Supporting Information

A Concise Synthesis of a β-Lactamase Inhibitor

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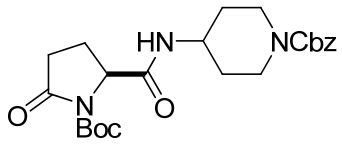
General Information. Commercial reagents were purified prior to use following the guidelines of Perrin and Armarego.[1] Non-aqueous reagents were transferred under nitrogen via syringe or cannula. All reactions were carried out under nitrogen in oven-dried glassware unless otherwise noted. Organic solutions were concentrated under reduced pressure on a Buchi rotary evaporator using a water bath. Chromatographic purification of products was accomplished using forced-flow chromatography on ICN 60 32-64 mesh silica gel 63 according to the method of Still.[2] Thin-layer chromatography (TLC) was performed on EM Reagents 0.25 mm silica gel 60-F plates. Visualization of

[1] Perrin, D. D.; Armarego, W. L. F. *Purification of Laboratory Chemicals*; 3rd ed., Pergamon Press, Oxford, 1988.
[2] Still, W. C.; Kahn, M.; Mitra, A. J. *J. Org. Chem.* **1978**, *43*, 2923.

the developed chromatogram was performed by fluorescence quenching or by anisaldehyde stain.

^{1}H and ^{13}C NMR spectra were recorded on a Bruker 400 (400 MHz and 100 MHz) as noted, and are internally referenced to residual protio solvent signals. Data for ^{1}H NMR are reported as follows: chemical shift (δ ppm), multiplicity (s = singlet, d = doublet, t = triplet, q = quartet, m = multiplet), integration and coupling constant (Hz). Data for ^{13}C NMR are reported in terms of chemical shift. Mass spectra were obtained from an Agilent LC/MSD TOF model G1969A.

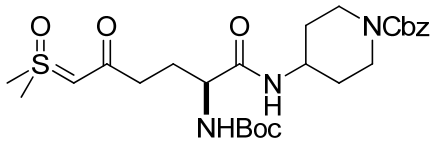


Preparation of Benzyl 4-{[1-(tert-butoxycarbonyl)-5-oxo-L-prolyl]amino}piperidine-carboxylate (7)

Benzyl 4-aminopiperidine-1-carboxylate (20 g, 85 mmol) and hydroxybenzotriazole hydrate (0.654 g, 4.27 mmol) were combined in dichloromethane (200 ml). To the solution was added 1-(3-dimethylaminopropyl)-3-ethylcarbodiimide hydrochloride (19.64 g, 102 mmol) followed by L-pyroglutamic acid (11.02 g, 85 mmol). A cold water bath was used to keep the temperature between 25 and 35 °C. After 30 min, the solution was quenched into 1 N HCl (100 ml). Sodium chloride (3 g) was added to aid phase separation. The organic layer was collected and washed with sodium bicarbonate (7%, 100 ml), then concentrated to a white solid.

The solid was suspended in acetonitrile and concentrated again to a wet solid. The residue was suspended in acetonitrile (200 ml). To the thick suspension was added di-tert-butyl dicarbonate (20.1 g, 92 mmol) followed by 4-dimethylaminopyridine (0.495 g, 4.05 mmol). After 3 h between 20 and 25 °C, the reaction was quenched with water (560 ml) containing 3% NaCl and the mixture was extracted with ethyl acetate (560 ml). The organic layer was washed with aqueous 3% NaCl (300 mL) and concentrated to a white solid. The residue was suspended in isopropyl acetate (350 mL) and the suspension was

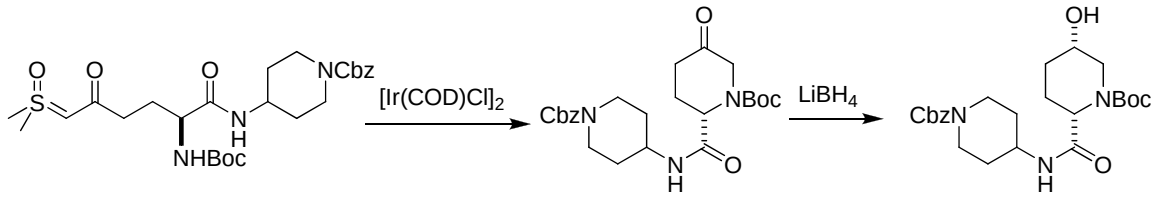
warmed to 45 °C, then allowed to cool to room temp. The suspension was filtered, rinsing with 1 : 1 heptane IPAc. The solid was dried under vacuum at 35 °C to give the title compound as a white solid (32.92 g, 73.9 mmol, 87%). ^{1}H NMR ($CDCl_3$, 400 MHz) δ 7.33 (5H, m), 6.62 (1H, m), 5.13 (2H, s), 4.48 (1H, dd, *J* = 9.0, 3.8 Hz), 4.15 (2H, m), 3.97 (1H, m), 2.95 (2H, m), 2.70 (1H, m), 2.46 (1H, m), 2.31 (1H, m), 2.15 (1H, m), 1.94 (2H, m), 1.45 (9H, s). ^{13}C NMR ($CDCl_3$, 100 MHz) δ 174.2, 170.3, 155.1, 149.6, 136.7, 128.5, 128.0, 127.9, 83.8, 67.2, 60.6, 46.9, 43.0, 42.9, 31.7, 31.5, 28.0, 22.1; HRMS calculated for $C_{23}H_{31}N_3O_3$ (M+Na): 468.2111, found: 468.2113. $[\alpha]_D^{25}$ = 5.64 (c = 1.0, MeOH).



Preparation of Benzyl 4-({N-(tert-butoxycarbonyl)-6-[dimethyl(oxido)-λ^4-sulfanylidene]-5-oxo-L-norleucyl}amino)piperidine-1-carboxylate (8)

Potassium tert-butoxide (28.1 g, 251 mmol) was added as a solid charge to a suspension of trimethyl sulfoxonium iodide (62.6 g, 284 mol) in DMSO (334 mL) at 23 °C. The suspension was aged at 23°C for one hour, followed by addition of benzyl 4-{[1-(tert-butoxycarbonyl)-5-oxo-L-prolyl]amino}piperidine-1-carboxylate (**7**, 74.5 g, 167 mmol) as a single solid charge, and the suspension was then aged for one hour at 23 °C. Water (120 mL) was added dropwise until there was slight cloudiness in the solution, at this time 25 mg seed crystal was added and the suspension stirred for 30 minutes. At this time a further 600 mL water was added (total 2:1 water:DMSO) slowly over 30 minutes, and the solution was cooled to 0 °C for 3 hours with stirring. The resulting suspension was then filtered and washed 6x with cold water (150 mL each). There was 6% product loss by HPLC in the filtration, a further 2% loss to the wash. The filter cake was dried initially via flushing with nitrogen while pulling vacuum for three hours. The resulting white powder was dried in a vacuum oven held at 50 °C for 24 hours, providing **8** (64.0 g, 119 mmol, 71.2 % yield) as a white solid. ^{1}H NMR ($CDCl_3$, 400 MHz) δ 7.49 (1H, br s),

7.33 (5H, m), 5.87 (1H, br s), 5.09 (2H, s), 4.50 (1H, s), 4.04 (3H, m), 3.91 (1H, m), 3.41 (3H, s), 3.37 (3H, s), 2.98 (2H, m), 2.36 (1H, m), 2.20 (1H, m), 1.90 (4H, m), 1.39 (12H, s). ^{13}C NMR ($CDCl_3$, 100 MHz) δ 189.9, 171.4, 155.7, 155.2, 136.7, 128.5, 128.0, 127.8, 79.6, 71.6, 67.1, 53.7, 46.2, 42.7, 41.9, 41.8, 36.4, 31.6, 29.5, 28.4; HRMS calculated for $C_{26}H_{39}N_3O_7S$ (M+H): 538.2587, found: 538.2582. $[\alpha]_D^{25}$ = 9.0 (c = 1.0, MeOH).

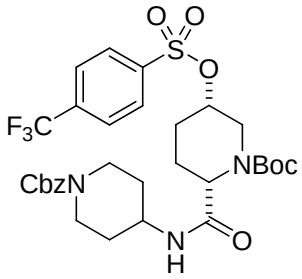


Preparation of tert-butyl (2S)-2-[({1-[(benzyloxy)carbonyl]piperidin-4-yl}amino)carbonyl]-5-oxopiperidine-1-carboxylate (10)

A suspension of benzyl 4-({N-(tert-butoxycarbonyl)-6-[dimethyl(oxido)-λ^4-sulfanylidene]-5-oxo-L-norleucyl}amino)piperidine-1-carboxylate (60.0 g., 112 mmol) in toluene (1000 mL) was degassed via nitrogen sparging for 30 minutes. The suspension was then added over 1 hour to a 80 °C degassed solution of $[Ir(COD)Cl]_2$ (747 mg, 1.12 mol) in toluene (500 mL). The reaction mixture was aged at 80 °C for 10 hours, and then cooled to 20°C. The toluene was concentrated to 300 mL, and 30 mL methanol was then added. The solution was cooled to -15 °C and then added dropwise over 30 minutes to a 300 mL toluene solution of lithium borohydride (4M solution in THF, 112 mmol, 28 mL) that had also been cooled to -15 °C. After addition was complete the resulting solution was aged at -15 °C for an additional 1 hour. At this time, HPLC shows the reaction to be complete with a 14:1 ratio of diastereomers. The reaction was quenched via addition of 50 mL n-propanol followed inverse addition to 300 mL 5% NaHCO3 solution and allowed to warm to room temperature with vigorous stirring. The stirring continued for 1 hour at which time the aqueous layer was separated, then the organic layer was washed with 100 mL water. The organics were then concentrated, and flushed with toluene with evaporation providing a tan oil. The oil was taken up in 240 mL toluene and warmed with stirring to 55 °C. Around 40 °C the oil had turned into a white precipitate, then at

55 °C 36 mL n-PrOH was slowly added (minimal amount to dissolve solids) at which time the heat was removed, the solution seeded with 200 mg of seed crystal, and the solution allowed to cool to room temperature with stirring. The solution was then cooled further to 0 °C and kept stirring for an additional 16 hours. At this time the slurry had become very thick, and was filtered with a mother liquor loss of 8% as determined by HPLC. The filtered material was dried under nitrogen to provide **10** (34.6 g, 75 mmol, 67 % yield) as a crystalline white solid.

^{1}H NMR ($CDCl_3$, 400 MHz) δ 7.33 (5H, m), 6.22 (1H, br s), 5.13 (2H, s), 4.60 (1H, m), 4.08 (3H, m), 3.93 (1H, m), 3.62 (1H, m), 2.98 (2H, t, *J* = 11.8 Hz), 2.84 (s, 1H), 2.62 (1H, dd, *J* = 12.7, 10.1 Hz), 2.30 (1H, m), 1.90 (3H, m), 1.63 (2H, m), 1.48 (9H, s) and 1.34 (2H, m). ^{13}C NMR ($CDCl_3$, 100 MHz) δ 170.2, 155., 155.2, 136.6, 128.5, 128.1, 127.9, 81.2, 77.3, 67.2, 66.3, 55.0, 52.9, 48.3, 46.5, 42.8, 32.0, 31.8, 29.9, 28.3, 23.7; HRMS calculated for $C_{24}H_{35}N_3O_6$ (M+Na): 484.2424, found: 484.2420. $[\alpha]_D^{25}$ = -6.8 (c = 1.0, MeOH).

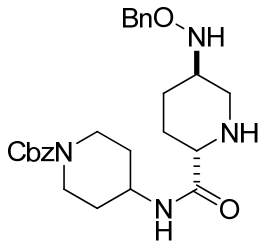


Preparation of tert-butyl (2S,5S)-2-[({1-[(benzyloxy)carbonyl]piperidin-4-yl}amino)carbonyl]-5-({[4-(trifluoromethyl)phenyl]sulfonyl}oxy)piperidine-1-carboxylate (11)

To a reaction vessel containing alcohol **10** (6.0 g, 13 mmol) in DCM (24 mL) was added 4-(Trifluoromethyl)benzene-1-sulfonyl chloride (3.82 g, 15.6 mmol), triethylamine (2.54 mL, 18.2 mmol) and catalytic amount of DMAP (60 mg). The reaction was warmed gently to 35 °C and held at that temperature for 3h then assayed for reaction completion. The reaction was then cooled to 10 C and diluted with MTBE (60 mL) and the organic layer was successively washed with aq $NaHCO_3$ (30 mL), aq NH_4Cl (2 x 30 mL) then

10 % aq brine solution (30 mL). The resulting organic layer was concentrated using rotary evaporator and flushed with additional MTBE to azeotrope dry. The resulting concentrate was diluted with MTBE (52 mL) then seeded. Heptanes (26.1 mL) was then added slowly and the resulting solids were filtered and washed with 40 % heptane/MTBE (2 x 17.4 mL); dried under vacuum to provide **11** as a crystalline white solid (8.38 g, 12.5 mmol, 96 % yield).

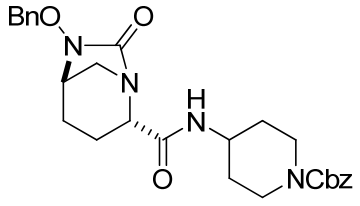
^{1}H NMR ($CDCl_3$, 400 MHz) δ 8.06 (2H, d, *J* = 8.2 Hz), 7.85 (2H, d, *J* = 8.2 Hz), 7.33 (5H, m), 6.13 (1H, br s), 5.13 (2H, s), 4.59 (1H, m), 4.47 (1H, m), 4.11 (3H, m), 3.91 (1H, m), 2.96 (2H, t, *J* = 11.6 Hz), 2.75 (1H, m), 2.33 (1H, m), 1.58 (1H, m), 1.46 (9H, s) and 1.35 (2H, m). ^{13}C NMR ($CDCl_3$, 100 MHz) δ 169.2, 155.1, 140.7, 136.7, 136.0, 135.7, 135.4, 135.0, 128.5, 128.2, 128.1, 127.9, 127.1, 126.6, 126.5, 126.4, 124.4, 121.7, 119.0, 81.9, 76.6, 67.2, 52.4, 46.6, 45.4, 42.7, 32.0, 31.8, 28.2, 27.4, 27.0, 23.5; HRMS calculated for $C_{31}H_{38}F_3N_3O_8S$ (M+Na): 692.2229, found: 692.2235. $[\alpha]_D^{25}$ = -10.6 (c = 1.0, MeOH).



Preparation of Benzyl 4-[({(2S,5R)-5-[(benzyloxy)amino]piperidin-2-yl}carbonyl)amino]piperidine-1-carboxylate (12)

N-Boc-O-benzylhydroxylamine (8.65 g, 38.7 mmol, as a solution in DMAC volume 38 mL) was added to a solution of potassium tert-butoxide (4.35 g, 38.7 mmol) in DMAC (80 mL), while maintaining the temperature between 18°C and 25°C. The solution was aged for 30 minutes after which time it became a slurry. Sulfonate **11** (20 g, 29.9 mmol) dissolved in DMAC (40 mL) was added to the slurry over 15 minutes at 20°C, and the resulting mixture was heated to 40°C for 3.5 hours and then left at 20°C overnight. Water (350 mL) was added to the mixture while maintaining the temperature at < 30°C. DCM

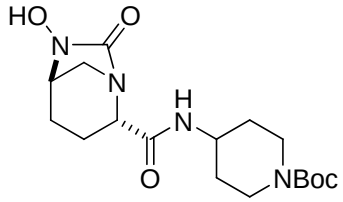
(350 mL) was then added, and the phases separated. The organic phase was washed three times with water (350 mL x 3). The washed organic phase was then distilled under atmospheric pressure to a volume of 90 mL, after which methanesulfonic acid (10 mL) was added and the solution heated to 35-40 °C for 8 hours. The solution was then cooled to 20°C and 2N NaOH (200 mL) added, followed by addition of DCM (90 mL). The phases were separated, and the organic phase was washed with water (90 mL), and then solvent switched at atmospheric pressure to acetonitrile, volume 50mL. p-Toluenesulfonic acid (4 g, 1 equiv. based on product assay) was added as a solution in acetonitrile (40mL) at 40°C to crystallize the product. MTBE (45 mL) was then added and the slurry was cooled 20°C, aged at 20°C for 1 hour, and then filtered to give the title product as a mono-tosylate crystalline salt (9.8 g, 53 %). ^{1}H NMR ($CDCl_3$, 400 MHz) δ 7.90 (1H, br s), 7.62 (2H, d, *J* = 7.2 Hz), 7.36 (5H, m), 7.23 (3H, m), 7.14 (2H, d, *J* = 7.2 Hz), 6.98 (2H, d, *J* = 7.8 Hz), 5.12 (2H, m), 4.40 (2H, s), 3.88 (3H, m), 3.62 (2H, m), 3.23 (2H, m), 2.70 (2H, m), 2.22 (3H, s), 1.59 (5H, m), 1.28 (3H, m). ^{13}C NMR ($CDCl_3$, 100 MHz) δ 168.2, 155.0, 141.6, 140.8, 137.5, 136.8, 128.9, 128.5, 128.3, 128.2, 128.0, 127.9, 127.8, 125.7, 76.1, 67.1, 57.3, 53.1, 46.9, 45.8, 42.4, 31.0, 30.8, 26.3, 25.7, 21.2; HRMS calculated for the free amine $C_{26}H_{34}N_4O_4$ (M+H): 467.2658, found: 467.2654. $[\alpha]_D^{25}$ = 17.1 (c = 1.0, MeOH).



Preparation of Benzyl 4-({[(2S,5R)-6-(benzyloxy)-7-oxo-1,6-diazabicyclo[3.2.1]oct-2-yl]carbonyl}amino)piperidine-1-carboxylate (14)

Benzyl 4-[({(2S,5R)-5-[(benzyloxy)amino]piperidin-2-yl}carbonyl)amino]piperidine-1-carboxylate in the form of a tosylate salt (26.2 g, 41.0 mmol) was slurried in dichloromethane (262 mL), after which 5 wt % $NaHCO_3$ (138 mL, 82.0 mmol) was

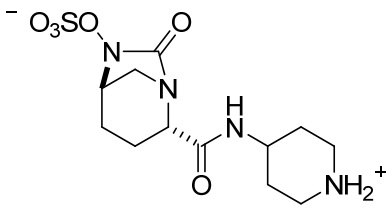
added and the resulting biphasic mixture was stirred vigorously for 30 minutes. The phases were separated, and the organic phase was washed with water (110 mL). The organic phase was then evaporated to a yellow-orange oil and flushed once with DCM. DCM (383 mL) was charged, followed by DIPEA (22.92 mL, 131 mmol) and the batch cooled to -10 °C. Triphosgene (9.74 g, 32.8 mmol) was added portion-wise, maintaining the temperature at <0°C. After 30 minutes, a 10% phosphoric acid solution (300 mL) was added, and the batch aged at 20°C overnight. The phases were separated and the organic phase was washed with 5 wt % $NaHCO_3$ (120 mL, pH 8) and water (80 mL). The organic phase was then distilled under reduced pressure and flushed twice with ethanol to a volume of ~75 mL, with concomitant crystallization of the product. Heptane (400 mL) was added dropwise. The slurry was then cooled to 0°C, filtered, washed with 3:1 heptane:ethanol (500 L), and dried on the filter under nitrogen stream to give the title product (17.48 g, 87%). ^{1}H NMR ($CDCl_3$, 400 MHz) δ 7.35 (10 H, m), 6.65 (1H, d, *J* = 7.8 Hz), 5.11 (2H, s), 5.03 (1H, d, *J* = 11.4 Hz), 4.90 (1H, d, *J* = 11.4 Hz), 4.13 (2H, m), 3.95 (1H, m), 3.87 (1H, d, *J* = 7.6 Hz), 3.31 (1H, s), 2.99 (3H, m), 2.66 (1H, d, *J* = 11.5 Hz), 2.35 (1H, dd, *J* = 14.0, 6.6 Hz), 1.94 (4H, m), 1.62 (2H, m) and 1.34 (2H, m). ^{13}C NMR ($CDCl_3$, 100 MHz) δ 168.9, 167.4, 155.1, 136.7, 135.6, 129.2, 128.8, 128.5, 128.0, 127.9, 78.2, 67.2, 60.4, 57.8, 47.5, 46.6, 42.8, 42.7, 31.9, 31.7, 20.8, 17.4; HRMS calculated for $C_{27}H_{32}N_4O_5$ (M+H): 493.2451, found: 493.2449. $[\alpha]_D^{25}$ = 16.9 (c = 1.0, $CHCl_3$).



Preparation of tert-Butyl 4-({[(2S,5R)-6-hydroxy-7-oxo-1,6-diazabicyclo[3.2.1]oct-2-yl]carbonyl}amino)piperidine-1-carboxylate (15)

Benzyl 4-({[(2R,5S)-6-(benzyloxy)-7-oxo-1,6-diazabicyclo[3.2.1]oct-2-yl]carbonyl}

amino)piperidine-1-carboxylate starting material (24.0 g., 48.7 mmol) and Boc_2O (11.2 g., 51.2 mmol) were charged to a glass bottle, and the solids were dissolved in THF (192 mL). The solution was then charged to a hydrogenation reactor along with $Pd(OH)_2$ (20 wt%, 2.4 g, 0.68 mmol) and another portion of THF (140 mL). The reaction was carried out at 45 psig H_2, 23 °C for 20 hours. After the reaction was complete as determined by HPLC analysis, the solution was filtered through solka flok to remove the catalyst and the filter cake was washed with THF. The filtrate and washes were then solvent switched by vacuum distillation to EtOAc to a volume of 110 mL. Approximately 380 mL EtOAc was used during the solvent switch with a constant volume distillation (110 mL at a maximum temperature of 20°C. The resulting EtOAc slurry was aged at room temperature for 1 hour, after which hexanes (50 mL) was added over 1 hour at room temperature. The slurry was aged for an additional 1 hour after which the supernatant concentration was measured (target: ~ 6 mg/g). The solids were then filtered and washed with 60 % EtOAc/hexanes solution (3 x 40 mL) and dried under vacuum and N_2 at room temperature to afford the title product (14.7 g., 39.9 mmol, 82% isolated yield). ^{1}H NMR (400 MHz, $CDCl_3$): δ 6.78 (d, *J* = 8.0 Hz, 1H), 4.02 – 3.95 (m, 2H), 3.94 – 3.86 (m, 1H), 3.81 (d, *J* = 7.8 Hz, 1H), 3.70 (m, 1H), 3.11 (dt, *J* = 11.2, 2.9 Hz, 1 H), 2.84 (t, *J* = 11.9 Hz, 2H) 2.78 (d, *J* = 11.3 Hz, 1H), 2.34 (dd, *J* = 15.0, 6.7 Hz, 1H), 2.15-2.08 (m, 1H), 1.96-1.80 (m, 3H), 1.74-1.63 (m, 1H), 1.41 (s, 9H), 1.37-1.24 (m, 2H); ^{13}C NMR ($CDCl_3$, 100 MHz) δ 169.1, 167.8, 154.8, 79.9, 59.7, 59.3, 47.9, 46.8, 42.6, 31.8, 31.6, 28.4, 20.5, 17.4; HRMS calculated for $C_{17}H_{28}N_4O_5$ (M+H): 369.2138, found: 369.2140. $[\alpha]_D^{25}$ = -18.2 (c = 1.0, $CHCl_3$).



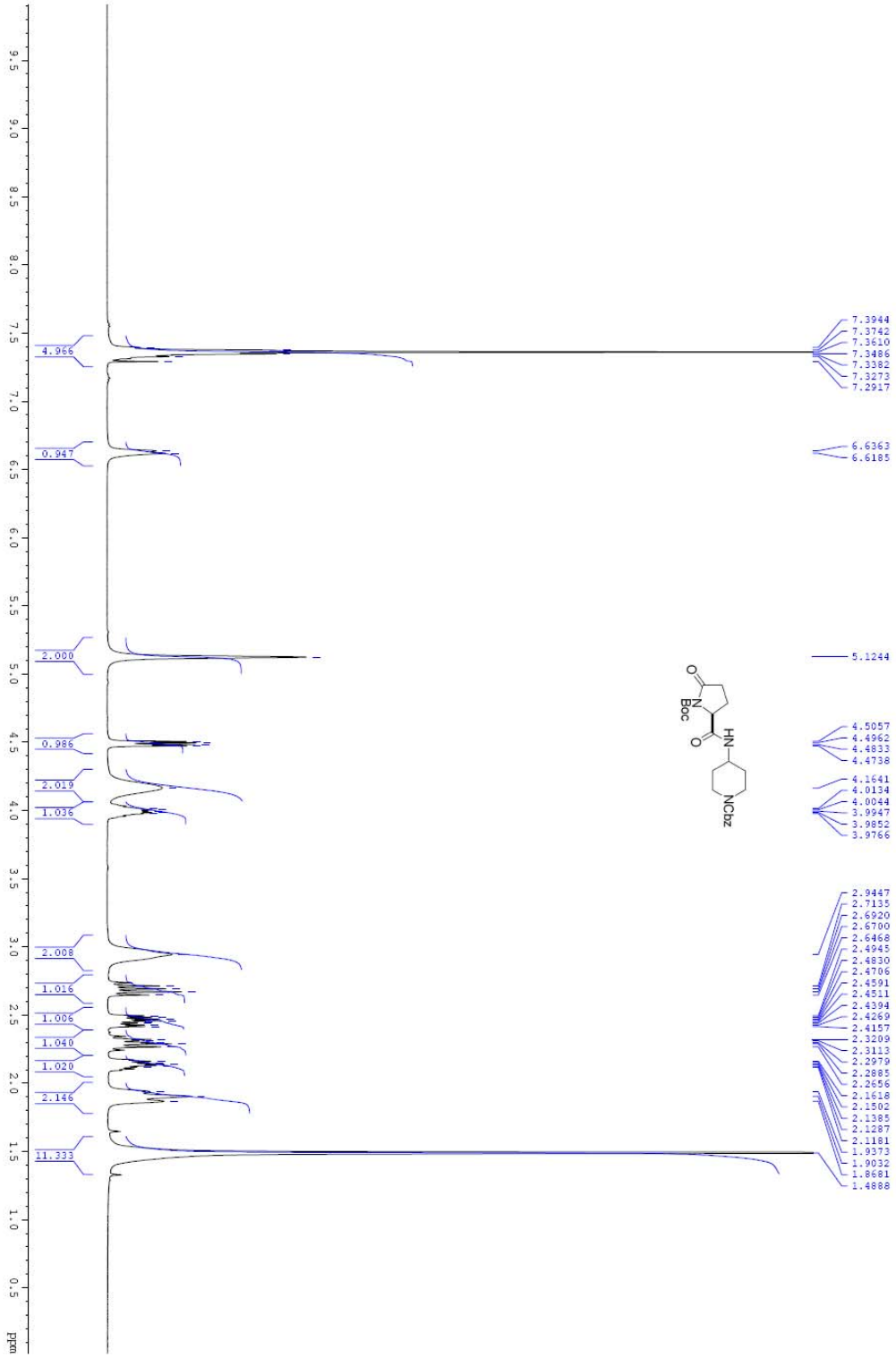
Preparation of (2S,5R)-7-Oxo-N-piperidin-4-yl-6-(sulfooxy)-1,6-diazabicyclo[3.2.1]octane-2-carboxamide (1)

tert-Butyl 4-({[(2S,5R)-6-hydroxy-7-oxo-1,6-diazabicyclo[3.2.1]oct-2-yl] carbonyl}amino)piperidine-1-carboxylate, (76 g, 196 mmol), THF (760 mL), 2-picoline (38.8 mL, 392 mL) and pyridine-SO_3 complex (109 g, 686 mmol) were charged to a flask under nitrogen. No exotherm was observed. The heterogeneous mixture was allowed to stir overnight (~15 h). DCM (312 mL) was then added and the mixture was concentrated by vacuum distillation, removing ~450 mL of THF/DCM. Additional DCM (600 mL) was added. The flask was placed in an ice bath and 0.5 M K_2HPO_4 (607 mL, 304 mmol) was added over 4 minutes. Bu_4NHSO_4 (73.2 g, 216 mmol) was then added over 10 minutes followed by additional water (4 L). The biphasic mixture was stirred for 30 minutes, after which the layers were separated (aqueous pH 3.5). The organic layer was returned to the separatory funnel and washed with water (150 mL); pH was 4.5. The mixture was flushed with DCM and solvent-switched to 2,2,2-trifluoroethanol by vacuum distillation (810 mL final volume TFE) and used as is in the next step. Water content by Karl-Fisher titration was 900 ppm.

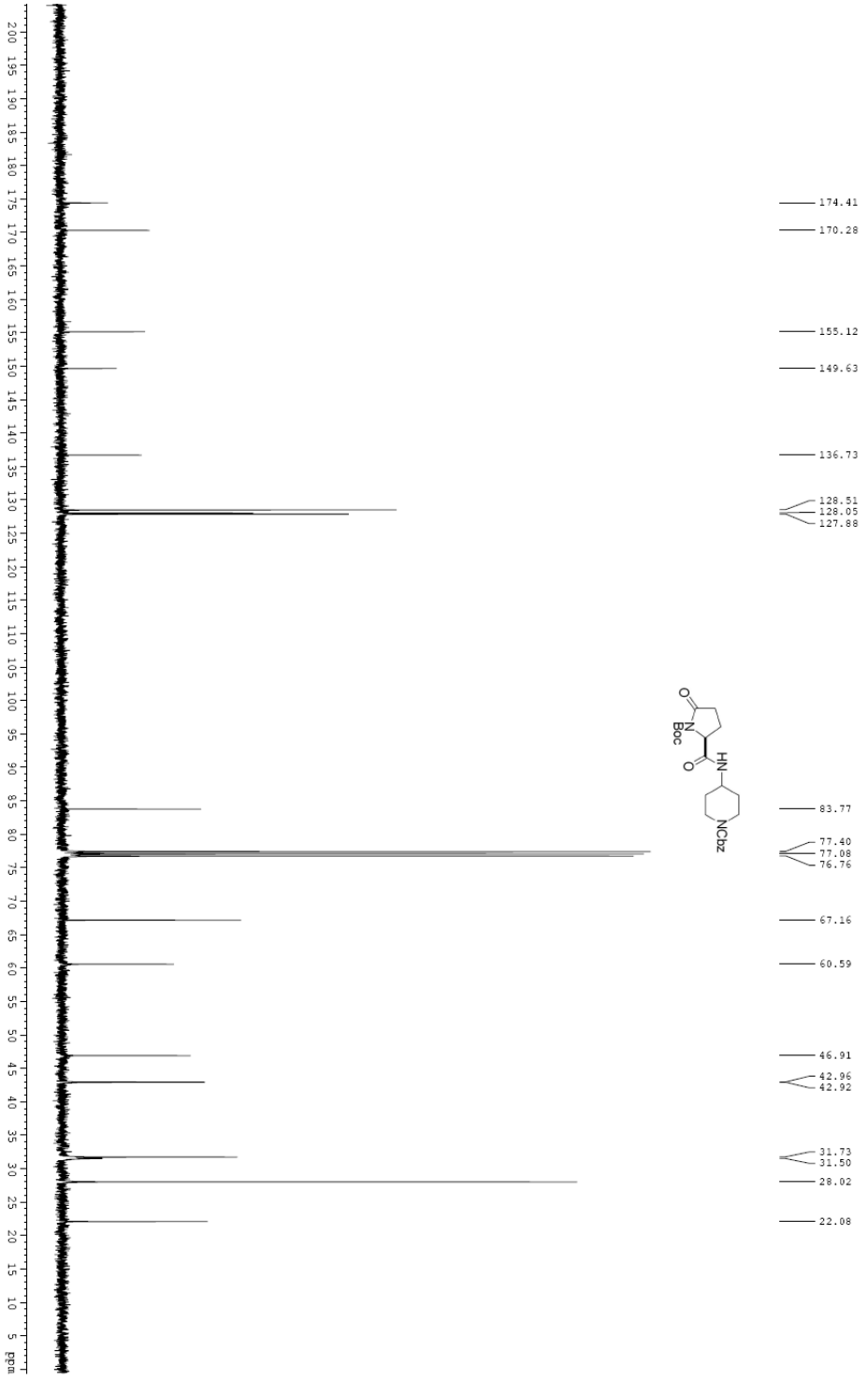
The solution of $Bu_4N^+ {}^-OSO_3$ salt in TFE (810 mL) was used with an assumed yield of 100% (135 g, 196 mmol). The reaction mixture was cooled in an ice bath, and $HBF_4 \cdot Et_2O$ (37.8 mL, 274 mmol) was added via addition funnel over 5 minutes between 18°C and 22°C. The resulting white slurry was allowed to stir overnight (12 hours). TFE (~500 mL) was removed by vacuum distillation. DCM (800 mL) was then added. To a 2-L flask was charged pyrogen-free water (814 mL) and $NaHCO_3$ (6.57 g, 78 mmol), and the solution was cooled to 13°C. The reaction mixture was transferred by vacuum into the flask with temperature of 11-13°C. The reaction flask was rinsed with additional and the suspension also transferred to the extractor. The reaction mixture was warmed to 18.5 °C and de-pyrogenated water (200 mL) was added to solubilize all the solids. The final pH was 5. The organic layer was separated, and the aqueous layer was washed with DCM (2 x 540 mL).

The aqueous layer was charged to a clean flask. The solution was concentrated by vacuum distillation followed by azeotropic distillation with IPA. At this time, ^{1}H NMR analysis of the IPA:H_2O ratio indicated the presence of 415 mL of water and additional IPA was added to a total of 1.25 mL. The white crystalline solid was filtered and washed with 7:1 IPA:de-pyrogenated water (400 mL) and dried under vacuum and nitrogen at room temperature to afford the title product in the form of a crystalline channel hydrate, 1.5 wt% water. (Yield = 48.9 g, 68%). ^{1}H NMR (400 MHz, DMSO-d_6): δ 8.30 (br s, 2H), 8.20 (d, *J* = 7.8 Hz, 1H), 4.01 (s, 1H), 3.97-3.85 (m, 1H), 3.75 (d, *J* = 6.5 Hz, 1H), 3.28 (dd, *J* = 12.9, 2.5 Hz, 2H), 3.05-2.93 (m, 4H), 2.08-1.97 (m, 1H), 1.95-1.79 (m, 3H), 1.73-1.59 (m, 4H); ^{13}C NMR (DMSO-d_6, 100 MHz) δ 169.7, 166.9, 59.8, 58.3, 46.9, 44.3, 42.9, 28.5, 28.3, 20.8, 18.9; HRMS calculated for $C_{12}H_{20}N_4O_6S$ (M+H): 349.1182, found: 349.1183. $[\alpha]_D^{25}$ = -23.3 (c = 1.0, $CHCl_3$).

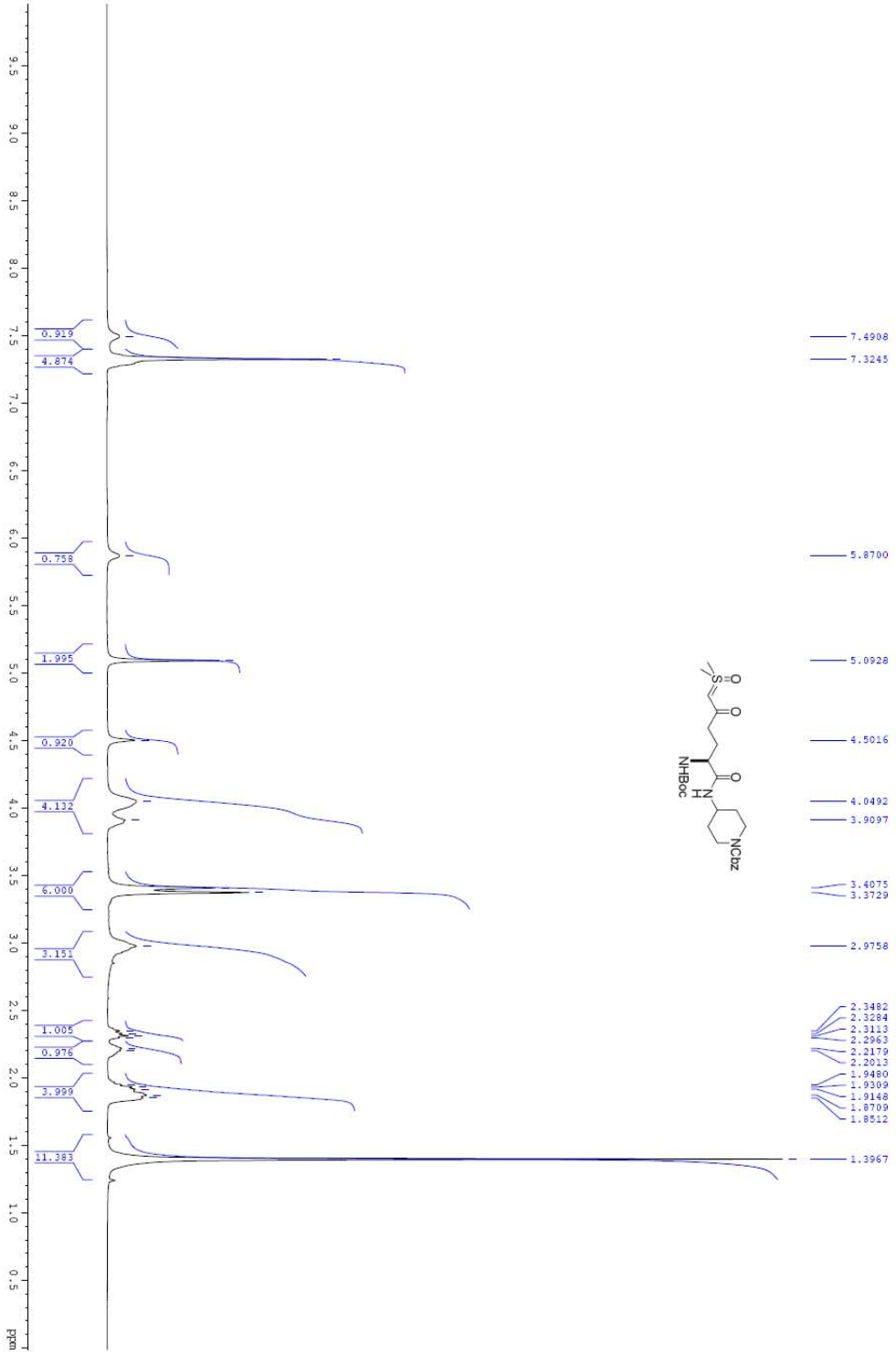
Benzyl 4-{[1-(tert-butoxycarbonyl)-5-oxo-L-prolyl]amino}piperidine-carboxylate (7). ^{1}H NMR (400 MHz).



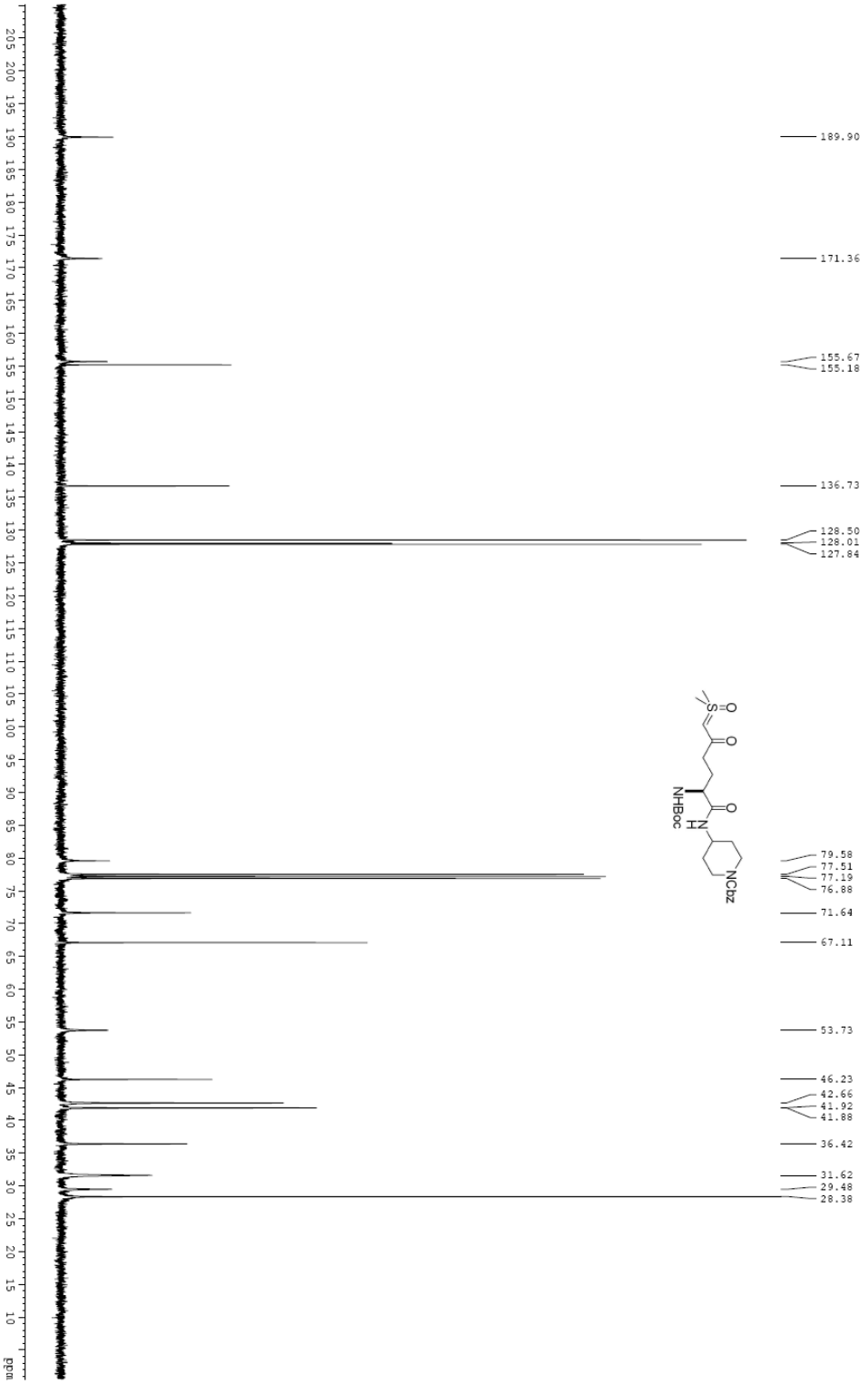
Benzyl 4-{[1-(tert-butoxycarbonyl)-5-oxo-L-prolyl]amino}piperidine-carboxylate (7). ^{13}C NMR (100 MHz).



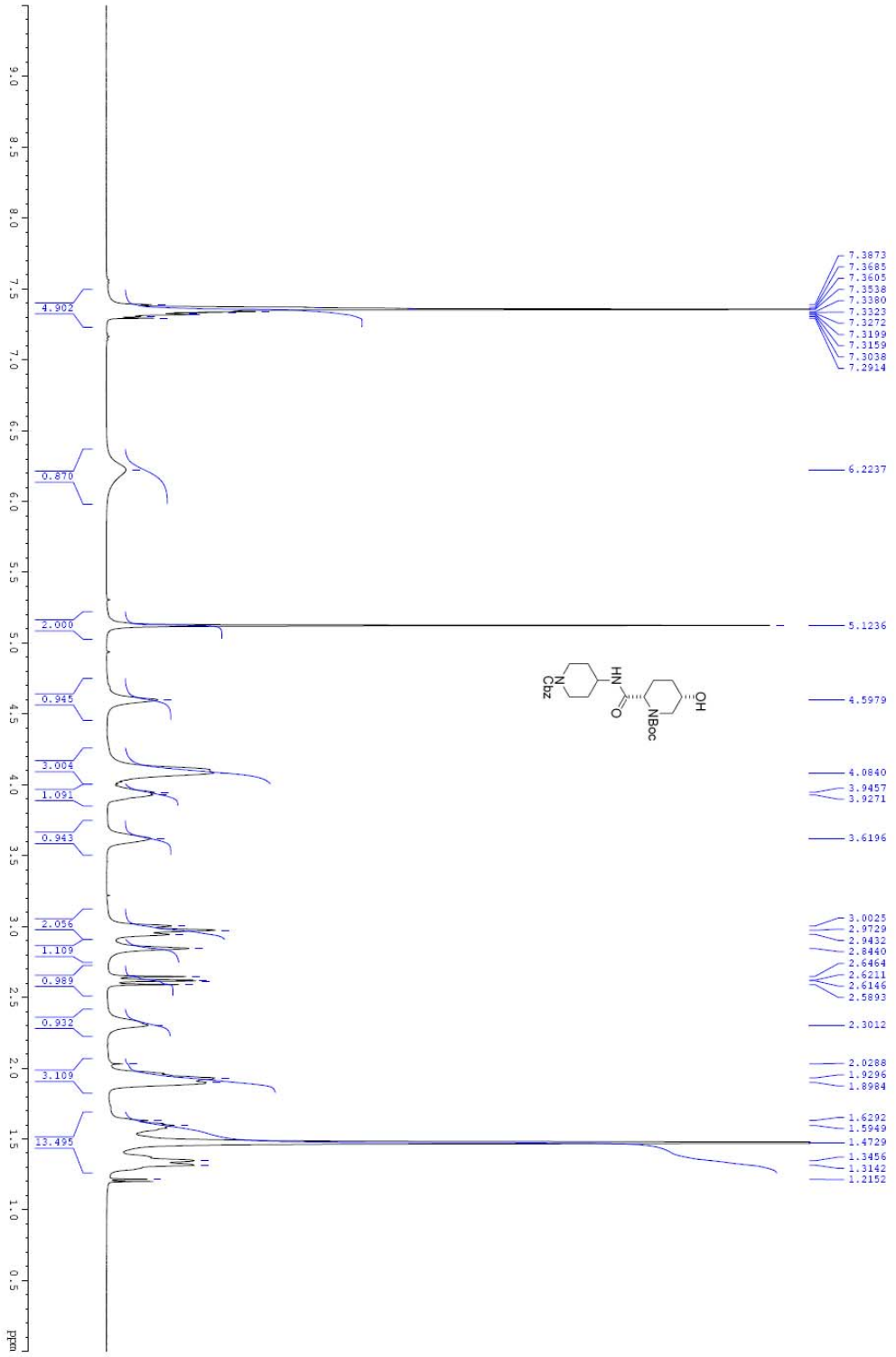
Benzyl 4-({N-(tert-butoxycarbonyl)-6-[dimethyl(oxido)-λ ^{4}-sulfanylidene]-5-oxo-L-norleucyl}amino)piperidine-1-carboxylate (8). ^{1}H NMR (400 MHz).



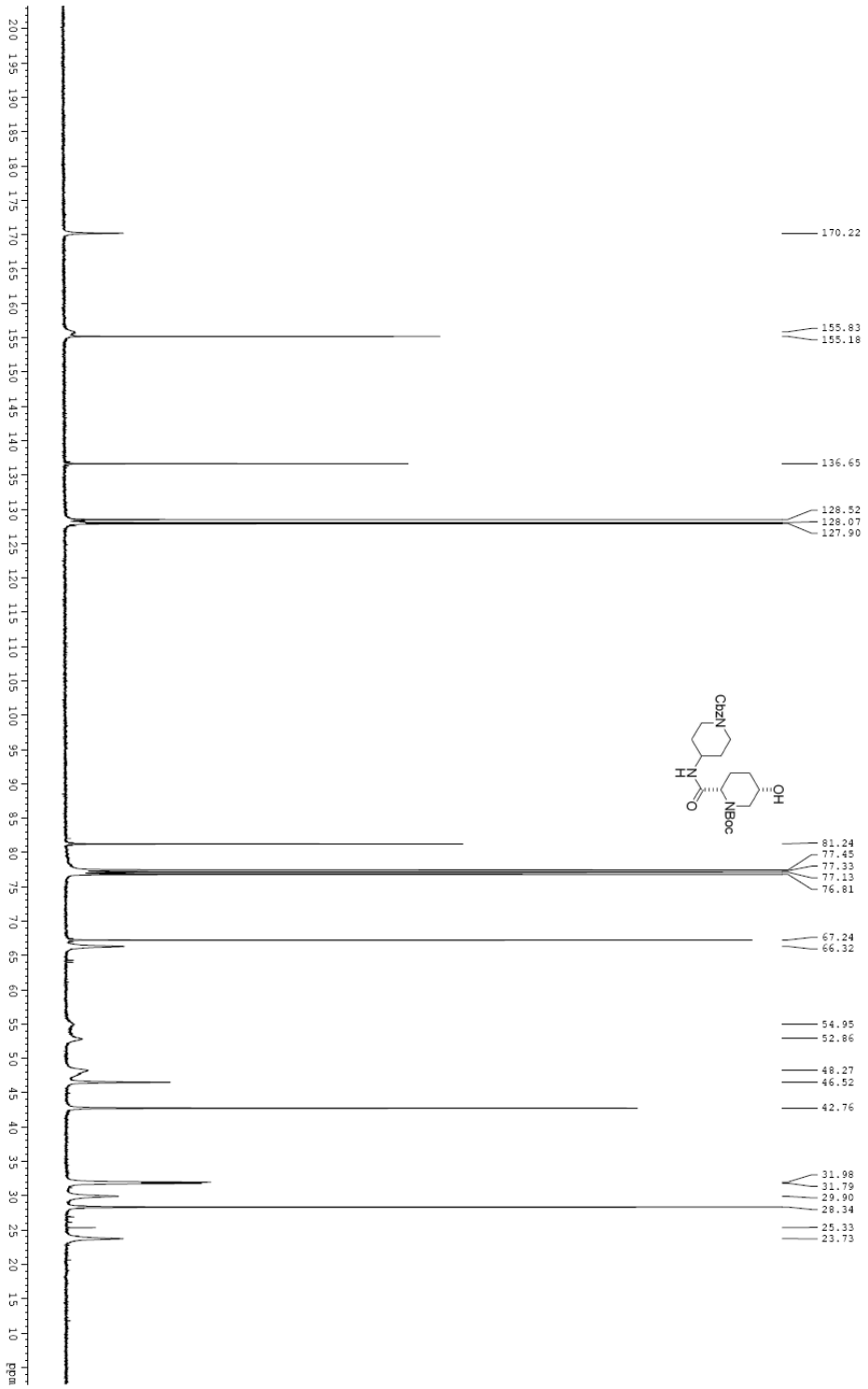
Benzyl 4-({N-(tert-butoxycarbonyl)-6-[dimethyl(oxido)-λ ^{4}-sulfanylidene]-5-oxo-L-norleucyl}amino)piperidine-1-carboxylate (8). ^{13}C NMR (100 MHz)



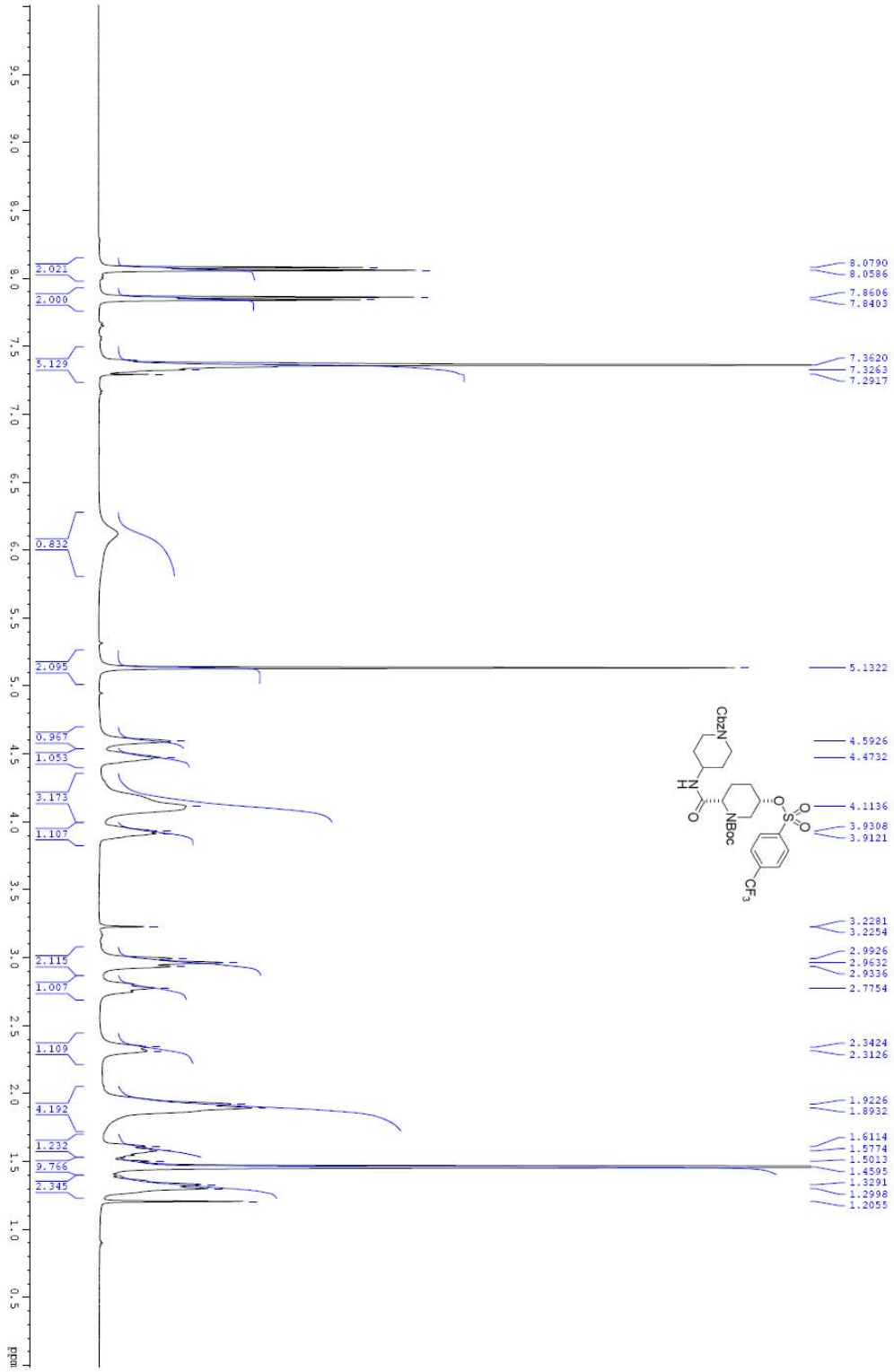
tert-butyl (2S)-2-[({1-[(benzyloxy)carbonyl]piperidin-4-yl}amino)carbonyl]-5-oxopiperidine-1-carboxylate (10). ^{1}H NMR (400 MHz).



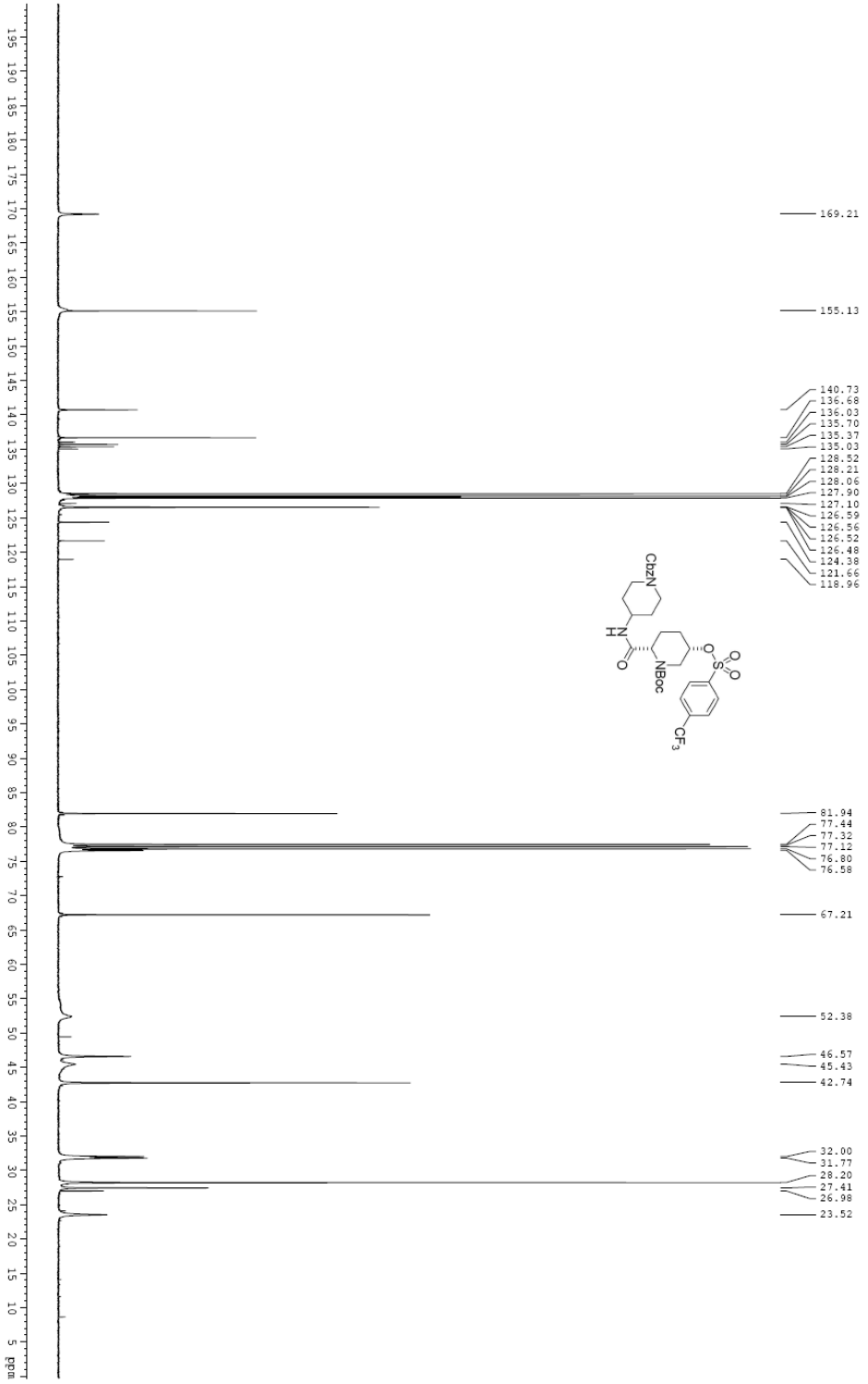
tert-butyl (2S)-2-[({1-[(benzyloxy)carbonyl]piperidin-4-yl}amino)carbonyl]-5-oxopiperidine-1-carboxylate (10). ^{13}C NMR (100 MHz).



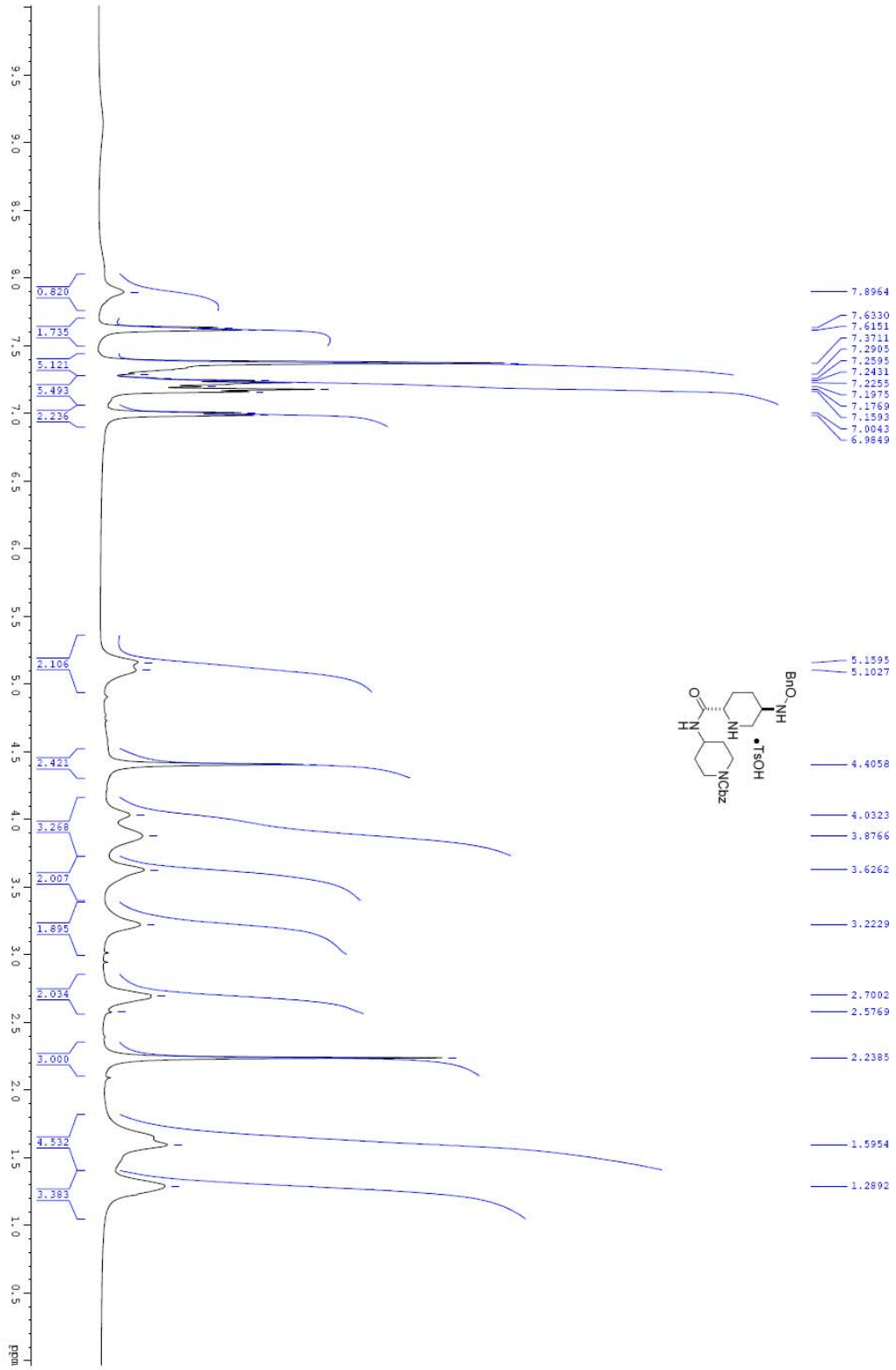
tert-butyl (2S,5S)-2-[({1-[(benzyloxy)carbonyl]piperidin-4-yl}amino)carbonyl]-5-({[4-(trifluoromethyl)phenyl]sulfonyl}oxy)piperidine-1-carboxylate (11). ^{1}H NMR (400 MHz).



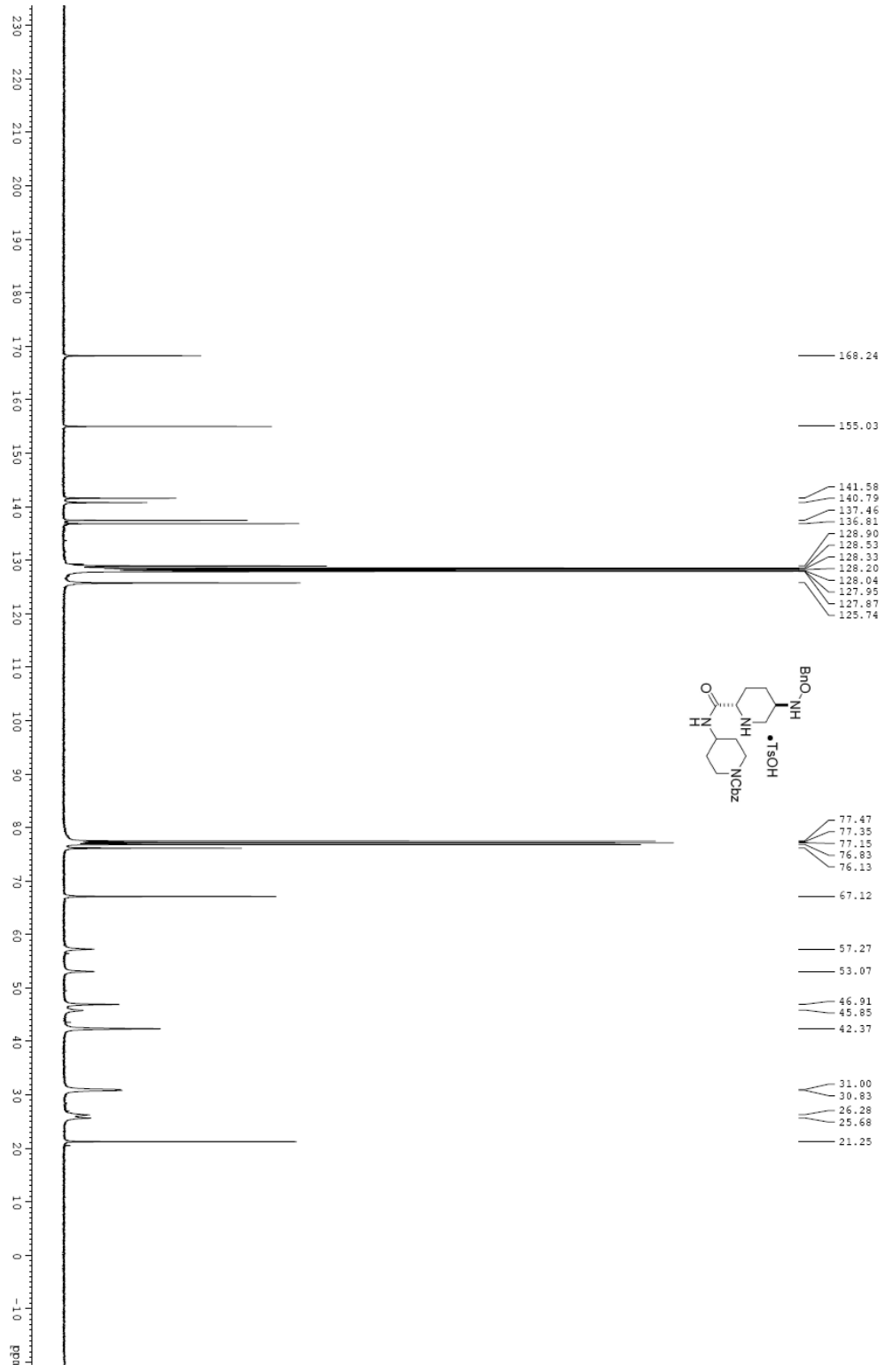
tert-butyl (2S,5S)-2-[({1-[(benzyloxy)carbonyl]piperidin-4-yl}amino)carbonyl]-5-({[4-(trifluoromethyl)phenyl]sulfonyl}oxy)piperidine-1-carboxylate (11). ^{13}C NMR (100 MHz).



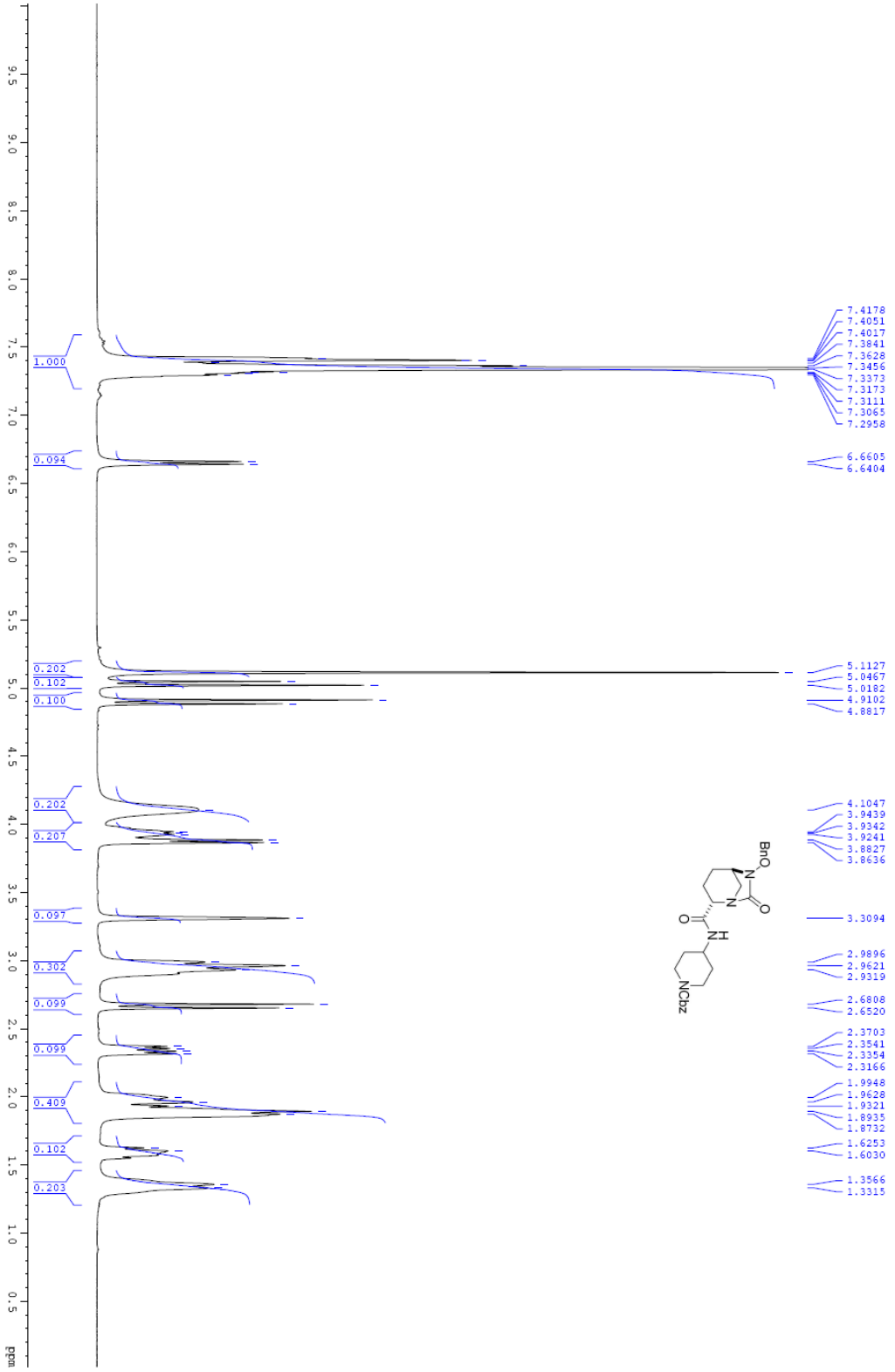
Benzyl 4-[({(2S,5R)-5-[(benzyloxy)amino]piperidin-2-yl}carbonyl)amino]piperidine-1-carboxylate (12). ^{1}H NMR (400 MHz).



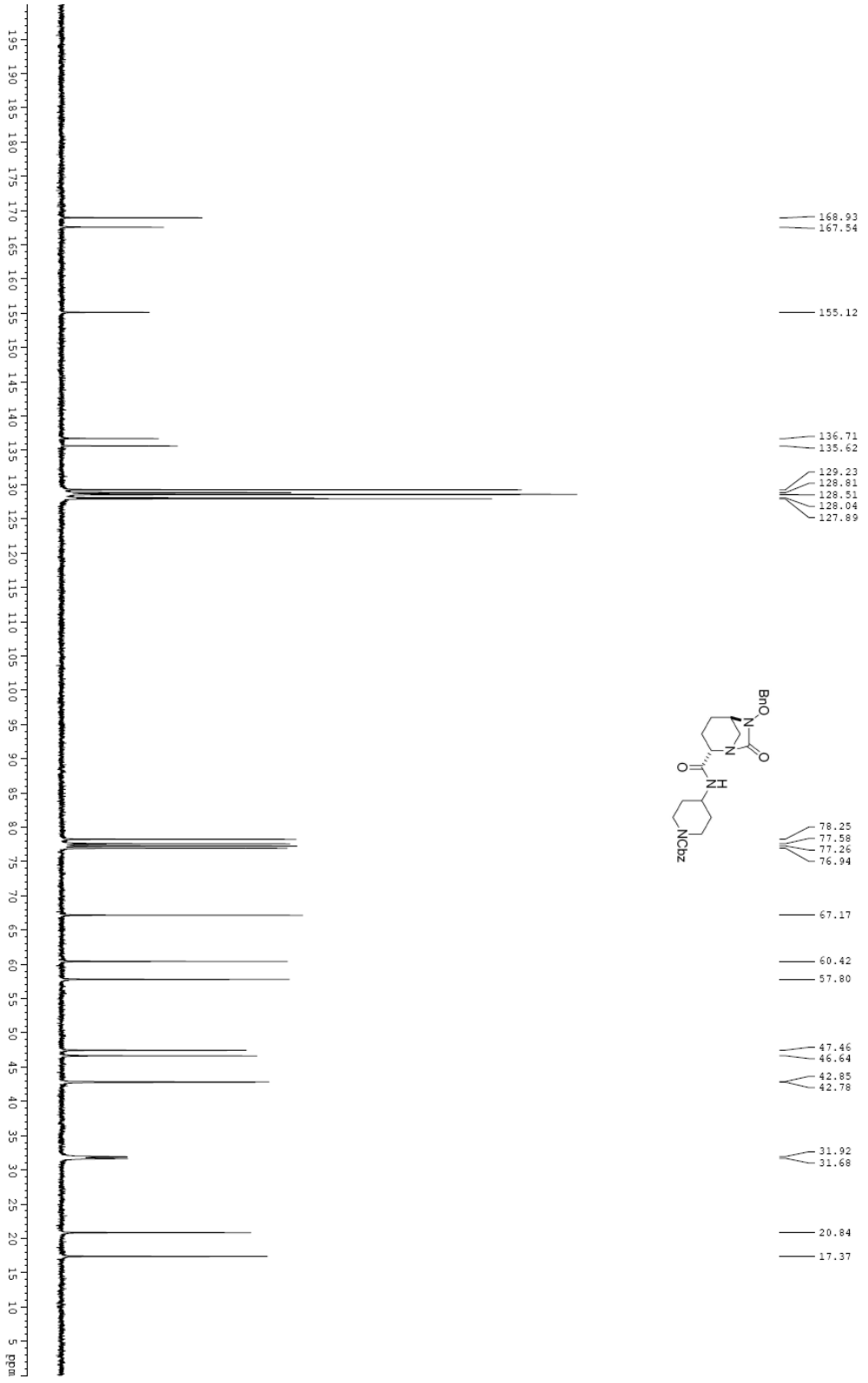
Benzyl 4-[({(2S,5R)-5-[(benzyloxy)amino]piperidin-2-yl}carbonyl)amino]piperidine-1-carboxylate (12). ^{13}C NMR (100 MHz).



Benzyl 4-({[(2S,5R)-6-(benzyloxy)-7-oxo-1,6-diazabicyclo[3.2.1]oct-2-yl]carbonyl}amino)piperidine-1-carboxylate (14). ^{1}H NMR (400 MHz).

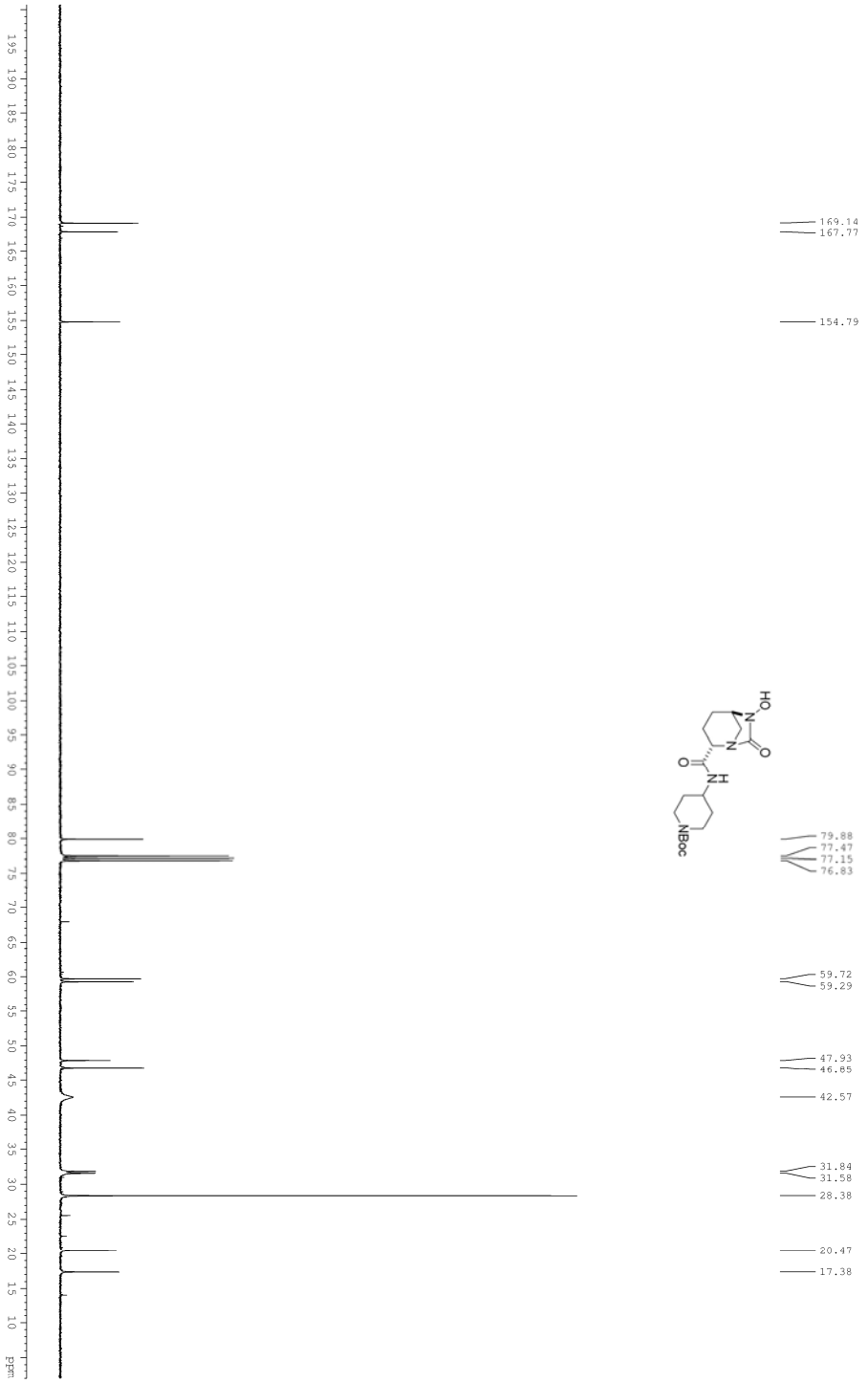


Benzyl 4-({[(2S,5R)-6-(benzyloxy)-7-oxo-1,6-diazabicyclo[3.2.1]oct-2-yl]carbonyl}amino)piperidine-1-carboxylate (14). ^{13}C NMR (100 MHz).

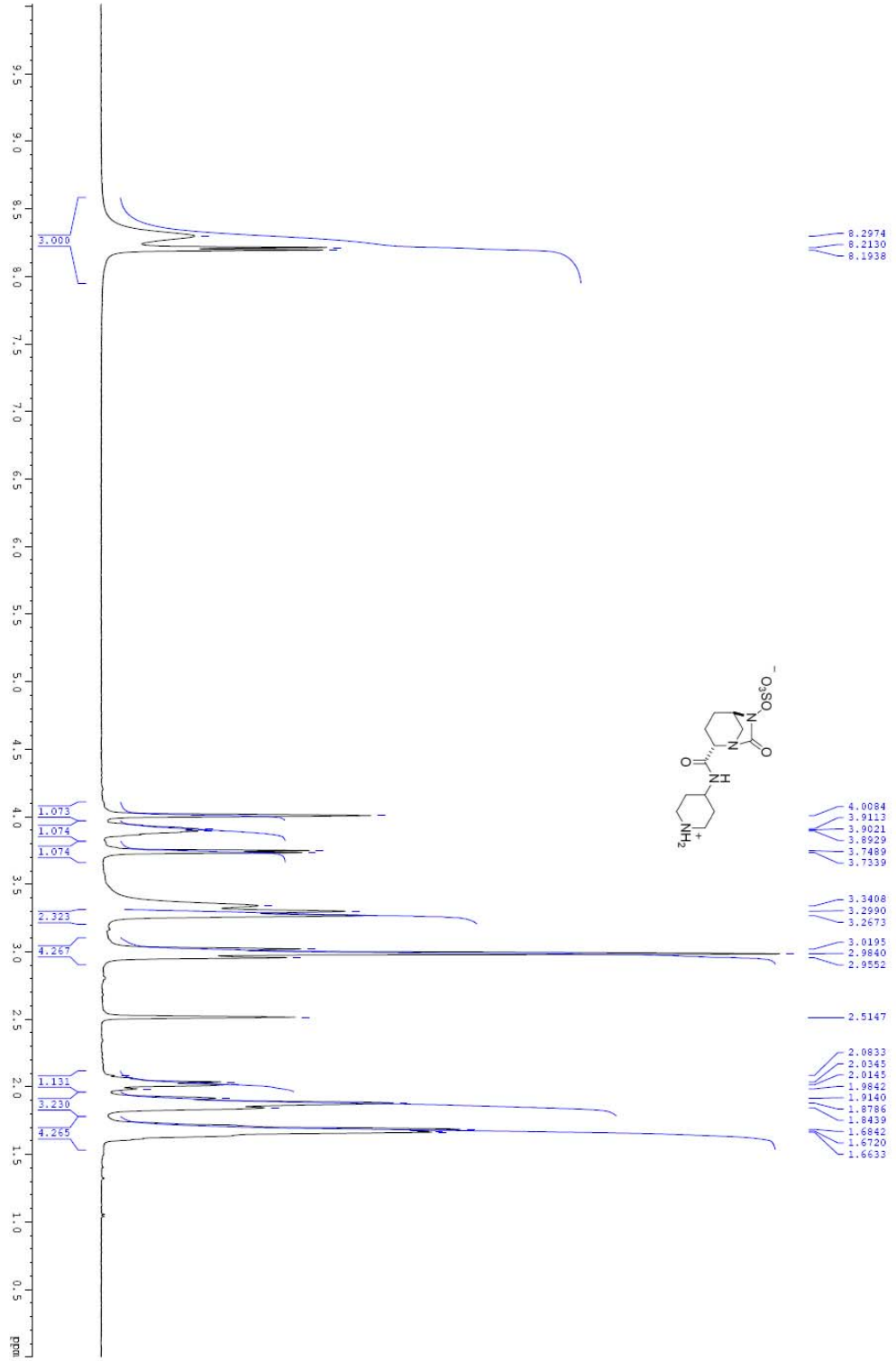


tert-Butyl 4-({[(2S,5R)-6-hydroxy-7-oxo-1,6-diazabicyclo[3.2.1]oct-2-yl]carbonyl}amino)piperidine-1-carboxylate (15). ^{1}H NMR (400 MHz).

tert-Butyl 4-({[(2S,5R)-6-hydroxy-7-oxo-1,6-diazabicyclo[3.2.1]oct-2-yl]carbonyl}amino)piperidine-1-carboxylate (15). ^{13}C NMR (100 MHz).



(2S,5R)-7-Oxo-N-piperidin-4-yl-6-(sulfooxy)-1,6-diazabicyclo[3.2.1]octane-2-carboxamide (1). ^{1}H NMR (400 MHz).



(2S,5R)-7-Oxo-N-piperidin-4-yl-6-(sulfooxy)-1,6-diazabicyclo[3.2.1]octane-2-carboxamide (1). ^{13}C NMR (100 MHz).