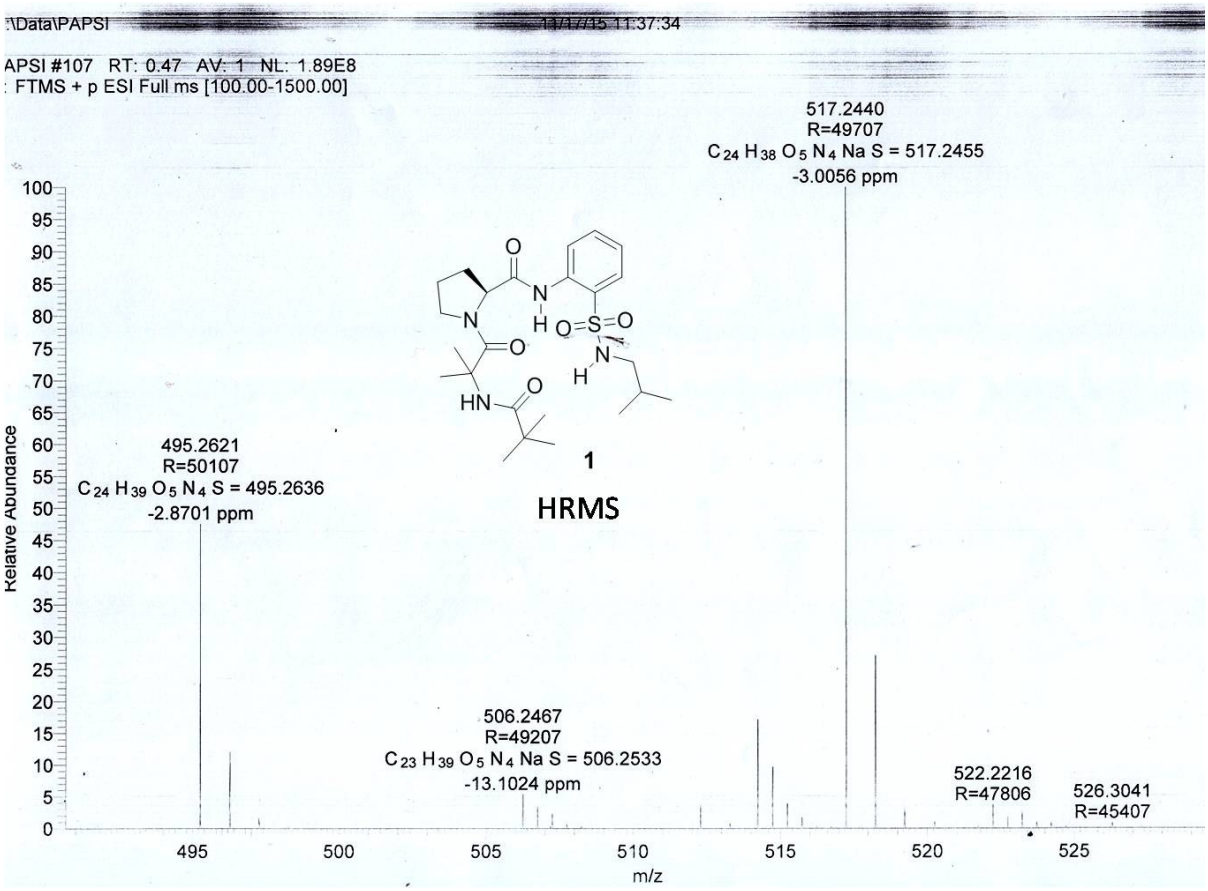
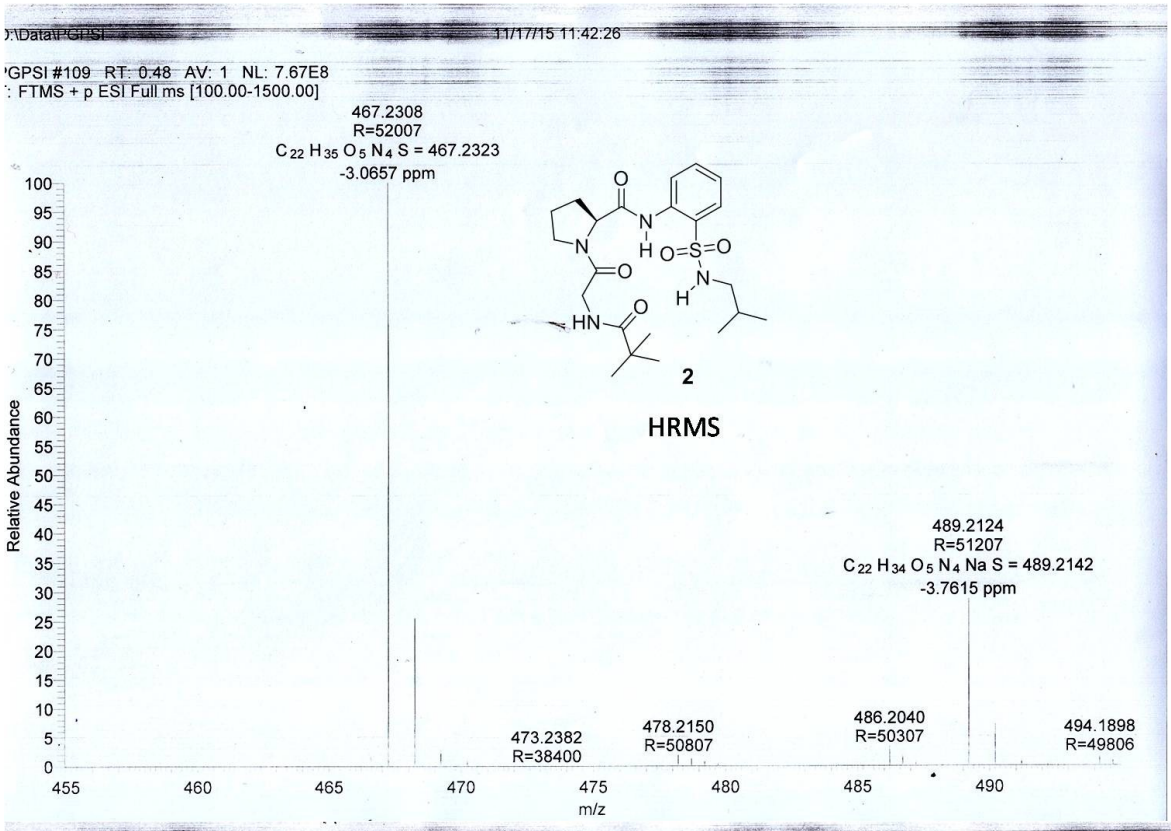
2. Bruker (2006). APEX2, SAINT, and SADABS. Bruker AXS Inc.,Madison, Wisconsin, USA.
3. G. M. Sheldrick, *Acta Cryst*. 2008, **A64**, 112 – 122.
4. C. F. Macrae, I. J. Bruno, J. A. Chisholm, P. R. Edgington, P. McCabe, E. Pidcock, L. Rodriguez-Monge, R. Taylor, J. van de Streek and P. A. Wood, *J. Appl. Crystallogr*., 2008, **41**, 466.

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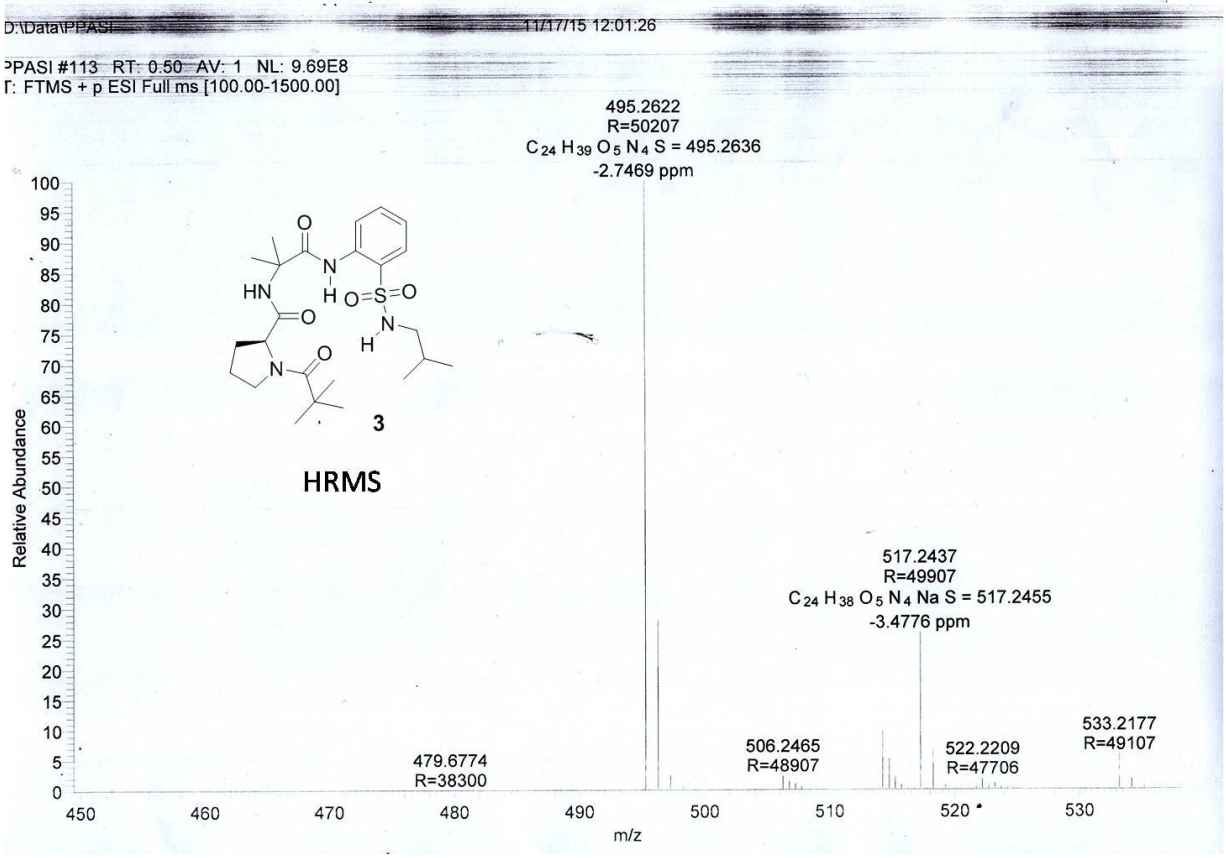
R=52007
C22 H35 O5 N4 S = 467.2323
-3.0657 ppm
2
HRMS
489.2124
R=51207
C22 H34 O5 N4 Na S = 489.2142
-3.7615 ppm
473.2382
R=38400
478.2150
R=50807
486.2040
R=50307
494.1898
R=49806
Relative Abundance
m/z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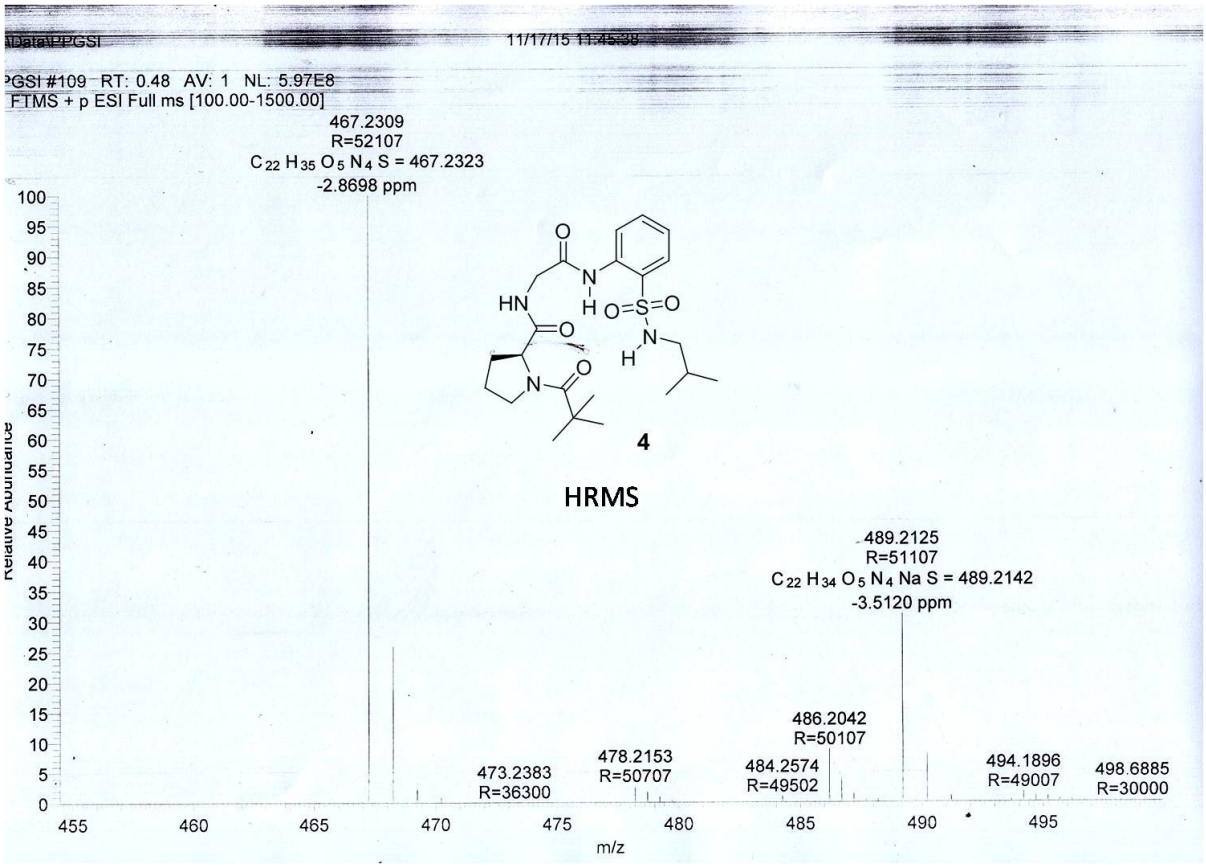
R=50207
C24 H39 O5 N4 S = 495.2636
-2.7469 ppm
3
HRMS
517.2437
R=49907
C24 H38 O5 N4 Na S = 517.2455
-3.4776 ppm
479.6774
R=38300
506.2465
R=48907
522.2209
R=47706
533.2177
R=49107
Relative Abundance
m/z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C22 H35 O5 N4 S = 467.2323
-2.8698 ppm
4
HRMS
489.2125
R=51107
C22 H34 O5 N4 Na S = 489.2142
-3.5120 ppm
486.2042
R=50107
473.2383
R=36300
478.2153
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484.2574
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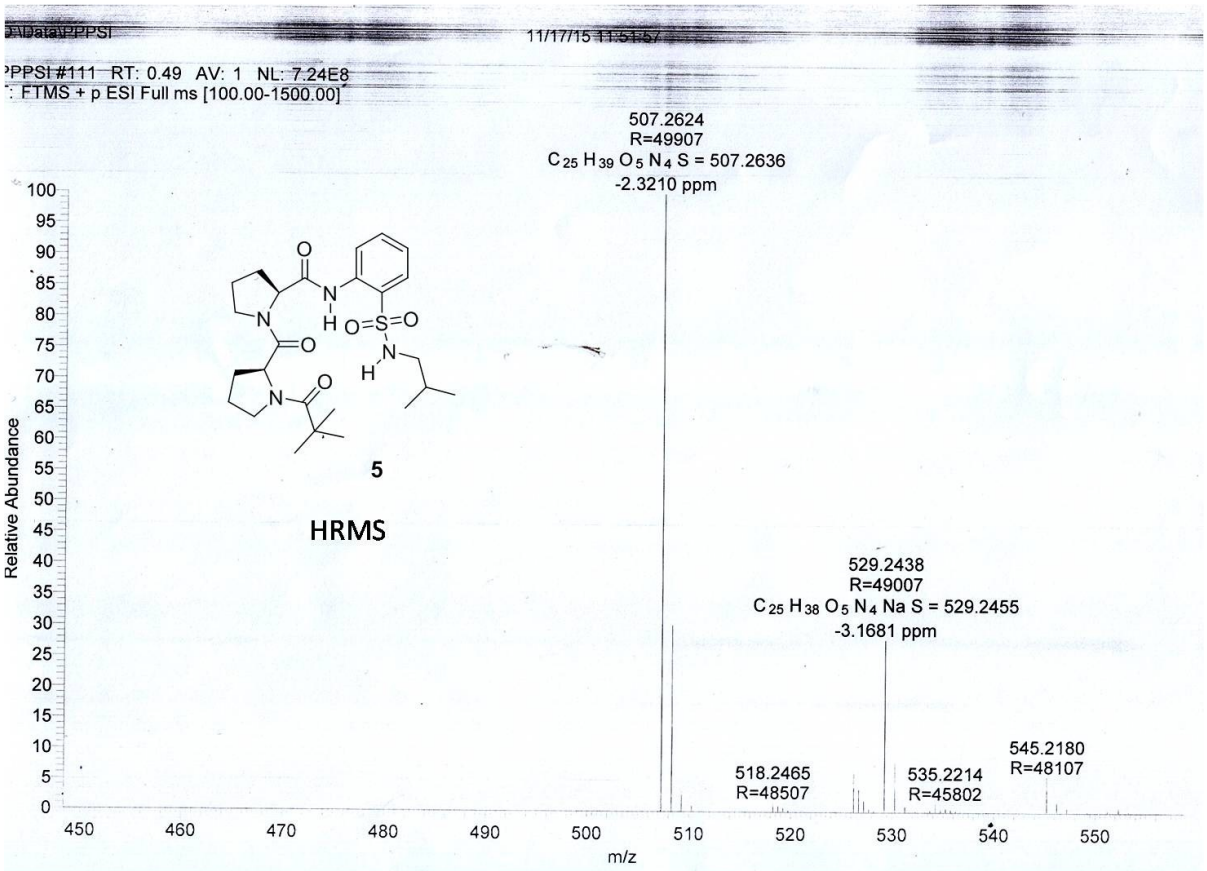
498.6885
R=30000
Relative Abundance
m/z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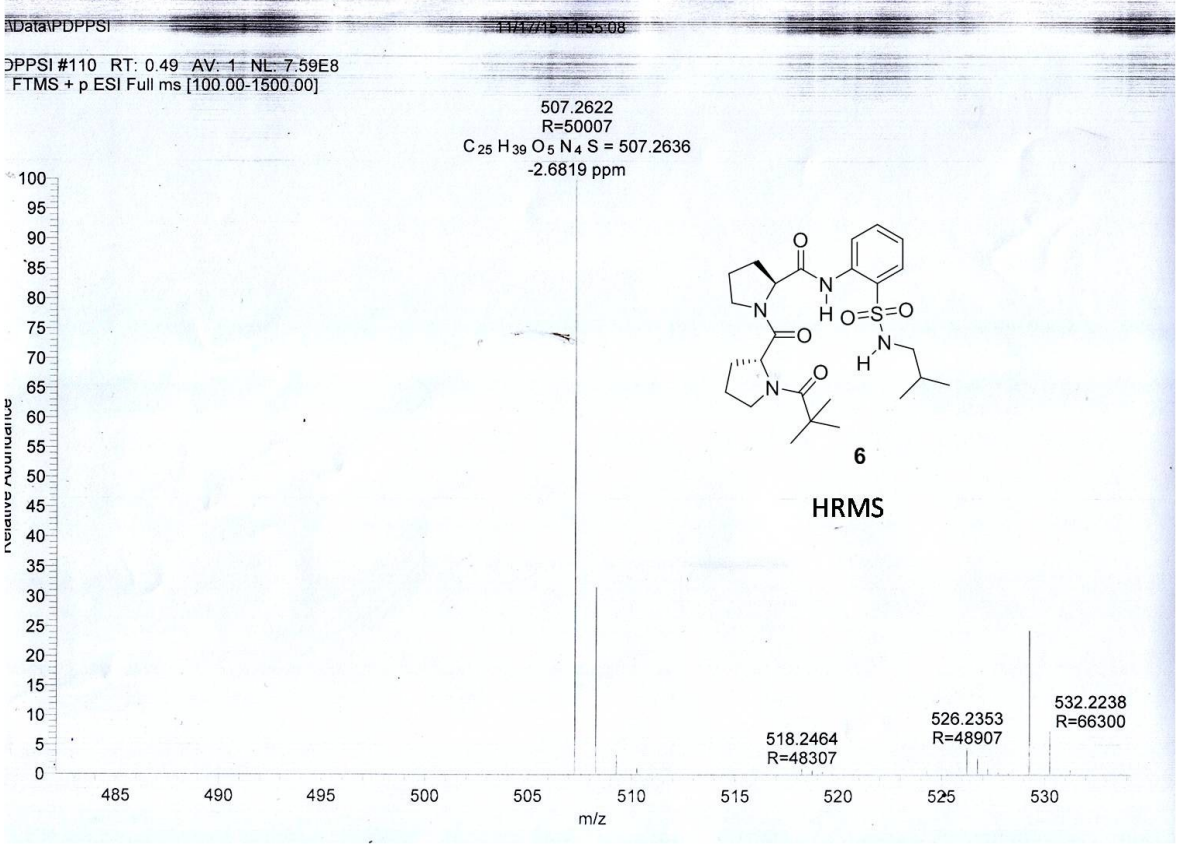
R=49907
C25 H39 O5 N4 S = 507.2636
-2.3210 ppm
529.2438
R=49007
C25 H38 O5 N4 Na S = 529.2455
-3.1681 ppm
518.2465
R=48507
535.2214
R=45802
545.2180
R=48107
Relative Abundance
m/z

5

HRMS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C25 H39 O5 N4 S = 507.2636
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518.2464
R=48307
526.2353
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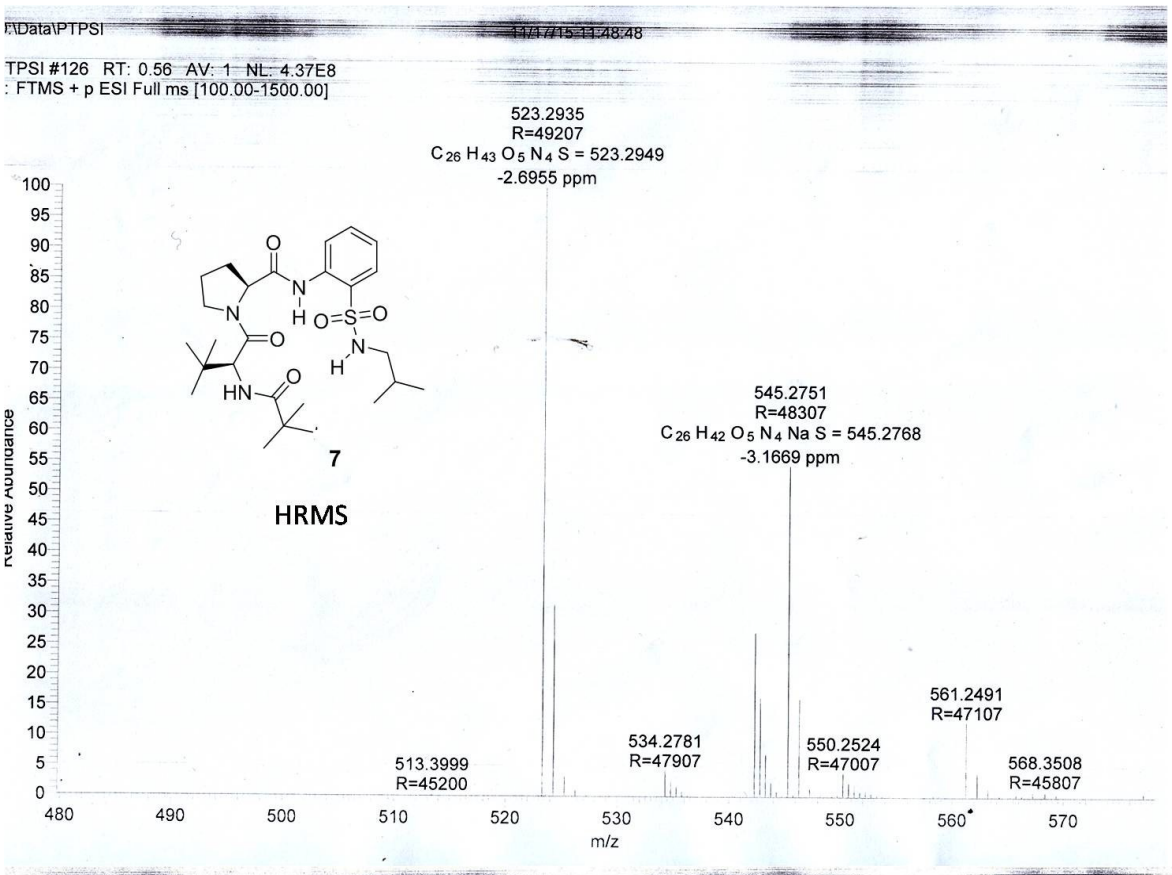
532.2238
R=66300
m/z

6

HRMS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R=49207
C26 H43 O5 N4 S = 523.2949
-2.6955 ppm
7
HRMS
545.2751
R=48307
C26 H42 O5 N4 Na S = 545.2768
-3.1669 ppm
561.2491
R=47107
534.2781
R=47907
550.2524
R=47007
513.3999
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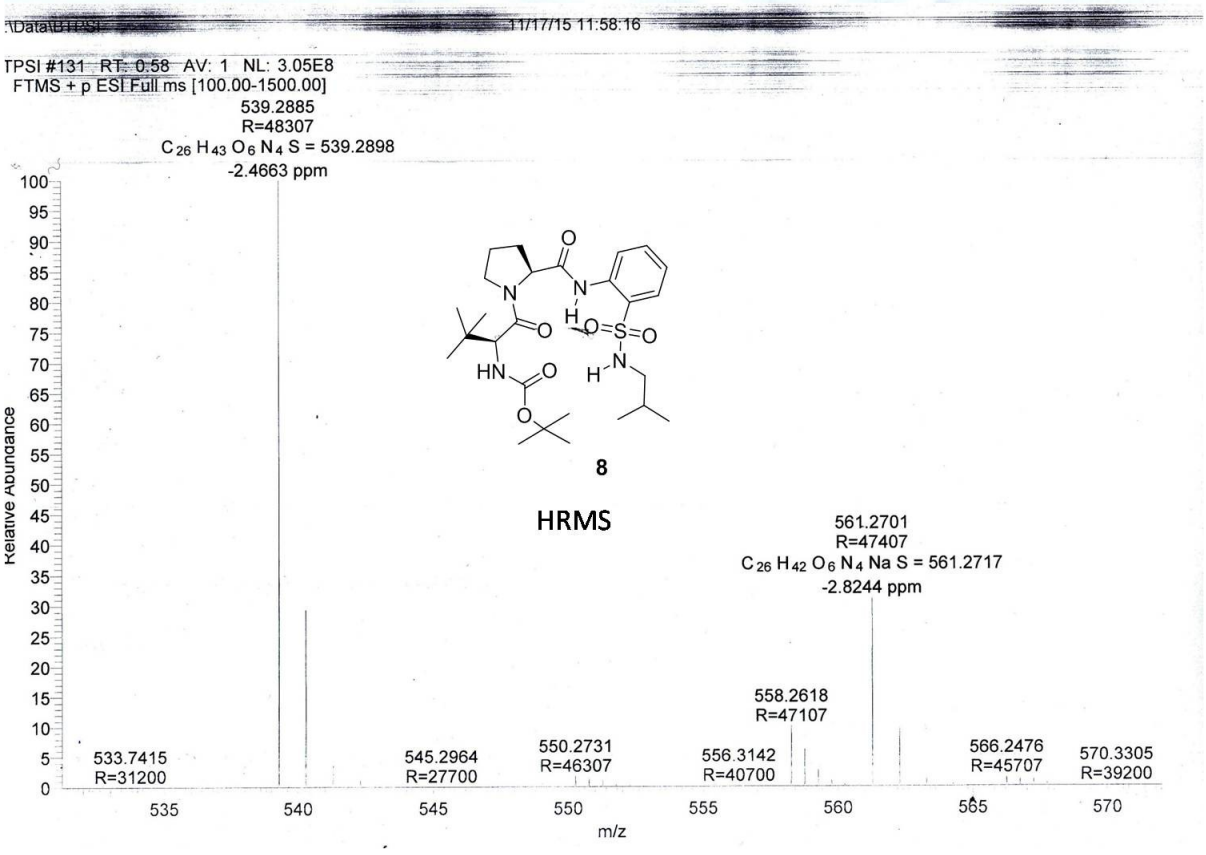
568.3508
R=45807
Relative Abundance
m/z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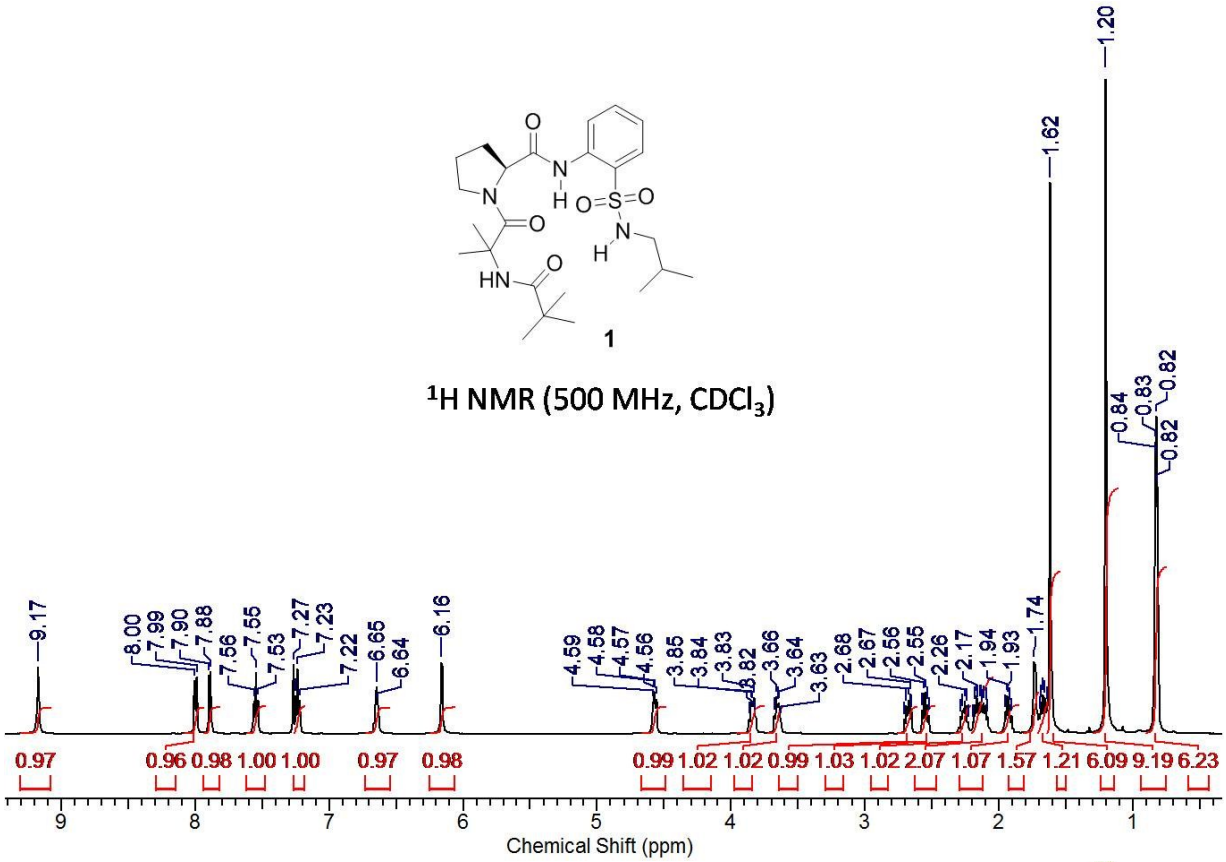
R=48307
C26 H43 O6 N4 S = 539.2898
-2.4663 ppm
8
HRMS
561.2701
R=47407
C26 H42 O6 N4 Na S = 561.2717
-2.8244 ppm
558.2618
R=47107
533.7415
R=31200
545.2964
R=27700
550.2731
R=46307
556.3142
R=40700
566.2476
R=45707
570.3305
R=39200
Relative Abundance
m/z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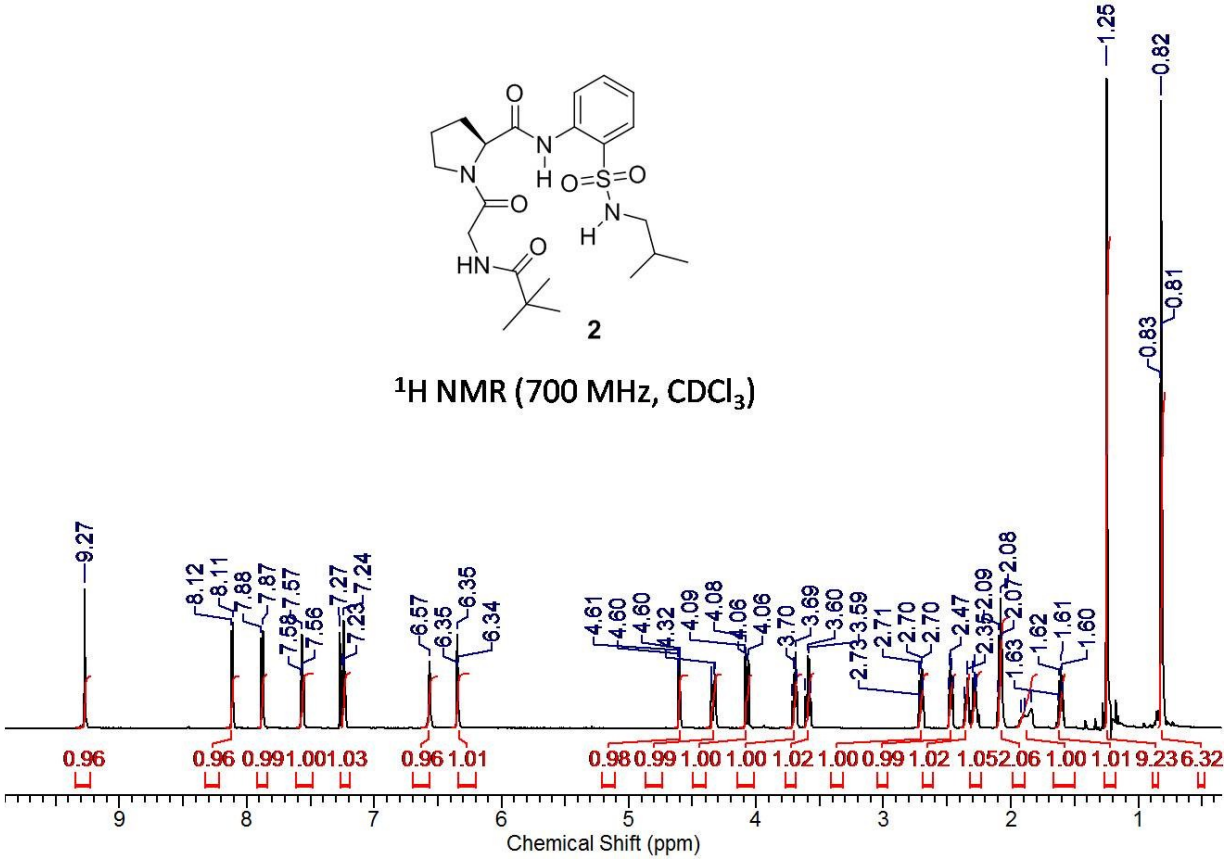
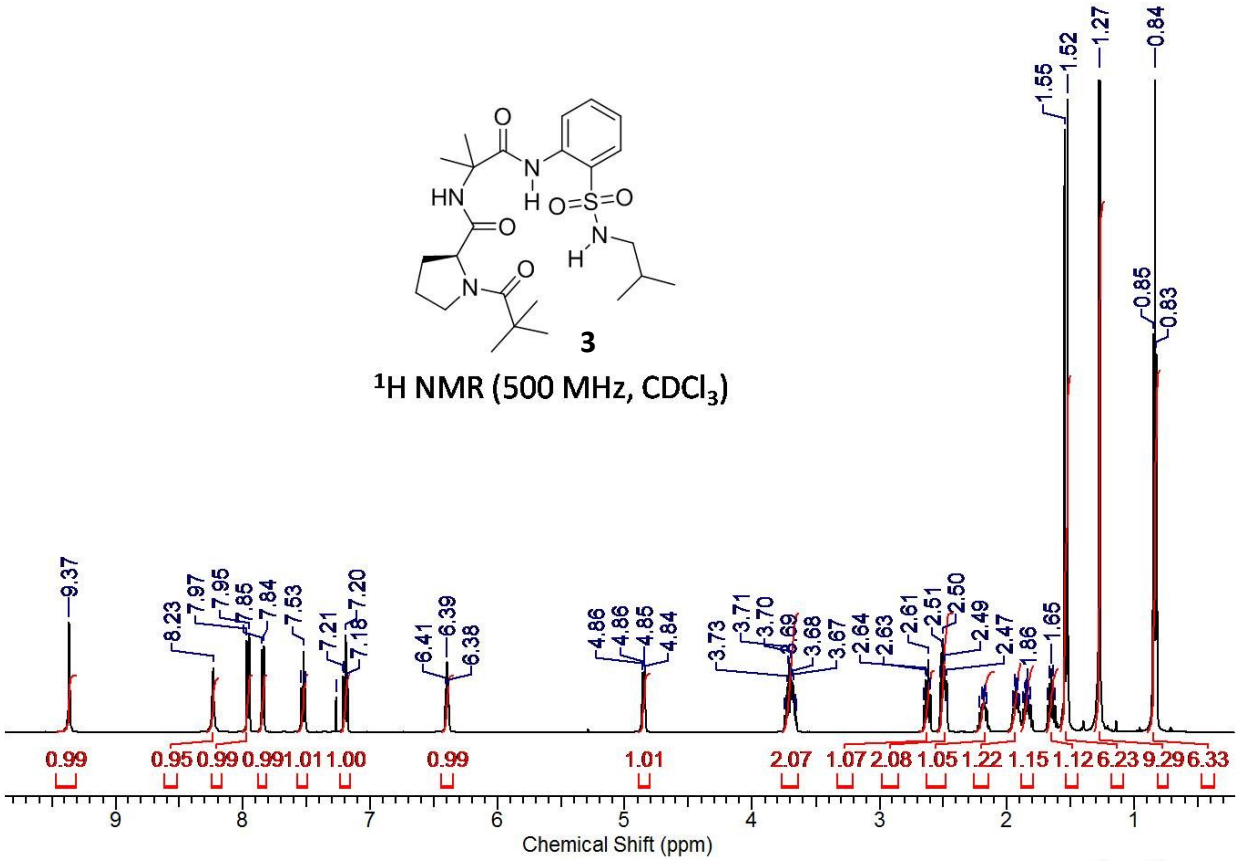
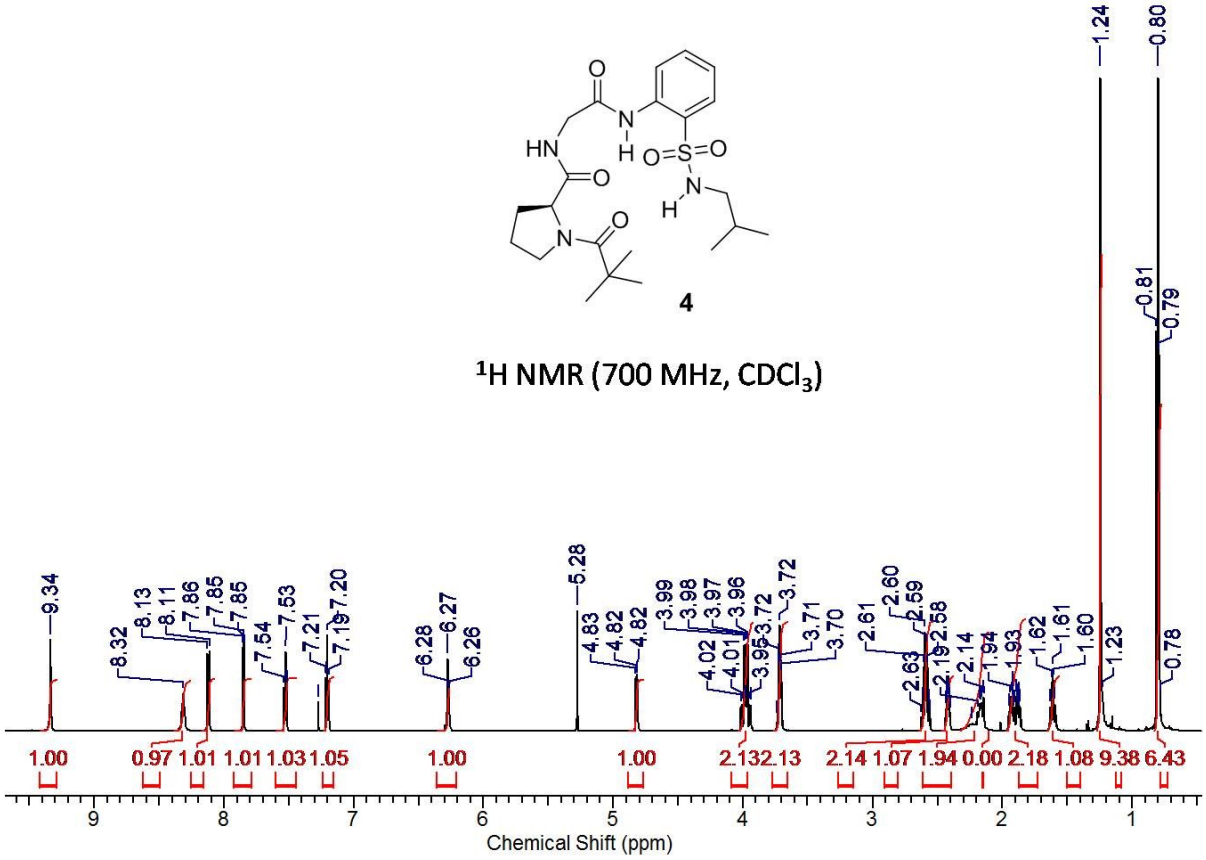
Chemical Shift (ppm)


2
1H NMR (700 MHz, CDCl3)
Chemical Shift (ppm)


3
1H NMR (500 MHz, CDCl3)
Chemical Shift (ppm)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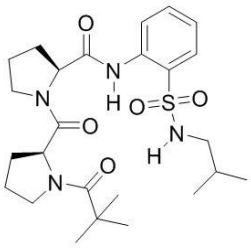
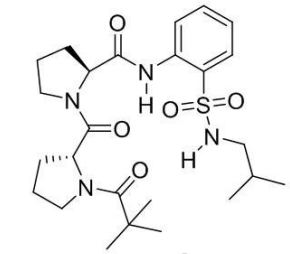
1H NMR (700 MHz, CDCl3)
Chemical Shift (ppm)



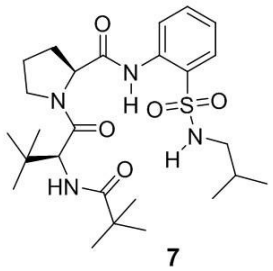
5

^{1}H NMR (700 MHz, $CDCl_3$)



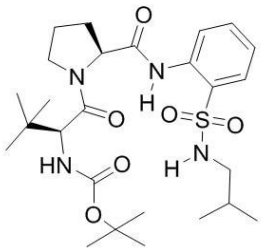
6

^{1}H NMR (700 MHz, $CDCl_3$)



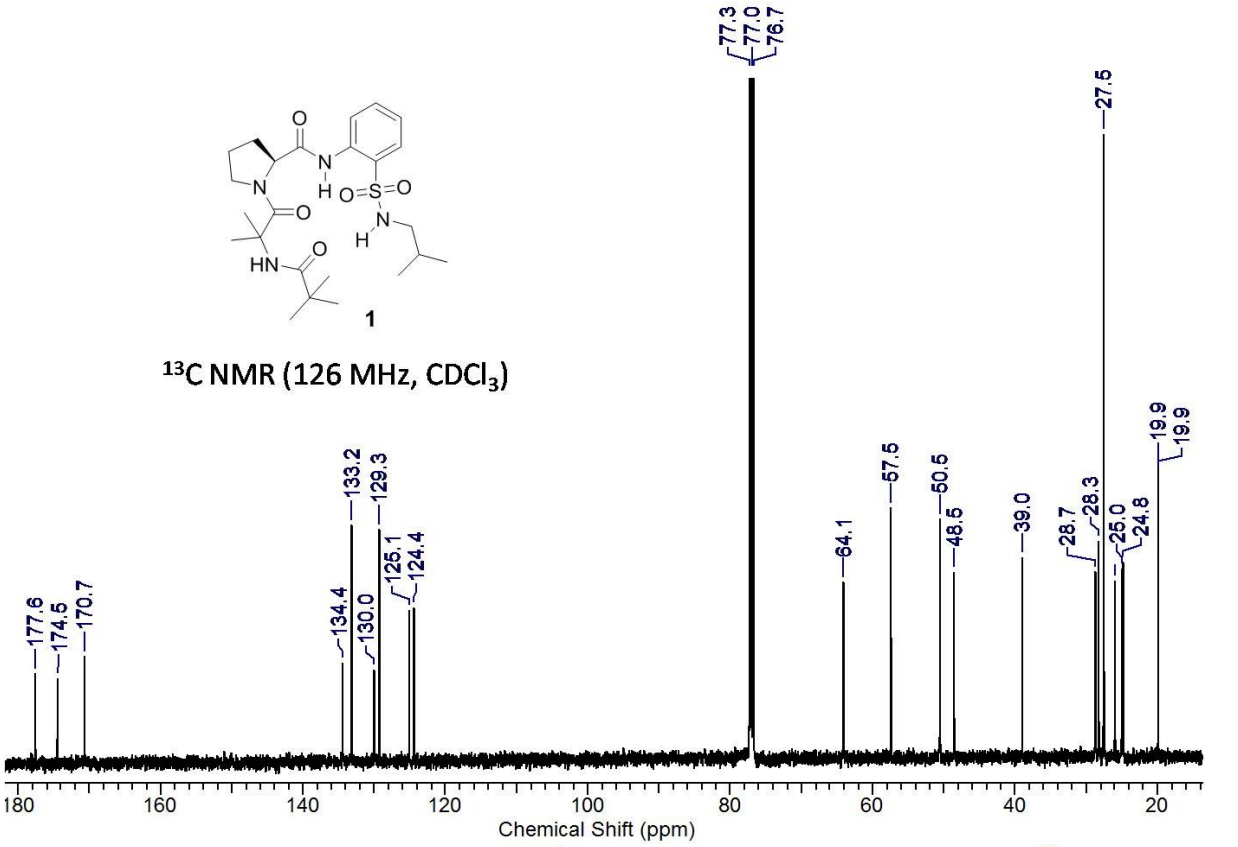
7

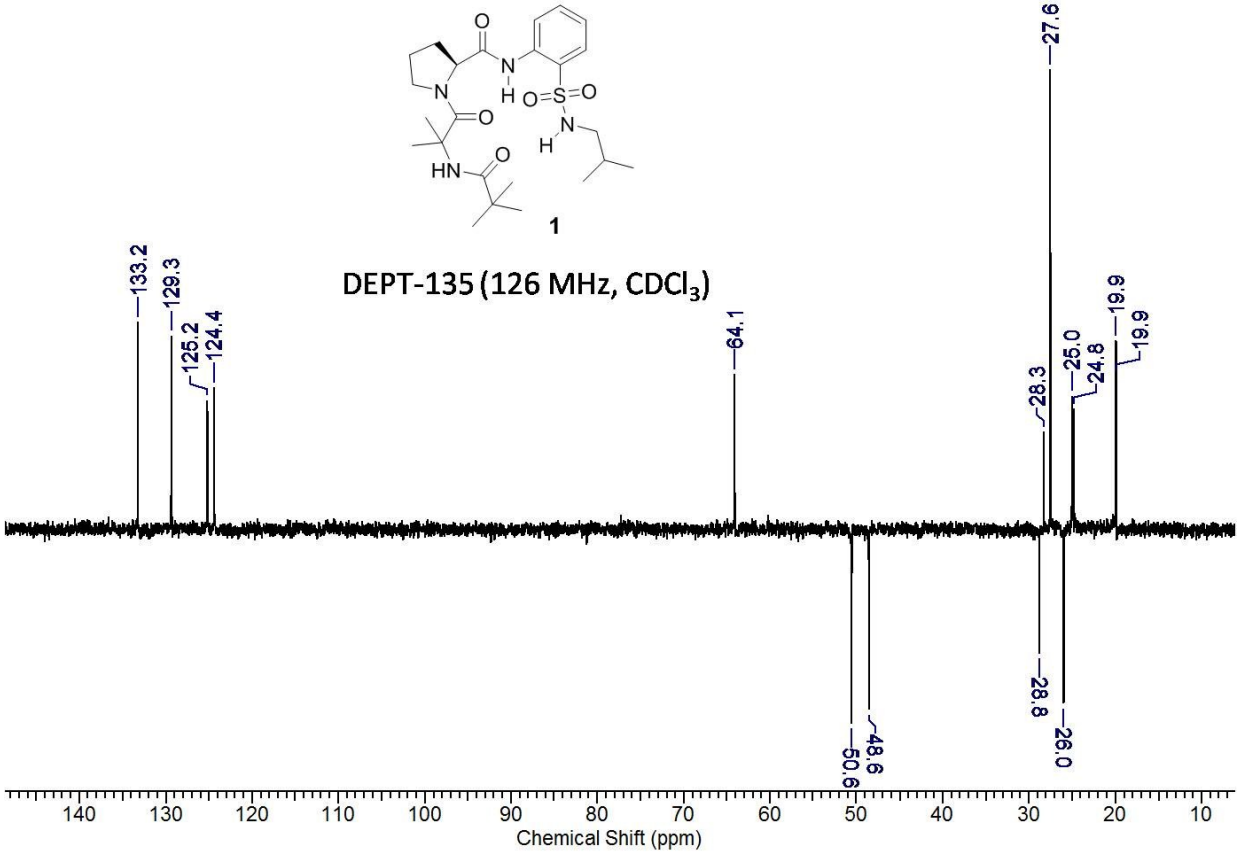
^{1}H NMR (400 MHz, $CDCl_3$)

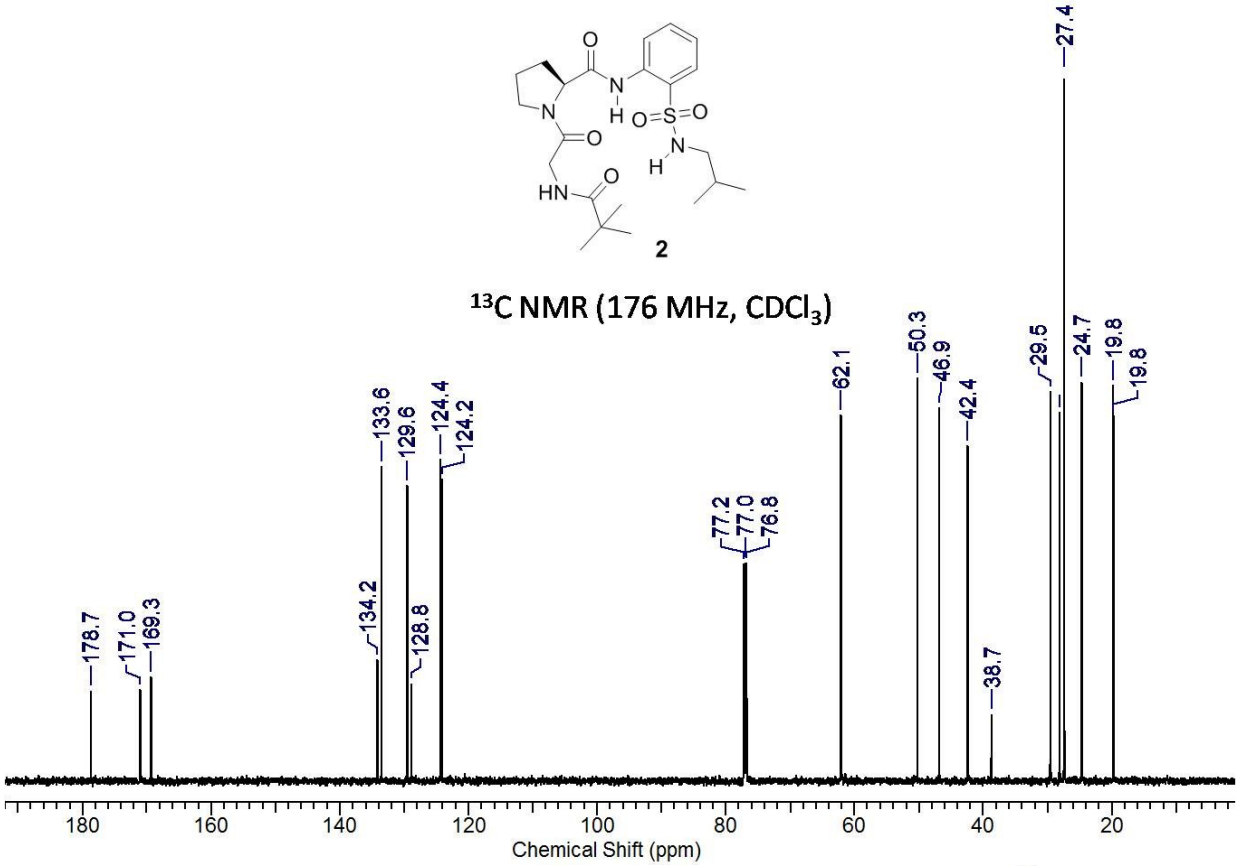


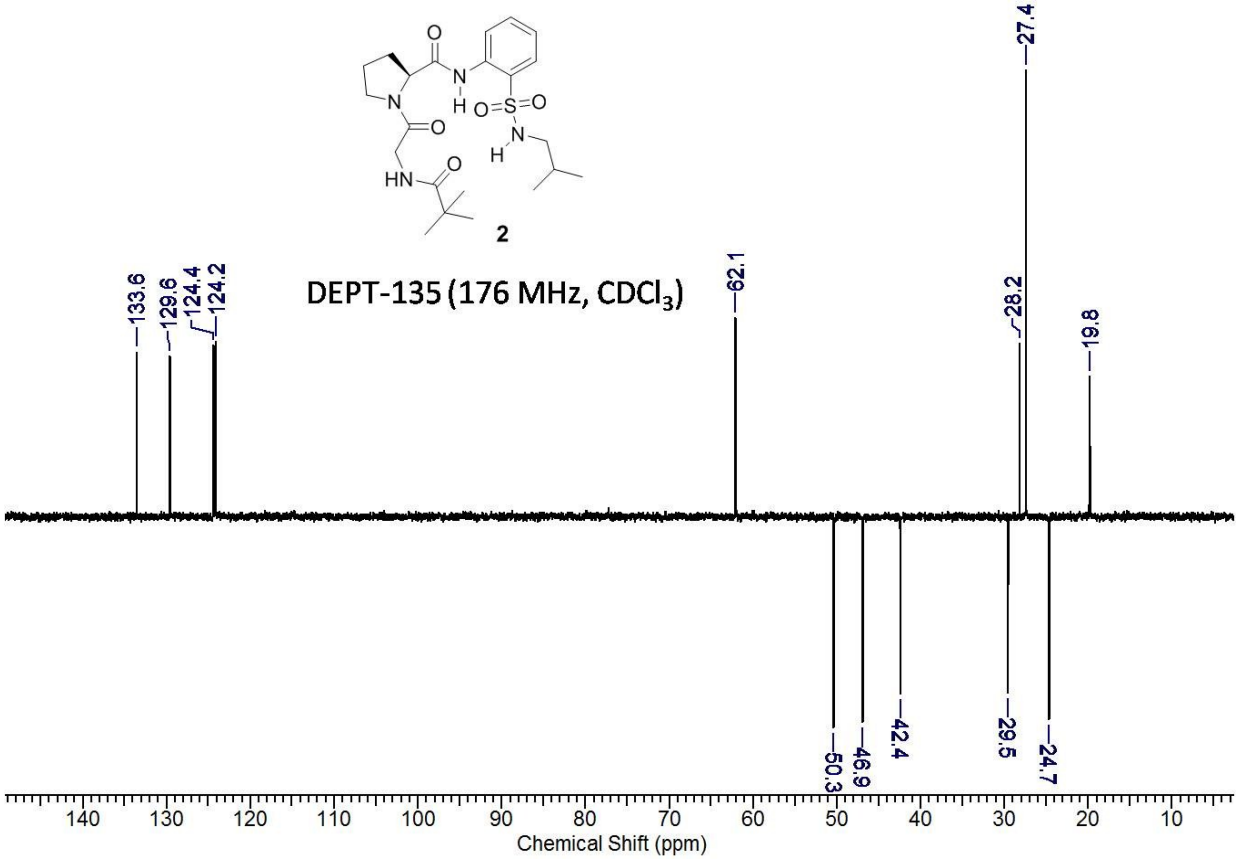
8

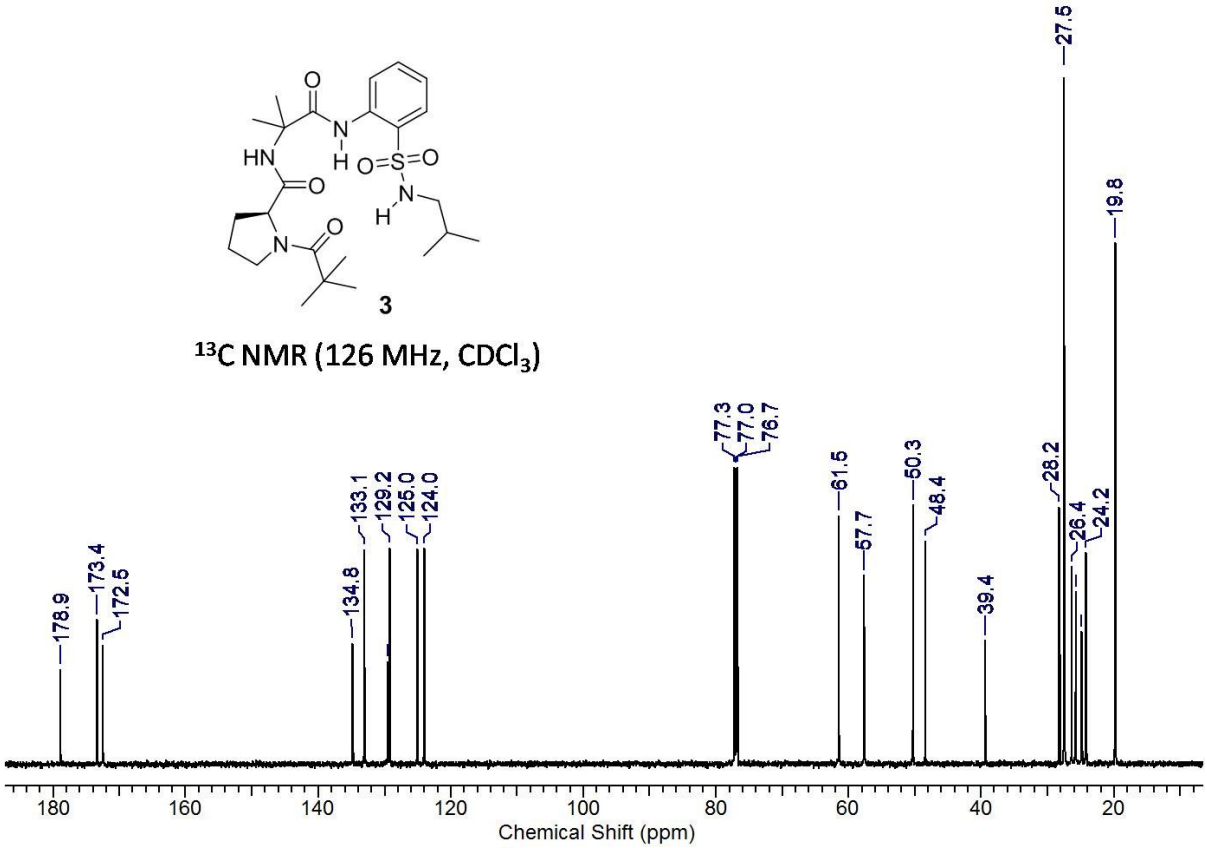
^{1}H NMR (400 MHz, $CDCl_3$)

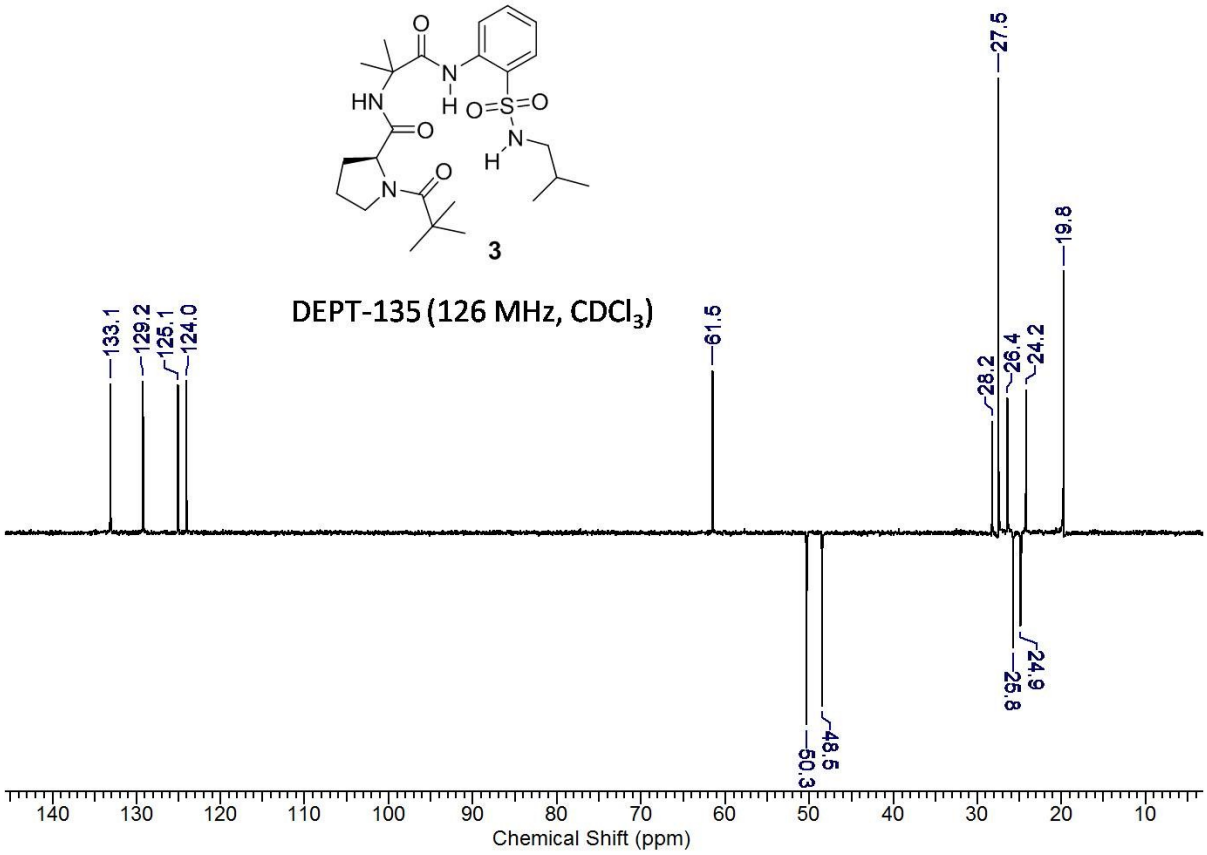

1
13C NMR (126 MHz, CDCl3)
77.3
77.0
76.7
27.5
177.6
174.5
170.7
134.4
133.2
130.0
129.3
125.1
124.4
64.1
57.5
50.5
48.5
39.0
28.7
28.3
25.0
24.8
19.9
19.9
Chemical Shift (ppm)


1
DEPT-135 (126 MHz, CDCl3)
133.2
129.3
125.2
124.4
64.1
27.6
28.3
25.0
24.8
19.9
19.9
60.6
48.6
28.8
26.0
Chemical Shift (ppm)


2
^{13}C NMR (176 MHz, CDCl$_3$)
178.7
171.0
169.3
134.2
133.6
129.6
128.8
124.4
124.2
77.2
77.0
76.8
62.1
50.3
46.9
42.4
38.7
29.5
27.4
24.7
19.8
19.8
Chemical Shift (ppm)


2
DEPT-135 (176 MHz, CDCl$_3$)
133.6
129.6
124.4
124.2
62.1
28.2
27.4
19.8
50.3
46.9
42.4
29.5
24.7
Chemical Shift (ppm)


3
^{13}C NMR (126 MHz, $CDCl_3$)
178.9
173.4
172.6
134.8
133.1
129.2
125.0
124.0
77.3
77.0
76.7
61.5
57.7
50.3
48.4
39.4
28.2
27.5
26.4
24.2
19.8
Chemical Shift (ppm)


3
DEPT-135 (126 MHz, $CDCl_3$)
133.1
129.2
125.1
124.0
61.5
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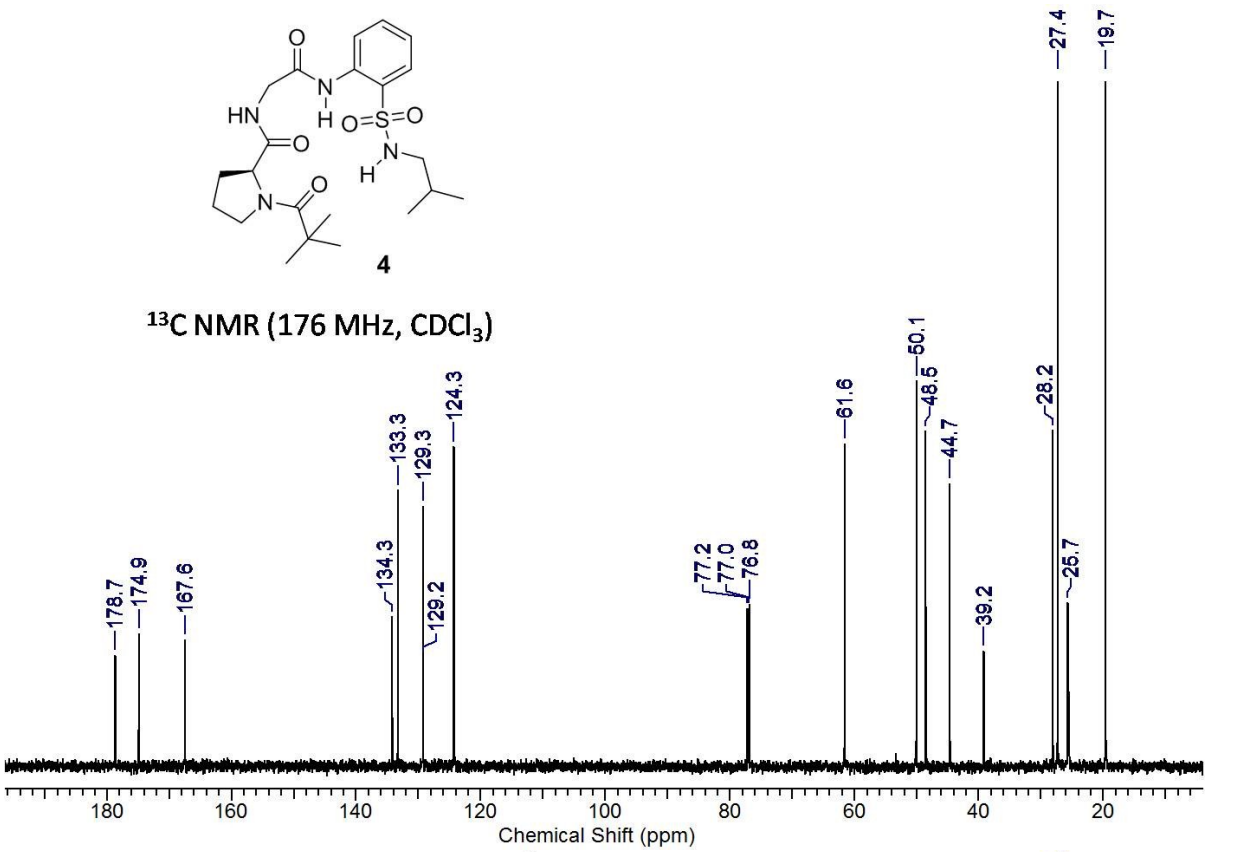
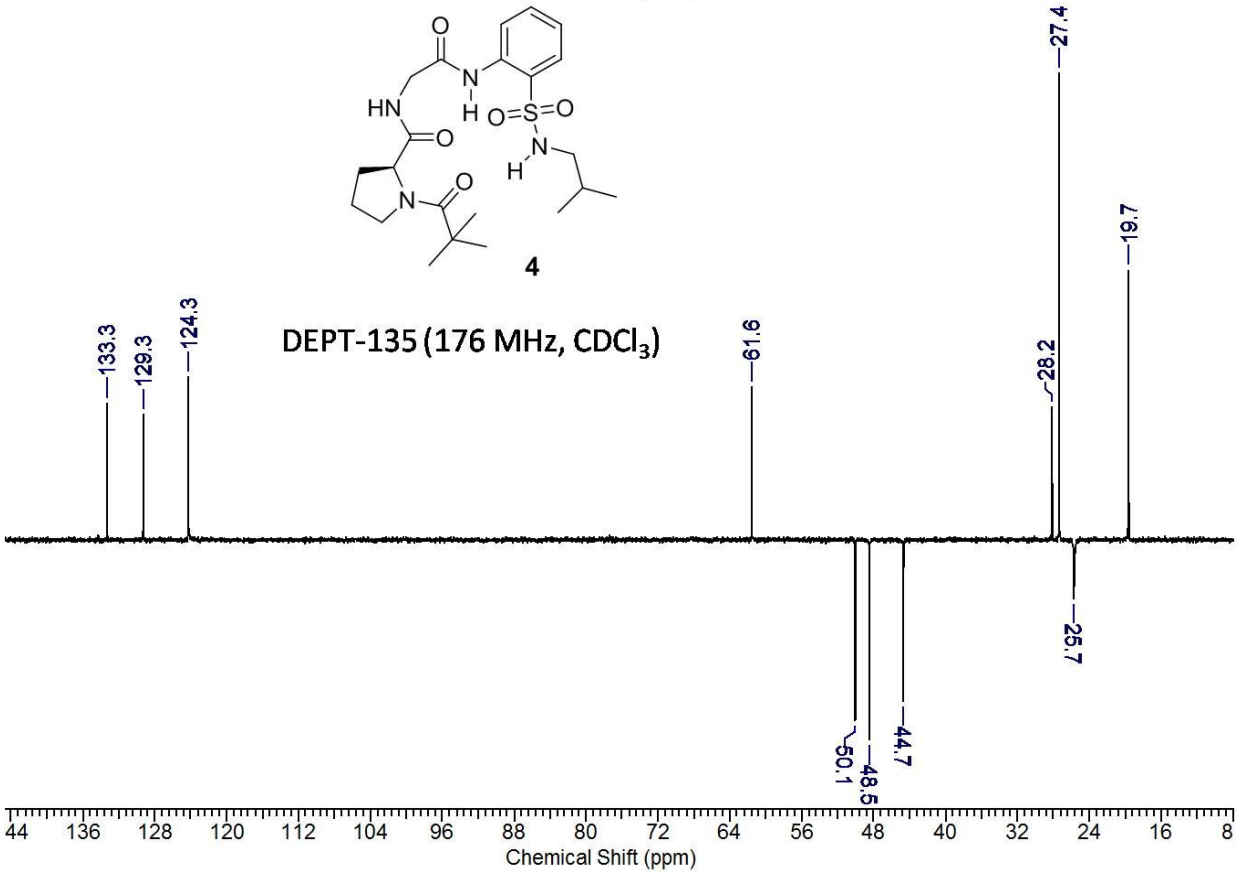
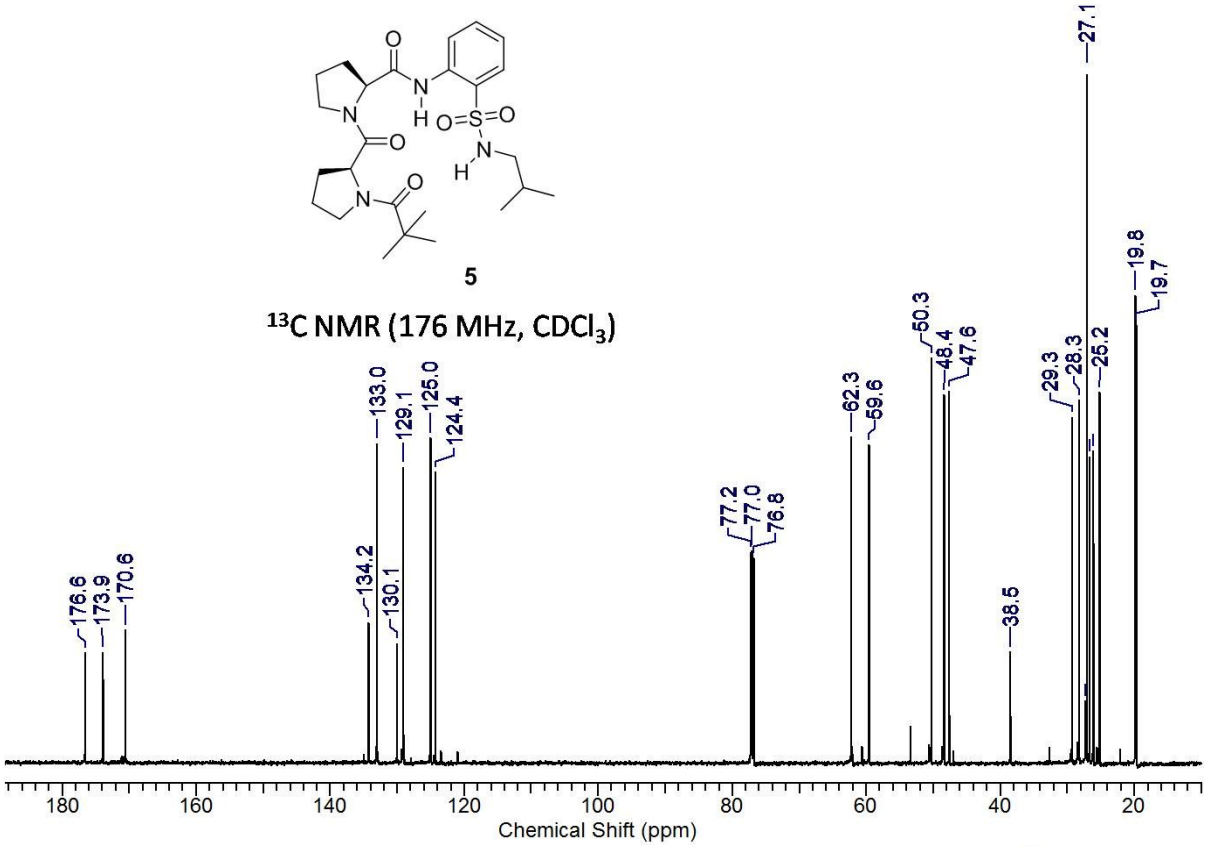
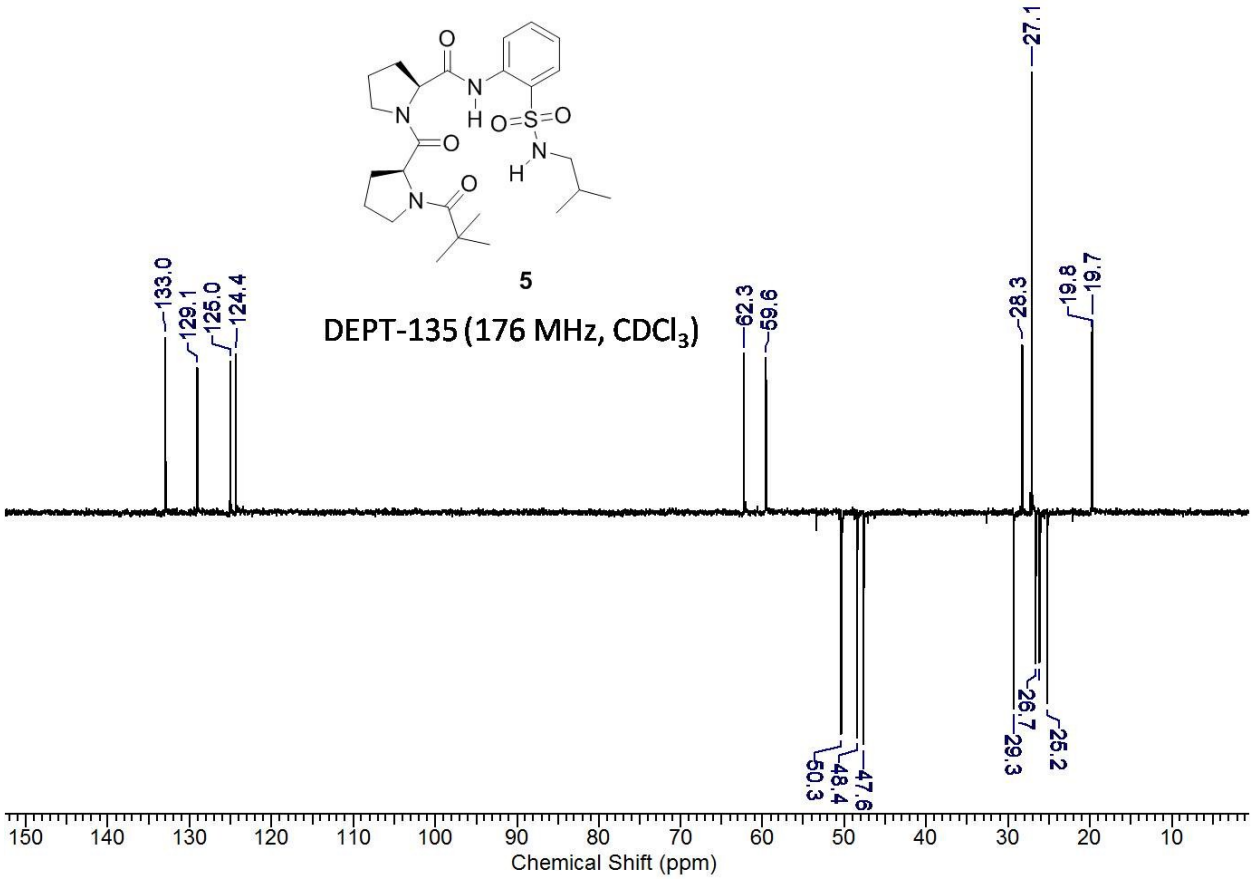
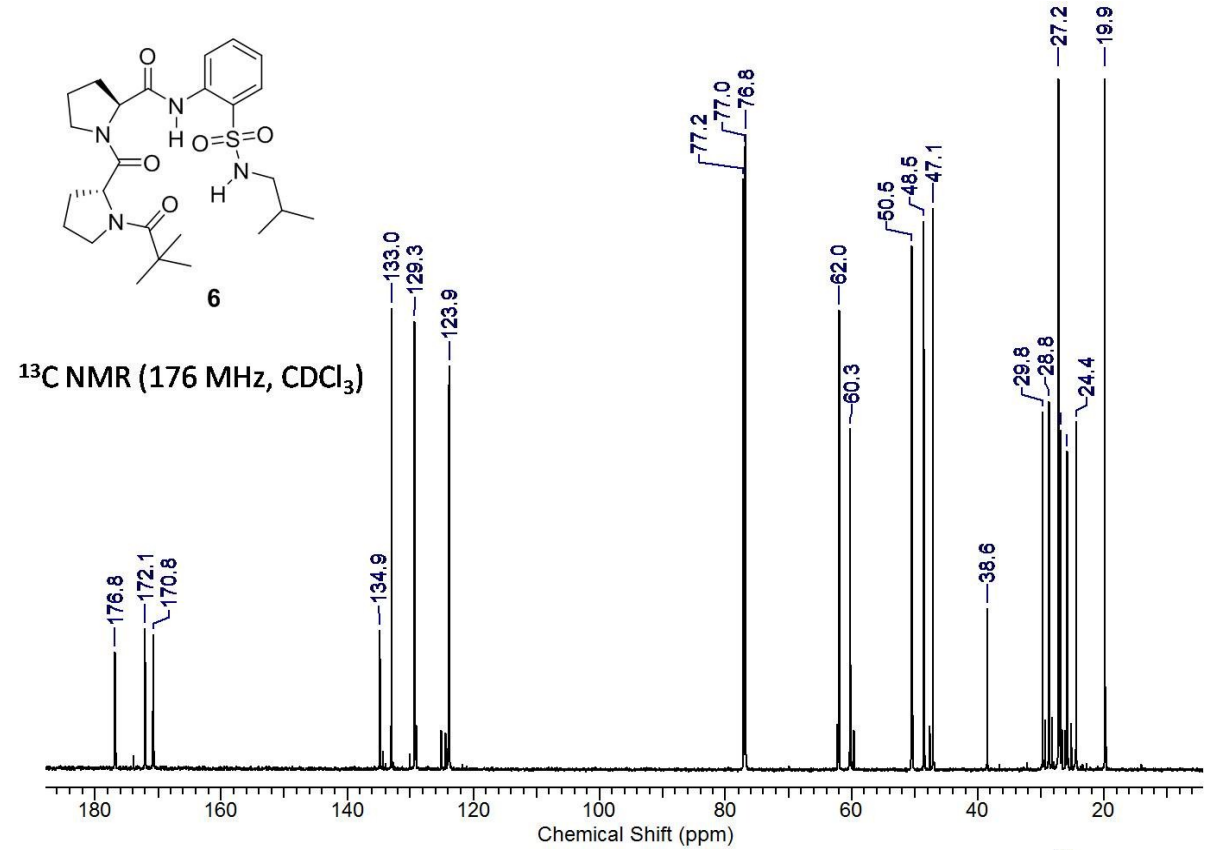
27.5
26.4
24.2
19.8
50.3
48.6
26.8
24.9
Chemical Shift (ppm)

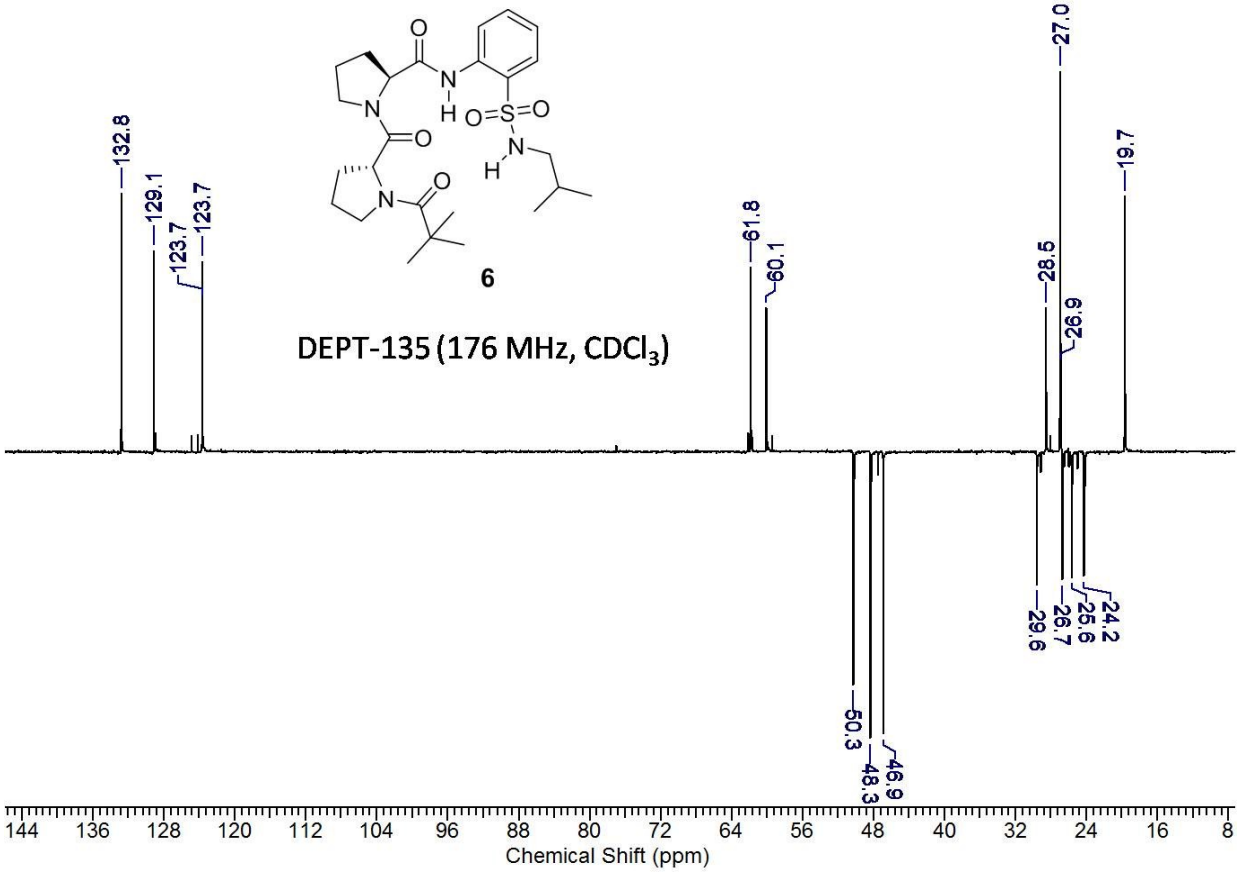

4
^{13}C NMR (176 MHz, CDCl$_3$)
178.7
174.9
167.6
134.3
133.3
129.3
129.2
124.3
77.2
77.0
76.8
61.6
50.1
48.5
44.7
39.2
28.2
27.4
25.7
19.7
180
160
140
120
100
80
60
40
20
Chemical Shift (ppm)

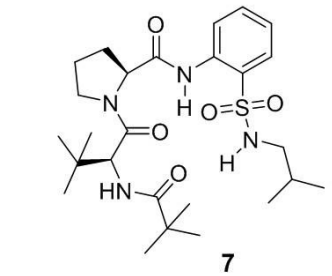

4
DEPT-135 (176 MHz, CDCl$_3$)
133.3
129.3
124.3
61.6
28.2
27.4
19.7
26.7
50.1
48.5
44.7
44
136
128
120
112
104
96
88
80
72
64
56
48
40
32
24
16
8
Chemical Shift (ppm)


5
^{13}C NMR (176 MHz, CDCl$_3$)
176.6
173.9
170.6
134.2
133.0
130.1
129.1
125.0
124.4
77.2
77.0
76.8
62.3
59.6
50.3
48.4
47.6
38.5
29.3
28.3
27.1
25.2
19.8
19.7
Chemical Shift (ppm)


5
DEPT-135 (176 MHz, CDCl$_3$)
133.0
129.1
125.0
124.4
62.3
59.6
28.3
27.1
19.8
19.7
60.3
48.4
47.6
28.3
26.7
26.2
Chemical Shift (ppm)

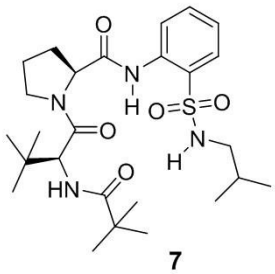

6
^{13}C NMR (176 MHz, $CDCl_3$)
176.8
172.1
170.8
134.9
133.0
129.3
123.9
77.2
77.0
76.8
62.0
60.3
50.5
48.5
47.1
38.6
29.8
28.8
27.2
24.4
19.9
Chemical Shift (ppm)


6
DEPT-135 (176 MHz, $CDCl_3$)
132.8
129.1
123.7
123.7
61.8
60.1
50.3
48.3
46.9
29.6
28.5
26.9
26.7
26.6
24.2
27.0
19.7
Chemical Shift (ppm)



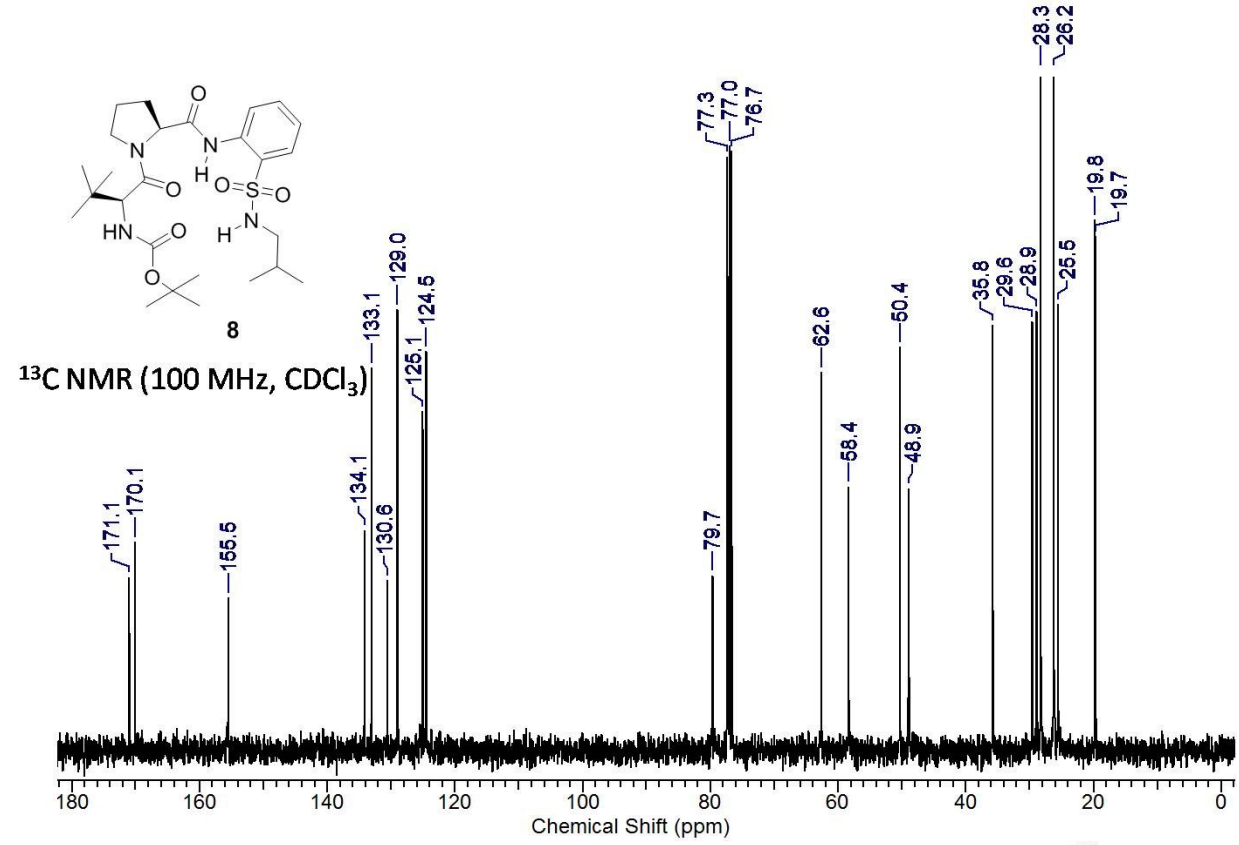
7

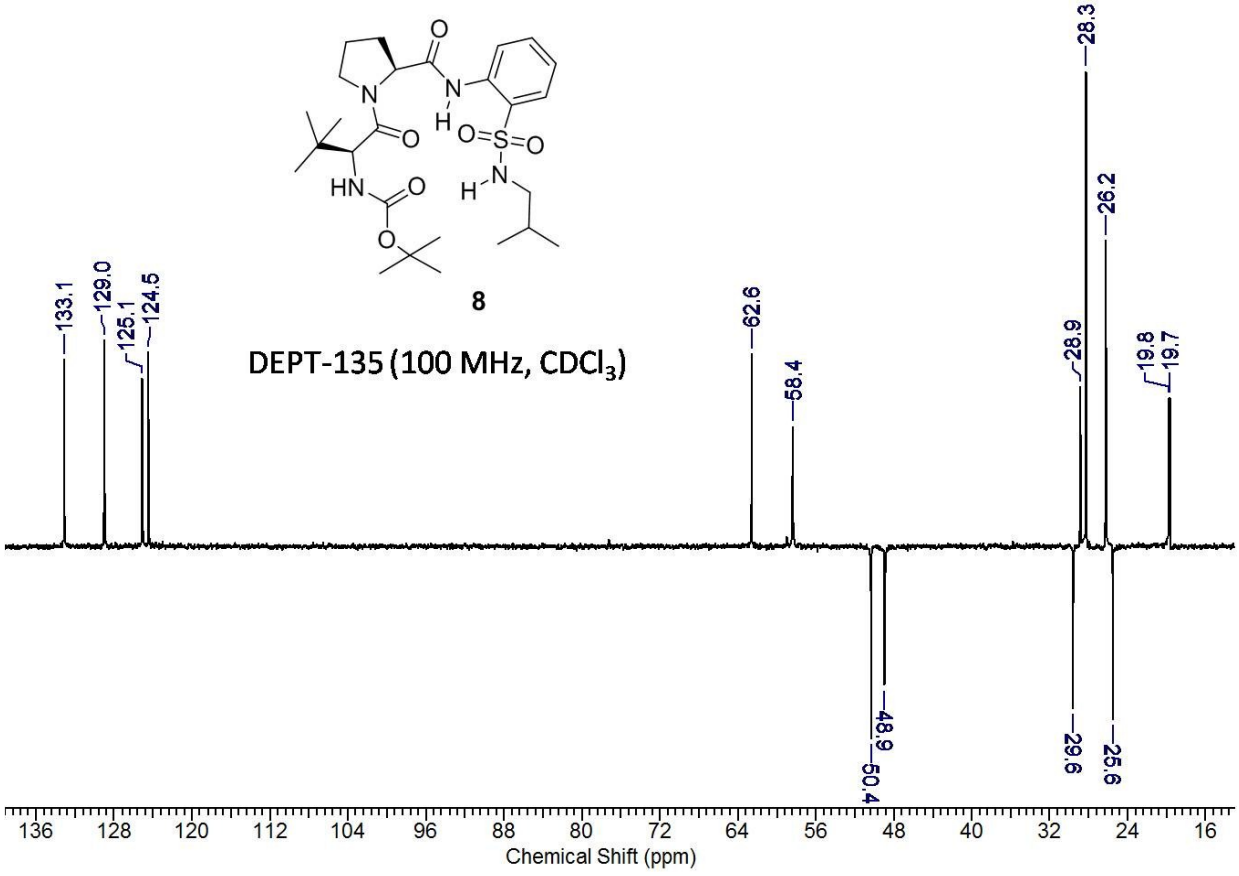
^{13}C NMR (100 MHz, $CDCl_3$)



7

DEPT-135 (100 MHz, $CDCl_3$)


8
^{13}C NMR (100 MHz, $CDCl_3$)
171.1
170.1
155.5
134.1
133.1
130.6
129.0
125.1
124.5
79.7
77.3
77.0
76.7
62.6
58.4
50.4
48.9
35.8
29.6
28.9
28.3
26.2
25.5
19.8
19.7
180
160
140
120
100
80
60
40
20
0
Chemical Shift (ppm)


8
DEPT-135 (100 MHz, $CDCl_3$)
133.1
129.0
125.1
124.5
62.6
58.4
48.9
50.4
28.3
26.2
28.9
29.6
19.8
19.7
26.6
136
128
120
112
104
96
88
80
72
64
56
48
40
32
24
16
Chemical Shift (ppm)

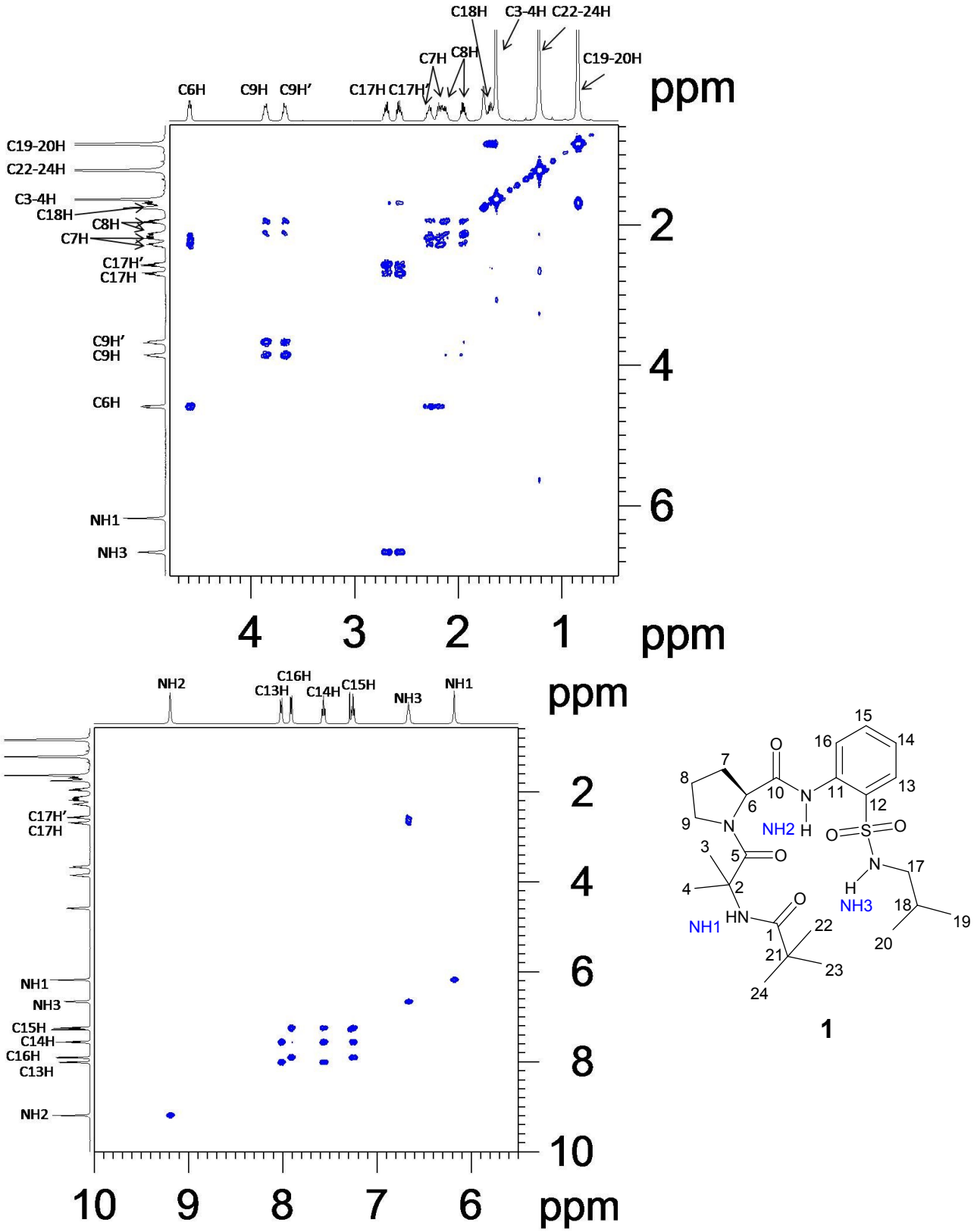


Figure: Partial COSY spectra of **1** (500 MHz, $CDCl_3$): aliphatic (upper excerpt) and aromatic (lower excerpt) regions.

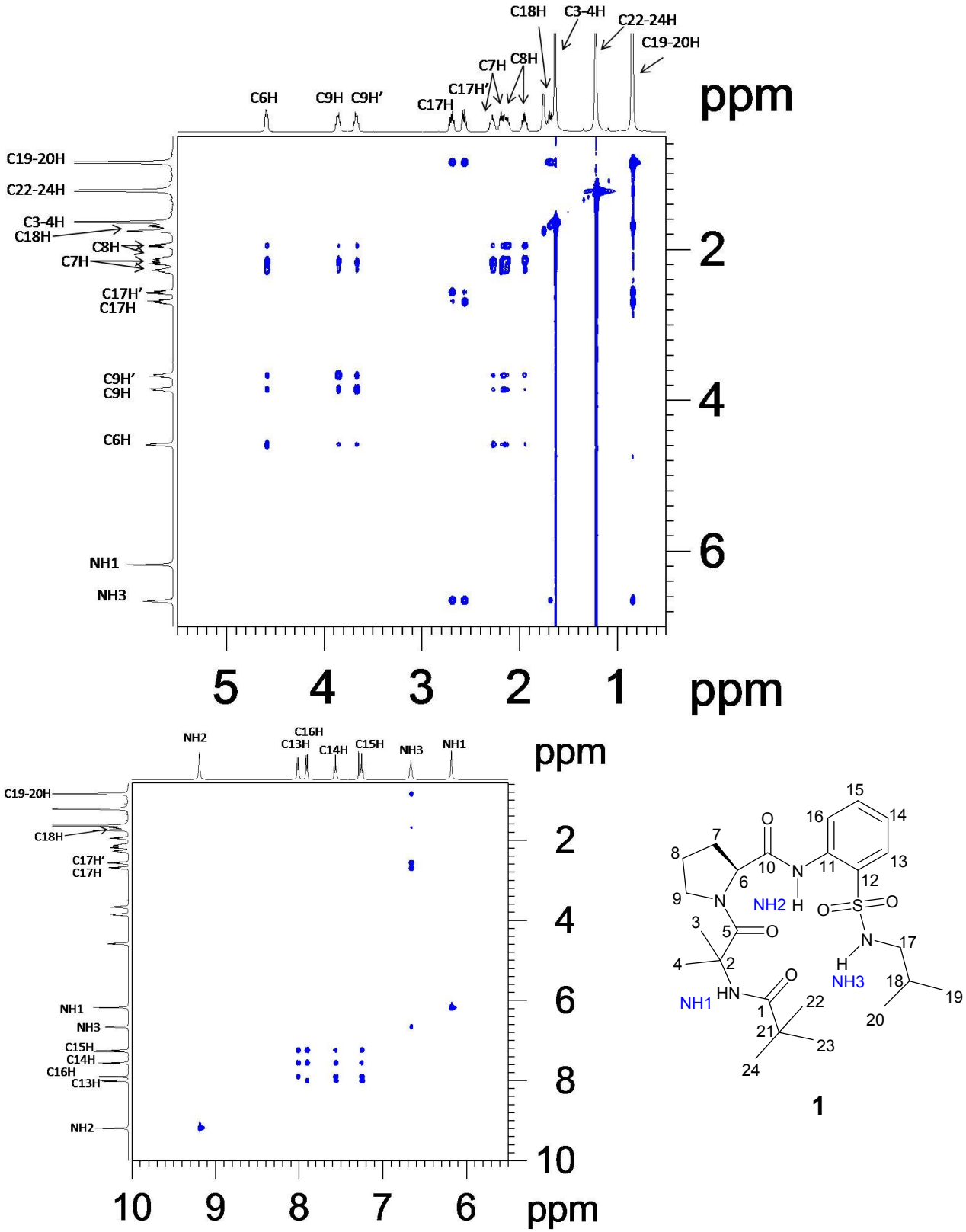


Figure: Partial TOCSY spectra of **1** (500 MHz, $CDCl_3$): aliphatic (upper excerpt) and aromatic (lower excerpt) regions.

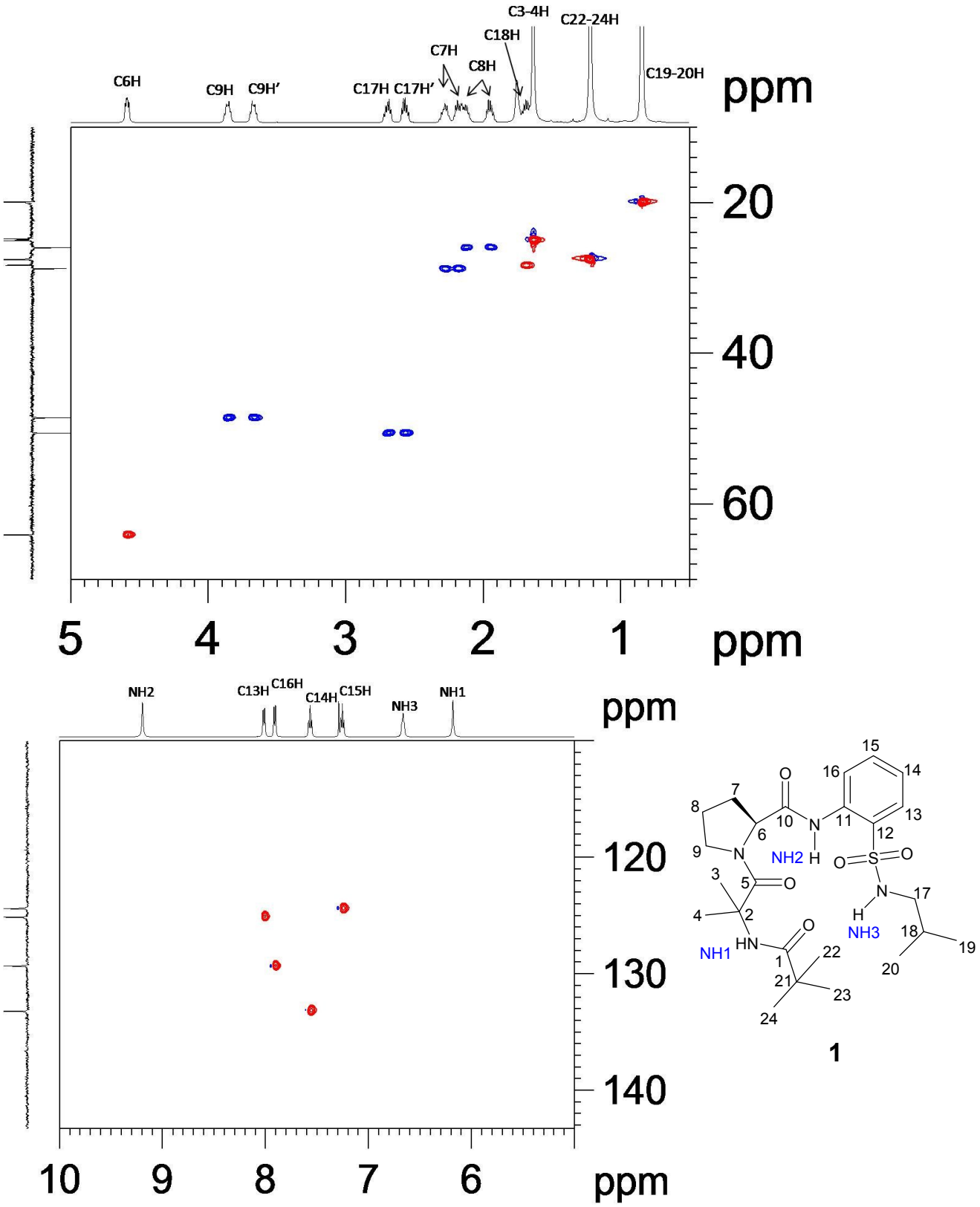


Figure: Partial HSQC spectra of **1** (500 MHz, $CDCl_3$): aliphatic (upper excerpt) and aromatic (lower excerpt) regions.

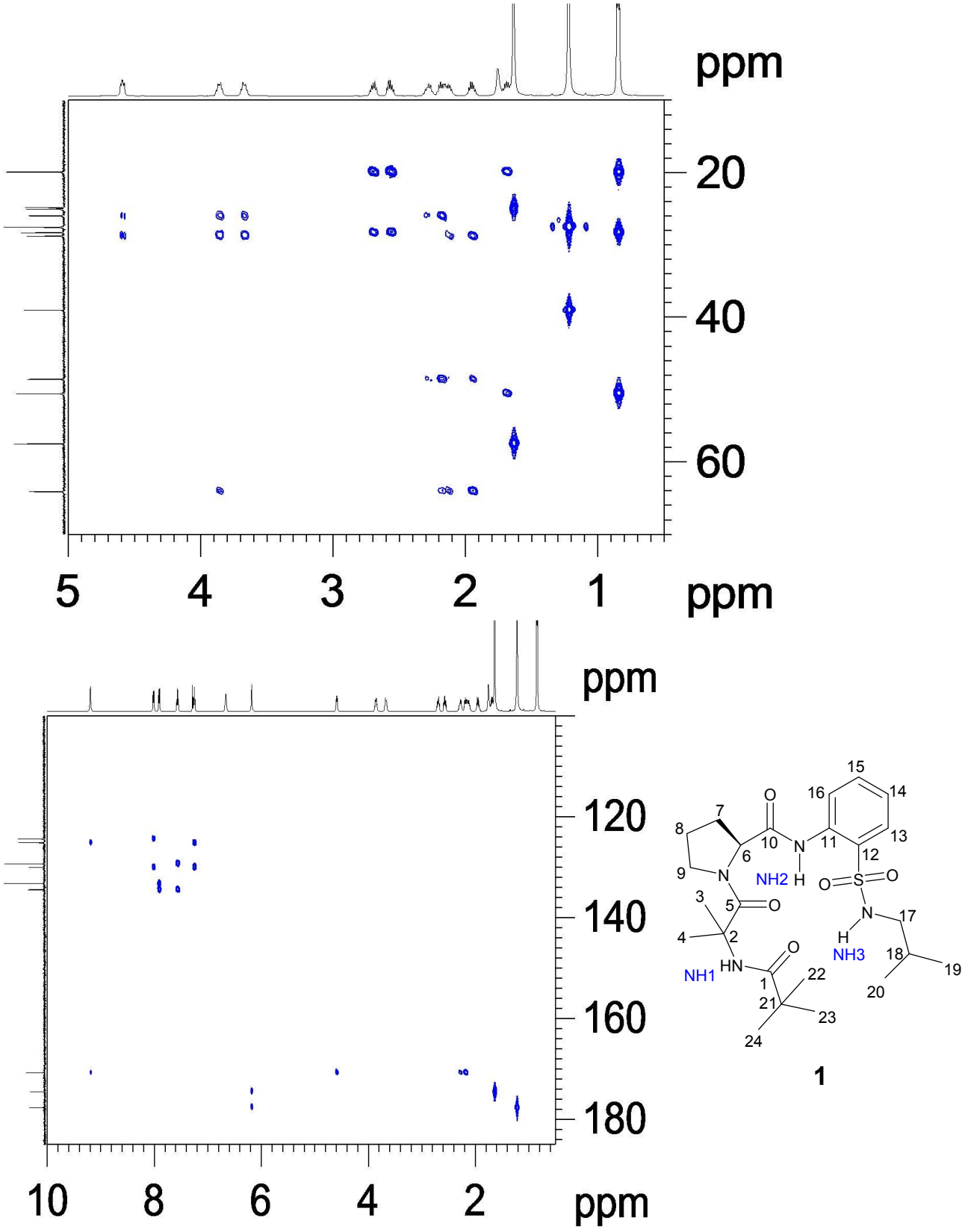


Figure: Partial HMBC spectra of **1** (500 MHz, $CDCl_3$): aliphatic (upper excerpt) and aromatic (lower excerpt) regions.

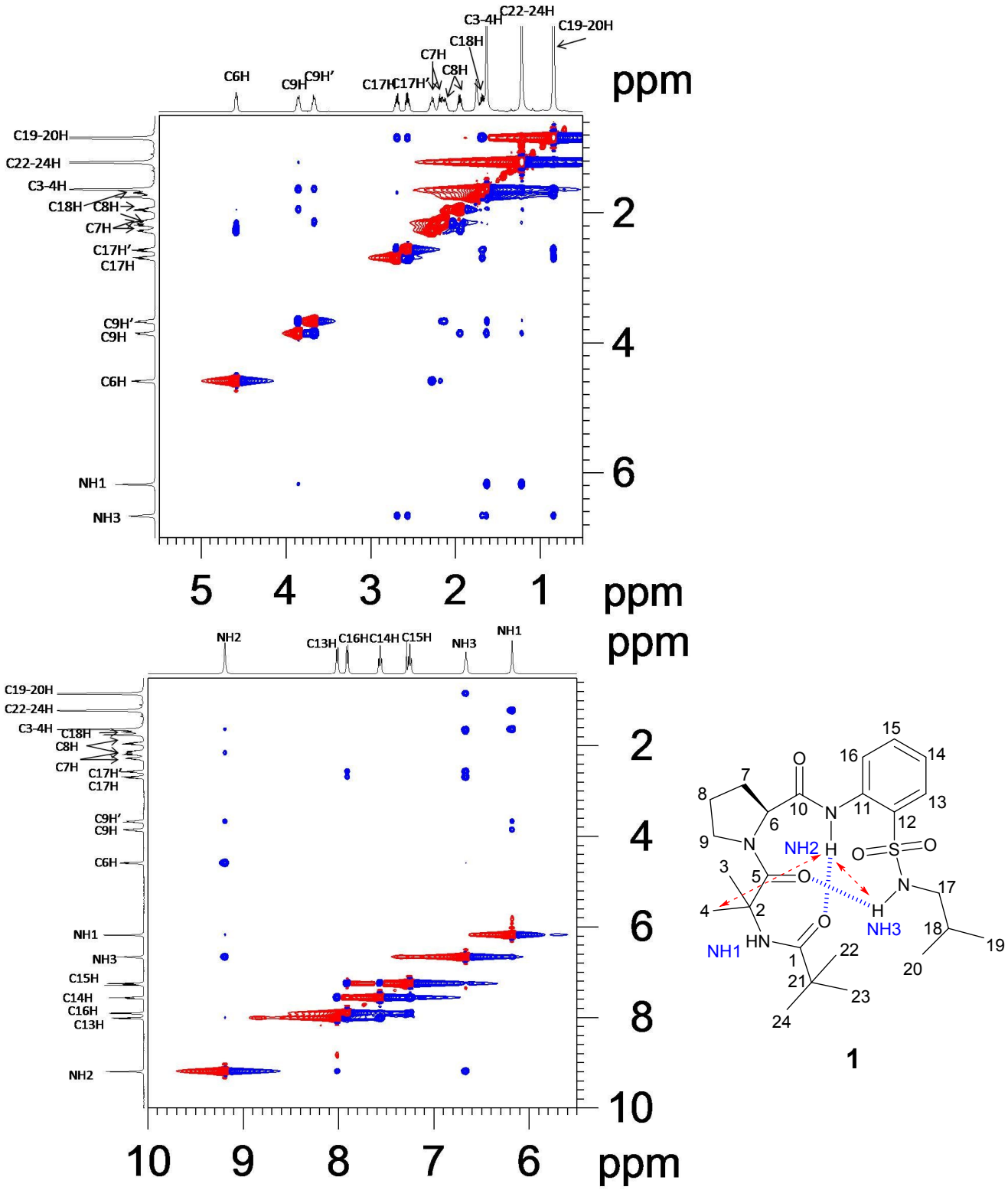


Figure: Partial NOESY spectra of **1** (500 MHz, $CDCl_3$): aliphatic (upper excerpt) and aromatic (lower excerpt) regions.

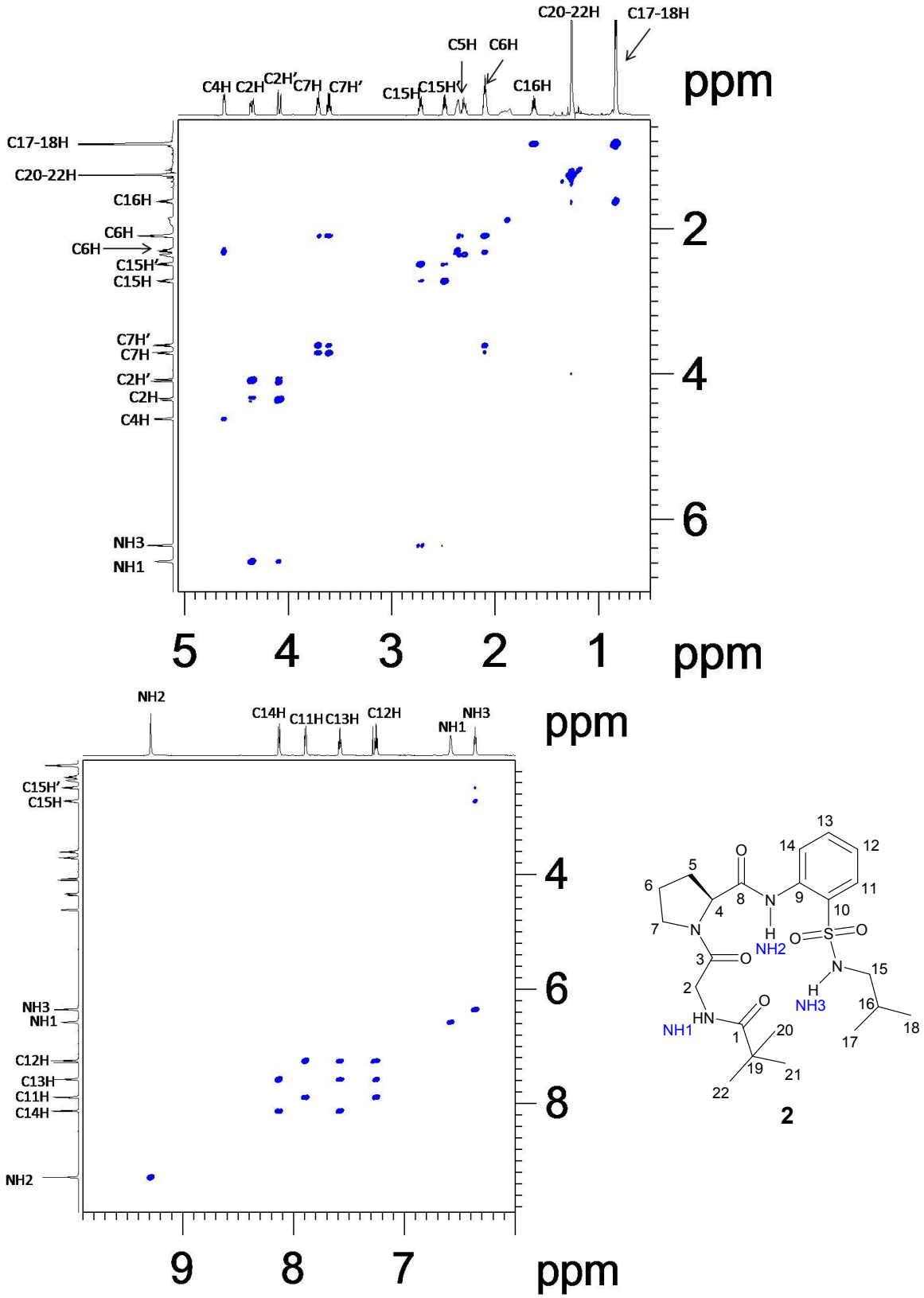


Figure: Partial COSY spectra of **2** (700 MHz, $CDCl_3$): aliphatic (upper excerpt) and aromatic (lower excerpt) regions.

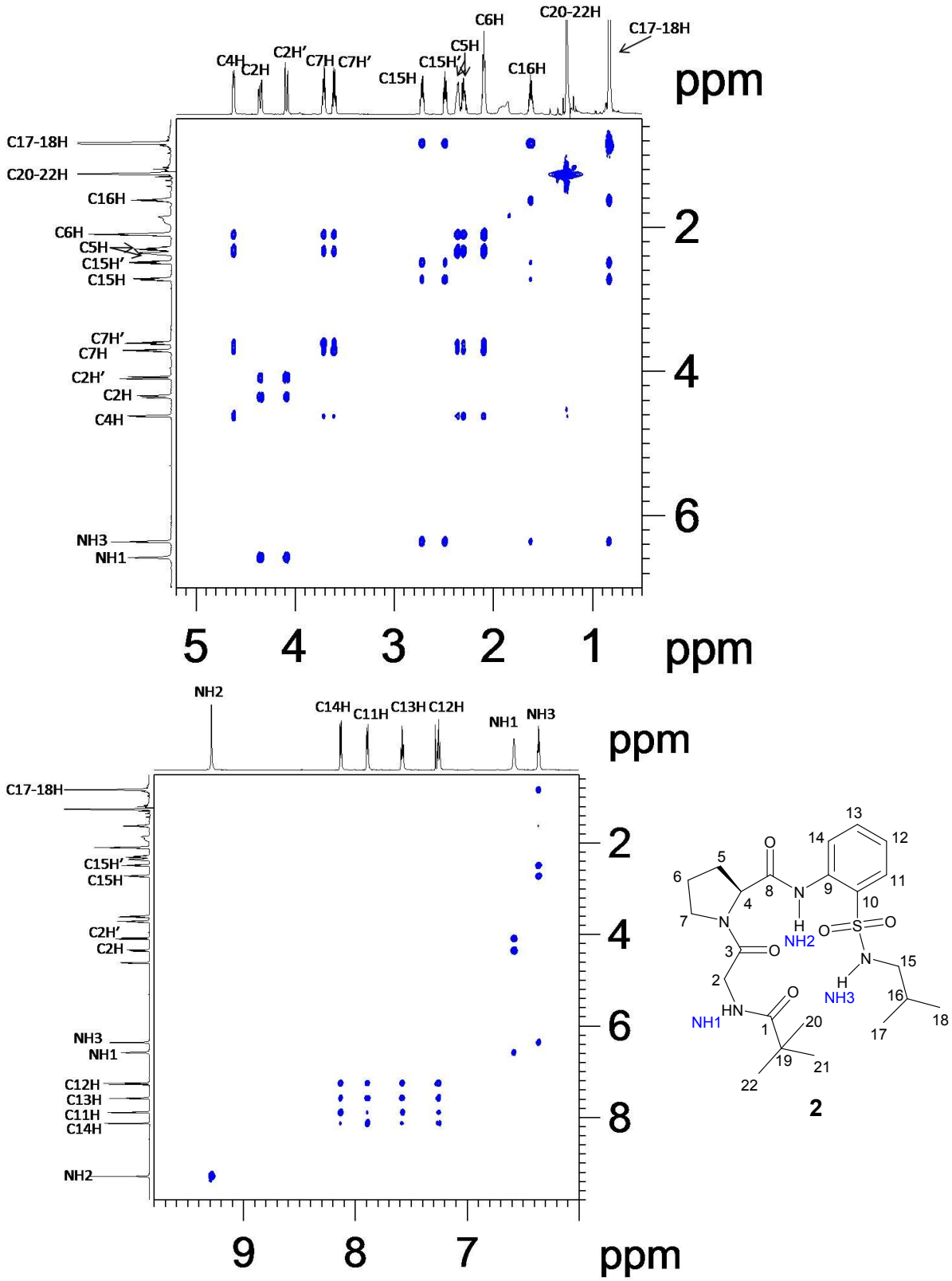


Figure: Partial TOCSY spectra of **2** (700 MHz, $CDCl_3$): aliphatic (upper excerpt) and aromatic (lower excerpt) regions.

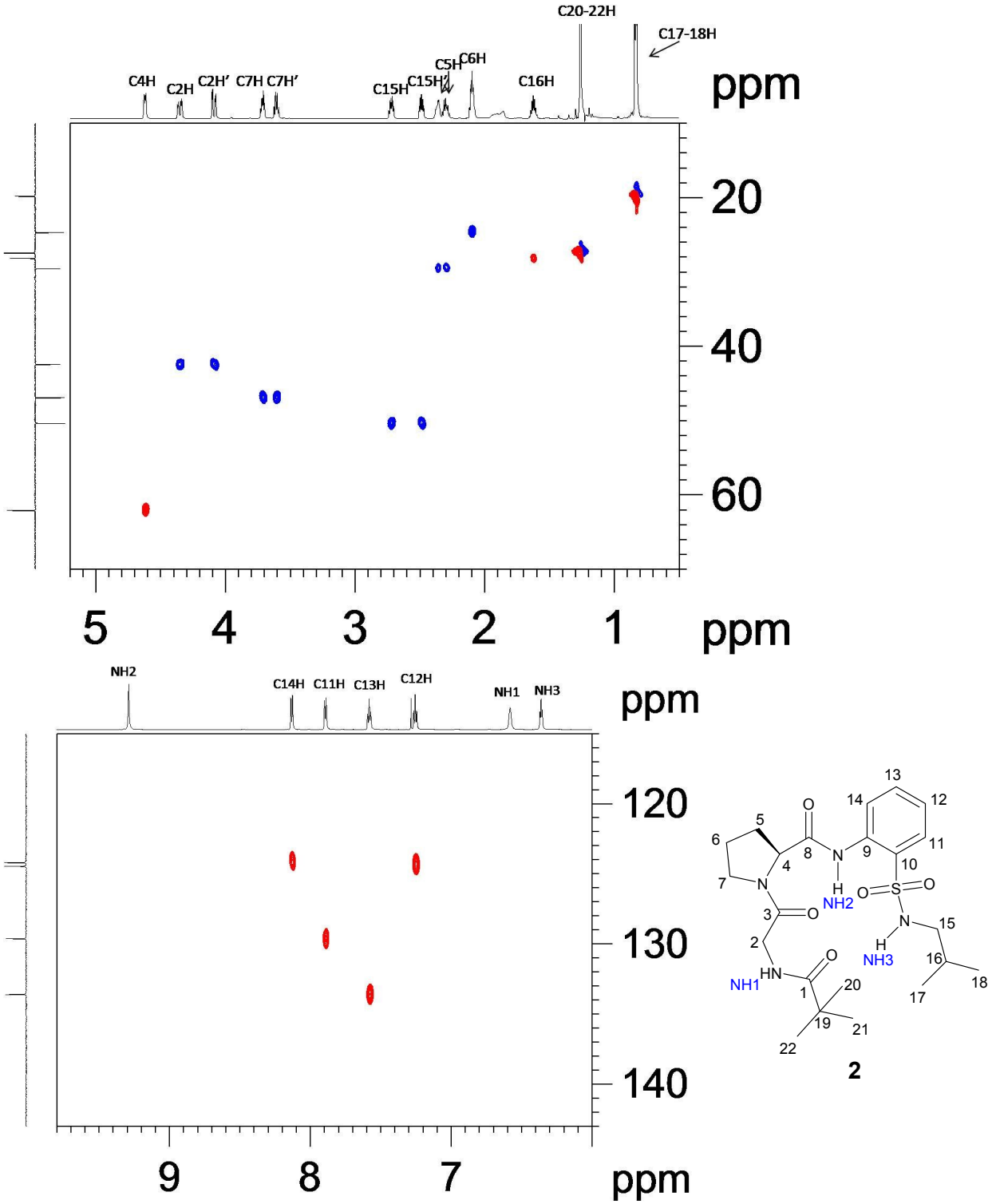


Figure: Partial HSQC spectra of **2** (700 MHz, $CDCl_3$): aliphatic (upper excerpt) and aromatic (lower excerpt) regions.

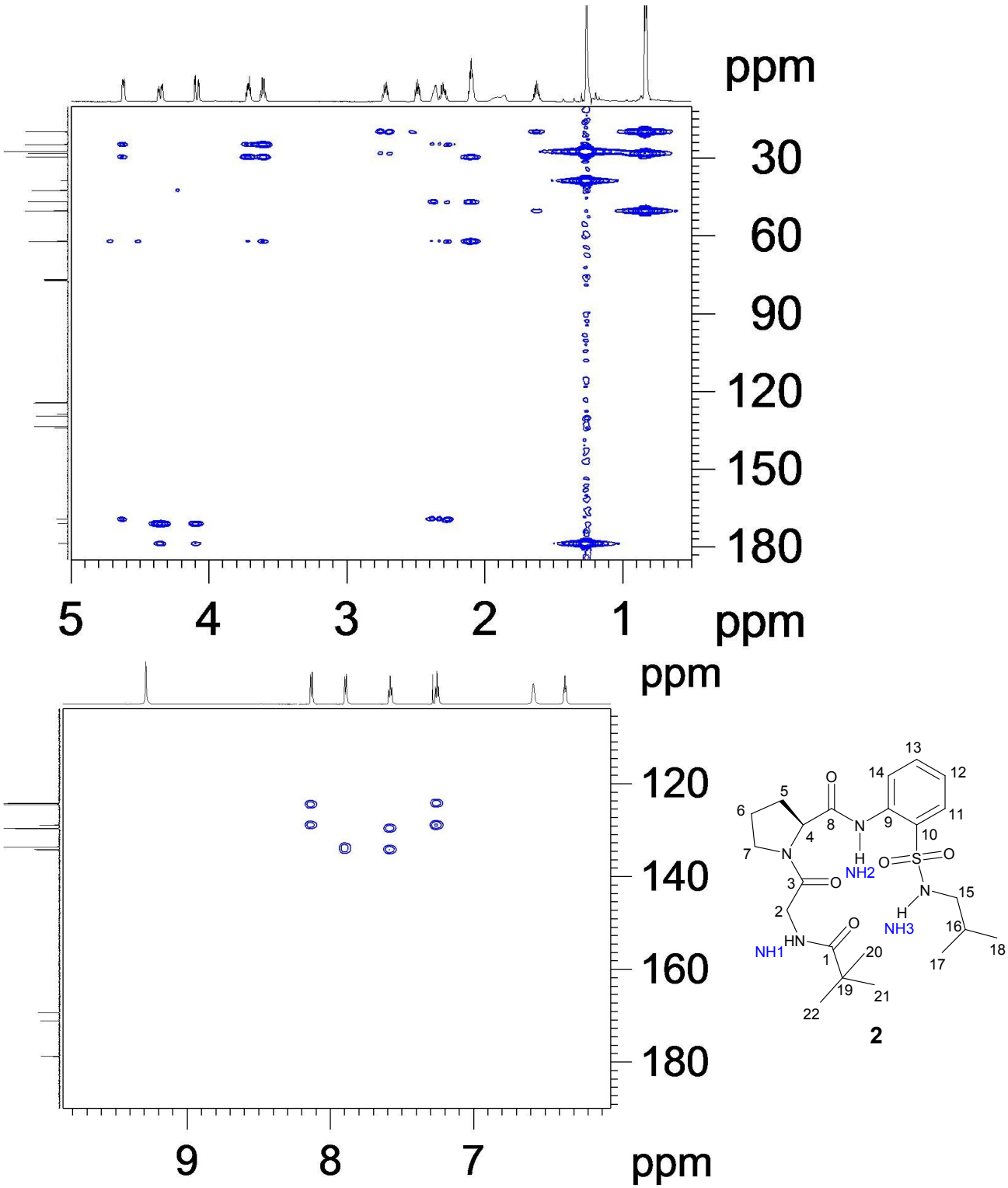


Figure: Partial HMBC spectra of **2** (700 MHz, $CDCl_3$): aliphatic (upper excerpt) and aromatic (lower excerpt) regions.

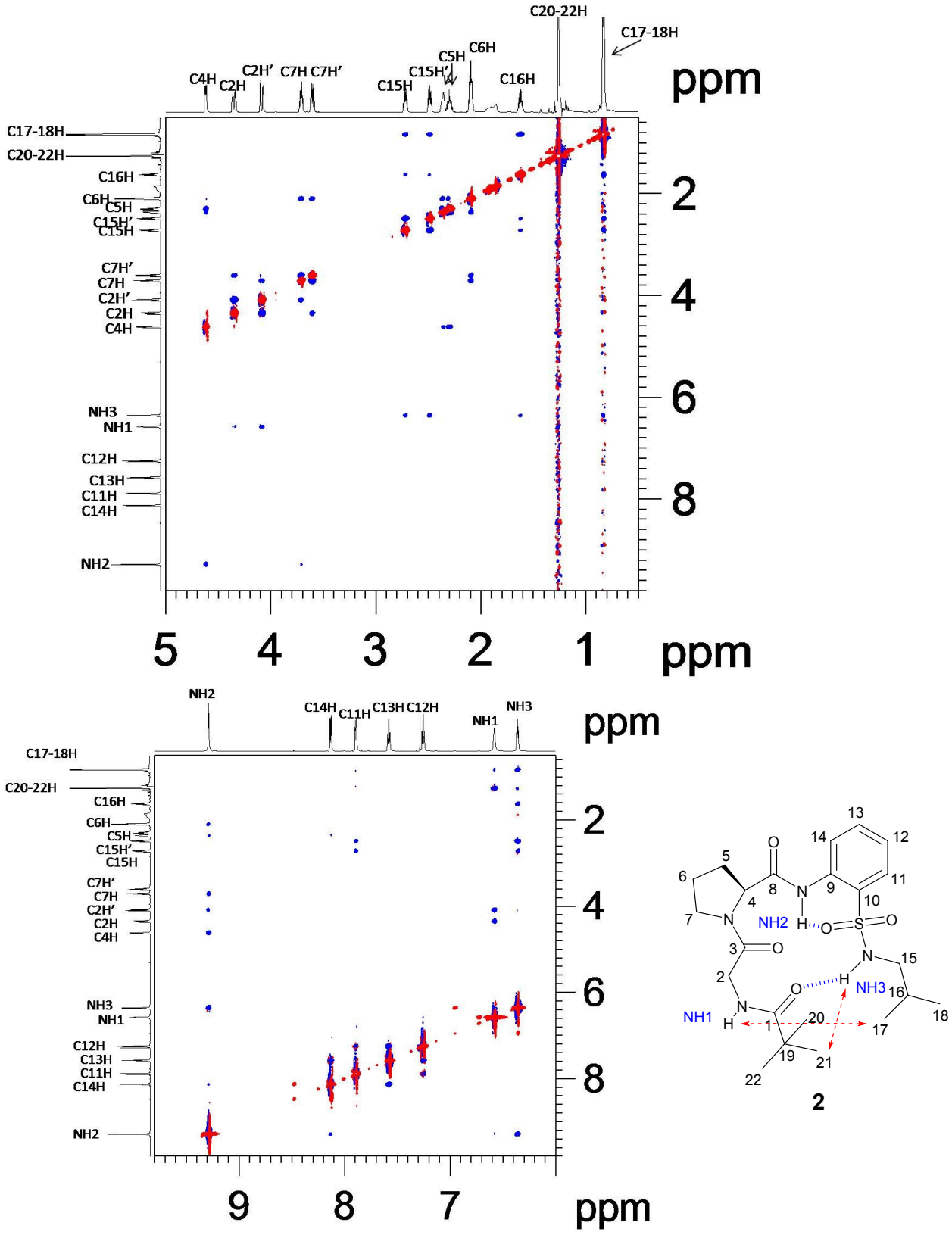


Figure: Partial NOESY spectra of **2** (700 MHz, $CDCl_3$): aliphatic (upper excerpt) and aromatic (lower excerpt) regions.

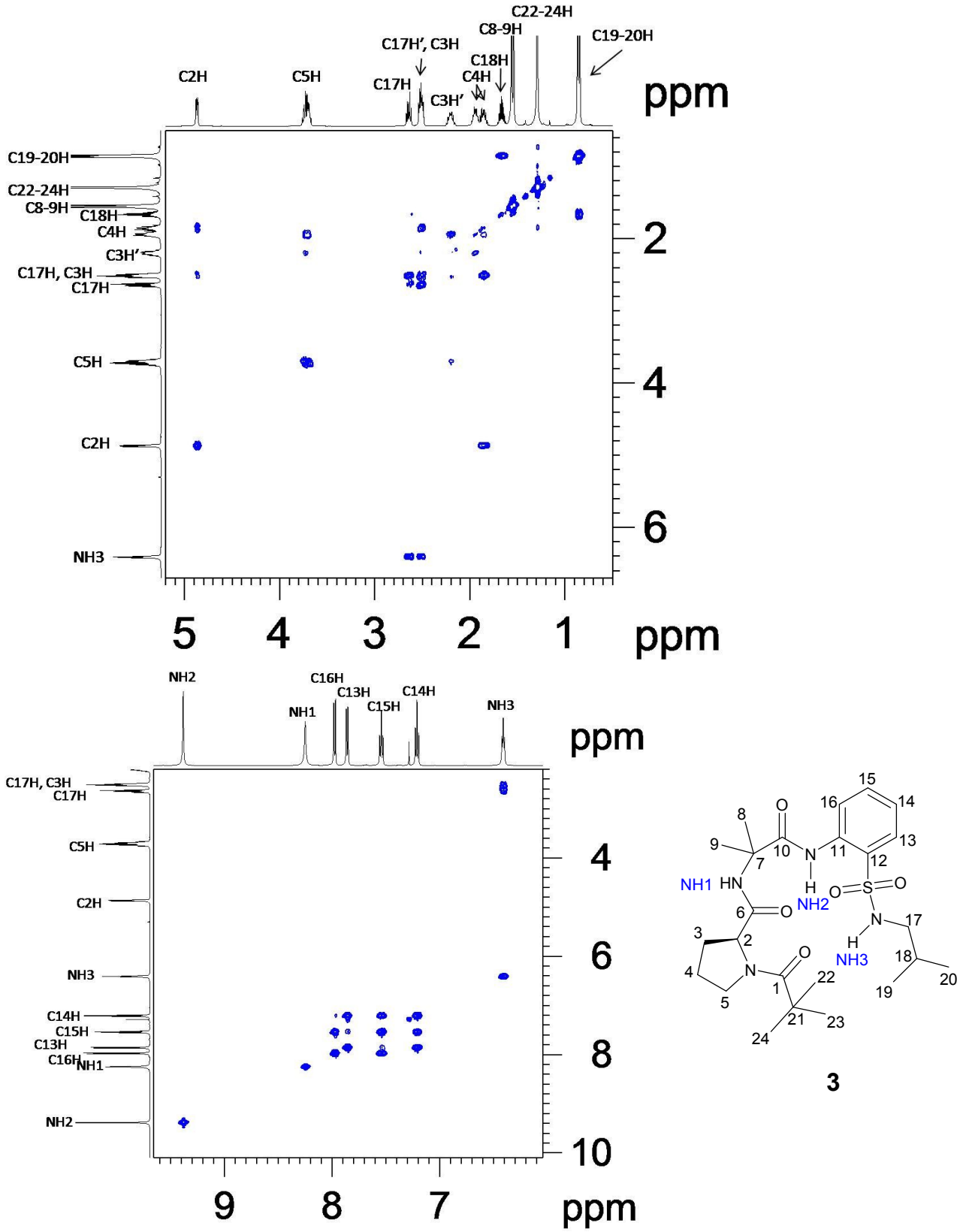


Figure: Partial COSY spectra of **3** (500 MHz, $CDCl_3$): aliphatic (upper excerpt) and aromatic (lower excerpt) regions.

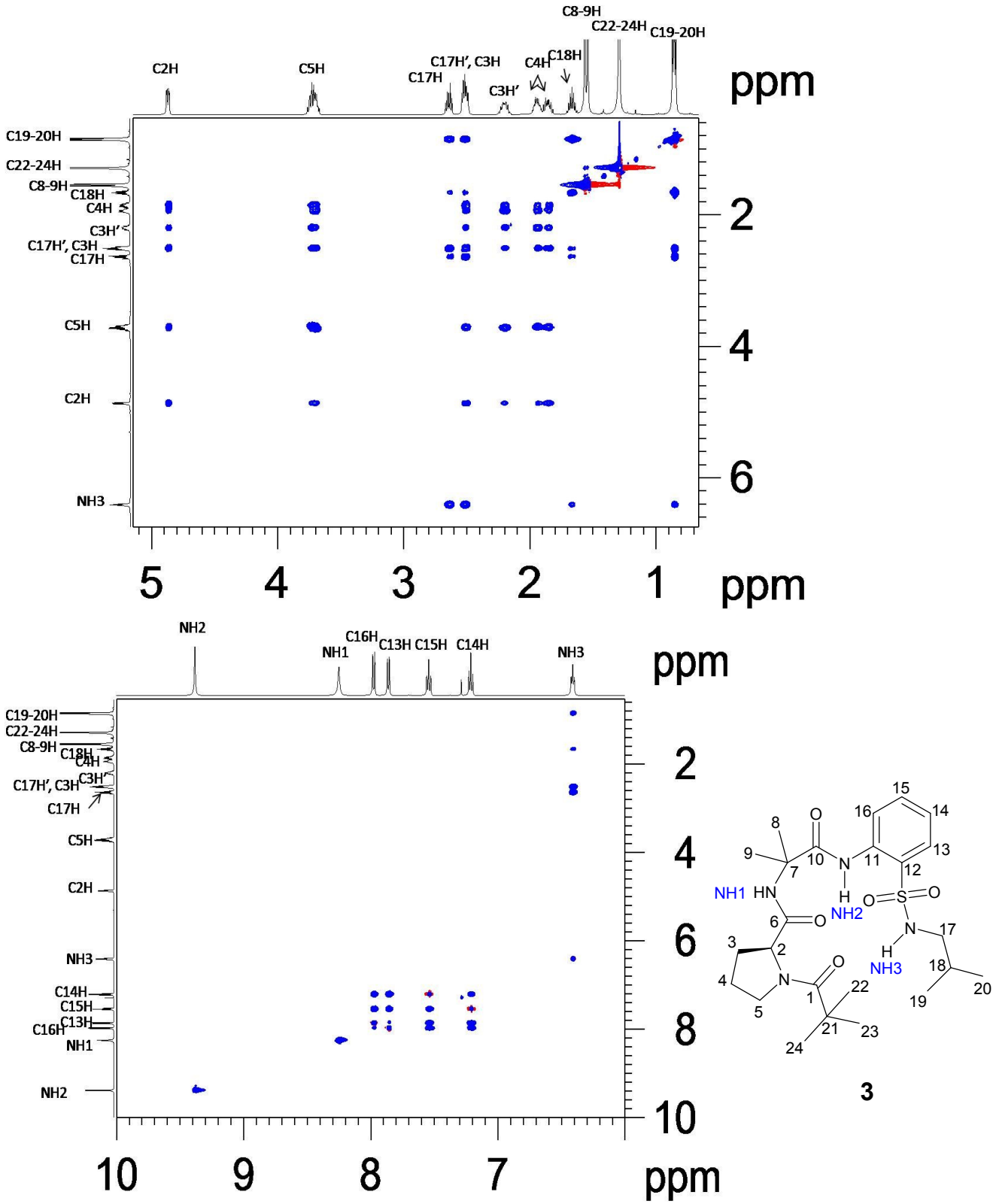


Figure: Partial TOCSY spectra of **3** (500 MHz, $CDCl_3$): aliphatic (upper excerpt) and aromatic (lower excerpt) regions.

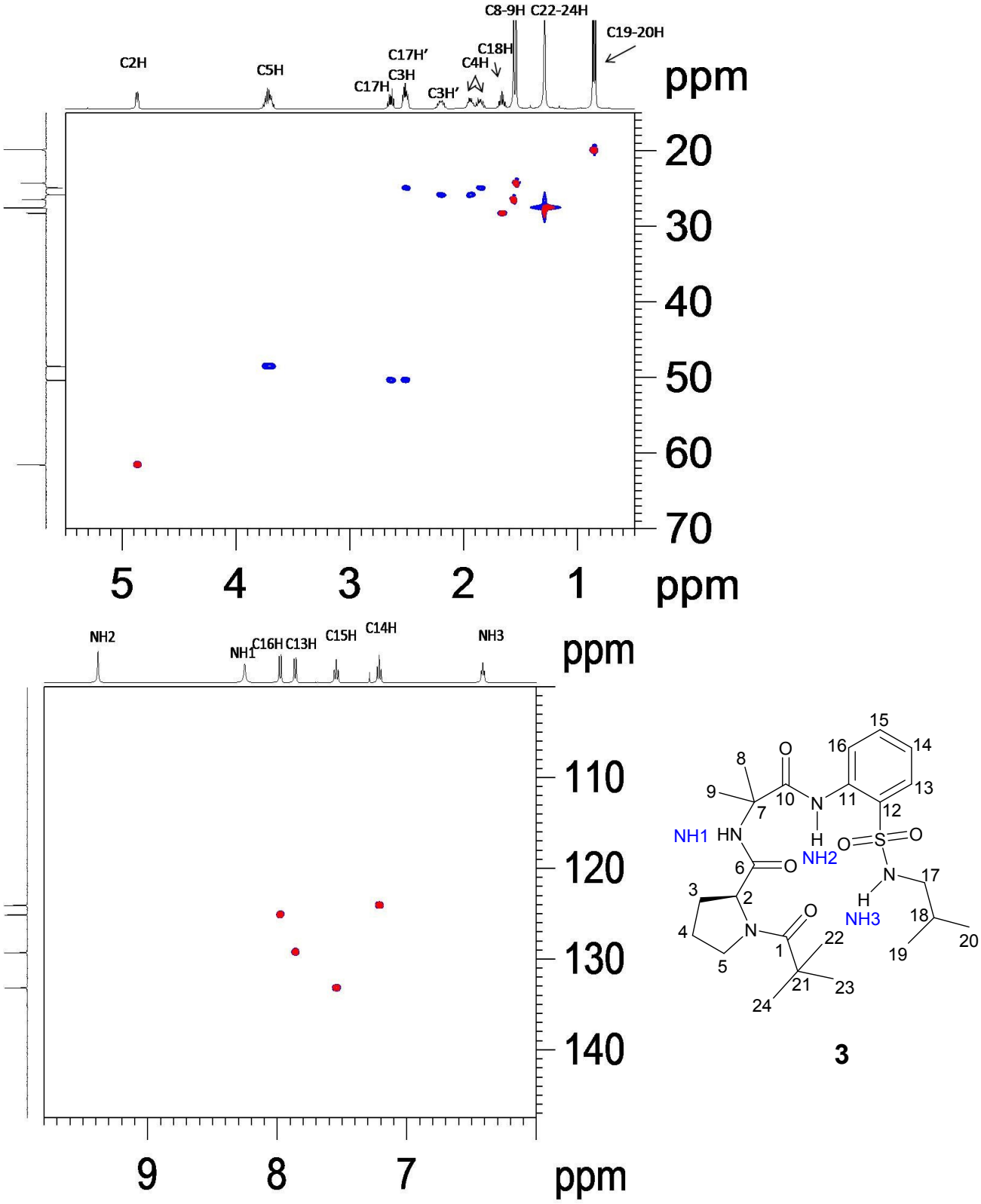


Figure: Partial HSQC spectra of **3** (500 MHz, $CDCl_3$): aliphatic (upper excerpt) and aromatic (lower excerpt) regions.

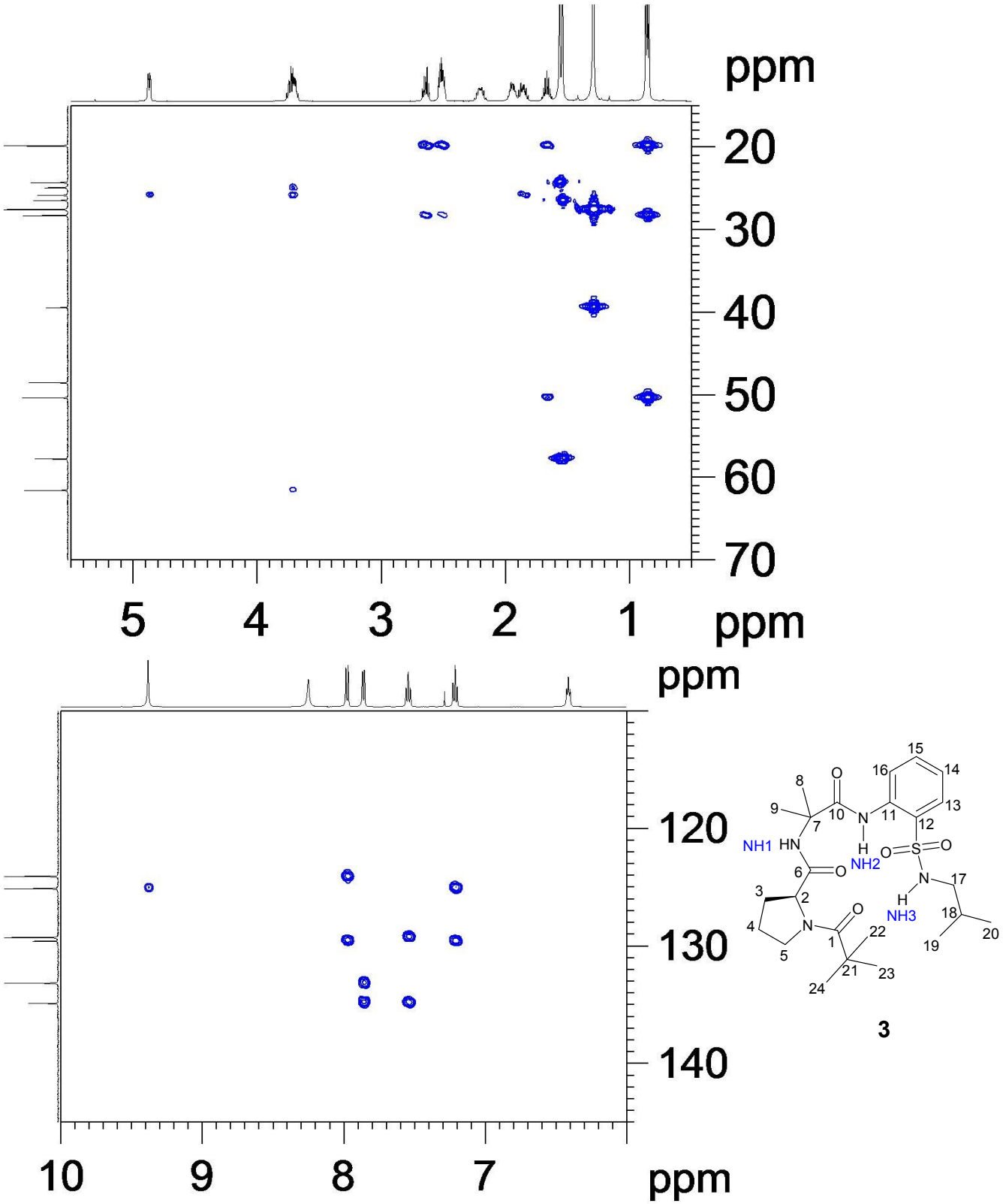


Figure: Partial HMBC spectra of **3** (500 MHz, $CDCl_3$): aliphatic (upper excerpt) and aromatic (lower excerpt) regions.

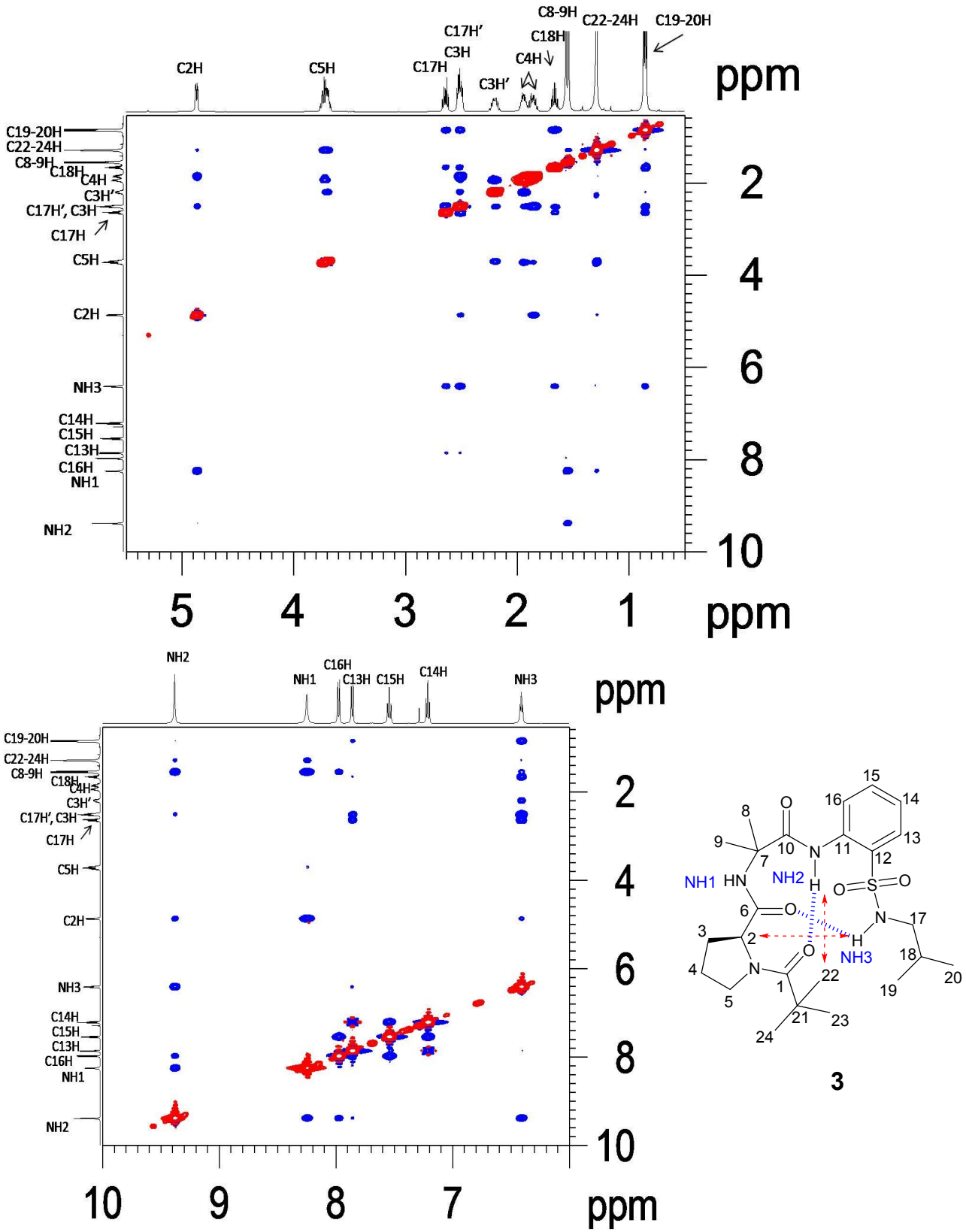


Figure: Partial NOESY spectra of **3** (500 MHz, $CDCl_3$): aliphatic (upper excerpt) and aromatic (lower excerpt) regions.

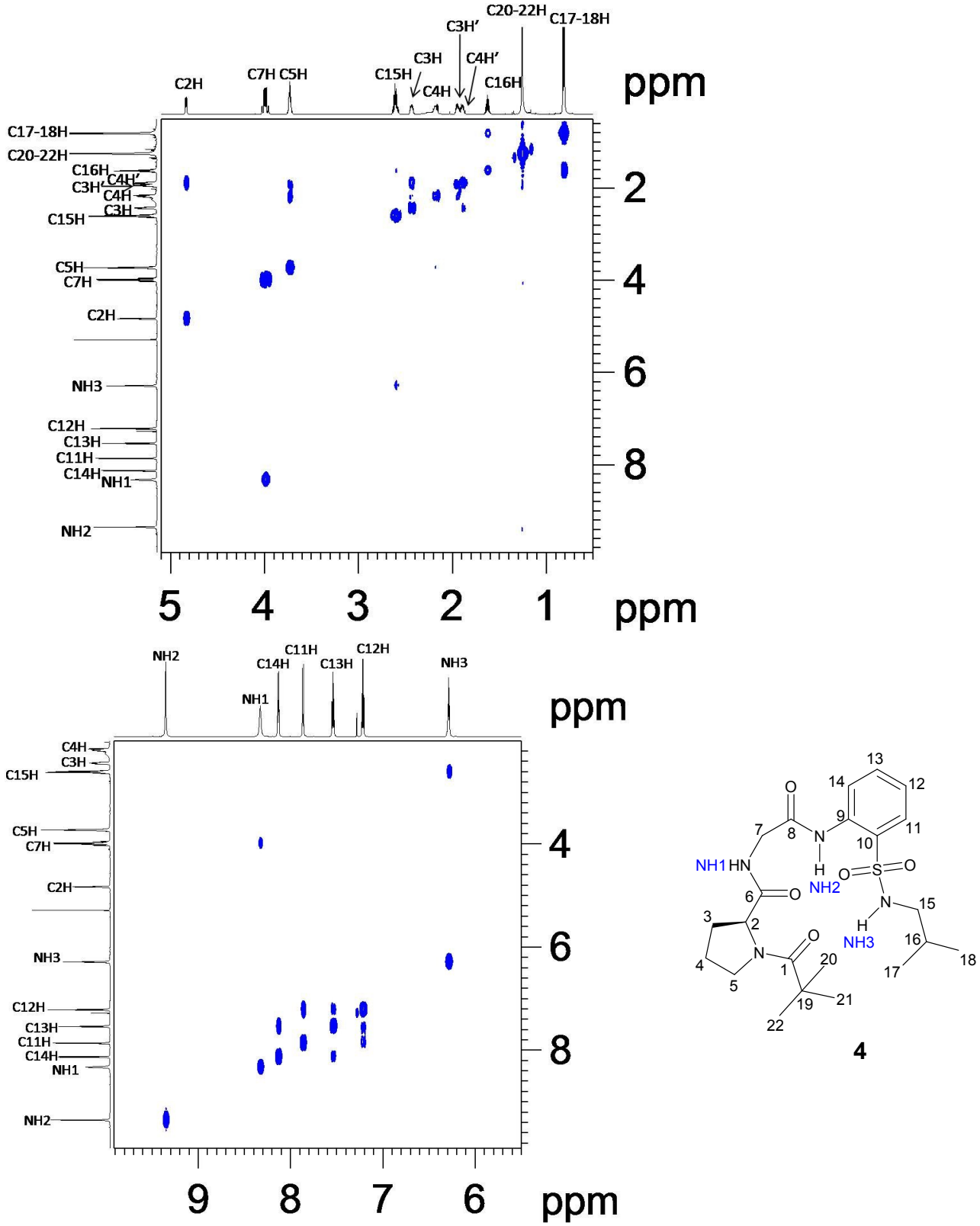


Figure: Partial COSY spectra of **4** (700 MHz, $CDCl_3$): aliphatic (upper excerpt) and aromatic (lower excerpt) regions.

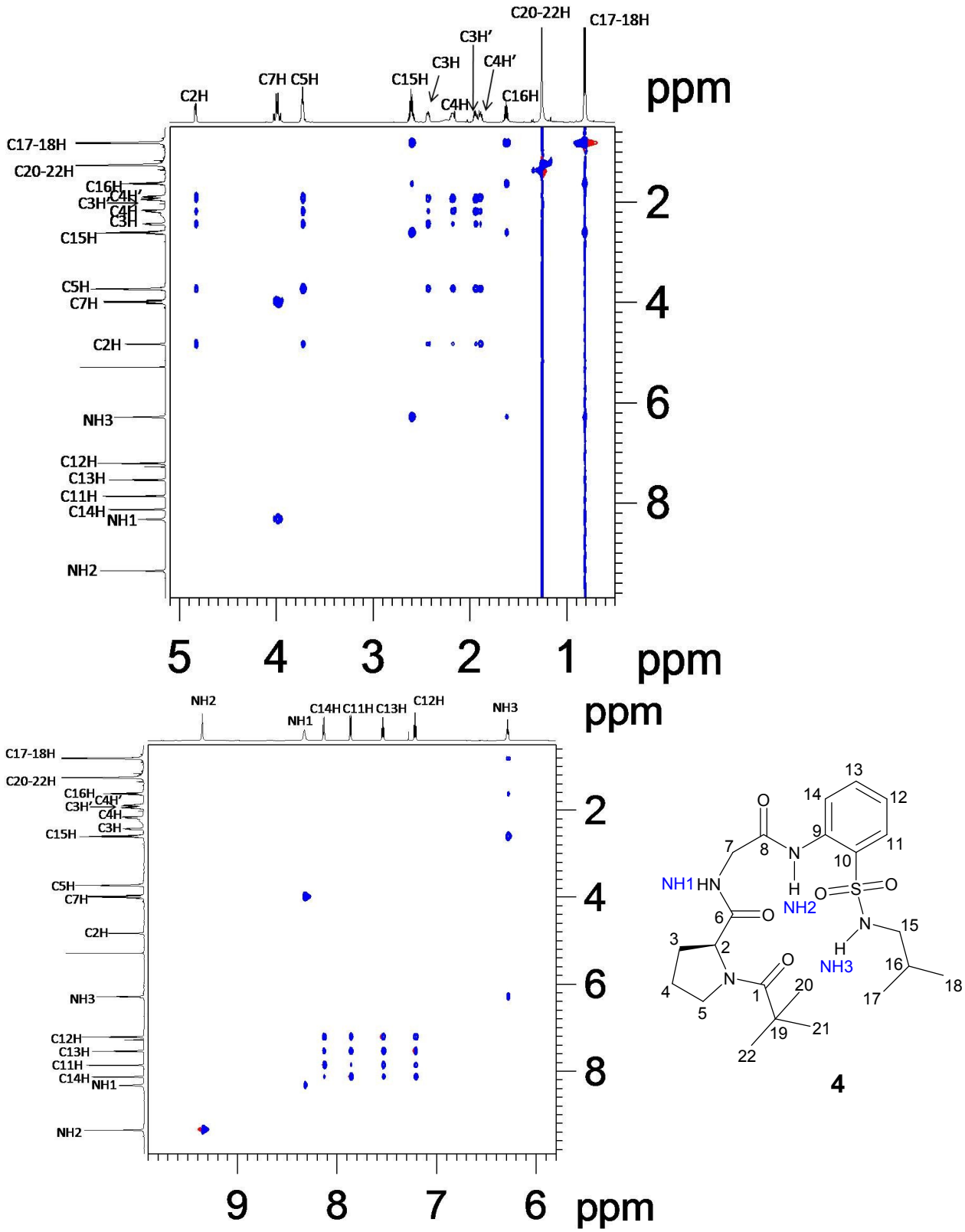
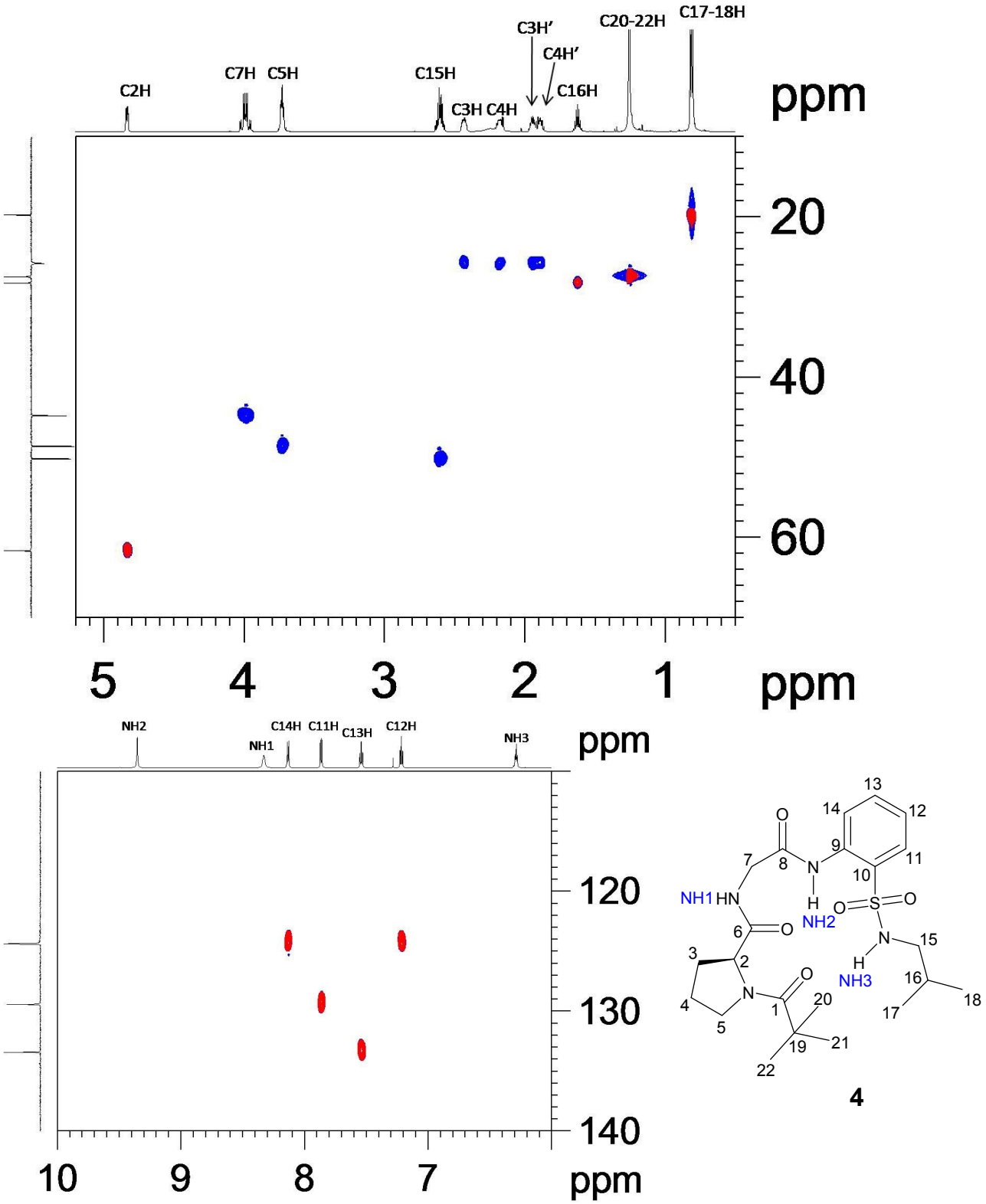


Figure: Partial TOCSY spectra of **4** (700 MHz, $CDCl_3$): aliphatic (upper excerpt) and aromatic (lower excerpt) regions.



4

Figure: Partial HSQC spectra of **4** (700 MHz, $CDCl_3$): aliphatic (upper excerpt) and aromatic (lower excerpt) regions.

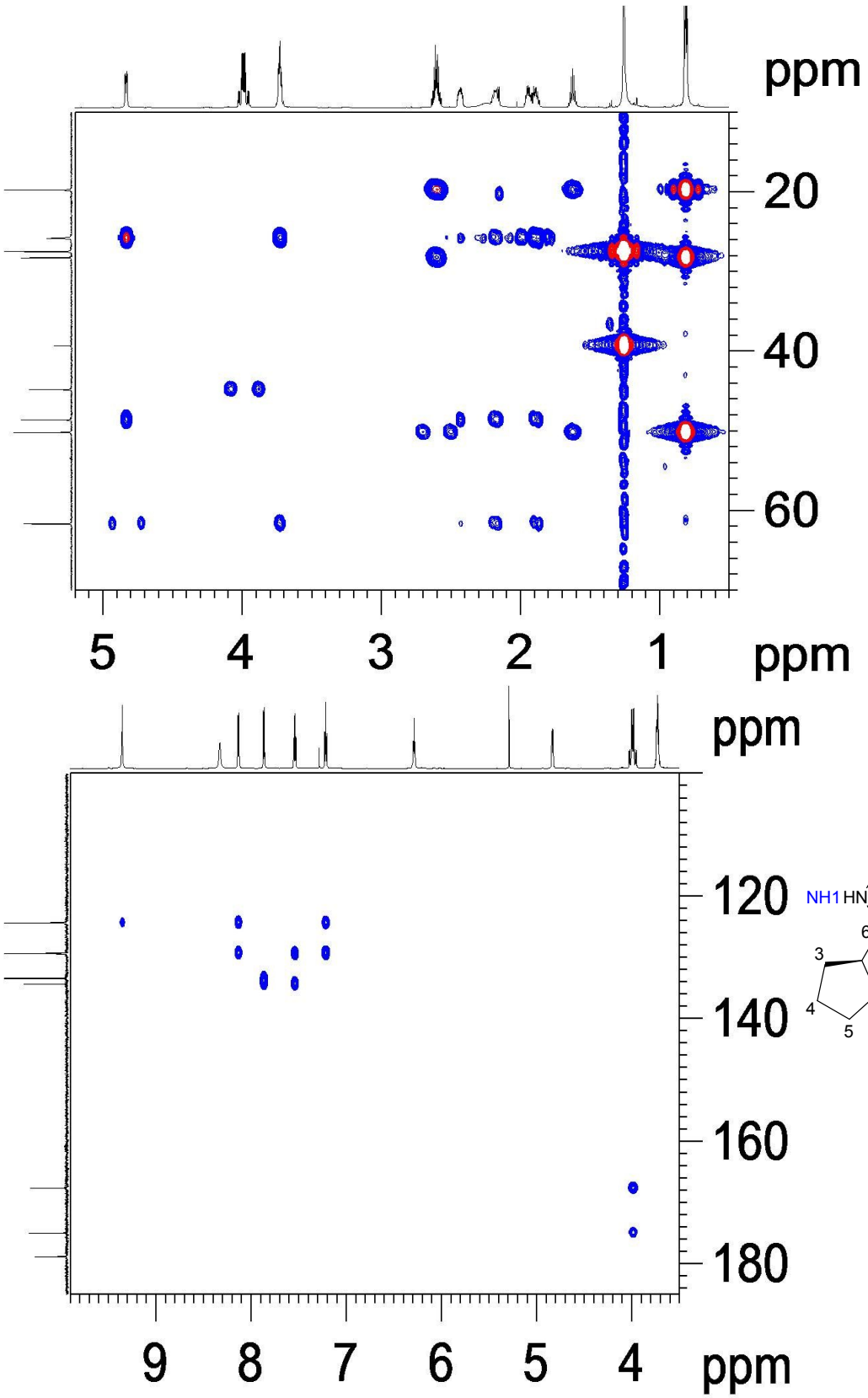


Figure: Partial HMBC spectra of **4** (700 MHz, $CDCl_3$): aliphatic (upper excerpt) and aromatic (lower excerpt) regions.

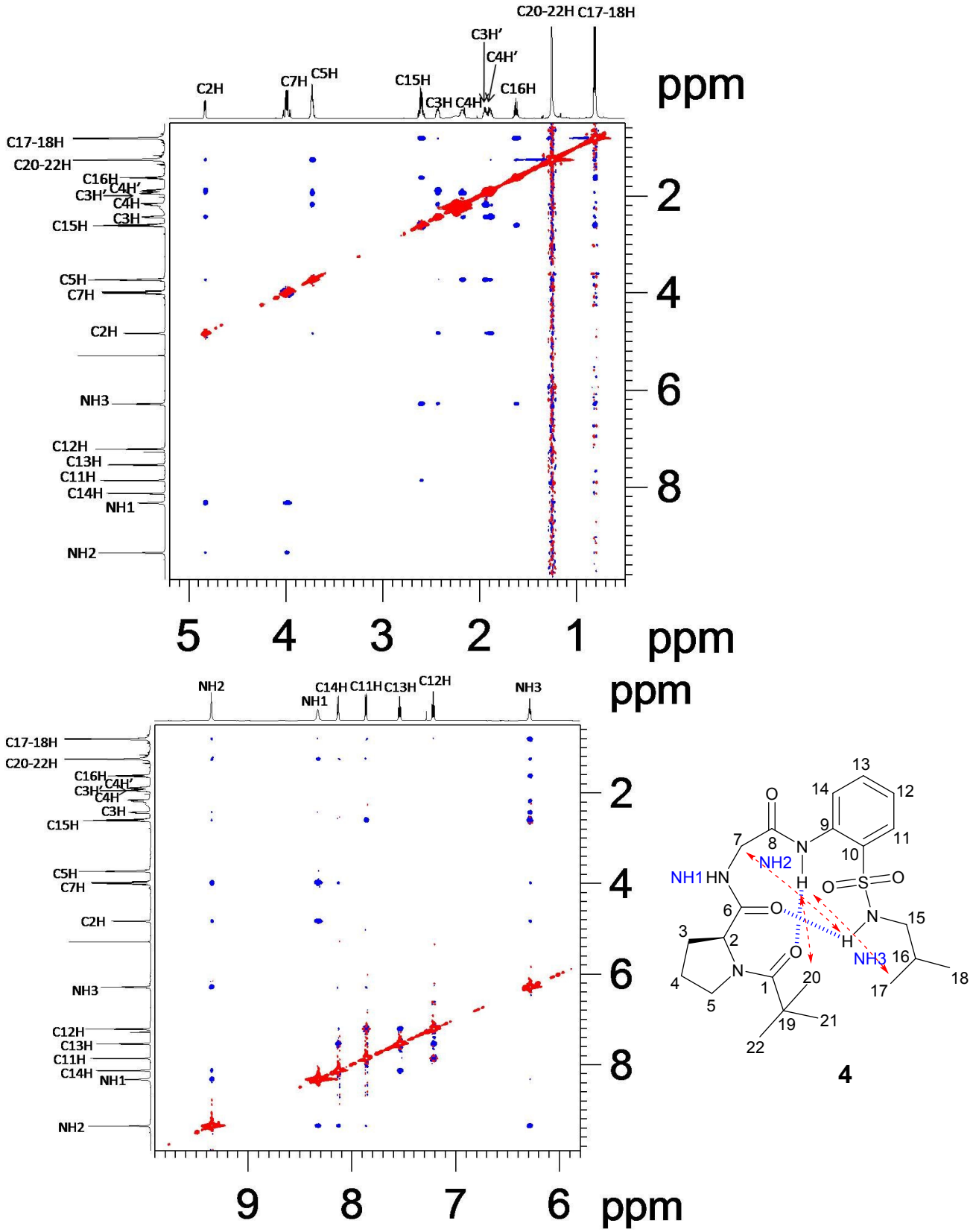


Figure: Partial NOESY spectra of **4** (700 MHz, $CDCl_3$): aliphatic (upper excerpt) and aromatic (lower excerpt) regions.

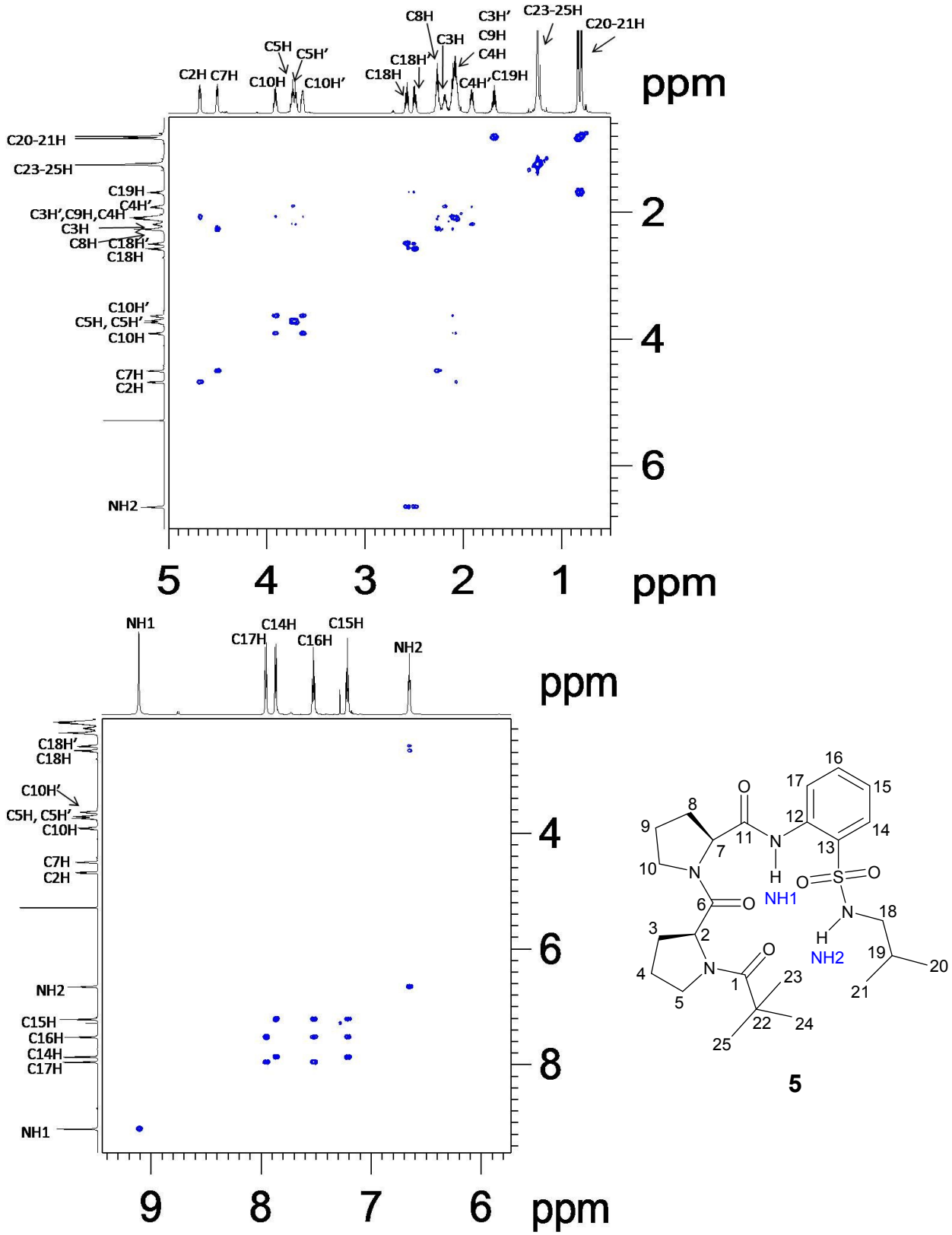
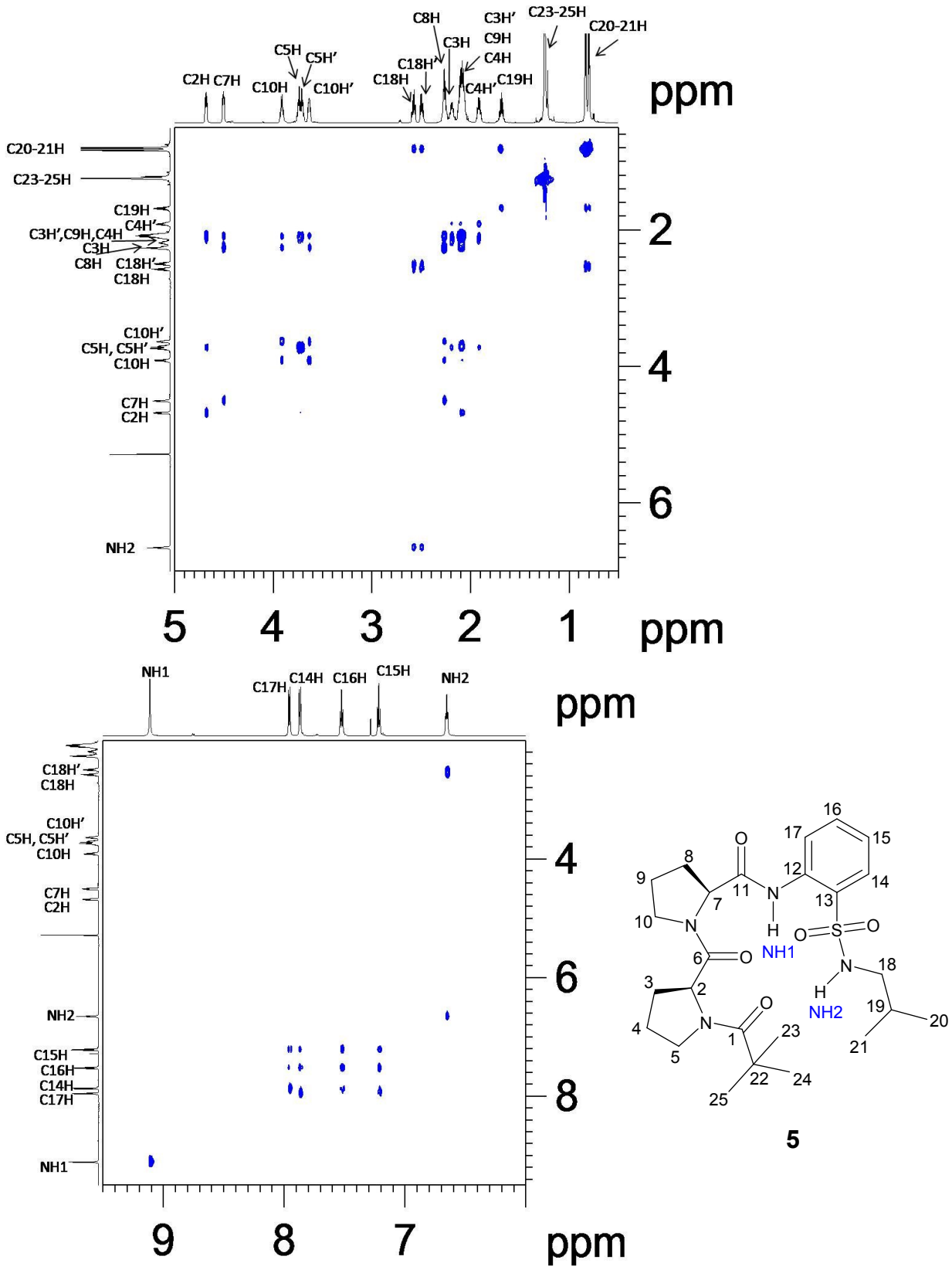


Figure: Partial COSY spectra of **5** (700 MHz, $CDCl_3$): aliphatic (upper excerpt) and aromatic (lower excerpt) regions.



5

Figure: Partial TOCSY spectra of **5** (700 MHz, $CDCl_3$): aliphatic (upper excerpt) and aromatic (lower excerpt) regions.

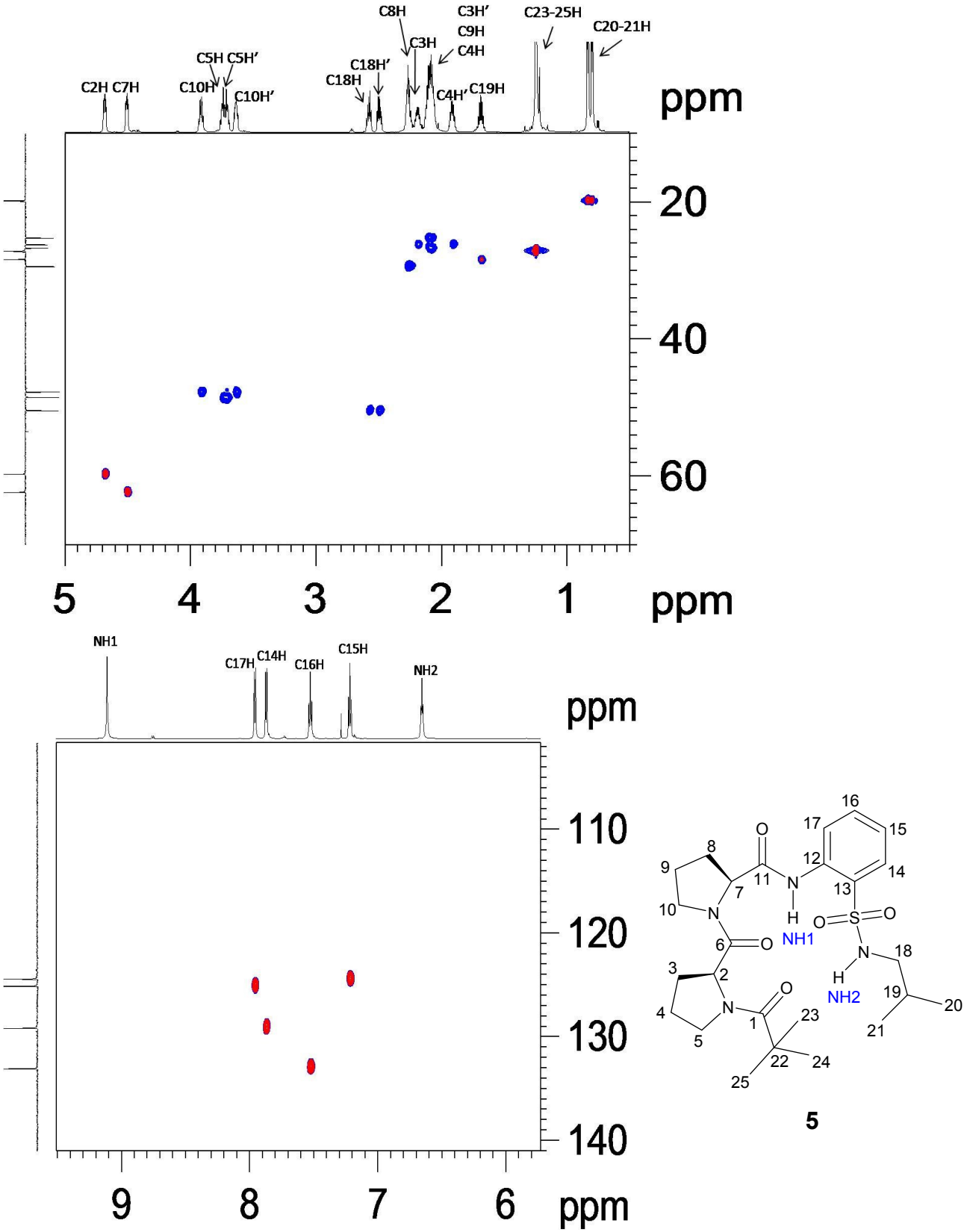
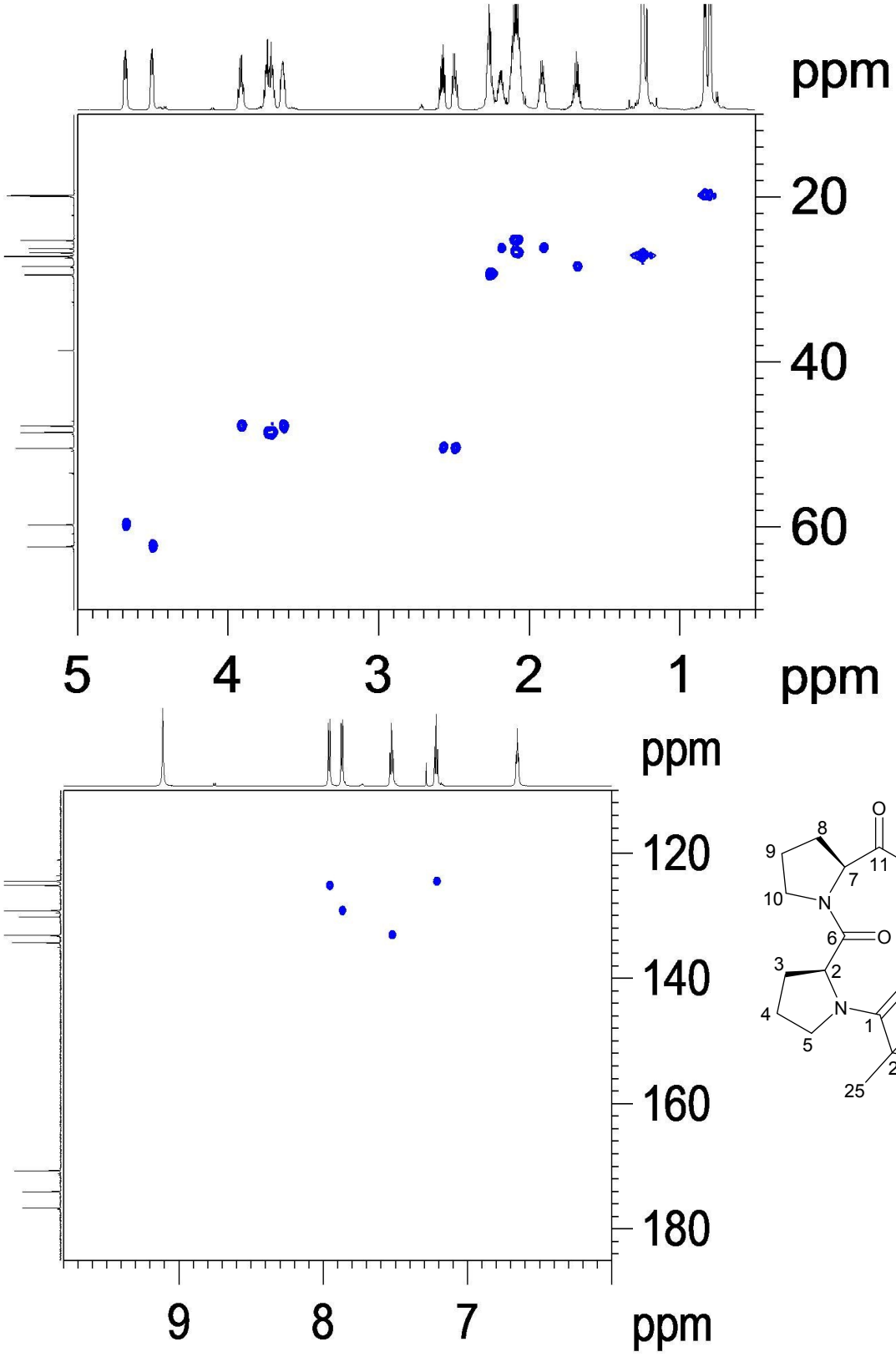
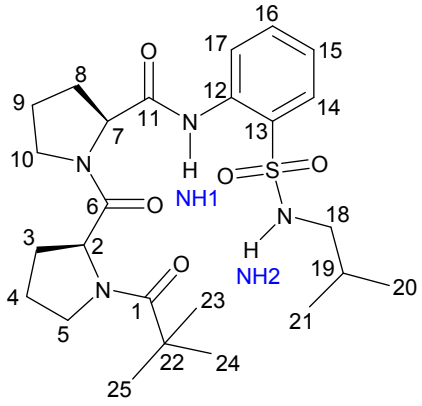


Figure: Partial HSQC spectra of **5** (700 MHz, $CDCl_3$): aliphatic (upper excerpt) and aromatic (lower excerpt) regions.





5

Figure: Partial HMBC spectra of **5** (700 MHz, $CDCl_3$): aliphatic (upper excerpt) and aromatic (lower excerpt) regions.

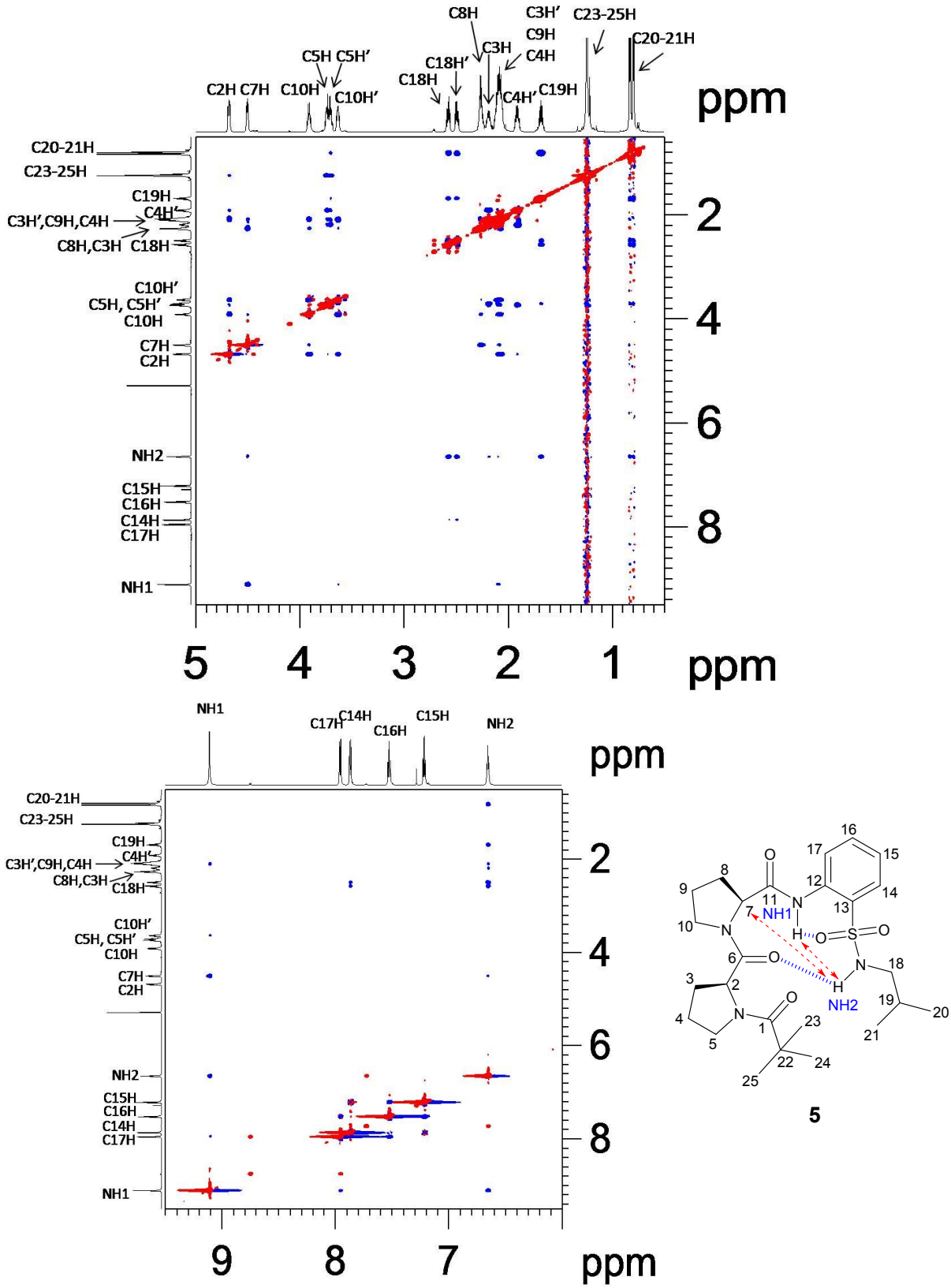
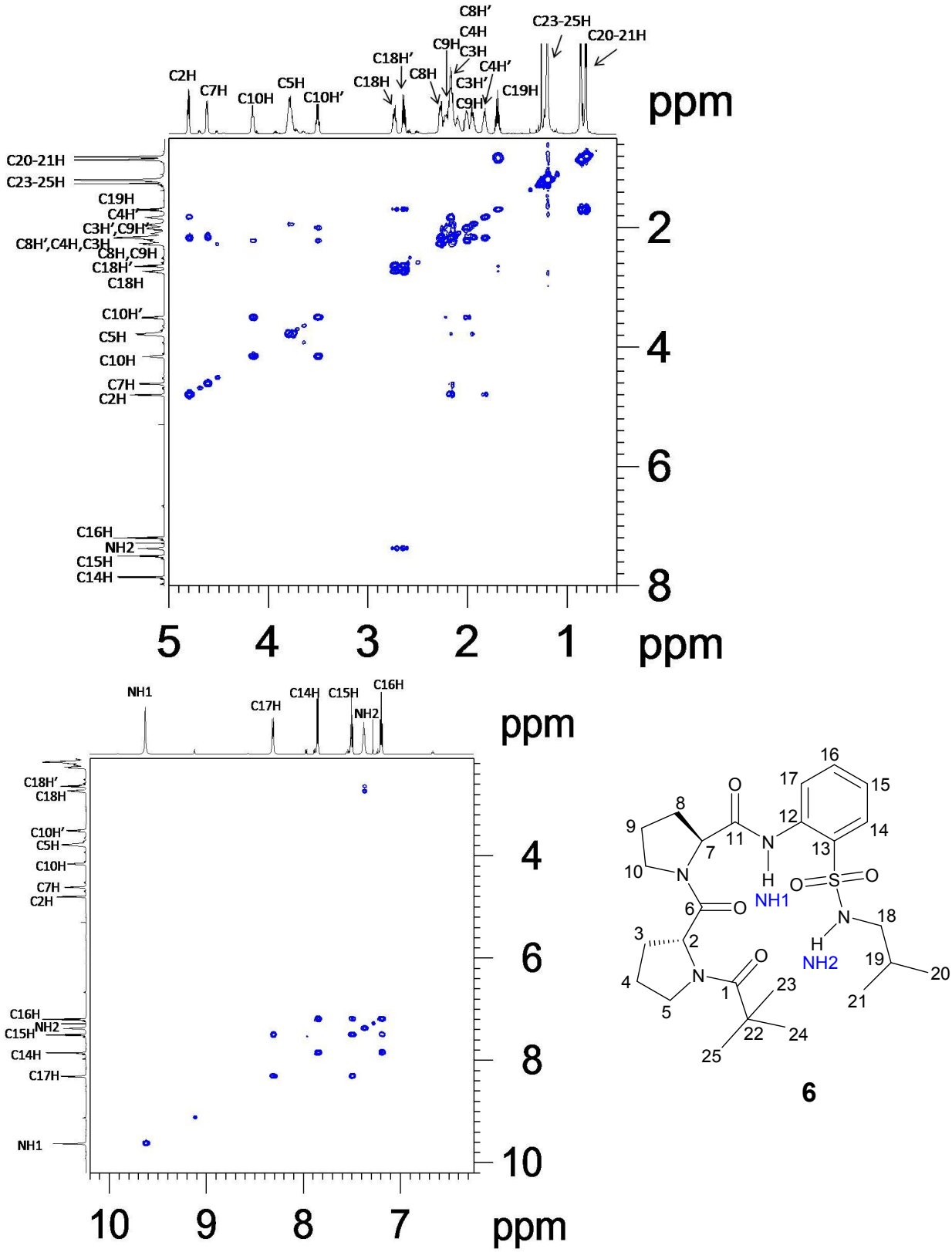


Figure: Partial NOESY spectra of **5** (700 MHz, $CDCl_3$): aliphatic (upper excerpt) and aromatic (lower excerpt) regions.



6

Figure: Partial COSY spectra of **6** (700 MHz, $CDCl_3$): aliphatic (upper excerpt) and aromatic (lower excerpt) regions.

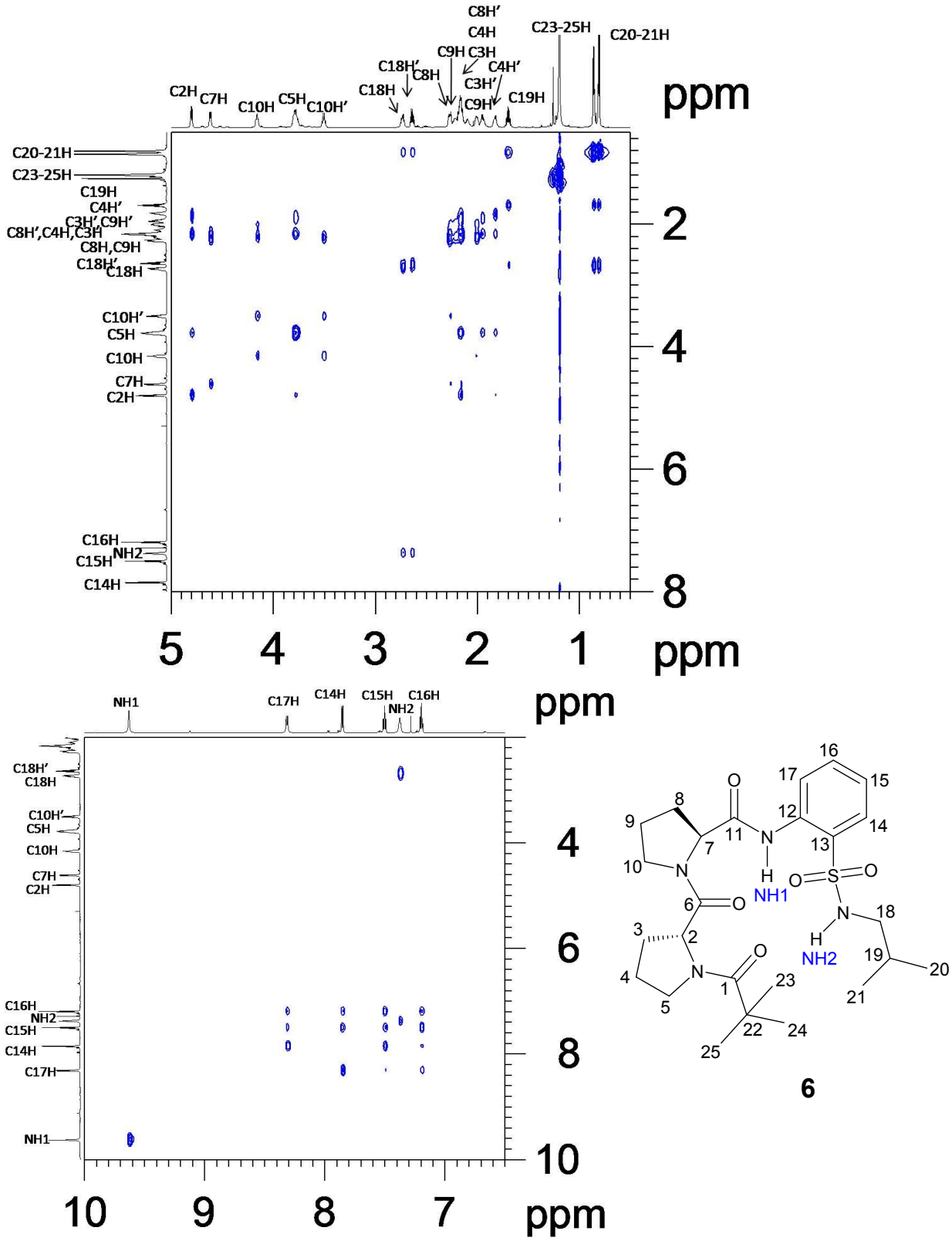


Figure: Partial TOCSY spectra of **6** (700 MHz, $CDCl_3$): aliphatic (upper excerpt) and aromatic (lower excerpt) regions.

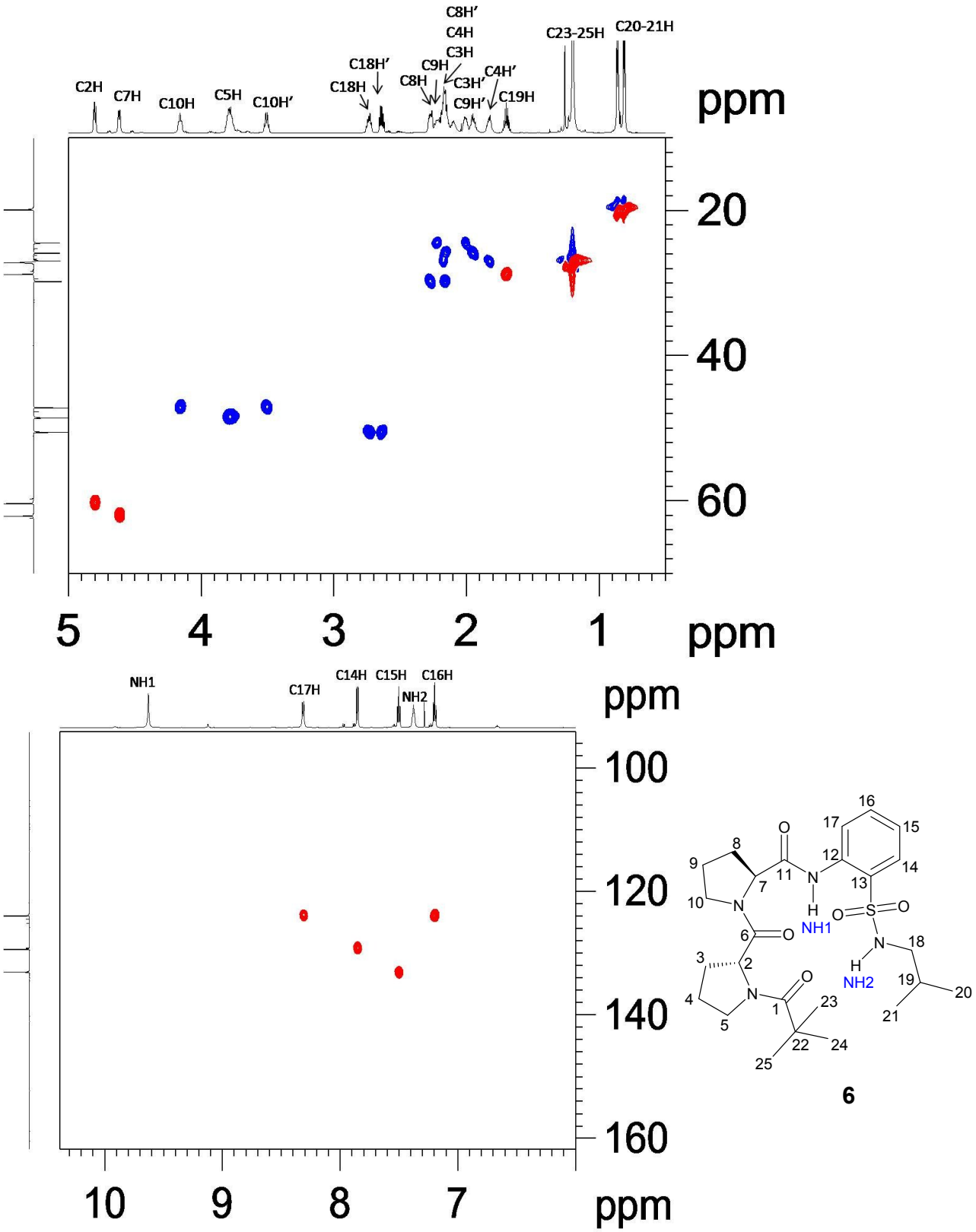


Figure: Partial HSQC spectra of **6** (700 MHz, $CDCl_3$): aliphatic (upper excerpt) and aromatic (lower excerpt) regions.

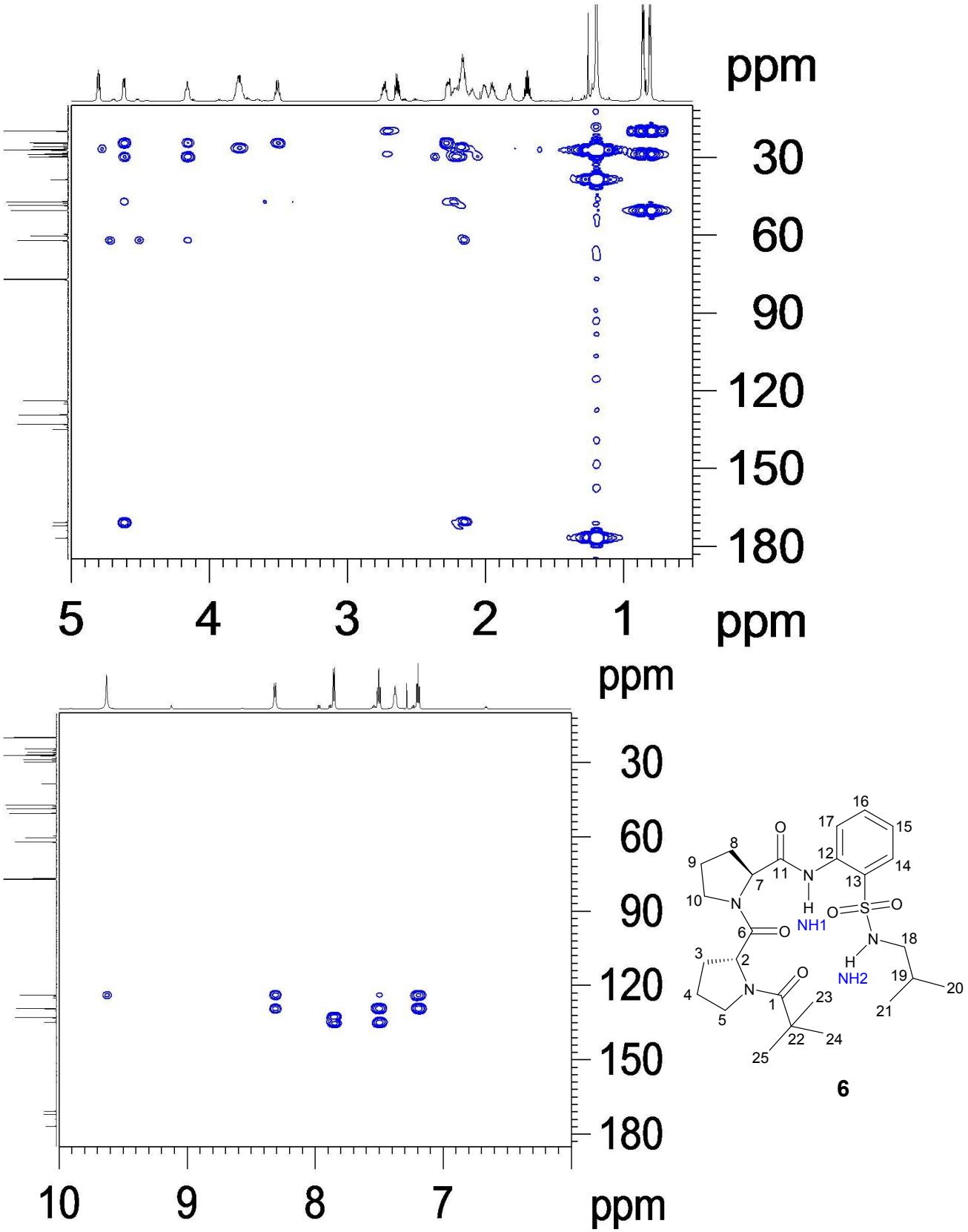


Figure: Partial HMBC spectra of **6** (700 MHz, $CDCl_3$): aliphatic (upper excerpt) and aromatic (lower excerpt) regions.

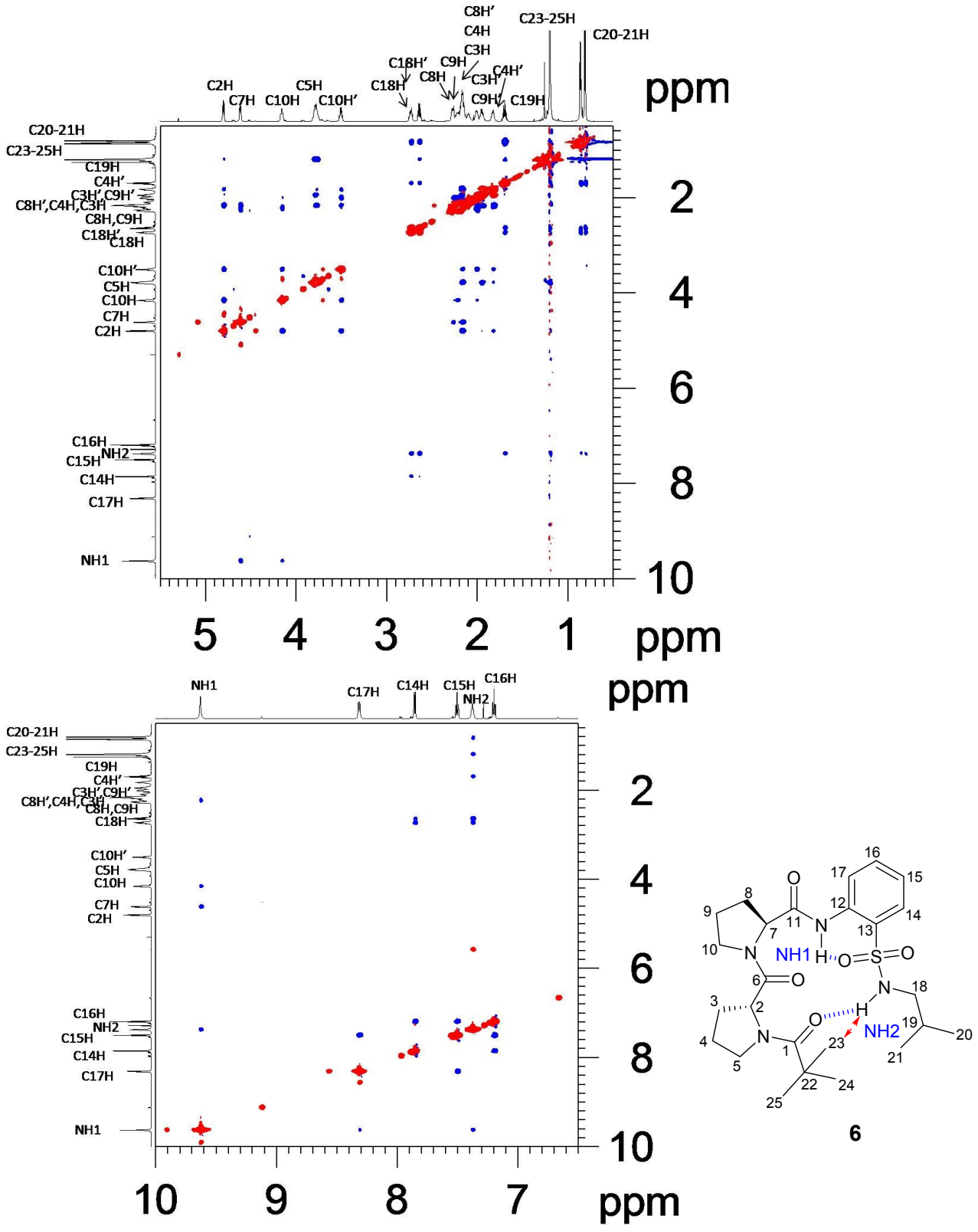


Figure: Partial NOESY spectra of **6** (700 MHz, $CDCl_3$): aliphatic (upper excerpt) and aromatic (lower excerpt) regions.

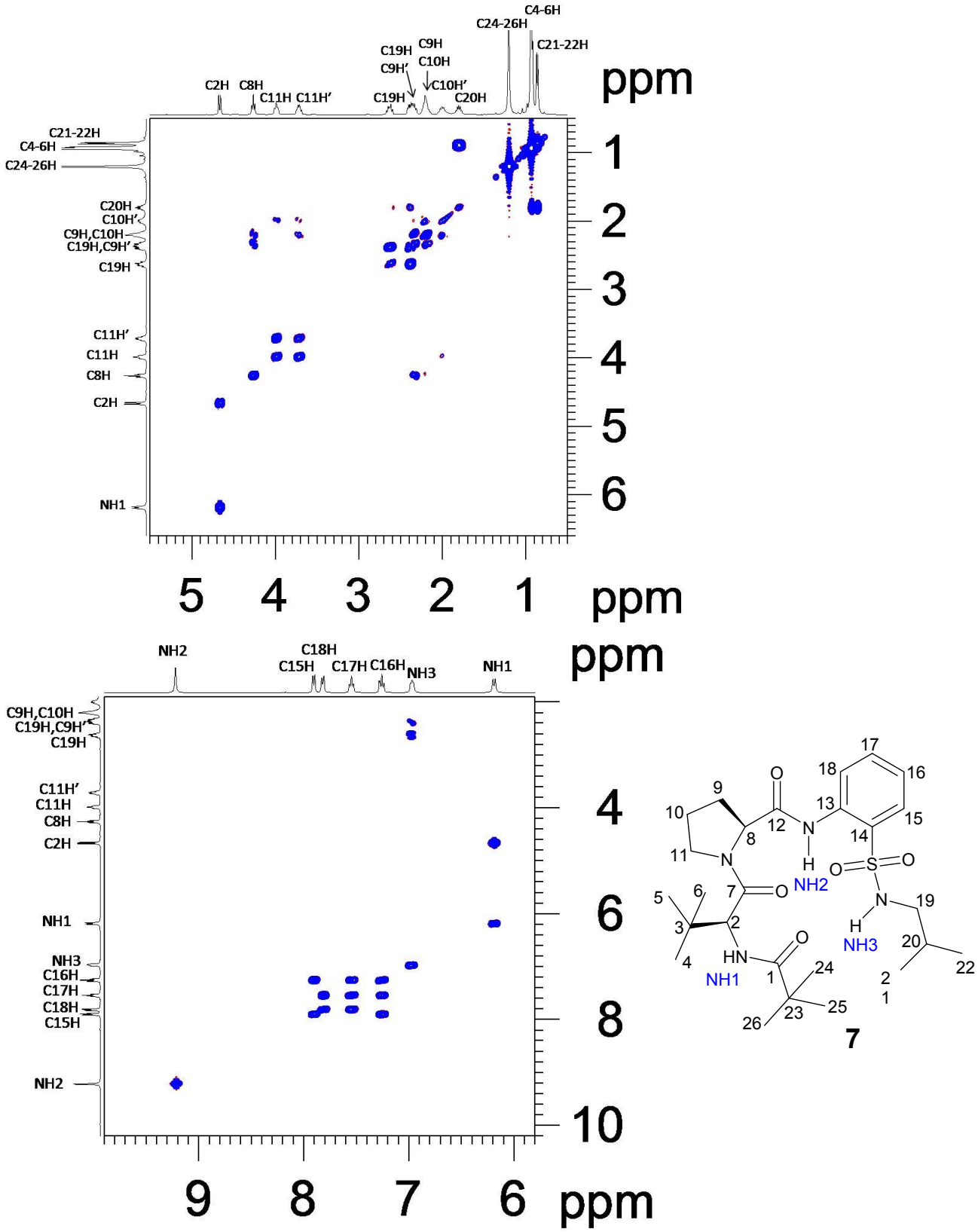


Figure: Partial COSY spectra of **7** (400 MHz, $CDCl_3$): aliphatic (upper excerpt) and aromatic (lower excerpt) regions.

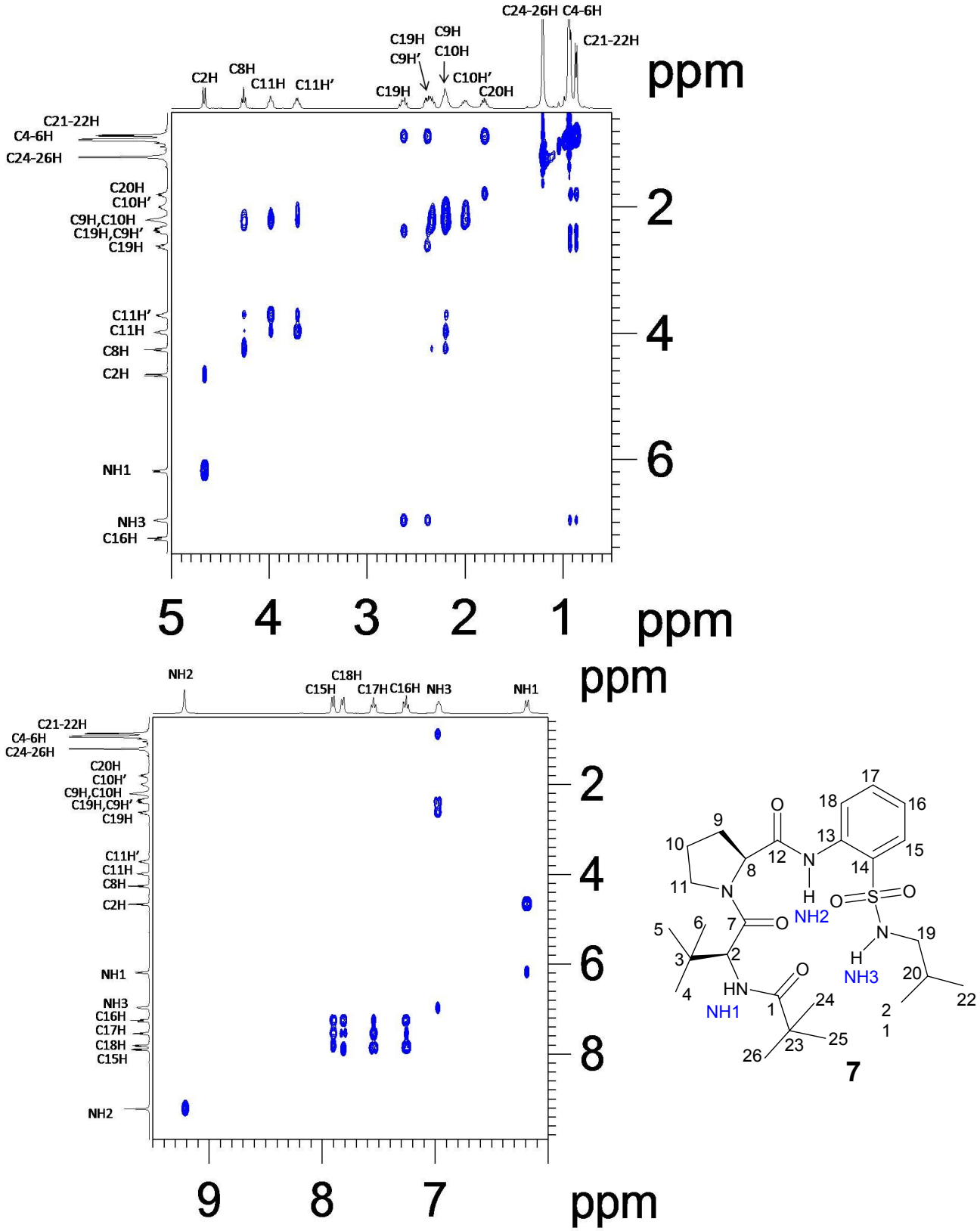


Figure: Partial TOCSY spectra of **7** (400 MHz, $CDCl_3$): aliphatic (upper excerpt) and aromatic (lower excerpt) regions.

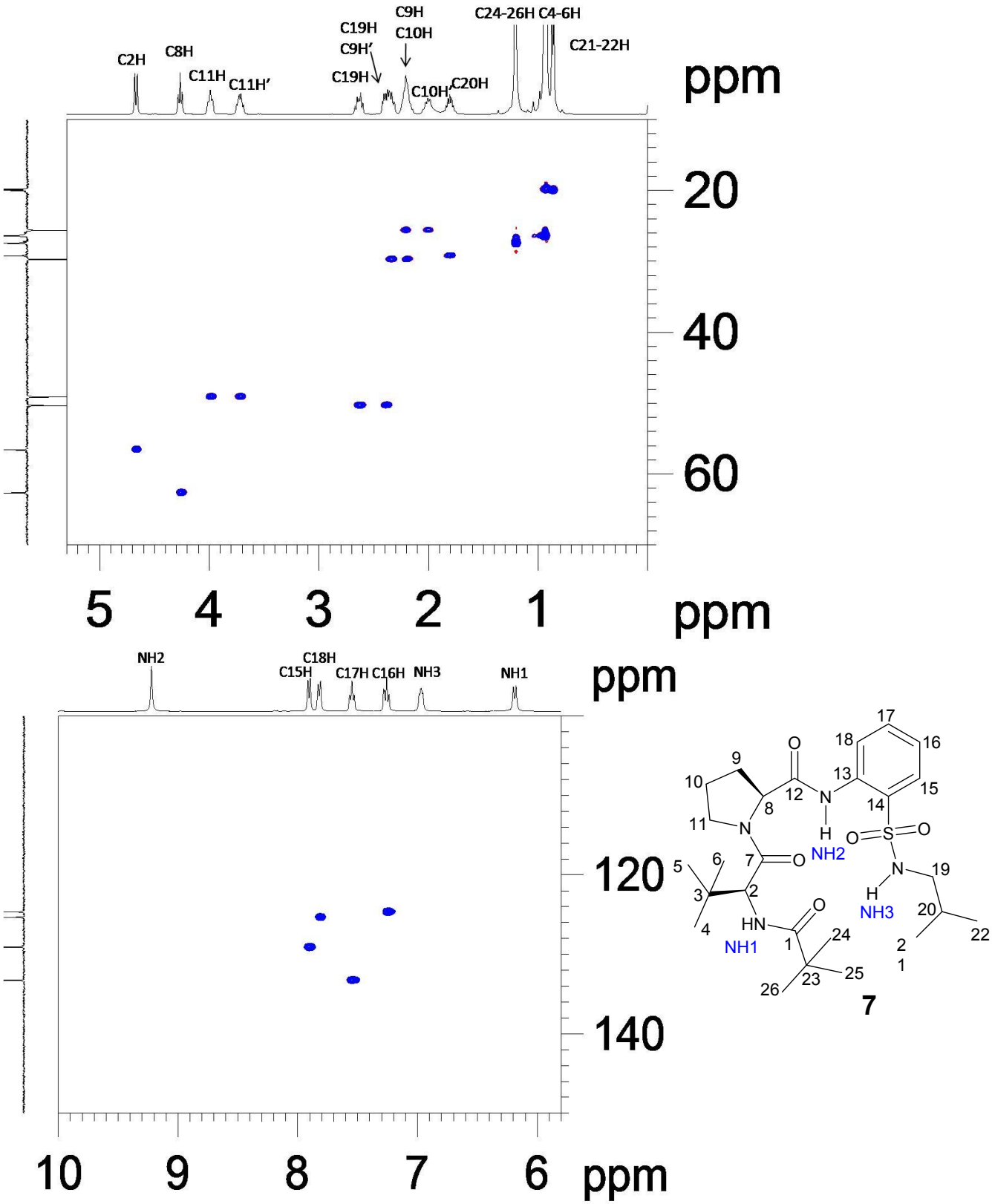


Figure: Partial HSQC spectra of **7** (400 MHz, $CDCl_3$): aliphatic (upper excerpt) and aromatic (lower excerpt) regions.

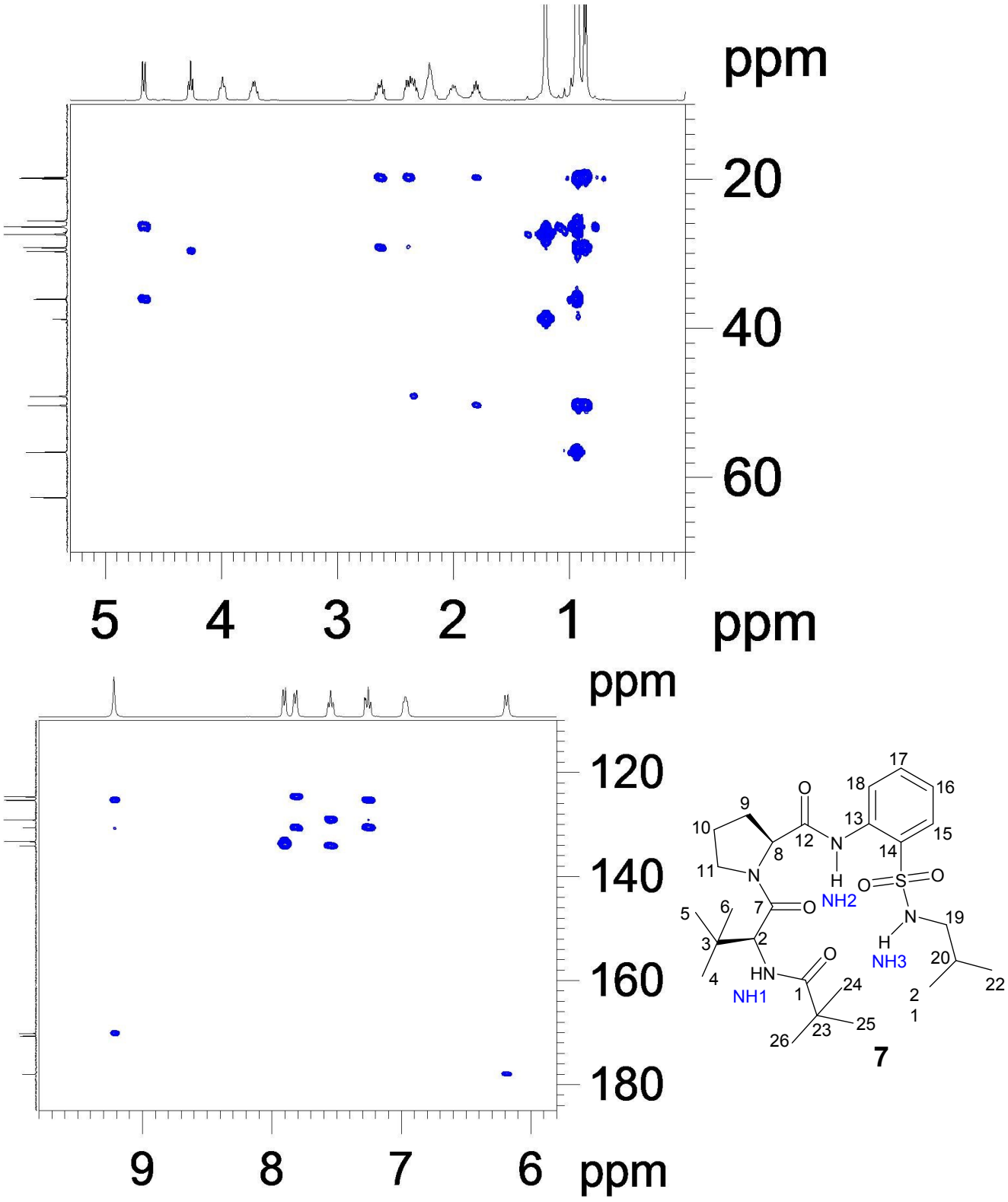


Figure: Partial HMBC spectra of **7** (400 MHz, $CDCl_3$): aliphatic (upper excerpt) and aromatic (lower excerpt) regions.

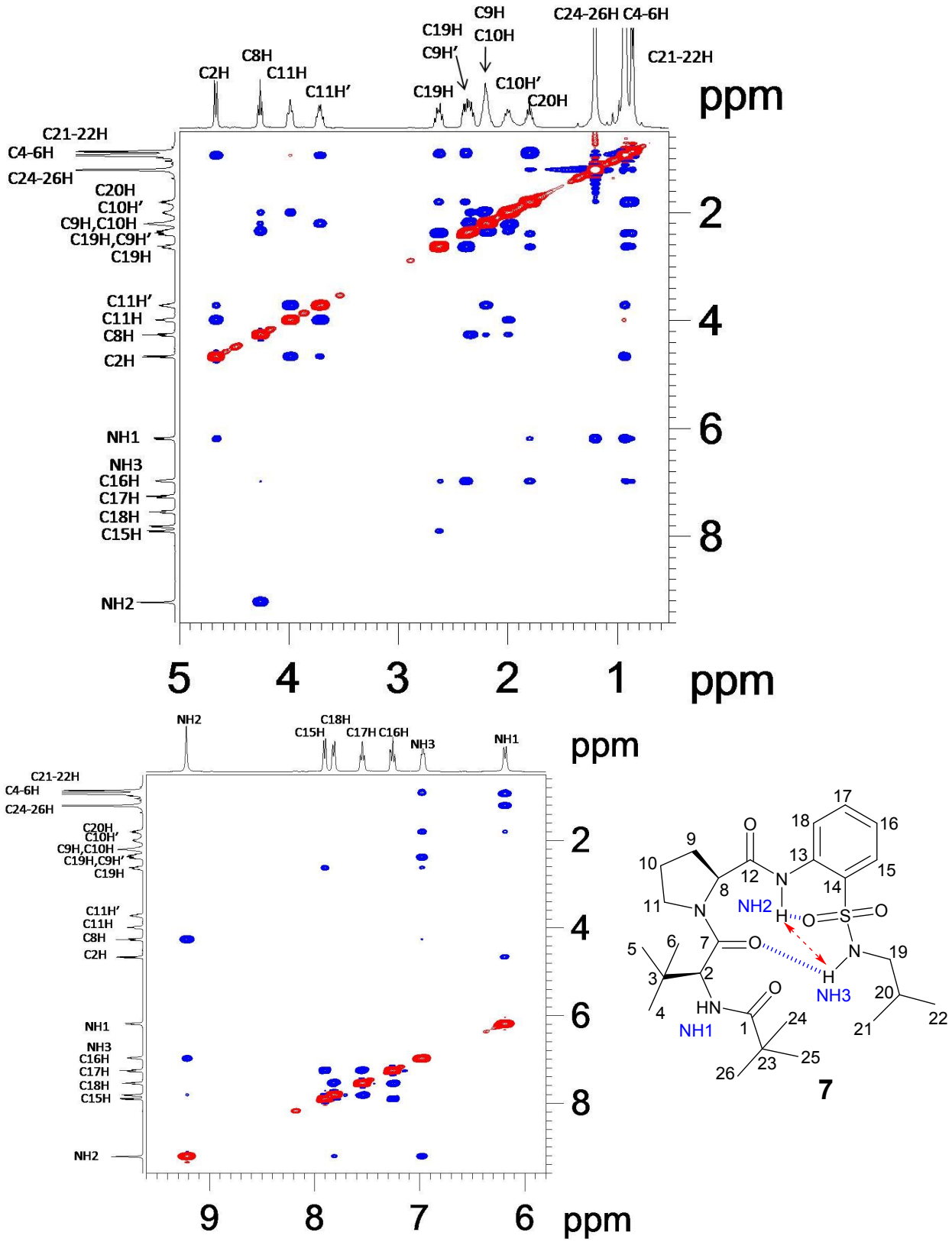
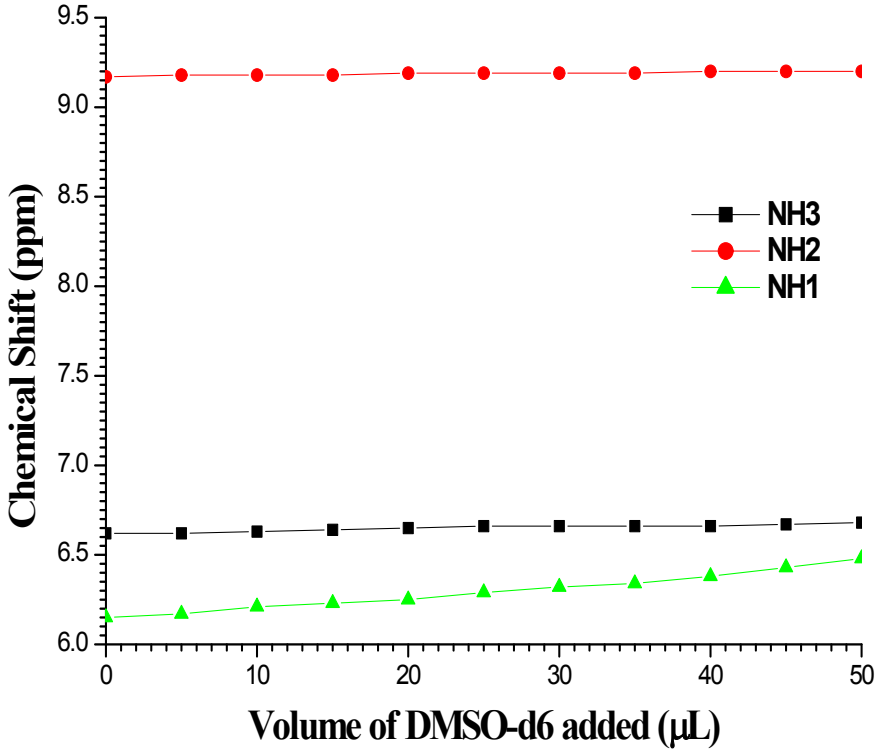


Figure: Partial NOESY spectra of **7** (400 MHz, $CDCl_3$): aliphatic (upper excerpt) and aromatic (lower excerpt) regions.

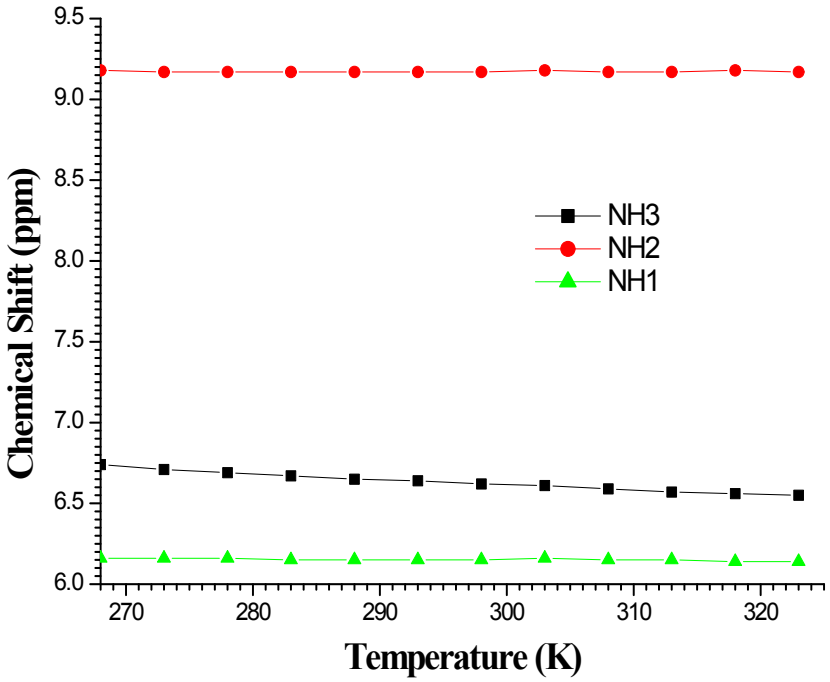
Table . DMSO-*d6* titration plots of compound 1 (5 mmol, 400 MHz, $CDCl_3$).



Volume of DMSO-d6 added (µL)	Chemical shift in (ppm)		
	NH3	NH2	NH1
0	6.62	9.17	6.15
5	6.62	9.18	6.17
10	6.63	9.18	6.21
15	6.64	9.18	6.23
20	6.65	9.19	6.25
25	6.66	9.19	6.29
30	6.66	9.19	6.32
35	6.66	9.19	6.34
40	6.66	9.20	6.38
45	6.67	9.20	6.43
50	6.68	9.20	6.48

(a) δNH1 = 0.33 ppm
(b) δNH2 = 0.03 ppm
(c) δNH3 = 0.06 ppm

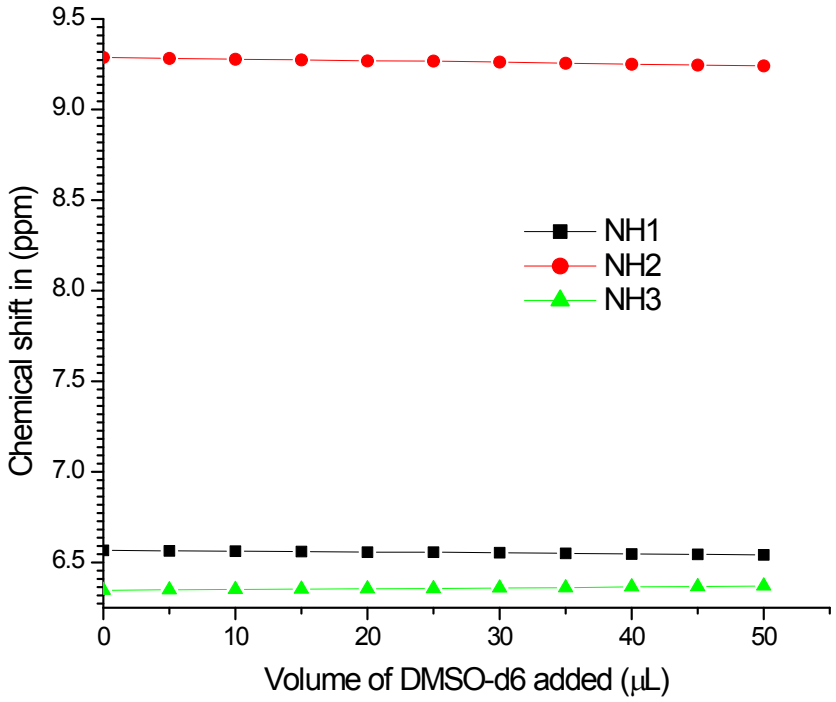
Table . Temperature Variation Study of Compound 1 (5 mmol, 400 MHz, $CDCl_3$).



Temperature (K)	Chemical shift in (ppm)		
	NH3	NH2	NH1
268	6.74	9.18	6.16
273	6.71	9.17	6.16
278	6.69	9.17	6.16
283	6.67	9.17	6.15
288	6.65	9.17	6.15
293	6.64	9.17	6.15
298	6.62	9.17	6.15
303	6.61	9.18	6.16
308	6.59	9.17	6.15
313	6.57	9.17	6.15
318	6.56	9.18	6.14
323	6.55	9.17	6.14

(a) δNH1 = 0.19 ppm
(b) δNH2 = 0.01 ppm
(c) δNH3 = 0.02 ppm

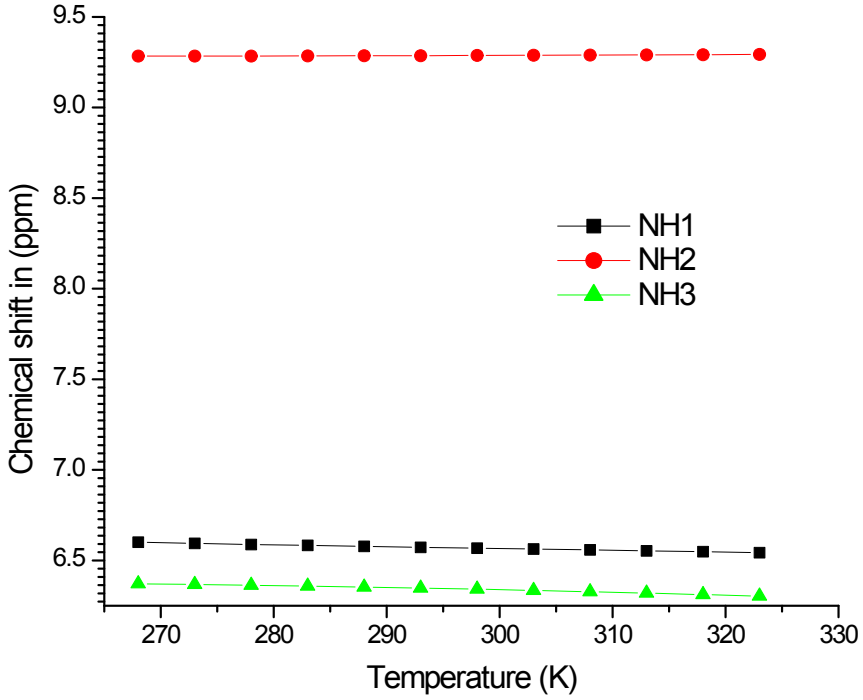
Table . DMSO-*d6* titration plots of compound 2 (10 mmol, 500 MHz, $CDCl_3$).



Volume of DMSO-d6 added (µL)	Chemical shift in (ppm)		
	NH2	NH1	NH3
0	9.29	6.57	6.35
5	9.28	6.57	6.35
10	9.27	6.56	6.36
15	9.25	6.55	6.36
20	9.25	6.55	6.37
25	9.23	6.54	6.37
30	9.23	6.54	6.38
35	9.22	6.53	6.38
40	9.21	6.53	6.39
45	9.21	6.52	6.39
50	9.20	6.52	6.40

(a) δNH1 = 0.05 ppm
(b) δNH2 = 0.09 ppm
(c) δNH3 = 0.05 ppm

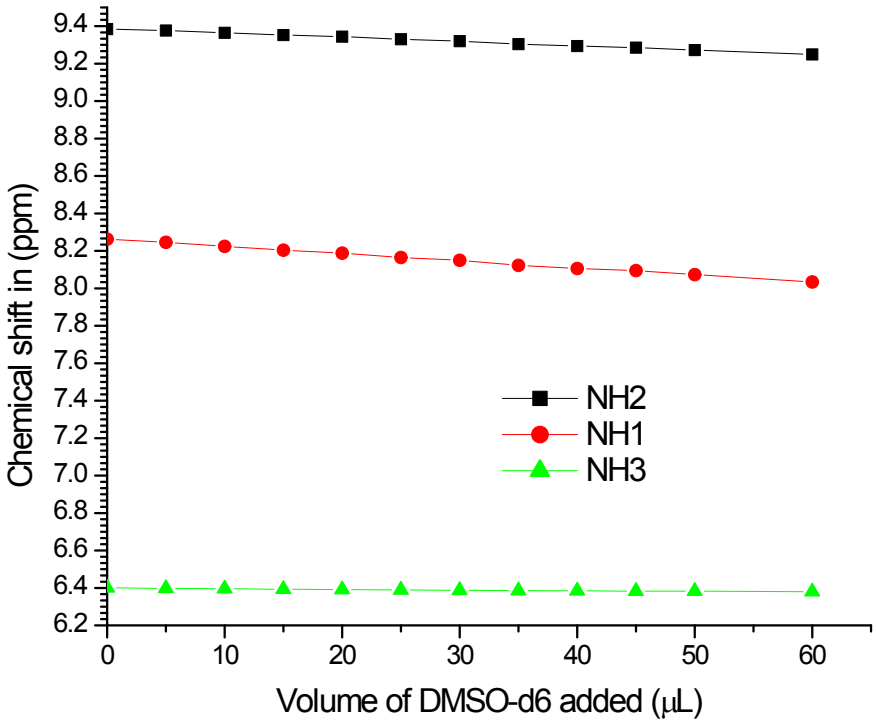
Table . Temperature Variation Study of Compound 2 (10 mmol, 700 MHz, $CDCl_3$).



Temperature (K)	Chemical shift in (ppm)		
	NH2	NH1	NH3
268	9.28	6.60	6.37
273	9.28	6.59	6.37
278	9.28	6.59	6.36
283	9.29	6.58	6.36
288	9.29	6.58	6.35
293	9.29	6.57	6.35
298	9.29	6.57	6.34
303	9.29	6.56	6.33
308	9.29	6.56	6.33
313	9.29	6.55	6.32
318	9.29	6.55	6.31
323	9.29	6.54	6.30

(a) δNH1 = 0.06 ppm
(b) δNH2 = 0.01 ppm
(c) δNH3 = 0.07 ppm

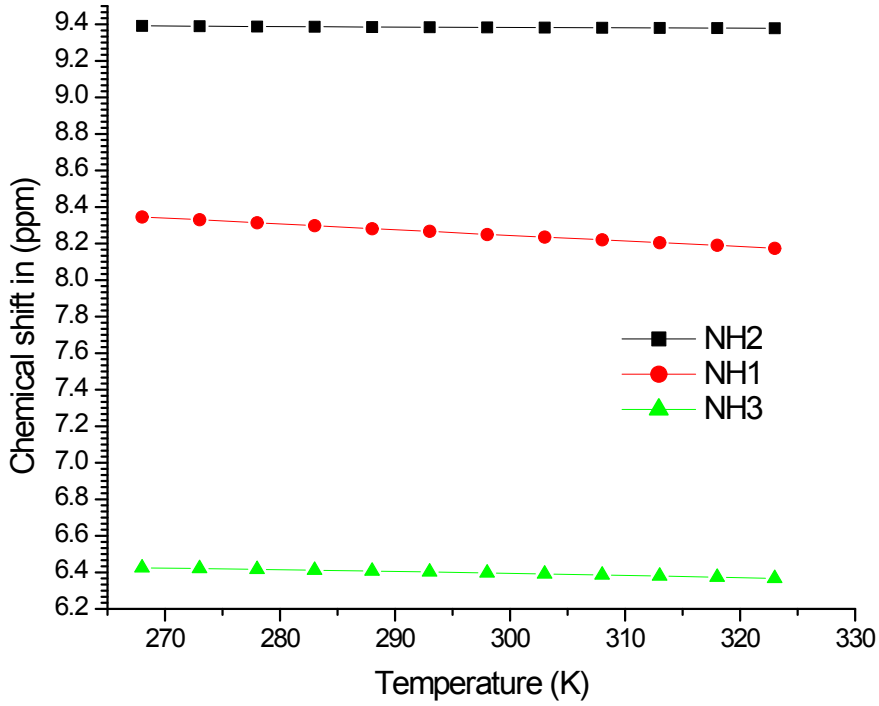
Table . DMSO-*d6* titration plots of compound 3 (10 mmol, 400 MHz, $CDCl_3$).



Volume of DMSO-d6 added (µL)	Chemical shift in (ppm)		
	NH2	NH1	NH3
0	9.38	8.26	6.40
5	9.38	8.25	6.40
10	9.37	8.22	6.40
15	9.35	8.20	6.39
20	9.34	8.19	6.39
25	9.33	8.16	6.39
30	9.32	8.15	6.39
35	9.30	8.12	6.39
40	9.29	8.11	6.38
45	9.29	8.09	6.38
50	9.27	8.07	6.38

(a) δNH1 = 0.19 ppm
(b) δNH2 = 0.10 ppm
(c) δNH3 = 0.02 ppm

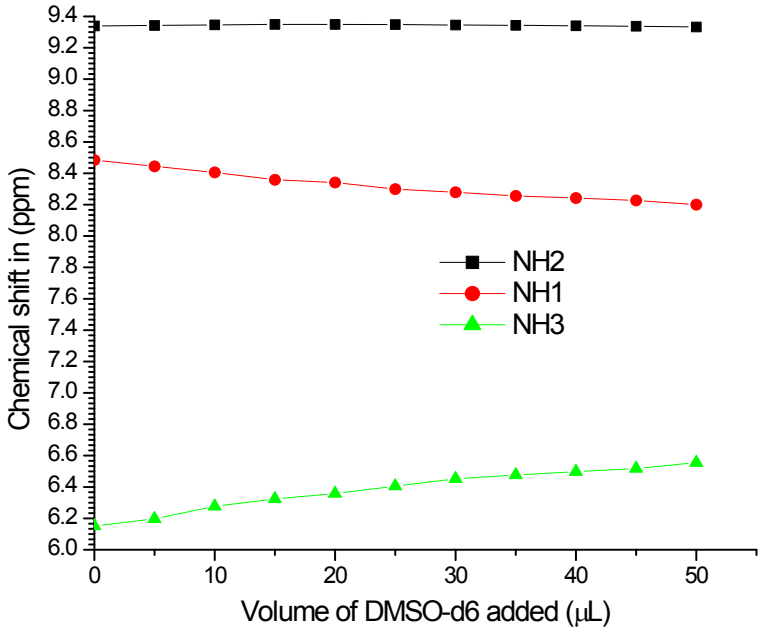
Table . Temperature Variation Study of Compound 3 (10 mmol, 400 MHz, $CDCl_3$).



Temperature (K)	Chemical shift in (ppm)		
	NH2	NH1	NH3
268	9.39	8.35	6.43
273	9.39	8.33	6.42
278	9.39	8.31	6.42
283	9.39	8.30	6.41
288	9.39	8.28	6.41
293	9.38	8.27	6.40
298	9.38	8.25	6.40
303	9.38	8.24	6.39
308	9.38	8.22	6.39
313	9.38	8.21	6.38
318	9.38	8.19	6.37
323	9.38	8.17	6.37

(a) δNH1 = 0.18 ppm
(b) δNH2 = 0.01 ppm
(c) δNH3 = 0.06 ppm

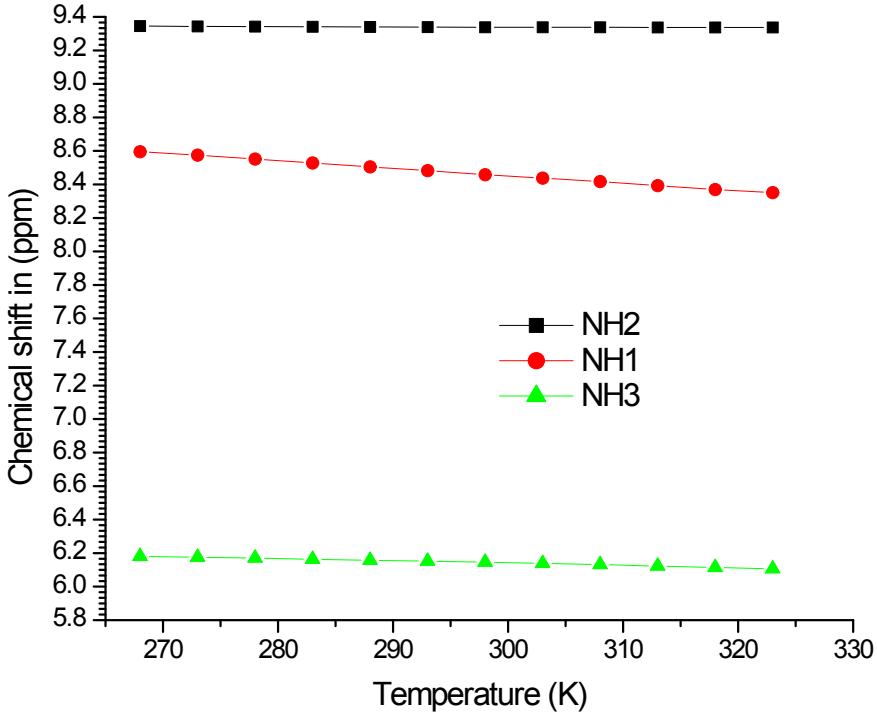
Table . DMSO-*d6* titration plots of compound 4 (10 mmol, 400 MHz, $CDCl_3$).



Volume of DMSO-d6 added (µL)	Chemical shift in (ppm)		
	NH2	NH1	NH3
0	9.34	8.48	6.15
5	9.34	8.44	6.20
10	9.35	8.41	6.28
15	9.35	8.36	6.32
20	9.35	8.34	6.36
25	9.35	8.30	6.41
30	9.35	8.28	6.45
35	9.34	8.26	6.48
40	9.34	8.24	6.50
45	9.34	8.23	6.52
50	9.33	8.20	6.56

(a) δNH1 = 0.28 ppm
(b) δNH2 = 0.01 ppm
(c) δNH3 = 0.41 ppm

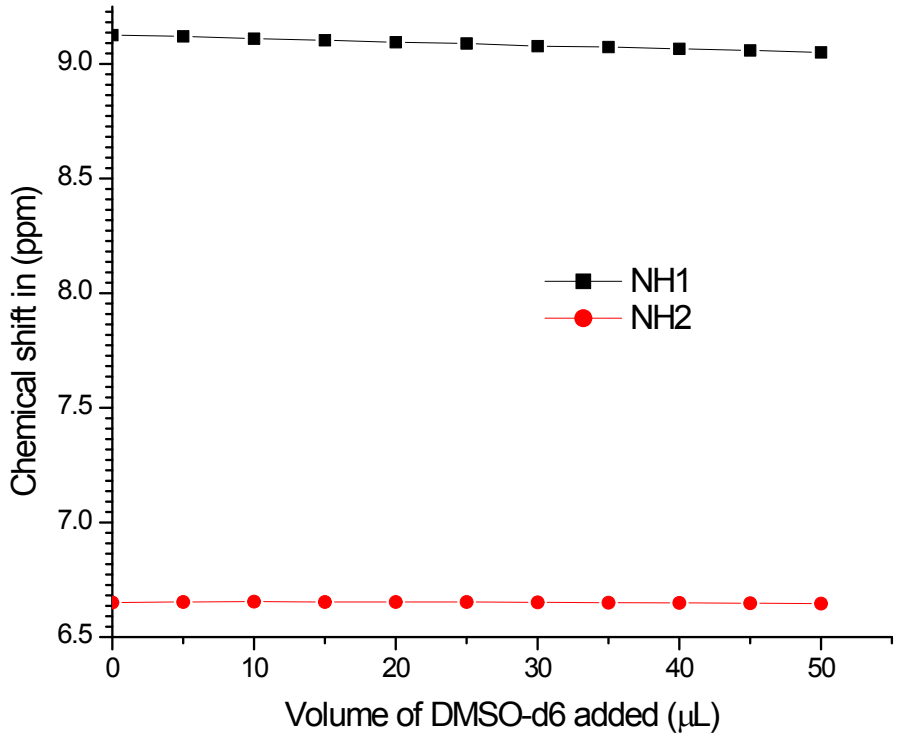
Table . Temperature Variation Study of Compound 4 (10 mmol, 400 MHz, $CDCl_3$).



Temperature (K)	Chemical shift in (ppm)		
	NH2	NH1	NH3
268	9.34	8.60	6.18
273	9.34	8.58	6.18
278	9.34	8.55	6.17
283	9.34	8.53	6.16
288	9.34	8.51	6.16
293	9.34	8.48	6.15
298	9.34	8.46	6.15
303	9.34	8.44	6.14
308	9.34	8.42	6.13
313	9.34	8.39	6.12
318	9.34	8.37	6.11
323	9.34	8.35	6.11

(a) δNH1 = 0.25 ppm
(b) δNH2 = 0.00 ppm
(c) δNH3 = 0.07 ppm

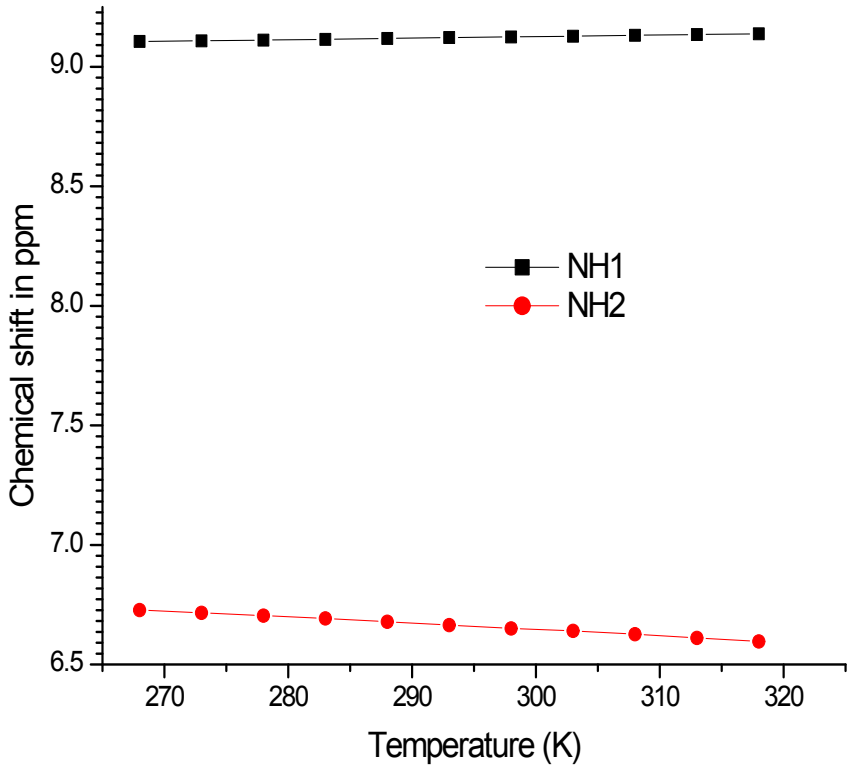
Table . DMSO-*d6* titration plots of compound 5 (10 mmol, 400 MHz, $CDCl_3$).



Volume of DMSO-d6 added (μL)	Chemical shift in (ppm)	
	NH1	NH2
0	9.13	6.65
5	9.12	6.65
10	9.11	6.65
15	9.10	6.65
20	9.09	6.65
25	9.09	6.65
30	9.08	6.65
35	9.07	6.65
40	9.07	6.65
45	9.06	6.65
50	9.05	6.65

(a) δNH1 = 0.08 ppm
(b) δNH2 = 0.00 ppm

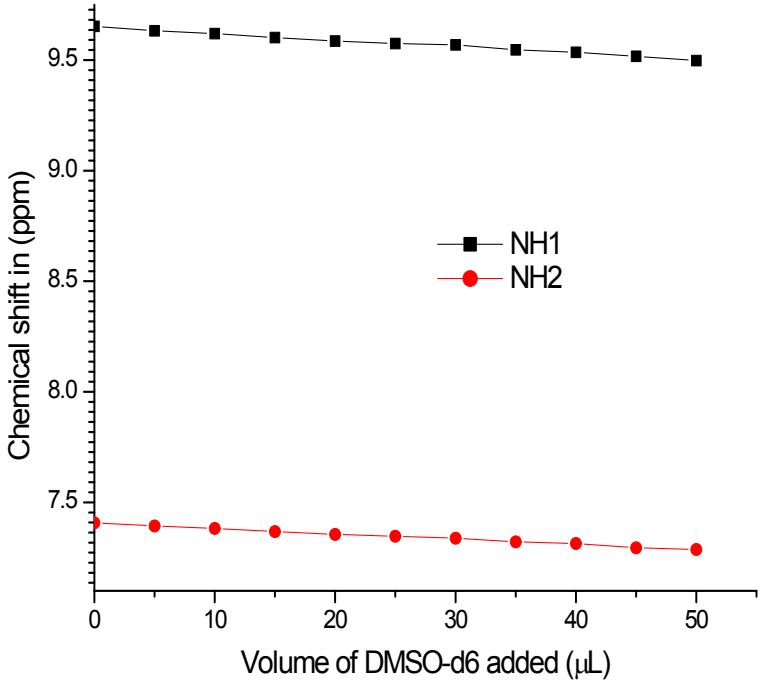
Table . Temperature Variation Study of Compound 5 (10 mmol, 400 MHz, $CDCl_3$).



Temperature (K)	Chemical shift in (ppm)	
	NH1	NH2
268	9.11	6.73
273	9.11	6.72
278	9.11	6.70
283	9.12	6.69
288	9.12	6.68
293	9.12	6.66
298	9.13	6.65
303	9.13	6.64
308	9.13	6.63
313	9.14	6.61
318	9.14	6.60
323	9.14	6.58

(a) δNH1 = 0.03 ppm
(b) δNH2 = 0.15 ppm

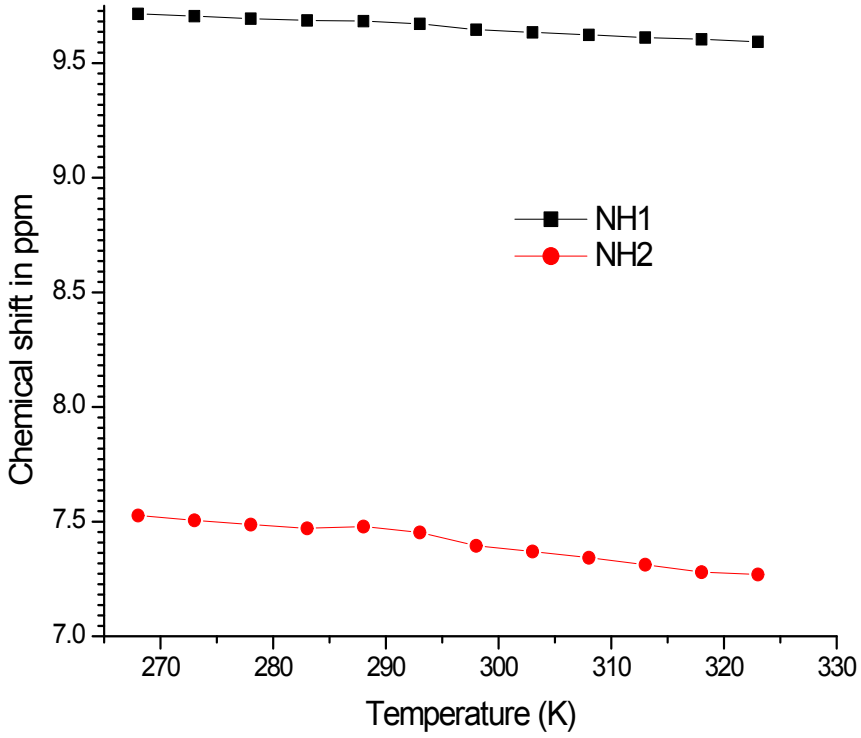
Table . DMSO-*d6* titration plots of compound 6 (10 mmol, 400 MHz, $CDCl_3$).



Volume of DMSO-d6 added (µL)	Chemical shift in (ppm)	
	NH1	NH2
0	9.65	7.41
5	9.63	7.39
10	9.62	7.38
15	9.60	7.37
20	9.59	7.36
25	9.58	7.35
30	9.57	7.34
35	9.55	7.32
40	9.54	7.31
45	9.52	7.30
50	9.50	7.29

(a) δNH1 = 0.15 ppm
(b) δNH2 = 0.12 ppm

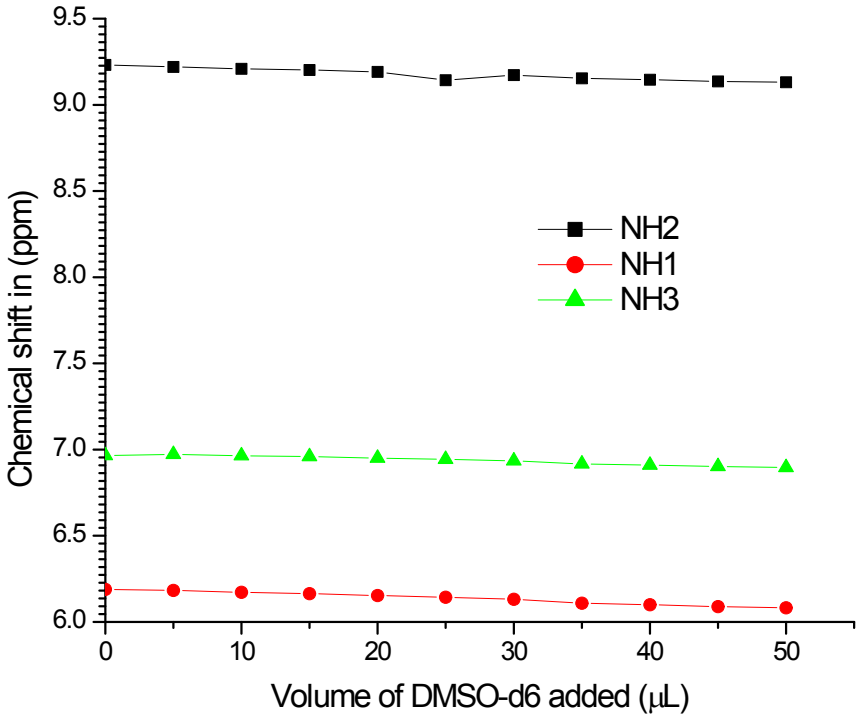
Table . Temperature Variation Study of Compound 6 (10 mmol, 400 MHz, $CDCl_3$).



Temperature (K)	Chemical shift in (ppm)	
	NH1	NH2
268	9.71	7.53
273	9.70	7.51
278	9.69	7.49
283	9.69	7.47
288	9.68	7.48
293	9.67	7.45
298	9.65	7.40
303	9.63	7.37
308	9.62	7.34
313	9.61	7.31
318	9.60	7.28
323	9.59	7.27

(a) δNH1 = 0.12 ppm
(b) δNH2 = 0.26 ppm

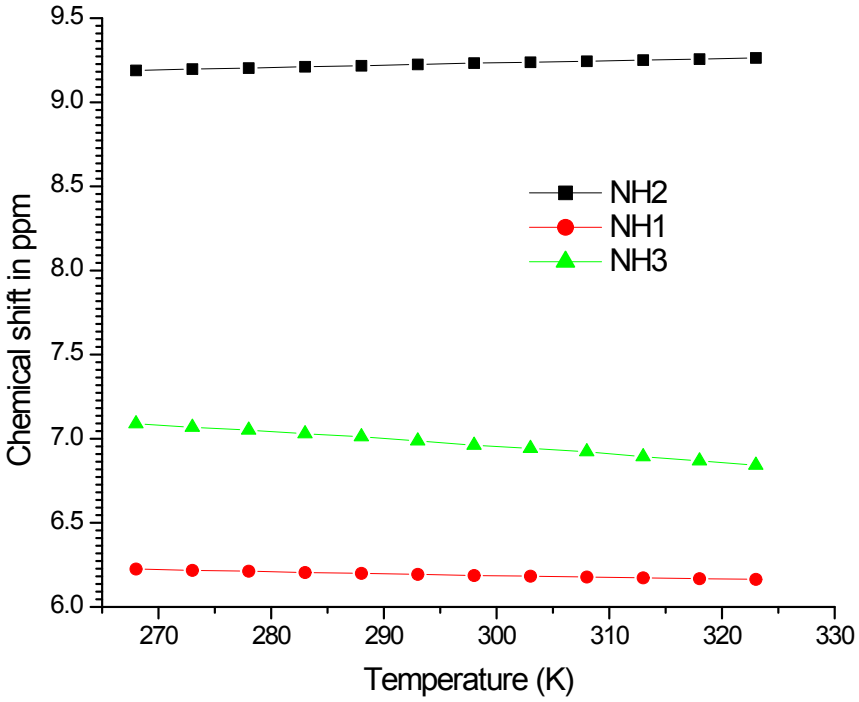
Table . DMSO-*d6* titration plots of compound 7 (10 mmol, 400 MHz, $CDCl_3$).



Volume of DMSO-d6 added (µL)	Chemical shift in (ppm)		
	NH2	NH1	NH3
0	9.23	6.19	6.97
5	9.22	6.18	6.97
10	9.21	6.17	6.96
15	9.20	6.16	6.96
20	9.19	6.15	6.95
25	9.14	6.14	6.94
30	9.17	6.13	6.93
35	9.15	6.11	6.92
40	9.15	6.10	6.91
45	9.14	6.09	6.90
50	9.13	6.08	6.90

(a) δNH1 = 0.11 ppm
(b) δNH2 = 0.10 ppm
(c) δNH3 = 0.11 ppm

Table . Temperature Variation Study of Compound 7 (10 mmol, 400 MHz, $CDCl_3$).



Temperature (K)	Chemical shift in (ppm)		
	NH2	NH1	NH3
268	9.19	6.23	7.09
273	9.20	6.22	7.07
278	9.20	6.21	7.05
283	9.21	6.21	7.03
288	9.22	6.20	7.01
293	9.23	6.19	6.99
298	9.23	6.19	6.96
303	9.24	6.18	6.94
308	9.24	6.18	6.92
313	9.25	6.17	6.89
318	9.26	6.17	6.87
323	9.26	6.16	6.84

(a) δNH1 = 0.07 ppm
(b) δNH2 = 0.07 ppm
(c) δNH3 = 0.25 ppm

Compound-1

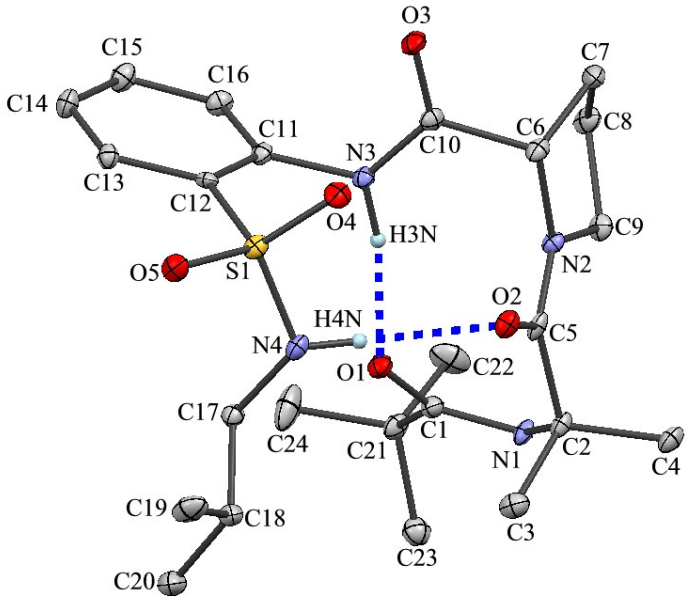


Figure: ORTEP diagram of **1**. Ellipsoids were drawn with 50 % probability.

Table: Torsion angles [°] for **1**

O(4)-S(1)-N(4)-C(17)	-176.2(3)
O(5)-S(1)-N(4)-C(17)	54.6(4)
C(12)-S(1)-N(4)-C(17)	-59.6(4)
C(2)-N(1)-C(1)-O(1)	8.3(7)
C(2)-N(1)-C(1)-C(21)	-173.9(4)
C(1)-N(1)-C(2)-C(4)	-169.0(4)
C(1)-N(1)-C(2)-C(3)	72.2(5)
C(1)-N(1)-C(2)-C(5)	-47.8(6)
C(9)-N(2)-C(5)-O(2)	171.0(4)
C(6)-N(2)-C(5)-O(2)	3.1(6)
C(9)-N(2)-C(5)-C(2)	-6.6(7)
C(6)-N(2)-C(5)-C(2)	-174.6(4)
N(1)-C(2)-C(5)-O(2)	135.3(4)
C(4)-C(2)-C(5)-O(2)	-103.9(5)
C(3)-C(2)-C(5)-O(2)	15.9(6)
N(1)-C(2)-C(5)-N(2)	-47.0(6)
C(4)-C(2)-C(5)-N(2)	73.8(5)

C(3)-C(2)-C(5)-N(2)	-166.4(4)
C(5)-N(2)-C(6)-C(7)	161.0(4)
C(9)-N(2)-C(6)-C(7)	-9.1(5)
C(5)-N(2)-C(6)-C(10)	-78.0(5)
C(9)-N(2)-C(6)-C(10)	112.0(4)
N(2)-C(6)-C(7)-C(8)	30.0(4)
C(10)-C(6)-C(7)-C(8)	-94.0(4)
C(6)-C(7)-C(8)-C(9)	-40.3(5)
C(5)-N(2)-C(9)-C(8)	175.1(4)
C(6)-N(2)-C(9)-C(8)	-16.2(5)
C(7)-C(8)-C(9)-N(2)	34.5(5)
C(11)-N(3)-C(10)-O(3)	0.1(7)
C(11)-N(3)-C(10)-C(6)	-179.2(4)
N(2)-C(6)-C(10)-O(3)	-179.8(4)
C(7)-C(6)-C(10)-O(3)	-62.5(5)
N(2)-C(6)-C(10)-N(3)	-0.4(6)
C(7)-C(6)-C(10)-N(3)	116.8(5)
C(10)-N(3)-C(11)-C(16)	92.1(5)
C(10)-N(3)-C(11)-C(12)	-87.0(6)
C(16)-C(11)-C(12)-C(13)	0.9(7)
N(3)-C(11)-C(12)-C(13)	-180.0(4)
C(16)-C(11)-C(12)-S(1)	179.3(3)
N(3)-C(11)-C(12)-S(1)	-1.6(6)
O(4)-S(1)-C(12)-C(11)	56.3(4)
O(5)-S(1)-C(12)-C(11)	-174.6(4)
N(4)-S(1)-C(12)-C(11)	-58.7(4)
O(4)-S(1)-C(12)-C(13)	-125.3(3)
O(5)-S(1)-C(12)-C(13)	3.8(4)
N(4)-S(1)-C(12)-C(13)	119.8(4)
C(11)-C(12)-C(13)-C(14)	-2.2(7)
S(1)-C(12)-C(13)-C(14)	179.3(4)
C(12)-C(13)-C(14)-C(15)	2.3(7)
C(13)-C(14)-C(15)-C(16)	-1.0(7)
C(14)-C(15)-C(16)-C(11)	-0.4(7)
C(12)-C(11)-C(16)-C(15)	0.4(7)
N(3)-C(11)-C(16)-C(15)	-178.7(4)

S(1)-N(4)-C(17)-C(18)	-122.1(4)
N(4)-C(17)-C(18)-C(20)	-173.4(4)
N(4)-C(17)-C(18)-C(19)	63.3(5)
O(1)-C(1)-C(21)-C(24)	-11.1(7)
N(1)-C(1)-C(21)-C(24)	171.0(5)
O(1)-C(1)-C(21)-C(23)	-131.4(5)
N(1)-C(1)-C(21)-C(23)	50.8(6)
O(1)-C(1)-C(21)-C(22)	109.1(5)
N(1)-C(1)-C(21)-C(22)	-68.7(5)

Compound-2

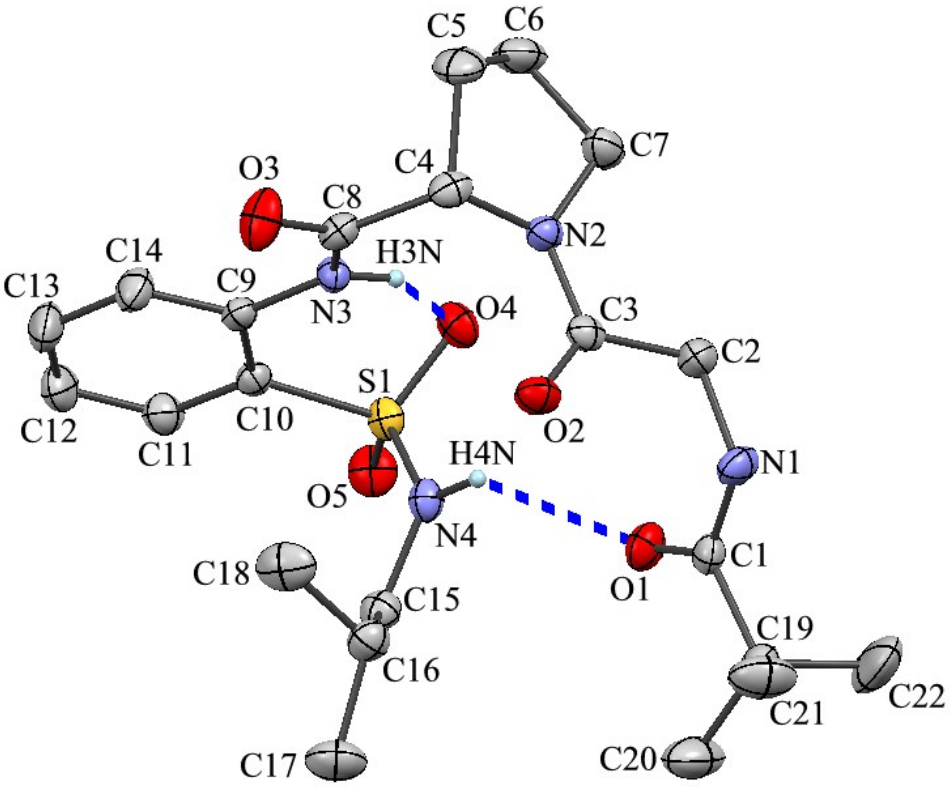


Figure: ORTEP diagram of **2**. Ellipsoids were drawn with 50 % probability.

Table: Torsion angles [°] for **2**

O(5)-S(1)-N(4)-C(15)	-42.9(3)
O(4)-S(1)-N(4)-C(15)	-173.8(2)

C(10)-S(1)-N(4)-C(15)	72.6(2)
C(2)-N(1)-C(1)-O(1)	-0.3(5)
C(2)-N(1)-C(1)-C(19)	177.6(3)
C(1)-N(1)-C(2)-C(3)	84.4(4)
C(4)-N(2)-C(3)-O(2)	12.0(4)
C(7)-N(2)-C(3)-O(2)	172.7(3)
C(4)-N(2)-C(3)-C(2)	-166.6(3)
C(7)-N(2)-C(3)-C(2)	-5.9(4)
N(1)-C(2)-C(3)-O(2)	3.5(5)
N(1)-C(2)-C(3)-N(2)	-177.9(3)
C(3)-N(2)-C(4)-C(8)	-81.4(3)
C(7)-N(2)-C(4)-C(8)	115.7(3)
C(3)-N(2)-C(4)-C(5)	157.4(3)
C(7)-N(2)-C(4)-C(5)	-5.5(3)
N(2)-C(4)-C(5)-C(6)	26.0(3)
C(8)-C(4)-C(5)-C(6)	-98.4(3)
C(4)-C(5)-C(6)-C(7)	-37.0(4)
C(3)-N(2)-C(7)-C(6)	-178.6(3)
C(4)-N(2)-C(7)-C(6)	-16.8(4)
C(5)-C(6)-C(7)-N(2)	32.6(4)
C(9)-N(3)-C(8)-O(3)	-0.1(5)
C(9)-N(3)-C(8)-C(4)	-176.1(2)
N(2)-C(4)-C(8)-O(3)	162.9(3)
C(5)-C(4)-C(8)-O(3)	-80.0(4)
N(2)-C(4)-C(8)-N(3)	-20.8(4)
C(5)-C(4)-C(8)-N(3)	96.2(3)
C(8)-N(3)-C(9)-C(14)	15.9(5)
C(8)-N(3)-C(9)-C(10)	-165.3(3)
C(14)-C(9)-C(10)-C(11)	1.9(4)
N(3)-C(9)-C(10)-C(11)	-177.0(3)
C(14)-C(9)-C(10)-S(1)	-176.9(3)
N(3)-C(9)-C(10)-S(1)	4.2(4)
O(5)-S(1)-C(10)-C(11)	8.2(3)
O(4)-S(1)-C(10)-C(11)	136.8(2)
N(4)-S(1)-C(10)-C(11)	-111.6(3)
O(5)-S(1)-C(10)-C(9)	-172.9(2)

O(4)-S(1)-C(10)-C(9)	-44.4(3)
N(4)-S(1)-C(10)-C(9)	67.3(3)
C(9)-C(10)-C(11)-C(12)	-1.2(5)
S(1)-C(10)-C(11)-C(12)	177.6(3)
C(10)-C(11)-C(12)-C(13)	-0.1(6)
C(11)-C(12)-C(13)-C(14)	0.8(6)
C(10)-C(9)-C(14)-C(13)	-1.3(5)
N(3)-C(9)-C(14)-C(13)	177.6(3)
C(12)-C(13)-C(14)-C(9)	0.0(6)
S(1)-N(4)-C(15)-C(16)	-142.3(2)
N(4)-C(15)-C(16)-C(18)	64.6(4)
N(4)-C(15)-C(16)-C(17)	-172.2(3)
O(1)-C(1)-C(19)-C(21)	-139.1(3)
N(1)-C(1)-C(19)-C(21)	43.1(4)
O(1)-C(1)-C(19)-C(22)	101.4(4)
N(1)-C(1)-C(19)-C(22)	-76.5(4)
O(1)-C(1)-C(19)-C(20)	-19.5(4)
N(1)-C(1)-C(19)-C(20)	162.6(3)

Compound-6

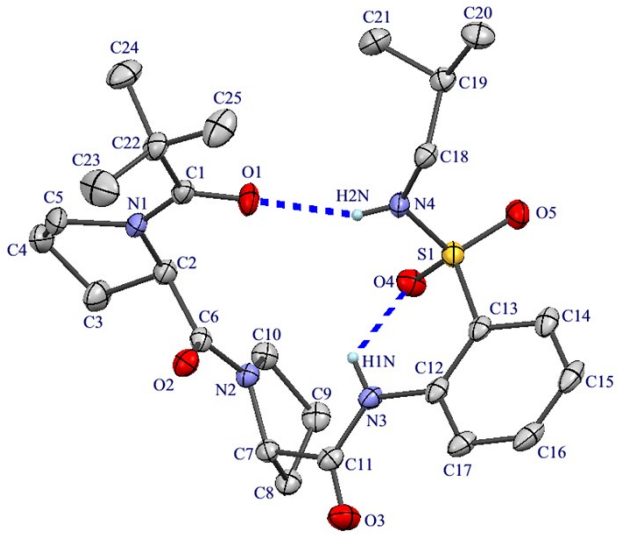


Figure: ORTEP diagram of **6**. Ellipsoids were drawn with 50 % probability.

Table: Torsion angles [°] for **6**

O(5)-S(1)-N(4)-C(18)	-37.7(3)
O(4)-S(1)-N(4)-C(18)	-167.8(3)
C(13)-S(1)-N(4)-C(18)	76.5(3)
C(2)-N(1)-C(1)-O(1)	3.8(5)
C(5)-N(1)-C(1)-O(1)	-172.9(4)
C(2)-N(1)-C(1)-C(22)	-175.4(3)
C(5)-N(1)-C(1)-C(22)	7.9(6)
C(1)-N(1)-C(2)-C(6)	66.9(4)
C(5)-N(1)-C(2)-C(6)	-115.7(3)
C(1)-N(1)-C(2)-C(3)	-176.4(3)
C(5)-N(1)-C(2)-C(3)	1.0(4)
N(1)-C(2)-C(3)-C(4)	22.3(4)
C(6)-C(2)-C(3)-C(4)	140.7(3)
C(2)-C(3)-C(4)-C(5)	-36.7(4)
C(1)-N(1)-C(5)-C(4)	153.0(4)
C(2)-N(1)-C(5)-C(4)	-23.9(4)
C(3)-C(4)-C(5)-N(1)	37.2(4)
C(7)-N(2)-C(6)-O(2)	13.2(4)
C(10)-N(2)-C(6)-O(2)	174.0(3)
C(7)-N(2)-C(6)-C(2)	-162.5(2)
C(10)-N(2)-C(6)-C(2)	-1.7(4)
N(1)-C(2)-C(6)-O(2)	23.1(4)
C(3)-C(2)-C(6)-O(2)	-90.9(4)
N(1)-C(2)-C(6)-N(2)	-161.2(2)
C(3)-C(2)-C(6)-N(2)	84.7(3)
C(6)-N(2)-C(7)-C(11)	-85.2(3)
C(10)-N(2)-C(7)-C(11)	111.4(3)
C(6)-N(2)-C(7)-C(8)	154.9(2)
C(10)-N(2)-C(7)-C(8)	-8.4(3)
N(2)-C(7)-C(8)-C(9)	29.4(3)
C(11)-C(7)-C(8)-C(9)	-93.6(3)
C(7)-C(8)-C(9)-C(10)	-39.8(3)
C(6)-N(2)-C(10)-C(9)	-177.4(3)
C(7)-N(2)-C(10)-C(9)	-15.7(3)

C(8)-C(9)-C(10)-N(2)	33.6(3)
C(12)-N(3)-C(11)-O(3)	5.2(5)
C(12)-N(3)-C(11)-C(7)	-170.6(3)
N(2)-C(7)-C(11)-O(3)	169.1(3)
C(8)-C(7)-C(11)-O(3)	-75.5(4)
N(2)-C(7)-C(11)-N(3)	-14.9(4)
C(8)-C(7)-C(11)-N(3)	100.5(3)
C(11)-N(3)-C(12)-C(13)	163.4(3)
C(11)-N(3)-C(12)-C(17)	-16.2(4)
C(17)-C(12)-C(13)-C(14)	2.5(4)
N(3)-C(12)-C(13)-C(14)	-177.1(3)
C(17)-C(12)-C(13)-S(1)	-177.5(2)
N(3)-C(12)-C(13)-S(1)	2.9(4)
O(5)-S(1)-C(13)-C(12)	-162.4(2)
O(4)-S(1)-C(13)-C(12)	-33.1(3)
N(4)-S(1)-C(13)-C(12)	81.6(3)
O(5)-S(1)-C(13)-C(14)	17.6(3)
O(4)-S(1)-C(13)-C(14)	146.9(2)
N(4)-S(1)-C(13)-C(14)	-98.4(2)
C(12)-C(13)-C(14)-C(15)	-1.0(4)
S(1)-C(13)-C(14)-C(15)	179.0(2)
C(13)-C(14)-C(15)-C(16)	-0.9(5)
C(14)-C(15)-C(16)-C(17)	1.3(5)
C(15)-C(16)-C(17)-C(12)	0.2(5)
C(13)-C(12)-C(17)-C(16)	-2.0(4)
N(3)-C(12)-C(17)-C(16)	177.6(3)
S(1)-N(4)-C(18)-C(19)	90.6(3)
N(4)-C(18)-C(19)-C(20)	-173.4(3)
N(4)-C(18)-C(19)-C(21)	63.4(3)
O(1)-C(1)-C(22)-C(25)	-9.6(5)
N(1)-C(1)-C(22)-C(25)	169.7(3)
O(1)-C(1)-C(22)-C(23)	-129.1(4)
N(1)-C(1)-C(22)-C(23)	50.1(4)
O(1)-C(1)-C(22)-C(24)	107.3(4)
N(1)-C(1)-C(22)-C(24)	-73.5(4)

Compound-7

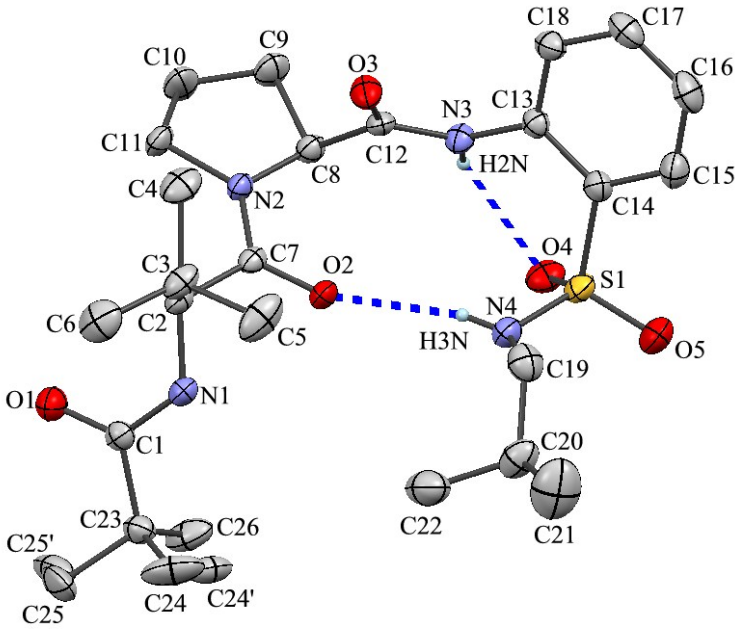


Figure: ORTEP diagram of **7**. Ellipsoids were drawn with 50 % probability.

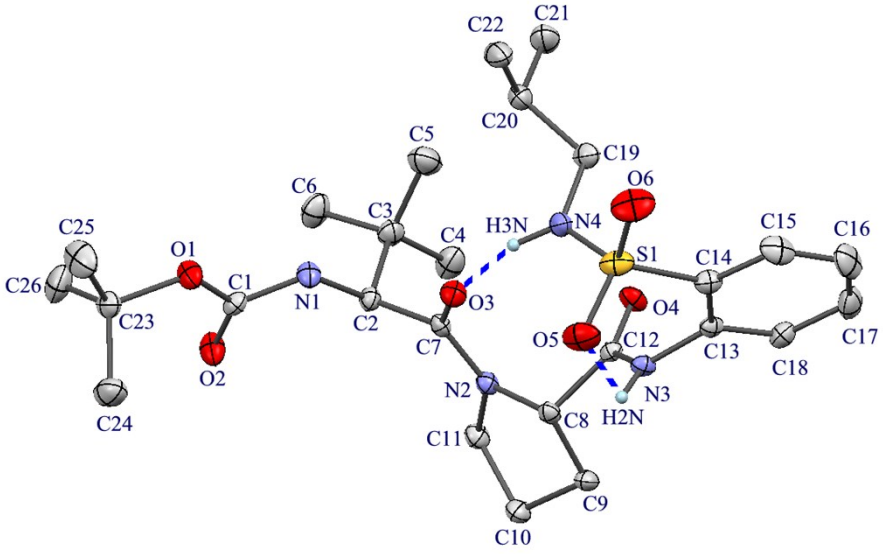
Table: Torsion angles [°] for **7**

O(4)-S(1)-N(4)-C(19)	172.6(3)
O(5)-S(1)-N(4)-C(19)	42.6(3)
C(14)-S(1)-N(4)-C(19)	-71.8(3)
C(2)-N(1)-C(1)-O(1)	-4.4(5)
C(2)-N(1)-C(1)-C(23)	175.7(3)
C(1)-N(1)-C(2)-C(7)	-121.0(3)
C(1)-N(1)-C(2)-C(3)	114.7(3)
N(1)-C(2)-C(3)-C(4)	177.4(3)
C(7)-C(2)-C(3)-C(4)	56.8(4)
N(1)-C(2)-C(3)-C(6)	-63.2(3)
C(7)-C(2)-C(3)-C(6)	176.2(3)
N(1)-C(2)-C(3)-C(5)	58.3(4)
C(7)-C(2)-C(3)-C(5)	-62.3(4)
C(8)-N(2)-C(7)-O(2)	1.6(4)
C(11)-N(2)-C(7)-O(2)	173.3(3)

C(8)-N(2)-C(7)-C(2)	-179.5(3)
C(11)-N(2)-C(7)-C(2)	-7.8(4)
N(1)-C(2)-C(7)-O(2)	-42.4(4)
C(3)-C(2)-C(7)-O(2)	80.7(3)
N(1)-C(2)-C(7)-N(2)	138.7(3)
C(3)-C(2)-C(7)-N(2)	-98.3(3)
C(7)-N(2)-C(8)-C(12)	-64.6(3)
C(11)-N(2)-C(8)-C(12)	122.4(3)
C(7)-N(2)-C(8)-C(9)	176.6(3)
C(11)-N(2)-C(8)-C(9)	3.6(3)
N(2)-C(8)-C(9)-C(10)	-17.9(4)
C(12)-C(8)-C(9)-C(10)	-135.7(4)
C(8)-C(9)-C(10)-C(11)	26.2(5)
C(7)-N(2)-C(11)-C(10)	-160.7(3)
C(8)-N(2)-C(11)-C(10)	11.5(4)
C(9)-C(10)-C(11)-N(2)	-23.5(5)
C(13)-N(3)-C(12)-O(3)	2.5(5)
C(13)-N(3)-C(12)-C(8)	-178.4(3)
N(2)-C(8)-C(12)-O(3)	-40.0(4)
C(9)-C(8)-C(12)-O(3)	74.8(4)
N(2)-C(8)-C(12)-N(3)	140.9(3)
C(9)-C(8)-C(12)-N(3)	-104.4(3)
C(12)-N(3)-C(13)-C(18)	-50.4(4)
C(12)-N(3)-C(13)-C(14)	130.7(3)
C(18)-C(13)-C(14)-C(15)	-1.8(5)
N(3)-C(13)-C(14)-C(15)	177.1(3)
C(18)-C(13)-C(14)-S(1)	177.5(2)
N(3)-C(13)-C(14)-S(1)	-3.7(4)
O(4)-S(1)-C(14)-C(15)	-134.1(3)
O(5)-S(1)-C(14)-C(15)	-4.1(3)
N(4)-S(1)-C(14)-C(15)	111.0(3)
O(4)-S(1)-C(14)-C(13)	46.7(3)
O(5)-S(1)-C(14)-C(13)	176.6(3)
N(4)-S(1)-C(14)-C(13)	-68.3(3)
C(13)-C(14)-C(15)-C(16)	1.5(5)
S(1)-C(14)-C(15)-C(16)	-177.8(3)

C(14)-C(15)-C(16)-C(17)	-0.3(6)
C(15)-C(16)-C(17)-C(18)	-0.5(6)
C(16)-C(17)-C(18)-C(13)	0.1(5)
C(14)-C(13)-C(18)-C(17)	1.0(5)
N(3)-C(13)-C(18)-C(17)	-177.8(3)
S(1)-N(4)-C(19)-C(20)	-114.1(3)
N(4)-C(19)-C(20)-C(22)	-69.0(4)
N(4)-C(19)-C(20)-C(21)	168.1(4)
O(1)-C(1)-C(23)-C(24)	-135.3(16)
N(1)-C(1)-C(23)-C(24)	44.6(16)
O(1)-C(1)-C(23)-C(26)	98.8(4)
N(1)-C(1)-C(23)-C(26)	-81.3(4)
O(1)-C(1)-C(23)-C(25)	-33.6(7)
N(1)-C(1)-C(23)-C(25)	146.2(7)
O(1)-C(1)-C(23)-C(25')	-5.4(6)
N(1)-C(1)-C(23)-C(25')	174.5(6)
O(1)-C(1)-C(23)-C(24')	-146.2(9)
N(1)-C(1)-C(23)-C(24')	33.7(9)

Compound-8



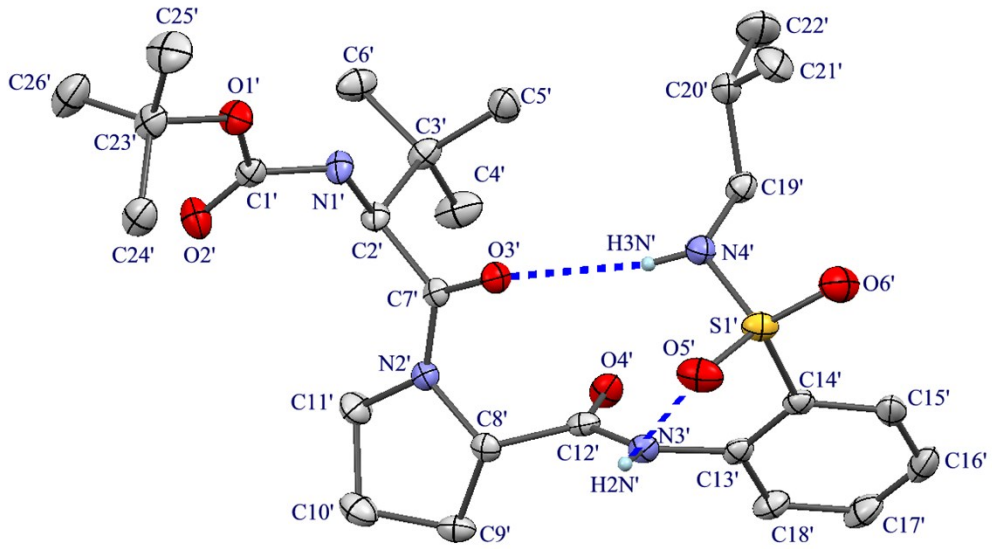


Figure: ORTEP diagram of **8**. Ellipsoids were drawn with 50 % probability. There are two molecules in the crystal packing of this molecules with slight different backbone torsions as shown above.

Table: Torsion angles [°] for **8**

O(5)-S(1)-N(4)-C(19)	-168.8(2)
O(6)-S(1)-N(4)-C(19)	60.8(3)
C(14)-S(1)-N(4)-C(19)	-52.4(3)
C(2)-N(1)-C(1)-O(2)	-1.5(5)
C(2)-N(1)-C(1)-O(1)	177.8(3)
C(23)-O(1)-C(1)-O(2)	5.6(5)
C(23)-O(1)-C(1)-N(1)	-173.7(3)
C(1)-N(1)-C(2)-C(7)	-128.4(3)
C(1)-N(1)-C(2)-C(3)	107.1(4)
N(1)-C(2)-C(3)-C(5)	63.0(4)
C(7)-C(2)-C(3)-C(5)	-57.5(4)
N(1)-C(2)-C(3)-C(4)	-175.6(3)
C(7)-C(2)-C(3)-C(4)	63.9(4)
N(1)-C(2)-C(3)-C(6)	-58.2(4)
C(7)-C(2)-C(3)-C(6)	-178.7(3)

C(8)-N(2)-C(7)-O(3)	5.3(4)
C(11)-N(2)-C(7)-O(3)	170.5(3)
C(8)-N(2)-C(7)-C(2)	-174.1(3)
C(11)-N(2)-C(7)-C(2)	-8.9(5)
N(1)-C(2)-C(7)-O(3)	-31.8(4)
C(3)-C(2)-C(7)-O(3)	92.0(4)
N(1)-C(2)-C(7)-N(2)	147.6(3)
C(3)-C(2)-C(7)-N(2)	-88.6(4)
C(7)-N(2)-C(8)-C(9)	176.3(3)
C(11)-N(2)-C(8)-C(9)	8.4(3)
C(7)-N(2)-C(8)-C(12)	-63.3(4)
C(11)-N(2)-C(8)-C(12)	128.8(3)
N(2)-C(8)-C(9)-C(10)	-30.4(3)
C(12)-C(8)-C(9)-C(10)	-153.0(3)
C(8)-C(9)-C(10)-C(11)	40.8(3)
C(7)-N(2)-C(11)-C(10)	-149.2(3)
C(8)-N(2)-C(11)-C(10)	17.0(3)
C(9)-C(10)-C(11)-N(2)	-35.5(3)
C(13)-N(3)-C(12)-O(4)	-7.5(5)
C(13)-N(3)-C(12)-C(8)	168.5(3)
N(2)-C(8)-C(12)-O(4)	-33.4(4)
C(9)-C(8)-C(12)-O(4)	83.8(4)
N(2)-C(8)-C(12)-N(3)	150.7(3)
C(9)-C(8)-C(12)-N(3)	-92.1(3)
C(12)-N(3)-C(13)-C(18)	-61.5(4)
C(12)-N(3)-C(13)-C(14)	120.0(3)
C(18)-C(13)-C(14)-C(15)	-4.3(5)
N(3)-C(13)-C(14)-C(15)	174.2(3)
C(18)-C(13)-C(14)-S(1)	174.2(2)
N(3)-C(13)-C(14)-S(1)	-7.3(4)
O(5)-S(1)-C(14)-C(13)	60.1(3)
O(6)-S(1)-C(14)-C(13)	-170.1(3)
N(4)-S(1)-C(14)-C(13)	-54.7(3)
O(5)-S(1)-C(14)-C(15)	-121.5(3)
O(6)-S(1)-C(14)-C(15)	8.4(3)
N(4)-S(1)-C(14)-C(15)	123.7(3)

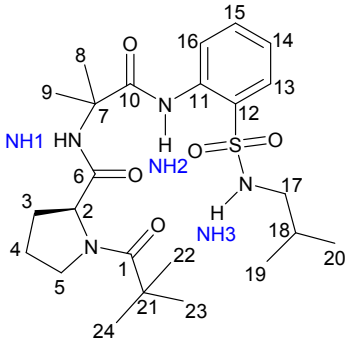
C(13)-C(14)-C(15)-C(16)	1.7(5)
S(1)-C(14)-C(15)-C(16)	-176.7(3)
C(14)-C(15)-C(16)-C(17)	1.6(6)
C(15)-C(16)-C(17)-C(18)	-2.3(6)
C(16)-C(17)-C(18)-C(13)	-0.3(5)
C(14)-C(13)-C(18)-C(17)	3.6(5)
N(3)-C(13)-C(18)-C(17)	-174.9(3)
S(1)-N(4)-C(19)-C(20)	-141.2(3)
N(4)-C(19)-C(20)-C(21)	-165.9(3)
N(4)-C(19)-C(20)-C(22)	71.5(4)
C(1)-O(1)-C(23)-C(26)	-64.6(4)
C(1)-O(1)-C(23)-C(24)	60.7(4)
C(1)-O(1)-C(23)-C(25)	178.7(3)
O(6')-S(1')-N(4')-C(19')	49.3(3)
O(5')-S(1')-N(4')-C(19')	179.8(3)
C(14')-S(1')-N(4')-C(19')	-64.4(3)
C(23')-O(1')-C(1')-O(2')	13.9(5)
C(23')-O(1')-C(1')-N(1')	-167.0(3)
C(2')-N(1')-C(1')-O(2')	1.8(5)
C(2')-N(1')-C(1')-O(1')	-177.3(3)
C(1')-N(1')-C(2')-C(7')	-110.1(3)
C(1')-N(1')-C(2')-C(3')	124.7(3)
N(1')-C(2')-C(3')-C(6')	-60.4(4)
C(7')-C(2')-C(3')-C(6')	176.1(3)
N(1')-C(2')-C(3')-C(4')	60.4(4)
C(7')-C(2')-C(3')-C(4')	-63.1(4)
N(1')-C(2')-C(3')-C(5')	-178.6(3)
C(7')-C(2')-C(3')-C(5')	57.9(4)
C(8')-N(2')-C(7')-O(3')	-2.0(4)
C(11')-N(2')-C(7')-O(3')	175.9(3)
C(8')-N(2')-C(7')-C(2')	176.9(3)
C(11')-N(2')-C(7')-C(2')	-5.2(5)
N(1')-C(2')-C(7')-O(3')	-49.1(4)
C(3')-C(2')-C(7')-O(3')	76.0(4)
N(1')-C(2')-C(7')-N(2')	132.0(3)
C(3')-C(2')-C(7')-N(2')	-102.9(3)

C(7')-N(2')-C(8')-C(12')	-58.7(4)
C(11')-N(2')-C(8')-C(12')	123.1(3)
C(7')-N(2')-C(8')-C(9')	-176.9(3)
C(11')-N(2')-C(8')-C(9')	4.9(4)
N(2')-C(8')-C(9')-C(10')	-25.2(3)
C(12')-C(8')-C(9')-C(10')	-144.3(3)
C(8')-C(9')-C(10')-C(11')	35.9(4)
C(7')-N(2')-C(11')-C(10')	-160.9(3)
C(8')-N(2')-C(11')-C(10')	17.0(4)
C(9')-C(10')-C(11')-N(2')	-32.3(4)
C(13')-N(3')-C(12')-O(4')	-10.3(5)
C(13')-N(3')-C(12')-C(8')	165.5(3)
N(2')-C(8')-C(12')-O(4')	-43.5(4)
C(9')-C(8')-C(12')-O(4')	70.8(4)
N(2')-C(8')-C(12')-N(3')	140.7(3)
C(9')-C(8')-C(12')-N(3')	-104.9(3)
C(12')-N(3')-C(13')-C(18')	-57.6(4)
C(12')-N(3')-C(13')-C(14')	123.2(4)
C(18')-C(13')-C(14')-C(15')	-3.0(5)
N(3')-C(13')-C(14')-C(15')	176.2(3)
C(18')-C(13')-C(14')-S(1')	176.0(3)
N(3')-C(13')-C(14')-S(1')	-4.8(5)
O(6')-S(1')-C(14')-C(15')	2.5(3)
O(5')-S(1')-C(14')-C(15')	-127.7(3)
N(4')-S(1')-C(14')-C(15')	117.6(3)
O(6')-S(1')-C(14')-C(13')	-176.5(3)
O(5')-S(1')-C(14')-C(13')	53.3(3)
N(4')-S(1')-C(14')-C(13')	-61.5(3)
C(13')-C(14')-C(15')-C(16')	2.5(5)
S(1')-C(14')-C(15')-C(16')	-176.6(3)
C(14')-C(15')-C(16')-C(17')	-0.5(6)
C(15')-C(16')-C(17')-C(18')	-0.9(6)
C(14')-C(13')-C(18')-C(17')	1.6(5)
N(3')-C(13')-C(18')-C(17')	-177.6(3)
C(16')-C(17')-C(18')-C(13')	0.3(6)
S(1')-N(4')-C(19')-C(20')	-124.5(3)

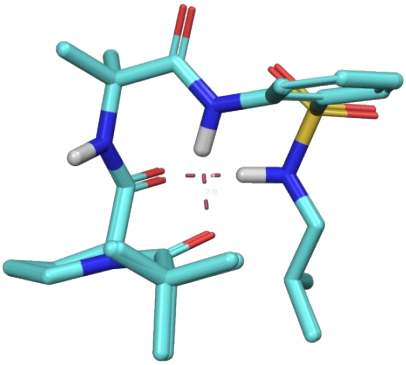
N(4')-C(19')-C(20')-C(21')	65.2(4)
N(4')-C(19')-C(20')-C(22')	-171.1(3)
C(1')-O(1')-C(23')-C(26')	-64.9(4)
C(1')-O(1')-C(23')-C(25')	176.9(3)
C(1')-O(1')-C(23')-C(24')	57.7(4)

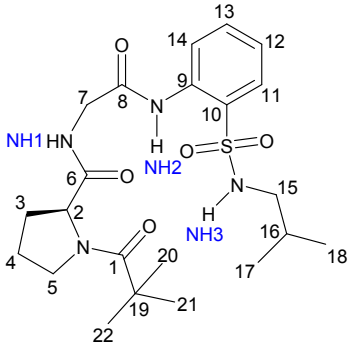
Molecular Dynamics

Molecular Dynamics NMR-based structures of compound **3**, **4** and **5** were derived from distant constraints from NOE cross peaks (given in table vide infra) by using macromodel-v10.8 from Schrödinger software. The seven lowest-energy superimposed structures of compound **3**, **4** and **5** showed root mean square deviation (RMSD) of 0.238 ± 0.104 Å, 0.098 ± 0.0447 Å and 0.289 ± 0.149 Å respectively. Chemical structures and their molecular models are as follows.



3





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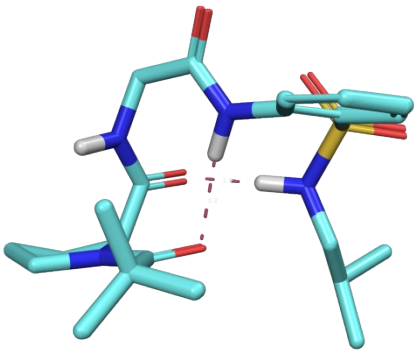

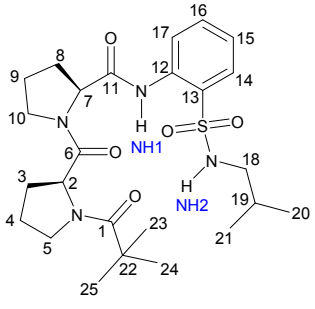

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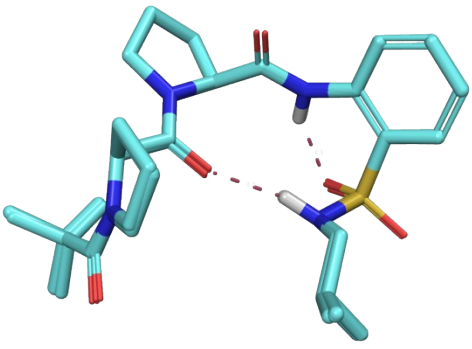

Distance constraints for peptide **3**

Atom1	Atom2	Upper bound(Å)	Lower bound(Å)
16H	15H	2.684	2.196
15H	14H	2.792609701	2.284862483
13H	14H	2.692696594	2.203115395
NH2	21H, 22H, 23H	5.110710753	4.181490616
NH2	8H,9H	3.144335617	2.572638232
NH2	3H	5.083634636	4.159337429
NH2	2H	4.338075351	3.549334378
NH2	NH3	3.190122588	2.6101003
NH2	16H	4.117541193	3.368897339
NH2	NH1	3.374946025	2.761319475
NH1	21H, 22H, 23H	4.135323888	3.383446818
NH1	8H,9H	2.803798066	2.2940166
NH1	5H	5.385741344	4.406515645
NH1	2H	2.801392853	2.292048698
16H	8H, 9H	4.020029143	3.289114753
13H	19H, 20H	5.00011728	4.091005047
13H	18H	5.537686336	4.530834275
13H	17H'	3.786326913	3.097903838
13H	17H	3.738633816	3.058882213
13H	NH3	5.29606777	4.333146357
NH3	19H,20H	3.357690315	2.747201167
NH3	3H	4.626613929	3.785411396
NH3	18H	3.501943519	2.865226515
NH3	3H'	4.001019228	3.273561186
NH3	17H'	2.892292413	2.366421065
NH3	17H	3.351138012	2.741840192
NH3	2H	4.85081087	3.968845258
2H	19H, 20H	5.817981604	4.760166767
2H	21H, 22H, 23H	4.096684704	3.35183294
2H	4H'	2.792276879	2.284590173
2H	3H'	5.12178258	4.190549384
2H	3H	3.438214857	2.813084883
2H	5H	4.150959215	3.396239357
5H	21H, 22H, 23H	2.575964823	2.107607582
5H	4H'	3.717108837	3.041270867
5H	4H	3.019314982	2.470348621
5H	3H'	3.094791691	2.532102293
5H	3H	4.369688261	3.575199486
17H	19H, 20H	2.995545642	2.450900979
17H	18H	3.485122827	2.851464131
17H	19H, 20H	2.907865198	2.379162435
17H	18H	3.389959176	2.773602962

3H	4H'	2.3073052	1.887795164
3H	4H	3.186830437	2.607406722
17H'	3H'	3.374934628	2.76131015
3H'	19H, 20H	4.210114914	3.444639475

Distance constraints for peptide **4**

Atom 1	Atom 2	Upper bound(Å)	Lower bound(Å)
14H	13H	2.684	2.196
13H	12H	2.746700908	2.247300743
NH2	17H, 18H	4.929825507	4.033493596
NH2	20H, 21H, 22H	4.568849707	3.73814976
NH2	7H	3.23132494	2.643811314
NH2	2H	4.18779576	3.426378349
NH2	NH3	3.068933394	2.510945504
NH2	14H	4.130715987	3.379676717
NH2	NH1	3.165223258	2.58972812
NH1	20H, 21H, 22H	4.019539516	3.28871415
NH1	7H	2.705998122	2.213998463
NH1	2H	2.776973746	2.272069428
11H	15H	3.287338202	2.689640347
NH3	17H, 18H	3.138100167	2.567536501
NH3	20H, 21H, 22H	4.494944872	3.677682168
NH3	16H	3.444536087	2.818256798
NH3	4H	4.005687337	3.277380548
NH3	3H	3.571699299	2.922299426
NH3	15H	2.813354691	2.301835656
NH3	7H	4.783404705	3.913694758
NH3	2H	4.581537716	3.748530859
2H	20H, 21H, 22H	3.838609211	3.140680263
2H	4H'	2.648720653	2.16713508
2H	3H	3.275239107	2.679741087
2H	5H	3.879448039	3.17409385
5H	20H, 21H, 22H	2.402339207	1.965550261
5H	3H'	2.75793645	2.256493459
5H	4H	2.927012388	2.394828318
5H	3H	4.225133818	3.456927669
15H	17H, 18H	2.487850659	2.035514176
15H	16H	2.970975467	2.430798109
15H	20H, 21H, 22H	4.723110935	3.864363492
3H	17H, 18H	4.02398909	3.29235471
3H	4H'	2.168363251	1.774115387
3H	4H	3.363910549	2.752290449
4H	17H, 18H	4.136547801	3.384448201
4H	20H, 21H, 22H	4.443159031	3.635311934
4H	4H'	2.293220283	1.876271141

16H	17H, 18H	2.37184052	1.940596789
3H'	20H, 21H, 22H	3.95707908	3.237610156
4H'	20H, 21H, 22H	3.777938673	3.091040733
16H	20H, 21H, 22H	3.398975017	2.780979559

Distance constraints for peptide **5**

Atom1	Atom2	Upper Bound (Å)	Lower Bound (Å)
17H	16H	2.684	2.196
16H	15H	2.668452476	2.183279299
NH1	17H	4.196725364	3.433684389
NH1	NH2	2.887480302	2.362483883
NH1	7H	2.589390481	2.118592212
NH1	10H'	4.186526584	3.425339933
NH1	9H	4.67689166	3.826547722
NH1	8H	3.687574362	3.017106296
14H	20H, 21H	4.722310804	3.86370884
14H	19H	5.027754489	4.113617309
14H	18H'	3.619415626	2.961340058
14H	18H	3.698077528	3.025699795
NH2	14H	4.455328868	3.645269074
NH2	20H, 21H	3.160170853	2.585594334
NH2	23H, 24H, 25H	4.516815581	3.695576384
NH2	19H	3.233978849	2.645982694
NH2	9H	3.790522504	3.101336594
NH2	3H	3.82973346	3.133418285
NH2	18H'	3.054151969	2.498851611
NH2	18H	2.9434568	2.408282837
NH2	5H	4.565952533	3.735779345
NH2	7H	3.925705304	3.211940703
2H	23H, 24H, 25H	3.902039706	3.192577941
2H	4H'	3.853269559	3.152675094
2H	4H	2.556260877	2.091486172
2H	3H	4.570609307	3.739589433
2H	10H'	2.820455865	2.307645707
2H	5H	3.768288463	3.083145106
2H	10H	2.438211773	1.994900542
7H	20H, 21H	4.764727635	3.898413519
7H	9H	3.641794717	2.979650223
7H	8H	2.48840582	2.035968398
7H	10H	4.250486197	3.477670525
10H	9H	2.865018447	2.344106002

10H	8H	3.483251338	2.849932913
5H	20H, 21H	3.589284633	2.936687427
5H	23H, 24H, 25H	2.301470259	1.883021121
5H	4H'	2.959428464	2.421350561
5H	4H	3.474262128	2.842578104
5H	3H	3.417368089	2.796028436
5H'	19H	3.997806806	3.270932842
5H'	4H	3.360408574	2.749425197
5H'	3H	2.999380287	2.454038417
10H'	9H	2.634965128	2.155880559
10H'	8H	4.344501866	3.554592435
18H	20H, 21H	2.735962717	2.23851495
18H'	20H, 21H	2.720568741	2.225919879
3H	20H, 21H	4.347786939	3.557280222
19H	20H, 21H	2.307782744	1.888185882
18H	19H	3.177807935	2.600024674
18H'	19H	3.266192651	2.672339442