Supporting Information

Total Synthesis of the Proposed Structure of Characellide B

Yong Wang†, Zhenwei Wang†, Zhe Wang†, Xiaoyu Liu, Yingjun Jiang, Xiaozhen Jiao* and Ping Xie*

State Key Laboratory Bioactive Substance and Function of Natural Medicine, Beijing Key Laboratory of Active Substance Discovery and Drugability Evaluation, Institute of Materia Medica, Peking Union Medical College and Chinese Academy of Medical Sciences, 1 Xiannongtan Street, Beijing, 100050, China

Email: *jiaoxz@imm.ac.cn
*xp@imm.ac.cn

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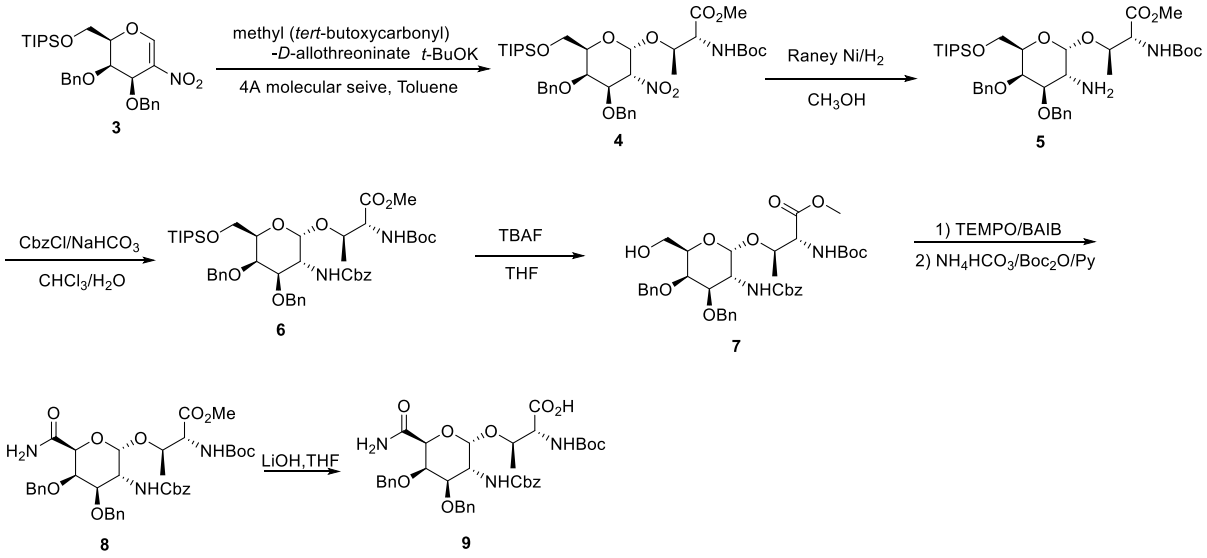
1. General Methods

All the solvents and chemicals were purchased from commercial sources: Sigma-Aldrich Chemical Co., Arcos Chemical Co., and J&K Chemical Co. with the purity of more than 95%. Flash column chromatography was performed on Biotage Isolera one. Column chromatography was carried out on silica gel (100-200 mesh). Thin-layer chromatography was performed using commercially available HSGF 254 pre-coated plates. ^{1}H NMR and ^{13}C NMR were recorded on Mercury 400, Bruker AV500, AV600 spectrometer. Coupling constants are given in Hz and chemical shifts are expressed as δ values in ppm. The following multiplicity abbreviations are used: (s) singlet, (d) doublet, (t) triplet, (q) quartet, (m) multiplet. IR spectra were recorded on a Thermo Nicolet 5700 FT-IR microscope Centaurμs spectrophotometer. ESI-HRMS data were measured on a LC-MS system which was performed on a ThermoFisher Exactive Plus mass spectrometer (ThermoFisher Scientific, Bremen, Germany) equipped with a ThermoFisher Accela HPLC system (ThermoFisher Scientific, Bremen, Germany). Optical rotations were measured with a PerkinElmer Polarimeter 341LC.

2. Experimental Procedures and Spectral Data of Products

2.1 Synthesis of Segment I

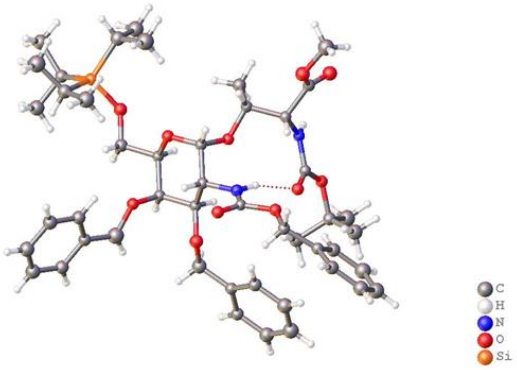


Methyl O-((2S,3R,4R,5R,6R)-4,5-bis(benzyloxy)-3-nitro-6-(((triisopropylsilyl)oxy) methyl)tetrahydro-2H- pyran-2-yl)-N-(tert-butoxycarbonyl)-D-allothreoninate (4) To a solution of compound **3** (200 mg, 0.38 mmol) and methyl (tert-butoxycarbonyl)-D-*allo*-threoninate (177 mg, 0.76 mmol) in dry toluene, 4A molecular sieve (263 mg) was added under argon atmosphere and stirred for 1 h. Then *t*-BuOK (76 μL, 1M in THF) was added dropwise and the mixture was stirred for 2.5 h. Subsequently, the reaction mixture was acidified by HOAc (76 μL) and filtered. The filtrate was diluted with EtOAc, washed with a saturated $NaHCO_3$ solution, H_2O, brine, dried over Na_2SO_4, filtered and concentrated *in vacuo*. The residue was purified by column chromatography on silica gel (petroleum ether/EtOAc=40:1→10:1) to give compound **4** (211 mg, 73%, α/β> 20:1, determined by NMR) as a colorless oil. $[\alpha]_D^{16}$ +7.4 (*c* 0.9, $CHCl_3$). IR (film)ν_{max} cm^{-1}: 3431, 3360, 3032, 2943, 2867,

1746, 1718, 1558, 1500, 1458, 1367, 1154, 1109, 1056, 883, 789, 748, 697. ^{1}H NMR (400 MHz, $CDCl_3$): δ 7.28-7.17 (m, 10H), 5.32 (d, J = 4.0 Hz, 1H), 5.11 (d, J = 7.6 Hz, 1H), 4.88 (dd, J = 4.4, 10.4 Hz, 1H), 4.75 (d, J = 10.8 Hz, 1H), 4.66 (q, J = 10.8 Hz, 2H), 4.45 (d, J = 11.2 Hz, 1H), 4.33 (dd, J = 3.2, 10.8 Hz, 1H), 4.22 (m, 1H), 3.91 (m, 2H), 3.77 (t, J = 6.4Hz ,1H), 3.70 (s, 3H), 3.64 (m, 2H), 1.38 (s, 9H), 1.26 (d, J = 6.4Hz, 3H), 0.97 (m, 21H); ^{13}C NMR (100 MHz, $CDCl_3$): δ 169.7, 155.0, 138.0, 137.4, 128.5, 128.3, 128.2, 128.1, 128.0, 127.8, 97.3, 84.2, 80.2, 77.3, 75.1, 75.0, 73.1, 71.9, 61.8, 57.9, 52.4, 28.3, 18.3, 18.0, 11.8; HRMS (ESI) m/z: $[M + H]^+$ Calcd for $C_{39}H_{61}O_{11}N_2Si$ 761.4039; Found: 761.4017.

methyl O-((2S,3R,4R,5R,6R)-3-amino-4,5-bis(benzyloxy)-6-(((triisopropylsilyl)oxy) methyl)tetrahydro-2H- pyran-2-yl)-N-(tert-butoxycarbonyl)-D-allothreoninate (5) A solution of compound **4** (500 mg, 0.66 mmol) in MeOH (10 mL) containing Raney Ni (50 mg) was stirred overnight at room temperature under an atmosphere of H_2. The suspension was then filtered, the combined filtrate was concentrated *in vacuo*, and the residue was purified by flash column chromatography on silica gel (DCM/MeOH=10:1) to give compound **5** (417 mg, 87%) as a colorless oil. $[\alpha]_D^{16}$ +17.9 (*c* 0.8, $CHCl_3$). IR (film)ν_{max} cm^{-1}: 3256, 3030, 2939, 2867, 1742, 1708, 1602, 1513, 1456, 1391, 1366, 1163, 1097, 1059, 1029, 883, 789, 735, 697. ^{1}H NMR (600 MHz, $CDCl_3$): δ 7.36-7.24 (m, 10H), 6.14 (d, J= 9.0Hz, 1H), 4.98 (d, J = 3.6 Hz, 1H), 4.85 (d, J = 11.4 Hz, 1H), 4.71 (d, J = 11.4 Hz, 1H), 4.63 (d, J = 11.4 Hz, 1H), 4.53 (d, J = 11.4 Hz, 1H), 4.42 (dd, J = 2.4, 9.0 Hz, 1H), 3.98 (m, 2H), 3.80 (t, J = 6.6 Hz, 1H), 3.74 (m, 2H), 3.71 (s, 3H), 3.42 (dd, J = 2.4, 10.8 Hz, 1H), 3.28 (dd, J = 3.6, 10.8 Hz, 1H), 1.43 (s, 9H), 1.27 (d, J = 6.6 Hz, 3H), 1.13-1.04 (m, 21H); ^{13}C NMR (150 MHz, $CDCl_3$): δ 170.7, 155.5, 138.7, 138.1, 128.5, 128.2, 128.0, 127.8, 127.7, 127.5, 102.3, 81.2, 79.8, 74.5, 72.5, 72.1, 71.8, 62.4, 58.3, 52.1, 51.5, 28.3, 18.4, 18.0, 11.8; HRMS (ESI) m/z: $[M + H]^+$ Calcd for $C_{39}H_{63}O_9N_2Si$ 731.4297; Found: 731.4299.

methyl O-((2S,3R,4R,5R,6R)-4,5-bis(benzyloxy)-3-(((benzyloxy)carbonyl)amino)-6-(((triisopropylsilyl)oxy) methyl)tetrahydro-2H-pyran-2-yl)-N-(tert-butoxycarbonyl)- D-allothreoninate (6) To a solution of amine **5** (335 mg, 0.46 mmol) in $CHCl_3$/H_2O (5 mL/10 mL) was added $NaHCO_3$ (118 mg, 1.41 mmol) and benzyl chloroformate (160 mg, 0.94 mmol). The reaction mixture was stirred at room temperature for 2 h and diluted with CH_2Cl_2. The organic phase was washed with H_2O, brine and dried over Na_2SO_4. After filtering and concentrated, the residue was purified by flash column chromatography on silica gel (petroleum ether/EtOAc=5:1) to give compound **6** as a white solid (392mg, 99%). m.p.58-61 ^{o}C; $[\alpha]_D^{16}$ +10.3 (*c* 0.7, $CHCl_3$). IR (film)ν_{max} cm^{-1}: 3842, 3284, 2990, 2891, 2864, 1740, 1715, 1689, 1553, 1529, 1455, 1356, 1257, 1164, 1139, 1096, 1083, 1064, 1029, 883, 731, 695. ^{1}H NMR (600 MHz, $CDCl_3$): δ 7.38-7.22 (m, 15H), 5.91 (d, J = 9.6 Hz, 1H), 5.29 (m, 2H), 5.06 (d, J = 11.4 Hz, 1H), 5.0 (d, J = 3.0 Hz, 1H), 4.98 (d, J = 11.4 Hz, 1H), 4.63 (t, J = 12.0 Hz, 1H), 4.58 (m, 2H), 4.50 (m, 2H), 4.03 (m,1H), 3.96 (m, 1H), 3.78-3.68 (m, 6H), 3.54 (d, J = 10.8 Hz, 1H), 1.40 (s, 9H), 1.18 (d, J = 6.0 Hz, 3H), 1.06 (m, 21H). ^{13}C NMR (150 MHz, $CDCl_3$): δ 170.5, 156.6, 155.4, 138.7, 138.4, 137.0, 128.30,128.26, 128.2, 128.1, 127.6, 127.4, 127.2, 100.5, 80.3, 78.7, 74.4, 73.1, 72.3, 66.3, 62.6, 57.9, 52.5, 51.3, 28.2, 17.9, 17.2, 11.8; HRMS (ESI) m/z: $[M + H]^+$ Calcd for $C_{47}H_{69}O_{11}N_2Si$ 865.4665; Found: 865.4606.



X-Ray structure of Compound **6** (CDCC 1988311) (displacement ellipsoids are drawn at 50% probability level)

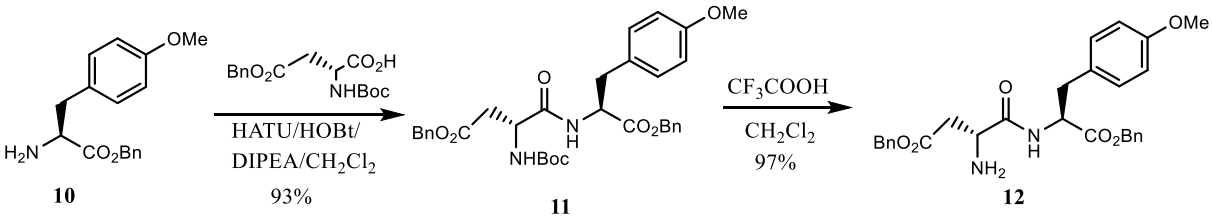
methyl O-((2S,3R,4R,5R,6R)-4,5-bis(benzyloxy)-3-(((benzyloxy)carbonyl)amino)-6-(hydroxymethyl) tetrahydro-2H-pyran-2-yl)-N-(tert-butoxycarbonyl)-D-allothreoninate (7) To a solution of compound **6** (350 mg, 0.41 mmol) in dry THF (5 mL), tetrabutylammonium fluoride (TBAF, 192 mg, 0.61 mmol) was added at 0 ºC. Then the reaction mixture was stirred at room temperature for 2 h. The solvent was removed under reduced pressure. The residue was dissolved in CH_2Cl_2, and washed with a saturated $NaHCO_3$ solution, H_2O, brine, and dried over Na_2SO_4. After filtering and concentrated, the residue was purified by column chromatography on silica gel (CH_2Cl_2/MeOH=50:1) to provide compound **7** (220 mg, 77%) as a white solid. m.p.140-142 ºC; $[\alpha]_D^{21}$ +52.7 (*c* 1.22, $CHCl_3$). IR (film)ν_{max} cm^{-1}: 3344, 3088, 3063, 3029, 2977, 2950, 2931, 2874, 1747, 1696, 1529, 1498, 1453, 1392, 1369, 1350, 1316, 1275, 1238, 1170, 1138, 1059, 1027, 979, 942, 902, 874, 737, 696. ^{1}H NMR (600 MHz, $CDCl_3$): δ 7.39-7.26 (m, 15H), 6.05 (d, *J* = 9.6 Hz, 1H), 5.33 (d, *J* = 8.4 Hz, 1H), 5.29 (d, *J* = 12.6 Hz, 1H), 5.08-4.99 (m, 3H), 4.67-4.51 (m, 5H), 4.06 (br., 1H), 3.89 (br., 1H), 3.80-3.73 (m, 2H), 3.69 (s, 3H), 3.55 (m, 2H), 1.76 (m, 1H), 1.41 (s, 9H), 1.16 (d, *J* = 6.0Hz, 3H); ^{1}H NMR (600 MHz, $CDCl_3$+D_2O): δ 7.39-7.26 (m, 15H), 6.06 (d, *J* = 9.6 Hz, 1H), 5.35 (d, *J* = 7.8 Hz, 1H), 5.28 (d, *J* = 12.6 Hz, 1H), 5.08-4.99 (m, 3H), 4.67-4.53 (m, 5H), 4.06 (br., 1H), 3.89 (br., 1H), 3.79-3.72 (m, 2H), 3.69 (s, 3H), 3.56-3.51 (m, 2H), 1.41 (s, 9H), 1.16 (d, *J* = 5.4 Hz, 3H); ^{13}C NMR (150 MHz, $CDCl_3$): δ 170.4, 156.6, 155.5, 138.1, 137.0, 128.7, 128.5, 128.4, 128.3, 127.9, 127.6, 127.5, 127.2, 100.6, 80.9, 80.3, 79.0, 78.7, 77.9, 76.9, 74.8, 74.1, 73.6, 73.0, 72.6, 71.2, 66.7, 66.4, 62.5, 57.9, 52.6, 51.2, 28.2, 17.1; HRMS (ESI) m/z: $[M + H]^+$ Calcd for $C_{38}H_{49}O_{11}N_2$ 709.3331; Found: 709.3324.

methyl O-((2S,3R,4R,5R,6S)-4,5-bis(benzyloxy)-3-(((benzyloxy)carbonyl)amino)-6-carbamoyltetrahydro- 2H-pyran-2-yl)-N-(tert-butoxycarbonyl)-D-allothreoninate (8) To a solution of compound **7** (560 mg, 0.79 mmol) in CH_2Cl_2/H_2O (10 mL/5 mL), 2,2,6,6-tetramethylpiperidinooxy (25 mg, 0.16 mmol) and (diacetoxyiodo)benzene (640 mg, 1.99 mmol) was added under vortex and continued stirring for 3 h at room temperature. A saturated $Na_2S_2O_3$ solution was added to the mixture and separated via separatory funnel. The inorganic phase was extracted by CH_2Cl_2 (3 mL×3), combined organic phase was washed with a saturated $Na_2S_2O_3$ solution, H_2O, brine, and dried over Na_2SO_4. After filtering and concentrated, the residue was purified by column chromatography on silica gel (CH_2Cl_2/MeOH=50:1) to give

white solid (470 mg, 82%). The solid was immediately dissolved in 1,4-dioxane (10 mL), and tert-butyldicarbonate (213 mg, 0.98 mmol) was added in pyridine (1 mL). The reaction was stirred for 15 min, then ammonium bicarbonate (77.4 mg, 0.98 mmol) was added. The reaction was quenched by with saturated $NaHCO_3$ solution after stirring for 3 h. The mixture was extracted by EtOAc, and the organic phase was washed with a saturated $NaHCO_3$ soulution, a 10%$KHSO_4$ solution, H_2O, brine, and dried over Na_2SO_4. After filtering and concentrated, the residue was purified by column chromatography on silica gel (CH_2Cl_2/EtOAc=5:1) to give compound **8** (416 mg, 73% over two steps) as a white solid. m.p.191-192 ºC; $[\alpha]_D^{19}$ +88.2 (*c* 0.958, $CHCl_3$). IR (film)ν_{max} cm^{-1}: 3347, 3227, 2982, 2934, 1746, 1694, 1643, 1534, 1056, 1018, 790, 736, 697.^{1}H NMR (600 MHz, $CDCl_3$): δ 7.39-7.21 (m, 15H), 6.52 (s, 1H), 5.91 (d, *J* = 9.6 Hz, 1H), 5.62 (d, *J* = 2.4 Hz, 1H), 5.36 (d, *J* = 8.4 Hz, 1H), 5.28 (d, *J* = 12.6 Hz, 1H), 5.10-5.06 (m, 2H), 4.91 (d, *J*=10.8 Hz, 1H), 4.65 (d, *J* = 12.0 Hz, 1H), 4.60 (d, *J* = 10.8 Hz, 1H), 4.51-4.44 (m, 4H), 4.26 (s, 1H), 4.06 (m, 1H), 3.68 (s, 3H), 3.56 (d, *J* = 10.8 Hz, 1H), 1.40 (s, 9H), 1.15 (d, *J* = 6.6 Hz, 3H); ^{13}C NMR (150 MHz, $CDCl_3$): δ 171.3, 170.1, 156.6, 155.4, 138.3, 137.9, 136.9, 128.34, 128.31, 128.13, 128.09, 127.7, 127.6, 127.54, 127.51, 127.2, 100.6, 80.4, 77.6, 77.4, 75.1, 74.5, 72.1, 71.8, 66.5, 57.9, 52.6, 50.8, 28.2, 17.3; HRMS (ESI) m/z: $[M + H]^+$ Calcd for $C_{38}H_{48}O_{11}N_3$ 722.3283; Found: 722.3263.

O-((2S,3R,4R,5R,6S)-4,5-bis(benzyloxy)-3-(((benzyloxy)carbonyl)amino)-6-carbamoyltetrahydro-2H-pyran-2-yl)-N-(tert-butoxycarbonyl)-D-allothreonine (9) To a solution of compound **8** (90 mg,0.13 mmol) in THF (2 mL) was added a LiOH solution (0.1M, 1.88 mL) dropwise at ice bath. The reaction was stirred for 30 min maintaining 0 ºC and for another 1.5 h at room temperature. Then the pH of the reaction mixture was adjusted to 7 with aq.10%$KHSO_4$. After removal of THF, the aqueous phase was adjusted to pH 1 with aq.10%$KHSO_4$, resulting in a white precipitate. After filtering and dried, compound **9** was afforded (70 mg) as a white solid, which was used in the next reaction without further purification.

2.2 Synthesis of Segment II

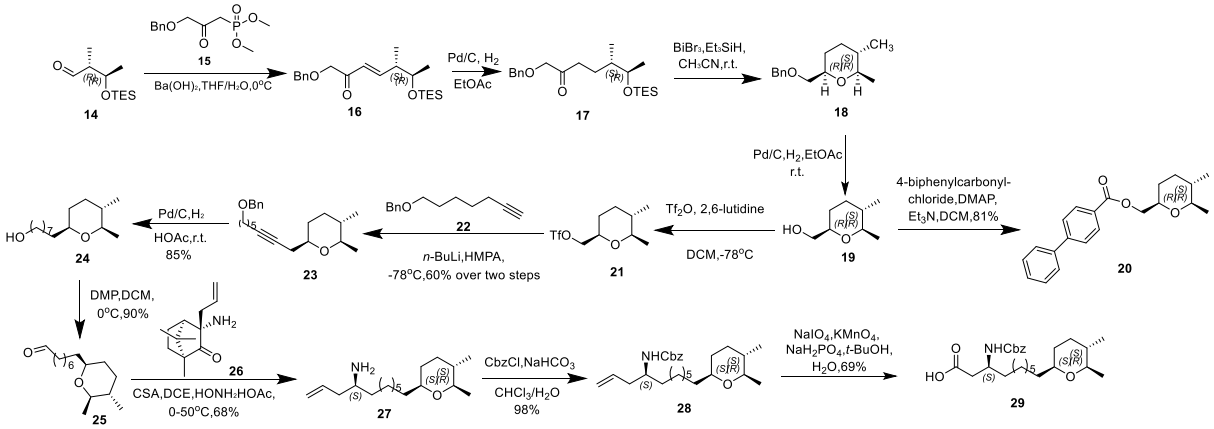


benzyl (R)-4-(((R)-1-(benzyloxy)-3-(4-methoxyphenyl)-1-oxopropan-2-yl)amino)-3-((tert- butoxycarbonyl) amino)-4-oxobutanoate (11) To a solution of compound **10** (710 mg, 2.2 mmol) in dry CH_2Cl_2 (10 mL) was added 1-Hydroxybenzotriazole (297 mg, 2.2 mmol), [dimethylamino(triazolo[4,5-b]pyridin-3-yloxy) methylidene]-dimethylazanium (836 mg, 2.2 mmol) and Boc-L-aspartic acid 4-benzyl ester(570 mg, 2.0 mmol). Then N,N-Diisopropylethylamine (774 mg, 6.0 mmol) was added dropwise at ice bath. The reaction was stirred overnight at room temperature. The reaction mixture was washed with a saturated $NaHCO_3$ solution, H_2O, brine, dried over Na_2SO_4, filtered and concentrated *in vacuo*. The residue was purified by column chromatography on silica gel (petroleum ether/EtOAc=10:1→5:1) to give compound **11** (1.1 g, 93%) as a white solid. m.p. 42-44 ºC; $[\alpha]_D^{24}$ -9.5 (*c* 0.63, $CHCl_3$).^{1}H NMR (400 MHz, $CDCl_3$): δ 7.39-7.28 (m, 10H), 6.98 (d, *J* =

4.8Hz, 1H), 6.90 (d, *J* = 8.8Hz, 2H), 6.72 (d, *J* = 8.8Hz, 2H), 5.58 (d, *J* = 4.8Hz, 1H), 5.11 (m, 4H), 4.82 (m, 1H), 4.54 (br., 1H), 3.73 (s, 3H), 3.06-2.97 (m, 3H), 2.66 (dd, *J* = 6, 17.2 Hz, 1H), 1.41 (s, 9H); ^{13}C NMR (100MHz, $CDCl_3$): δ 171.0, 170.3, 158.7, 135.5, 135.3, 130.4, 128.7, 128.5, 128.4, 127.6, 114.1, 67.3, 66.9, 55.2, 53.6, 37.1, 28.4; HRMS (ESI) m/z: $[M + H]^+$ Calcd for $C_{33}H_{39}O_8N_2$ 591.2701, Found: 591.2710.

Benzyl (R)-3-amino-4-(((R)-1-(benzyloxy)-3-(4-methoxyphenyl)-1-oxopropan-2-yl) amino)-4- oxobutanoate (12) To a solution of compound **11** (0.743 g, 2.6 mmol) in dry CH_2Cl_2 (10 mL) was added trifluoroacetic acid (2 mL) at ice bath and stirred for 3 h at room temperature. Then the reaction mixture was added 2N NaOH to adjust pH to 11 and separated via separatory funnel. The inorganic phase was extracted with CH_2Cl_2, and the combined organic phase was washed by H_2O, brine, dried over Na_2SO_4, filtered and concentrated *in vacuo*. The residue was purified by column chromatography on silica gel (CH_2Cl_2/MeOH=50:1) to give compound **12** (600 mg, 97%) as a white solid. m.p.56-58 ºC; $[\alpha]_D^{20}$ +10.6 (*c* 1.69, $CHCl_3$). IR (film)ν_{max} cm^{-1}: 3395, 3316, 3067, 3034, 2954, 2934, 2904, 2852, 1724, 1650, 1613, 1544, 1512, 1458, 1441, 1381, 1347, 1303, 1280, 1237, 1178, 1041, 992, 956, 900, 866, 823, 749, 698, 583, 552. ^{1}H NMR (400 MHz, $CDCl_3$) δ: 7.84(d, *J* = 8 Hz, 1H), 7.29-7.20 (m, 10H), 6.90 (d, *J* = 8.8 Hz, 2H), 6.68 (d, *J* = 8.4 Hz, 2H), 5.04 (m, 4H), 4.79 (m, 1H), 3.61 (m, 4H), 3.05-2.94 (m, 2H), 2.85 (dd, *J* = 3.6, 16.4Hz, 1H), 2.53 (dd, *J* = 8.4, 16.8Hz, 1H); ^{13}C NMR (150MHz, $CDCl_3$) δ: 172.6, 171.1, 170.8, 158.1, 135.3, 134.8, 129.8, 128.1, 128.04, 128.03, 128.0, 127.95, 127.9, 127.7, 127.64, 127.62, 127.60, 127.4, 113.4, 66.4, 65.8, 54.5, 52.8, 51.4,38.9, 36.4; HRMS (ESI) m/z: $[M + H]^+$ Calcd for $C_{28}H_{31}O_6N_2$ 491.2177, Found: 491.2180.

2.3 Synthesis of Segment III



(5S,6R,E)-1-(benzyloxy)-5-methyl-6-((triethylsilyl)oxy)hept-3-en-2-one (16) To a solution of the aldehyde **14** (5g, 23.11mmol) and the phosphonate **15** (7.55g, 27.73mmol) in THF/H_2O(100 mL: 5 mL), $Ba(OH)_2 \cdot 8H_2O$ (5.47g, 17.33mmol) was added portion-wise at 0℃ and the reaction continued stirring for 2h at the same temperature. Then the reaction mixture was carefully quenched with sat.aq. $NaHCO_3$ solution at 0 ℃ and filtered through Celite. The filtrate was extracted with EtOAc. The combined organic extracts were washed with H_2O, brine, dried (Na_2SO_4), filtered and concentrated in vacuo. Purification of the residue by flash column chromatography on silica gel (petroleum ether/Et_2O=98:2) provided compound **16** (5.11g, 66%) as a colorless oil. $[\alpha]_D^{19}$ +13.8 (c 1.55, $CHCl_3$); ^{1}H NMR(400MHz, $CDCl_3$) : δ 7.37-7.31 (m, 5H), 6.98-6.92 (dd, *J* = 16.0 , 8.0 Hz,1H), 6.27 (dd, *J* = 16.0 , 1.2 Hz,1H), 4.61 (s, 2H), 4.24 (s,

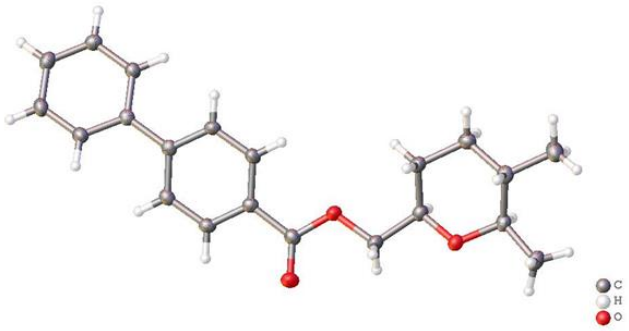
2H), 3.77 (m, 1H), 2.33 (m, 1H), 1.09 (d, J = 6.4Hz, 3H), 1.04 (d, J = 6.8Hz, 3H), 0.94 (t, J = 8.0 Hz, 9H), 0.58 (m, 6H); ^{13}C NMR (100MHz, $CDCl_3$) :δ196.9, 150.9, 137.4, 128.6, 126.1, 74.0, 73.4, 71.3, 44.9, 21.3, 15.2, 7.0, 5.1; HRMS (ESI) m/z: $[M + H]^+$ Calcd for $C_{21}H_{35}O_3Si$ 363.2356, Found: 363.2333.

(5S,6R)-1-(benzyloxy)-5-methyl-6-((triethylsilyl)oxy) heptan-2-one (17) A solution of olefin **16** (2 g, 5.52 mmol) in EtOAc (30ml) containing Pd/C (10%, 100 mg) was stirred overnight at room temperature under an atmosphere of H_2. The suspension was then filtered, the combined filtrate was concentrated *in vacuo*, and the residue was purified by flash column chromatography on silica gel (petroleum ether/EtOAc=95:5) to give compound **17** (1.82 g, 90%) as a colorless oil. $[\alpha]_D^{19}$ +70.4 (c 0.41, $CHCl_3$). IR (film)ν_{max} cm^{-1}: 3408, 2957, 2918, 2877, 2248, 2182, 2096, 1722, 1608, 1457, 1379, 1139, 742, 698, 614. ^{1}H NMR (400 MHz, $CDCl_3$): δ 7.37-7.31 (m, 5H), 4.59 (s, 2H), 4.07 (s, 2H), 3.69-3.63 (m, 1H), 2.57-2.49 (m, 1H), 2.46-2.37 (m, 1H), 1.79-1.70 (m, 1H), 1.47-1.41 (m, 1H), 1.36-1.29 (m, 1H), 1.06 (d, J = 6.4 Hz, 3H), 0.95 (t, J = 8 Hz, 9H), 0.84 (d, J = 6 Hz, 3H), 0.61-0.54 (m, 6H); ^{13}C NMR (100 MHz, $CDCl_3$): δ 209.1, 137.4, 128.7, 127.9, 110.0, 75.0, 73.5, 71.9, 40.3, 37.4, 19.8, 14.6, 7.1, 5.1; HRMS (ESI) m/z: $[M + H]^+$ Calcd for $C_{21}H_{37}O_3Si$ 365.2512, Found: 365.2517.

(2R,3S,6R)-6-((benzyloxy)methyl)-2,3-dimethyltetrahydro-2H-pyran (18) A solution of compound **17** (1.71 g, 4.93 mmol) in acetonitrile (50 mL) was added triethylsilane (688 mg, 5.92 mmol) and bismuth tribromide (110 mg, 0.25 mmol, prepared as a solution in acetonitrile at 1 mg/10μL) were added simultaneously via syringes. The reaction mixture was stirred for 30 min. The solvent was removed under reduced pressure to afford the crude reaction mixture, which was purified by flash chromatography (petroleum ether/EtOAc=98:2) to furnish tetrahydropyran **18** (898 mg, 82%, de = 94% according to ^{1}H-NMR spectrum) as a colorless oil. $[\alpha]_D^{19}$ +68.3 (*c* 0.47, $CHCl_3$). IR (film)ν_{max} cm^{-1}: 3030, 2966, 2926, 2873, 2851, 1734, 1604, 1496, 1454, 1380, 1261, 1228, 1206, 1104, 1018, 969, 876, 801, 736, 698. ^{1}H NMR (400 MHz, $CDCl_3$) :δ 7.35-7.26 (m, 5H), 4.63-4.52 (m, 2H), 3.58-3.48 (m, 2H), 3.41-3.38 (m, 2H), 3.08 (m, 1H), 1.76 (m, 1H), 1.60 (m, 2H), 1.35 (m, 1H), 1.21 (d, J = 6.4 Hz, 3H), 0.83 (d, J = 6.0 Hz, 3H); ^{13}C NMR (100 MHz, $CDCl_3$): δ 138.6, 128.5, 127.9, 127.7, 79.8, 76.8, 73.8, 73.5, 37.3, 32.5, 29.1, 19.9, 18.1; HRMS (ESI) m/z: $[M + H]^+$ Calcd for $C_{15}H_{23}O_2$ 235.1698, Found: 235.1677.

((2R,5S,6R)-5,6-dimethyltetrahydro-2H-pyran-2-yl) methanol (19) A solution of compound **18** (500 mg, 2.13 mmol) in EtOAc (15 ml) containing Pd/C (10%, 100 mg) was stirred overnight at room temperature under an atmosphere of H_2. The suspension was then filtered, the combined filtrate was concentrated *in vacuo* at 0 ºC due to its low boiling point. The residue **19** (300 mg, 97%) as a colorless oil was directly used for next step without further purification. $[\alpha]_D^{19}$ +37.6 (*c* 0.91, $CHCl_3$). ^{1}H NMR (400 MHz, $CDCl_3$) :δ 3.57-3.42 (m, 3H), 3.10-3.03 (m, 1H), 2.24 (s, 1H), 1.79-1.74 (m, 1H), 1.51-1.46 (m, 1H), 1.41-1.21 (m, 3H), 1.18 (d, J = 6.0 Hz, 3H), 0.82 (d, J = 6.0 Hz, 3H); ^{13}C NMR (100 MHz, $CDCl_3$): δ 79.7, 78.0, 66.4, 37.4, 32.3, 27.9, 19.8, 18.0; HRMS (ESI) m/z: $[M + H]^+$ Calcd for $C_8H_{17}O_2$ 145.1228, Found: 145.1219.

((2R,5S,6R)-5,6-dimethyltetrahydro-2H-pyran-2-yl)methyl[1,1'-biphenyl]-4-carboxylate (20) To a solution of compound **19** (200 mg, 1.39 mmol) and 4-Dimethylaminopyridine (DMAP, 33.89 mg, 0.28 mmol) in CH_2Cl_2 (10 mL), Et_3N (281 mg, 2.78 mmol) was added at ice bath. The reaction mixture was stirring for 1h at 0 ºC and raised up to room temperature stirring for another 1h. The mixture was diluted with H_2O (20 ml), extracted with EtOAc (20 mL). The organic extracts were washed with H_2O, brine, dried over Na_2SO_4, filtered and concentrated *in vacuo*. Purification of the residue by flash column chromatography on silica gel (petroleum ether/EtOAc=90:10) provided compound **20** (365 mg, 81%) as a white powder. m.p.55-57 ºC; $[\alpha]_D^{21}$ +41.0 (*c* 1.08, $CHCl_3$). IR (film)ν_{max} cm^{-1}: 3405, 3070, 2969, 2932, 2869, 2851, 1957, 1819, 1716, 1608, 1490, 1453, 1405, 1375, 1342, 1315, 1270, 1115, 1047, 1019, 995, 966, 943, 916, 875, 864, 783, 750, 695, 610. ^{1}H NMR (400 MHz, $CDCl_3$): δ 8.13 (d, J = 8.4 Hz, 2H), 7.67-7.62 (m, 4H), 7.47 (m, 2H), 7.41-7.38 (m, 1H), 4.33-4.30 (m, 2H), 3.70 (m, 1H), 3.15-3.08 (m, 1H), 1.85-1.80 (m, 1H), 1.74-1.68 (m, 1H), 1.51-1.41 (m, 1H),1.31 (m, 1H),1.23 (d, J = 6.0 Hz, 3H), 0.85 (d, J = 6.4 Hz, 3H); ^{13}C NMR (100 MHz, $CDCl_3$): δ 166.6, 145.8, 140.2, 130.4, 129.2, 129.1, 128.2, 127.4, 127.1, 79.9, 75.5, 68.0, 37.2, 32.4, 28.8, 19.8, 18.0; HRMS (ESI) m/z: $[M + H]^+$ Calcd for $C_{21}H_{25}O_3$ 325.1798, Found: 325.1793.



X-ray structure of compound **20** (CDCC 1988307) (displacement ellipsoids are drawn at 50% probability level)

(2R,3S,6R)-6-(7-(benzyloxy)hept-2-yn-1-yl)-2,3-dimethyltetrahydro-2H-pyran (23) Trifluoromethanesulfonic anhydride (201 mg, 0.71 mmol) was added to a solution of compound **19** (100 mg, 0.69 mmol) and 2,6-lutidine (222 mg, 2.17 mmol) in dry CH_2Cl_2 (5 ml) at -78 ºC. After stirring for 30 minutes, the solution was diluted with Et_2O (10 mL) and immediately washed with a saturated aqueous solution of sodium bicarbonate-ice mixture (1:1). The organic phase was quickly washed with 1N hydrochloric acid, H_2O, saturated $NaHCO_3$ solution, dried over Na_2SO_4, and filtered. The solvent was evaporated *in vacuo* at 0 ºC to give crude product **21** (190 mg) as a colorless oil, which was immediately submitted to the next step. *n*-BuLi (2.5M in hexane, 0.39 mL, 0.97 mmol), was added dropwise to a solution of compound **22** (208 mg, 1.10 mmol) in dry THF (5 mL) at -78 ºC. The mixture was stirred for 1 h at which time, HMPA (0.56 mL) was added. The freshly prepared triflate, diluted in dry THF (1 mL), was added to the reaction mixture via cannula. The reaction mixture stirred at -78 ºC for 5 h. The reaction was quenched by a saturated NH_4Cl solution and extracted with Et_2O (3mL×3). The combined organic phase was washed with H_2O, brine, dried over Na_2SO_4, filtered and concentrated *in vacuo*. The residue was purified by flash column chromatography (petroleum ether/Et_2O=95:5) to give compound **23** (130 mg, 60% over two steps) as a colorless oil. $[\alpha]_D^{21}$

+37.3 (*c* 1.02, $CHCl_3$). IR (film)ν_{max} cm^{-1}: 3292, 2929, 2852, 1960, 1603, 1495, 1454, 1377, 1366, 1313, 1095, 1073, 960, 950, 880, 736, 699, 615. ^1H NMR (400 MHz, $CDCl_3$): δ 7.35-7.27 (m, 5H), 4.50 (s, 2H), 3.47 (t, J = 6.4 Hz, 2H), 3.37 (m, 1H), 3.05 (m, 1H), 2.48-2.44 (m, 1H), 2.24 (m, 1H), 2.16 (m, 2H), 1.88-1.74 (m, 2H), 1.66-1.58 (m, 2H), 1.54-1.44 (m, 4H), 1.37-1.20 (m, 3H),1.18 (d, J = 6Hz, 3H), 0.82 (d, J = 6.4 Hz, 3H); ^{13}C NMR (100 MHz, $CDCl_3$): δ 138.8, 128.5, 127.8, 127.6, 81.8, 79.9, 76.9, 76.6, 73.0, 70.4, 37.2, 32.7, 31.5, 29.4, 29.0, 26.6, 25.6, 19.9, 18.9, 18.0; HRMS (ESI) m/z: $[M + H]^+$ Calcd for $C_{22}H_{33}O_2$ 329.2481, Found: 329.2492.

7-((2S,5S,6R)-5,6-dimethyltetrahydro-2H-pyran-2-yl)heptan-1-ol (24) A solution of compound **23** (500 mg, 1.59 mmol) in HOAc (10 mL) containing Pd/C (10%, 25 mg) was stirred overnight at room temperature under an atmosphere of H_2. The suspension was then filtered, the combined filtrate was concentrated *in vacuo*. The residue was purified by flash column chromatography on silica gel (petroleum ether/Et_2O=95:5) to give compound **24** (308 mg, 85%) as a colorless oil. $[\alpha]_D^{21}$ -12.5 (*c* 1.05, $CHCl_3$). IR (film)ν_{max} cm^{-1}: 3374, 2928, 2854, 1457, 1377, 1316, 1091, 1020, 749, 723. ^1H NMR (400 MHz, $CDCl_3$): δ 3.63 (t, J = 6.4 Hz, 2H), 3.23-3.18 (m, 1H), 3.04-2.97 (m, 1H), 1.76-1.71 (m, 1H), 1.62-1.48 (m, 4H), 1.42-1.21 (m, 15H), 1.17 (d, J = 6.4 Hz, 3H), 0.81 (d, J = 6.4 Hz, 3H); ^{13}C NMR (100 MHz, $CDCl_3$): δ 79.7, 77.9, 63.2, 37.5, 33.0, 32.9, 32.4, 29.8, 29.7, 29.5, 25.8, 19.9, 18.1; HRMS (ESI) m/z: $[M + Na]^+$ Calcd for $C_{15}H_{31}O_2$ 265.2138, Found: 265.2146.

7-((2S,5S,6R)-5,6-dimethyltetrahydro-2H-pyran-2-yl)heptanal (25) To a solution of compound **24** (500 mg, 2.19 mmol) in CH_2Cl_2 (20 mL), Dess-Martin periodinane (975 mg, 2.30 mmol) was added at ice bath and the reaction mixture stirred for 1 h. Then the mixture was filtered through Celite and filtrate stirred with a solution of 1:1(v/v) mixture of saturated $NaHCO_3$ and $Na_2S_2O_3$ (20 mL) for 10 min. The mixture was extracted with EtOAc, washed with H_2O, brine, dried (Na_2SO_4), filtrated, and concentrated *in vacuo*. The residue was purified by flash column chromatography on silica gel (petroleum ether/Et_2O=95:5) to give compound **25** (473 mg, 90%) as a colorless oil. $[\alpha]_D^{20}$ +3.0° (c 0.64, $CHCl_3$). ^1H NMR(400 MHz, $CDCl_3$): δ 9.75 (t, J =2.0 Hz, 1H), 3.23-3.16 (m, 1H), 3.03-2.96 (m, 1H), 2.42-2.38 (m, 2H), 1.75-1.70 (m, 1H), 1.64-1.56 (m, 3H), 1.53-1.45 (m, 1H), 1.38-1.36 (m, 1H), 1.33-1.24 (m, 9H), 1.22-1.18 (m, 2H), 1.16 (d, J = 5.0 Hz, 3H), 0.80 (d, J = 6.4 Hz, 3H); ^{13}C NMR (100 MHz, $CDCl_3$): δ 203.0, 79.7, 77.8, 44.0, 37.5, 36.6, 33.1, 32.4, 29.6, 29.4, 29.2, 25.8, 22.2, 19.9, 18.1; HRMS (ESI) m/z: $[M + H]^+$ Calcd for $C_{15}H_{29}O_2$ 241.2168, Found: 241.2157.

(1R,3S)-3-allyl-3-amino-1,7,7-trimethylbicyclo[2.2.1]heptan-2-one (26) To a solution of (1S) - (+) - camphorquinone (1.33 g, 8.0 mmol) in methanolic ammonia (ca.7M, 12 mL), allylboronoic acid pinacol ester (2.02 g, 12.0 mmol) was added dropwise at rt. After being stirred for 24 h, 3N hydrochloric acid was added slowly to adjust pH to 1. After being stirred for 30 min, the aqueous layer was washed with CH_2Cl_2 (20 mL), basified with 6N aqueous NaOH (pH ca. 10), and extracted with CH_2Cl_2 (15 mL×3). The later dichloromethane layers were dried over Na_2SO_4, filtered and concentrated *in vacuo*. The residue was purified by flash column chromatography on silica gel (petroleum ether/EtOAc=90:10) to give amine **26** (1.25g, 76%, >99%de) as a yellow oil. $[\alpha]_D^{25}$ -132.8 (c 1.20, $CHCl_3$). ^1H NMR (600 MHz, $CDCl_3$):δ

5.87-5.80 (m, 1H), 5.20-5.12 (m, 2H), 2.23 (dd, J = 14.4 , 6.6 Hz, 1H), 2.09 (dd, J = 14.4 Hz, 7.8 Hz, 1H), 1.90-1.83 (m, 2H), 1.67-1.62 (m, 2H), 1.48-1.43 (m, 1H), 1.41 (brs, 2H), 1.05 (s, 3H), 0.98 (s, 3H), 0.89 (s, 3H) ; ^{13}C NMR (150 MHz, $CDCl_3$) δ 222.6, 133.2, 119.2, 61.8, 58.5, 52.5, 46.2, 42.5, 30.1, 23.2, 22.9, 20.8, 9.7; HRMS (ESI) m/z: $[M + H]^+$ Calcd for $C_{13}H_{22}ON$ 208.1696, Found:208.1694.

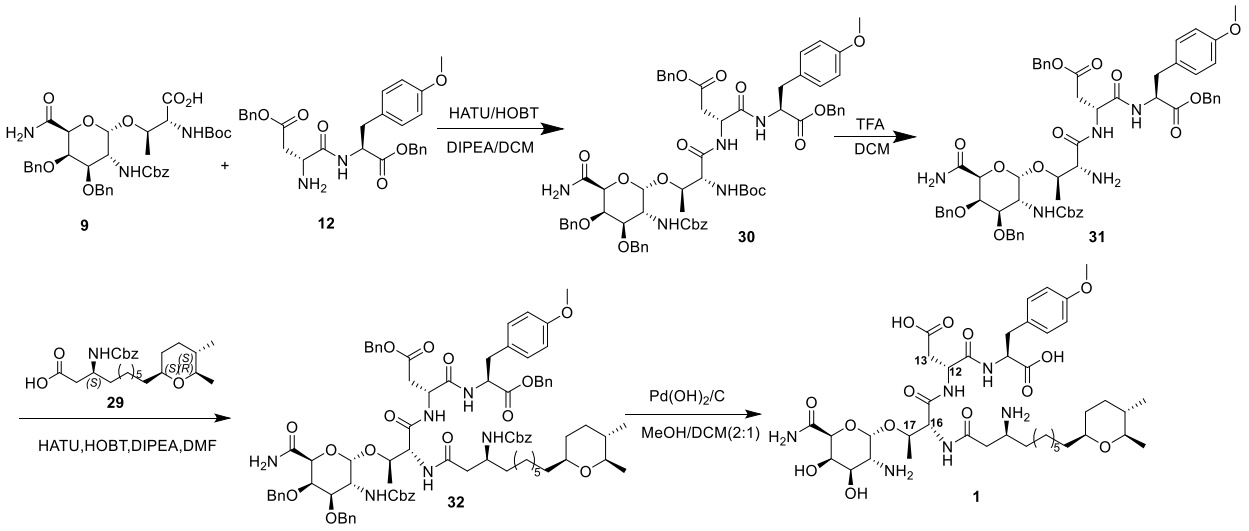
(S)-11-((2S,5S,6R)-5,6-dimethyltetrahydro-2H-pyran-2-yl)undec-1-en-4-amine (27) To a solution of chiral amine **26** (129 mg, 0.62 mmol) and aldehyde **25** (150 mg, 0.62 mmol) in 1,2-dichloroethane (5 mL) was added (+)-camphorquinone (14 mg, 0.06 mmol) at 0 ºC and continued stirring at room temperature for 30 h. Then a solution of $HONH_2 \cdot AcOH$ in methanol (0.5M, 2.5 mL, prepared from $HONH_2 \cdot HCl$, NaOH (solid, 1equiv), and AcOH (1equiv) in methanol) was added to the reaction mixture. After being stirred at 50 ºC for 3 h, the mixture was cooled to rt, and acidified with 1N aqueous HCl (pH ca.1). The mixture was washed with dichloromethane (10 mL), basified with 6N aqueous NaOH (pH ca.10), and extracted with dichloromethane (5 mL×3). The combined organic phase was dried over Na_2SO_4, filtered and concentrated *in vacuo*. The residue was purified by flash column chromatography on silica gel (CH_2Cl_2/MeOH= 20:1) to give compound **27** (174 mg, 68%) as a yellow oil. $[\alpha]_D^{22}$ -19.1 (c 1.12, $CHCl_3$). IR (film)ν_{max} cm^{-1}: 3073, 2928, 2855, 1641, 1561, 1454, 1401, 1380, 1317, 1091, 1013, 918, 648, 618. ^{1}H NMR (400 MHz,$CDCl_3$) :δ 5.85-5.74 (m, 1H), 5.14-5.10 (m, 2H), 3.26-3.17 (m, 2H), 3.03-3.00 (m, 1H), 2.90-2.83 (m, 1H), 2.31-2.25 (m, 1H), 2.13-2.04 (m, 1H), 1.75-1.71 (m, 1H), 1.60-1.58 (m, 1H), 1.50-1.21 (m, 18H), 1.17 (d, J = 6.0 Hz, 3H), 0.81 (d, J = 6.0 Hz, 3H); ^{13}C NMR (100 MHz, $CDCl_3$) : δ 135.0, 118.2, 79.7, 77.9, 51.1, 41.2, 37.5, 36.6, 36.3, 33.1, 32.4, 29.8, 29.7, 29.7, 26.1, 25.8, 20.0, 18.1; HRMS (ESI) m/z: $[M + H]^+$ Calcd for $C_{18}H_{36}ON$ 282.2797, Found:282.2794.

Benzyl ((S)-11-((2S,5S,6R)-5,6-dimethyltetrahydro-2H-pyran-2-yl)undec-1-en-4-yl)carbamate (28) To a solution of amine **27** (80 mg, 0.32 mmol) in $CHCl_3/H_2O$ (1 mL/2 mL) was added $NaHCO_3$(67 mg, 0.80 mmol) and benzyl chloroformate (81 mg, 0.47 mmol). The reaction mixture was stirred at room temperature for 2 h and diluted with CH_2Cl_2. The organic phase was washed with H_2O, brine, dried over Na_2SO_4, and purified by flash column chromatography on silica gel (petroleum ether/EtOAc=95:5) to give compound **28** as a white solid (116 mg, 98%). m.p.70-72 ºC; $[\alpha]_D^{20}$ +4.2 (*c* 0.40, $CHCl_3$). IR (film) ν_{max} cm^{-1}: 3323, 3066, 2926, 2852, 1688, 1541, 1453, 1267, 1090, 1047, 912, 731, 696, 675, 603. ^{1}H NMR (400 MHz, $CDCl_3$): δ 7.38-7.28 (m, 5H), 5.81-5.71 (m, 1H), 5.12-5.04 (m, 4H), 4.56-4.53 (m, 1H), 3.74-3.64 (m, 1H), 3.23-3.18 (m, 1H), 3.04-2.97 (m, 1H), 2.30-2.14 (m, 2H), 1.76-1.71 (m, 1H), 1.64-1.57 (m, 1H), 1.53-1.45 (m, 2H), 1.40-1.20 (m, 15H), 1.18 (d, J = 6.4 Hz, 3H), 0.81 (d, J = 6 Hz, 3H); ^{13}C NMR (100 MHz, $CDCl_3$): δ 156.1, 136.8, 134.4, 128.6, 128.2, 118.0, 79.7,77.9, 66.6, 50.8, 39.6, 37.5, 36.6, 34.7, 33.1, 32.4, 29.8, 29.6, 29.6, 26.0, 25.8, 20.0, 18.1; HRMS (ESI) m/z: $[M + H]^+$ Calcd for $C_{26}H_{42}O_3N$ 416.3165, Found:416.3156.

(S)-3-(((benzyloxy)carbonyl)amino)-10-((2S,5S,6R)-5,6-dimethyltetrahydro-2H-pyran-2-yl)decanoic acid (29) To a suspension of $NaIO_4$ (230 mg, 1.08 mmol) in pH 7.2 phosphate buffer (2 mL) was added $KMnO_4$ (21 mg, 0.13 mmol). After 15 min of violently stirring under argon atmosphere, the mixture was added to a solution of alkene **28** (50 mg, 0.13 mmol) in *t*-

BuOH (2 mL). The reaction mixture was vortexed at room temperature for 10 min, and the reaction was quenched with $Na_2S_2O_3$ (104 mg). The resulting mixture was poured into EtOAc (8 mL) and H_2O (13 mL). The organic layer was separated, and the aqueous layers was extracted with EtOAc (8 mL×3). The combined organic phases were washed with brine, dried over Na_2SO_4, filtered and concentrated *in vacuo*. The residue was purified by flash column chromatography on silica gel (petroleum ether/EtOAc/HOAc=90:3:1) to give compound **29** (40 mg, 69%) as a white solid. m.p.94-97 ºC; $[\alpha]_D^{18}$ -1 (c 0.22, $CHCl_3$); IR (film)ν_{max} cm^{-1}: 3256, 3030, 2939, 2867, 1742, 1708, 1602, 1513, 1460, 1366, 1252, 1212, 1163, 1060, 918, 883, 789, 735, 697. ^1H NMR (600 MHz, $CDCl_3$)：δ 7.40-7.29 (m, 5H), 5.20 (d, J = 8.4 Hz, 1H), 5.09 (m, 2H), 4.00-3.92 (m, 1H), 3.24-3.18 (m, 1H), 3.04-2.99 (m, 1H), 2.62-2.53 (m, 2H), 1.76-1.72 (m, 1H), 1.62-1.48 (m, 4H), 1.37-1.21 (m, 14H), 1.18 (d, J = 6.0 Hz, 3H), 0.81 (d, J = 6.6 Hz, 3H); ^{13}C NMR (150 MHz, $CDCl_3$) : 176.2, 156.1, 136.7, 128.7, 128.3, 128.2, 79.9, 78.0, 66.9, 48.2, 38.9, 37.5, 36.5, 34.5, 33.1, 32.4, 29.7, 29.5, 29.3, 26.2, 25.7, 19.9, 18.1; HRMS (ESI) m/z: $[M + H]^+$ Calcd for $C_{25}H_{38}O_5N$ 432.2750, Found: 432.2763.

2.4 Scheme 5. Synthesis of compound 1



Benzyl(6R,9R,12R)-9-(2-(benzyloxy)-2-oxoethyl)-6-((R)-1-(((2S,3R,4R,5R,6S)-4,5-bis(benzyloxy)-3-(((benzyloxy)carbonyl)amino)-6-carbamoyltetrahydro-2H-pyran-2-yl)oxy)ethyl)-12-(4-methoxybenzyl)-2,2-dimethyl-4,7,10-trioxo-3-oxa-5,8,11-triazatridecan-13-oate (30) To a solution of compound **9** (70 mg, 0.099 mmol) in dry CH_2Cl_2 (5 mL) was added 1-Hydroxybenzotriazole (14.7 mg, 0.109 mmol), [dimethylamino(triazolo[4,5-b]pyridin-3-yloxy) methylidene]-dimethylazanium (41.5 mg, 0.109 mmol) and compound **12** (58 mg, 0.118 mmol). Then N, N-Diisopropylethylamine (38.4 mg, 0.298 mmol) was added dropwise at ice bath. The reaction was stirred overnight at room temperature. The reaction mixture was washed with a saturated $NaHCO_3$ solution, H_2O, brine, dried over Na_2SO_4, filtered and concentrated *in vacuo*. The residue was purified by column chromatography on silica gel (CH_2Cl_2/MeOH=100:1→20:1) to give compound **30** (80 mg, 68%) as a white solid. m.p.207-210 ºC; $[\alpha]_D^{20}$ +92.8 (*c* 1.04, $CHCl_3$). IR (film)ν_{max} cm^{-1}: 3333, 3204, 3063, 3033, 2977, 2935, 1732, 1696, 1650, 1534, 1512, 1454, 1391, 1249, 1175, 1059, 1019, 843, 737, 698. ^1H NMR (600 MHz, DMSO-d_6): δ 8.54 (d, J =7.8 Hz, 1H), 8.14 (d, J =7.8 Hz, 1H), 7.48(s, 1H), 7.36-7.21 (m, 25H), 7.17 (d, J =6.0 Hz, 1H), 7.11 (d, J =3.6 Hz, 1H),

7.06 (d, *J* =8.4 Hz, 2H), 6.76 (d, *J* =7.8 Hz, 2H), 5.17 (d, *J* =12.6 Hz, 1H), 5.09-5.03(m, 5H), 4.91 (d, *J* =13.2 Hz, 1H), 4.77 (m, 1H), 4.67-4.62 (m, 2H), 4.53-4.41 (m, 4H), 4.29 (dd, *J* =2.4, 8.4 Hz, 1H), 4.14 (m, 2H), 3.97 (m, 1H), 3.70 (d, *J* =10.2 Hz, 1H), 3.63 (s, 3H), 2.97 (dd, *J* = 5.4, 12.6 Hz, 1H), 2.81 (dd, *J* =9.0, 13.2 Hz, 1H), 2.57 (dd, *J* = 3.6, 16.2 Hz, 1H), 2.45 (dd, *J* = 9.6, 16.2 Hz, 1H), 1.36 (s, 9H), 1.04 (d, *J* = 6.0 Hz, 3H); ^{13}C NMR (150 MHz, DMSO-d_6) *δ*: 171.0, 170.5, 170.0, 169.6, 168.2, 158.0, 156.3, 155.5, 138.8, 138.6, 137.1, 135.9,135.6, 130.6, 130.2, 128.9, 128.6, 128.5, 128.3, 128.2, 128.1, 128.00, 127.96, 127.8, 127.7, 127.6, 127.4, 127.3, 127.2, 126.9, 113.6, 99.6, 78.8, 77.2, 74.6, 74.2, 71.3, 71.2, 66.0, 65.8, 65.3, 58.4, 54.9, 53.8, 50.7, 48.9, 36.5, 36.0, 28.1, 16.5; HRMS (ESI) m/z: $[M + H]^+$ Calcd for $C_{65}H_{74}O_{16}N_5$ 1180.5125; Found: 1180.5140.

Benzyl(R)-3-((2R,3R)-2-amino-3-(((2S,3R,4R,5R,6S)-4,5-bis(benzyloxy)-3-(((benzyloxy)carbonyl)amino)-6-carbamoyltetrahydro-2H-pyran-2-yl)oxy)butanamido)-4-(((R)-1-(benzyloxy)-3-(4-methoxyphenyl)-1-oxopropan-2-yl)amino)-4-oxobutanoate

(31) To a solution of compound **30** (70 mg, 0.59 mmol) in dry CH_2Cl_2 (2 mL) was added trifluoroacetic acid (220 μL) at ice bath and stirred overnight at room temperature. Then the reaction mixture was added 2N NaOH to adjust pH to 11 and separated via separatory funnel. The inorganic phase was extracted with CH_2Cl_2, and the combined organic phase was washed by H_2O, brine, dried over Na_2SO_4, filtered and concentrated *in vacuo*. The residue was purified by column chromatography on silica gel (CH_2Cl_2/CH_3OH=30:1→15:1) to give compound **31** (47 mg, 73%) as a white solid. m.p.210-212 ºC; $[\alpha]_D^{21}$ +50.4 (*c* 0.08, $CHCl_3$); ^{1}H NMR (600 MHz, DMSO-d_6) *δ*: 8.58 (br., 1H), 7.46 (s, 1H), 7.42-7.20 (m, 28H), 7.08 (m, 2H), 6.76(m, 2H), 5.16 (m, 2H), 5.10-4.90 (m, 4H), 4.72-4.68 (m, 2H), 4.54 (d, *J* = 10.8 Hz, 2H), 4.47 (br., 2H), 4.43 (s, 1H), 4.16(s,1H), 4.02 (m, 1H), 3.88-3.79 (m, 2H), 3.66 (s, 3H), 3.38 (br., 1H), 3.30 (m, 1H), 3.02 (m, 1H), 2.86 (m, 1H), 2.66 (m, 1H), 2.50 (m, 1H), 1.84 (br. 2H), 1.01 (d, *J* = 6 Hz, 3H); ^{1}H NMR (600 MHz, DMSO-d_6+D_2O): *δ* 7.30-7.17 (m, 25H), 7.07 (d, *J* = 7.8 Hz, 1H), 7.03 (d, *J* = 8.4 Hz, 1H), 6.75(t, *J* = 7.5 Hz, 2H), 5.12 (d, *J*=12 Hz, 1H), 5.05 (m, 2H), 4.96 (m, 2H), 4.89 (m, 1H), 4.67 (m, 2H), 4.51 (m, 2H), 4.45 (br., 2H), 4.42 (br., 1H), 4.16(d, *J* = 10.2 Hz, 1H), 4.01 (dd, *J* = 2.4, 10.8 Hz, 1H), 3.88-3.78 (m, 2H), 3.64 (s, 3H), 3.36-3.28 (m, 2H), 2.99 (m, 1H), 2.82 (m, 2H), 2.59 (m, 1H), 2.48 (m, 1H), 1.01 (d, *J* = 5.4 Hz, 3H); ^{13}C NMR (150 MHz, DMSO-d_6): *δ* 175.3, 173.9, 172.7, 170.6, 168.0, 157.9, 156.3, 142.5, 138.8, 138.7, 137.1, 135.6, 130.2, 130.0, 128.8, 128.3, 128.1, 128.0, 127.98, 127.8, 127.7, 127.6, 127.44, 127.40, 127.3, 127.25, 126.6, 126.4, 113.7, 97.7, 76.4, 76.2, 74.7, 74.3, 71.3, 66.6, 65.3, 62.9, 57.7, 54.9, 53.4, 50.9, 48.0, 34.2, 32.6, 15.2. HRMS (ESI) m/z: $[M + H]^+$ Calcd for $C_{60}H_{66}O_{14}N_5$ 1080.4601; Found: 1080.4628.

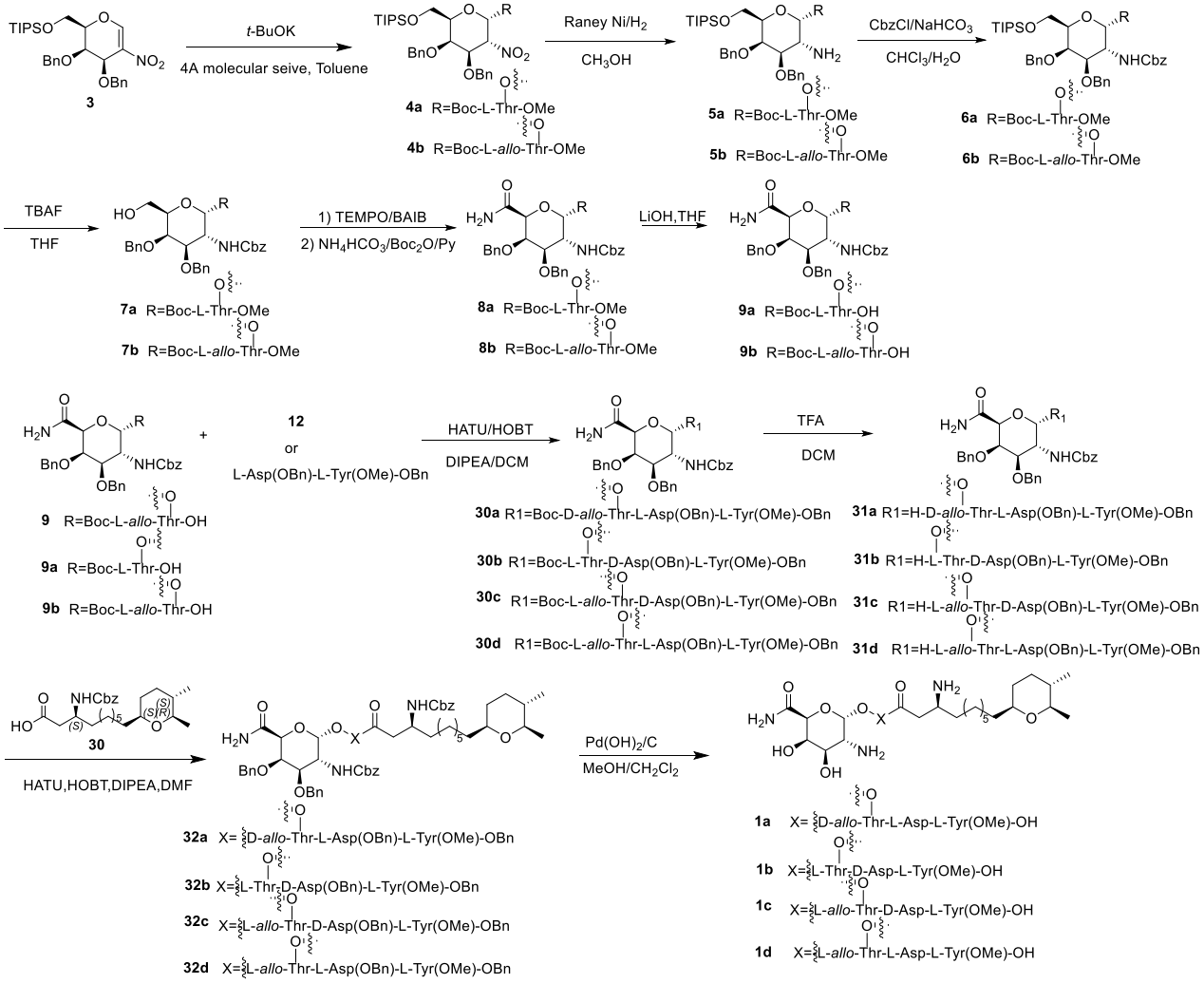
Benzyl(5S,9R,12R,15R)-12-(2-(benzyloxy)-2-oxoethyl)-9-((R)-1-(((2S,3R,4R,5R,6S)-4,5-bis(benzyloxy)-3-(((benzyloxy)carbonyl)amino)-6-carbamoyltetrahydro-2H-pyran-2-yl)oxy)ethyl)-5-(7-((2S,5S,6R)-5,6-dimethyltetrahydro-2H-pyran-2-yl)heptyl)-15-(4-methoxybenzyl)-3,7,10,13-tetraoxo-1-phenyl-2-oxa-4,8,11,14-tetraazahexadecan-16-oate

(32) To a solution of compound **29** (17.7 mg, 0.04 mmol) in dry DMF(1 mL) was added 1-Hydroxybenzotriazole (5.5 mg, 0.04 mmol), [dimethylamino(triazolo[4,5-b]pyridin-3-yloxy) methylidene]-dimethylazanium (15.5 mg, 0.04 mmol) and compound **31** (40 mg, 0.04 mmol). Then N, N-Diisopropylethylamine (14.3 mg, 0.11 mmol) was added dropwise at ice bath. The reaction was stirred for 3h at room temperature. The reaction mixture was washed with a saturated $NaHCO_3$ solution, H_2O, brine, dried over Na_2SO_4, filtered and concentrated *in vacuo*.

The residue was purified by column chromatography on silica gel (CH_2Cl_2/MeOH=50:1→20:1) to give compound **32** (40 mg, 72%) as a white solid. m.p.163-165 ºC; $[\alpha]_D^{19}$ -7.7 (*c* 0.168, $CHCl_3$). IR (film)ν_{max} cm^{-1}: 3334, 3064, 3034, 2927, 2854, 1732, 1692, 1656, 1643, 1543, 1512, 1454, 1251, 1057, 1020, 843, 736, 697. ^{1}H NMR (600 MHz, DMSO-d_6) δ: 8.44 (m, 2H), 7.84 (d, *J* = 7.8 Hz, 1H), 7.49 (s, 1H), 7.37-7.05 (m, 30H), 7.06 (d, *J* = 8.4Hz, 2H), 6.76 (d, *J* = 7.8Hz, 2H), 5.15-5.02 (m, 8H), 4.92-4.87 (m, 2H), 4.73-4.69 (m, 4H), 4.58 (d, *J* = 12.0 Hz, 1H), 4.53 (d, *J* = 10.8 Hz, 1H), 4.47-4.44 (m, 2H), 4.16-4.03 (m, 4H), 3.76 (m, 2H), 3.65 (s, 3H), 3.12 (m, 2H), 2.97 (dd, *J* = 5.4, 13.8 Hz, 1H), 2.92 (m, 1H), 2.82 (dd, *J* = 9.6, 13.8 Hz, 1H), 2.61 (m, 1H), 2.45-2.38 (m, 2H), 2.21 (m, 1H), 1.66 (d, *J* = 4.8 Hz, 1H), 1.49 (d, *J* = 9.6 Hz, 1H), 1.33-1.05 (m, 18H), 1.04 (d, *J* = 6.0 Hz, 3H), 0.95 (d, *J* = 6.0 Hz, 3H), 0.74 (d, *J* = 4.8 Hz, 3H); ^{13}C NMR (150 MHz, DMSO-d_6) δ: 171.0, 170.7, 169.9, 169.6, 167.9, 158.0, 156.4, 155.4, 138.9, 137.4, 137.1, 135.9, 135.6, 130.2, 128.7, 128.4, 128.3, 128.2, 128.1, 128.0, 127.9, 127.8, 127.7, 127.66, 127.6, 127.5, 127.3, 127.2, 127.1, 126.9,126.8, 113.6, 99.9, 78.6, 77.6, 77.0, 76.6, 75.1, 74.3, 71.4, 71.3, 66.0, 65.8, 65.3, 65.0, 55.9, 54.9, 53.8, 50.9, 49.1, 49.0, 41.0, 40.0, 36.9, 36.2, 35.9, 32.3, 31.8, 29.02, 28.97, 28.7, 25.2, 25.1, 19.7, 17.8, 15.7; HRMS (ESI) m/z: $[M + H]^+$ Calcd for $C_{85}H_{103}O_{18}N_6$ 1495.7323; Found: 1495.7310.

Compound 1 To a solution of compound **32** (12mg，0.014mmol) in MeOH/CH_2Cl_2 mixture (9ml v/v 2:1) was added $Pd(OH)_2$/C (25mg), the mixture was stirred at room temperature under an atmosphere of H_2 for 24 h. After filtering and concentration, the residue was purified by HPLC using a reverse C18 column (Thermo, 250 mm x 10 mm, 5 μm) to give compound **1** (5 mg, 71%) as a white solid. (The purification used a mixture of acetonitrile (containing 0.1% TFA) and H_2O (containing 0.1% TFA) as the eluent with a flow of 3 mL/min. The fraction of acetonitrile was 10% from 0 to 1 min, 10%-50% from 1 to 11 min, 50% from 11 to 17 min, 50%-95% from 17 to 18 min, 95% from 18 to 24 min, and then, it was gradually decreased to 10% from 24 to 25min). m.p.217-218 ºC; $[\alpha]_D^{19}$ +7.8 (*c* 0.26, CH_3OH). IR (film)ν_{max} cm^{-1}: 3240, 3060, 2934, 2858, 1670, 1544, 1515, 1437, 1249, 1202, 1141, 1085, 1039, 839, 800, 723, 601. ^{1}H NMR (600 MHz, MeOD-d_4) δ: 7.15 (d, *J*=7.8 Hz, 2H), 6.84 (d, *J* = 8.4 Hz, 2H), 5.31 (s, 1H), 4.66 (dd, *J* = 7.2 Hz, 1H), 4.58 (s, 1H), 4.48-4.42 (m, 1H), 4.29 (d, *J* = 2.4Hz, 1H), 4.24 (d, *J* = 2.4 Hz, 1H), 4.18-4.15 (m, 1H), 3.97 (d, *J* = 10.8 Hz, 1H), 3.76 (s, 3H), 3.55-3.51 (m, 1H), 3.48 (dd, *J* = 10.8, 3.6 Hz, 1H), 3.25 (m, 1H), 3.16 (dd, *J* = 13.8, 5.4 Hz, 1H), 3.06-3.01 (m, 1H), 2.93 (dd, *J* = 13.5, 8.4 Hz, 1H), 2.77-2.71 (m, 1H), 2.65-2.52 (m, 3H), 1.77-1.75 (m, 1H), 1.69-1.60 (m, 3H), 1.50-1.29 (m, 20H), 1.27-1.25 (m, 3H), 1.21-1.19 (m, 3H); ^{13}C NMR (150 MHz, MeOD-d_4) δ: 175.2, 173.4, 172.8, 172.6, 172.3, 171.8, 171.5, 160.1, 131.4, 130.3, 114.9, 97.8, 81.2, 79.3, 76.5, 73.5, 70.0, 68.0, 58.7, 55.7, 52.1, 51.6, 50.2, 38.7, 37.8, 37.4, 33.9, 33.4, 30.7, 30.4, 26.7, 26.2, 20.0, 18.2; HRMS (ESI) m/z: $[M + H]^+$ Calcd for $C_{41}H_{67}O_{14}N_6$ 867.4710; Found:867.4709.

2.5 Scheme 6. Synthesis of compound 1a-1d



Methyl O-((2S,3R,4R,5R,6R)-4,5-bis(benzyloxy)-3-nitro-6-(((triisopropylsilyl)oxy)methyl)tetrahydro-2H-pyran-2-yl)-N-(tert-butoxycarbonyl)-L-threoninate (4a). 4a was prepared from **3** (2.08 g, 3.94 mmol) following the procedure described for **4**. Purification by flash chromatography (petroleum ether/ethyl acetate = 40:1) gave the title compound (2.7 g, 3.55 mmol, 90%) as a colorless oil. $[\alpha]_D^{25}$ +59.4 (*c* 1.04, $CHCl_3$). IR (film)ν_{max} cm^{-1}: 3443, 3064, 3031, 2943, 2867, 1750, 1720, 1557, 1500, 1457, 1366, 1165, 1121, 1093, 1054, 914, 883, 789, 740, 697, 599. ^{1}H NMR (400 MHz, $CDCl_3$) δ 7.38 – 7.23 (m, 10H), 5.33 (d, J = 4.3 Hz, 1H), 5.05 (d, J = 9.8 Hz, 1H), 4.92 (dd, J = 4.3, 10.7 Hz, 1H), 4.82 (d, J = 11.1 Hz, 1H), 4.77 (d, J = 10.8 Hz, 1H), 4.72 (d, J = 10.8 Hz, 1H), 4.53 (d, J = 11.0 Hz, 1H), 4.41 (dd, J = 10.7, 3.0 Hz, 1H), 4.36 – 4.26 (m, 2H), 4.02 (d, J = 3.0 Hz, 1H), 3.87 (t, J = 6.7 Hz, 1H), 3.77 (s, 3H), 3.75 – 3.66 (m, 2H), 1.48 (s, 9H), 1.30 (d, J = 6.3 Hz, 3H), 1.14 – 1.00 (m, 21H). ^{13}C NMR (100 MHz, $CDCl_3$): δ 170.6, 156.2, 138.2, 137.5, 128.7, 128.5, 128.3, 128.2, 127.9, 97.7, 84.6, 80.3, 75.3, 75.2, 73.2, 73.2, 72.0, 61.9, 58.2, 52.9, 28.4, 18.4, 18.1, 11.9. HRMS (ESI) m/z: $[M + Na]^+$ Calcd for $C_{39}H_{60}O_{11}N_2SiNa$ 783.3858; Found: 783.3858.

MethylO-((2S,3R,4R,5R,6R)-4,5-bis(benzyloxy)-3-nitro-6-(((triisopropylsilyl)oxy)methyl)tetrahydro-2H-pyran-2-yl)-N-(tert-butoxycarbonyl)-L-

allothreoninate (4b). 4b was prepared from **3** (1.6 g, 3.03 mmol) following the procedure described for **4**. Purification by flash chromatography (petroleum ether/ethyl acetate = 40:1) gave the title compound (1.98 g, 2.60 mmol, 86%) as a colorless oil. $[\alpha]_D^{20}$ +97.3 (*c* 0.7, $CHCl_3$). IR (film)ν_{max} cm^{-1}: 3438, 3374, 3031, 2942, 2867, 1747, 1720, 1558, 1499, 1458, 1367, 1163, 1120, 1055, 916, 883, 787, 750, 697, 604. ^{1}H NMR (400 MHz, $CDCl_3$): δ 7.41 – 7.19 (m, 10H), 5.38 (d, *J* = 8.7 Hz, 1H), 5.33 (d, *J* = 4.3 Hz, 1H), 4.98 (dd, *J* = 10.6, 4.3 Hz, 1H), 4.84 (d, *J* = 10.9 Hz, 1H), 4.77 – 4.70 (m, 2H), 4.55 (d, *J* = 10.9 Hz, 1H), 4.43 – 4.35 (m, 2H), 4.04 (d, *J* = 2.9 Hz, 1H), 4.00 (m, 2H), 3.86 – 3.76 (m, 2H), 3.75 (s, 3H), 1.46 (s, 9H), 1.17 – 1.03 (m, 24H). ^{13}C NMR (100 MHz, $CDCl_3$): δ 170.3, 155.4, 138.3, 137.6, 128.6, 128.4, 128.4, 128.2, 128.2, 127.9, 94.9, 84.6, 80.1, 75.5, 75.3, 75.1, 73.3, 73.1, 72.1, 61.5, 58.0, 52.4, 28.4, 18.1, 15.3, 12.0. HRMS (ESI) m/z: $[M + H]^+$ Calcd for $C_{39}H_{61}O_{11}N_2Si$ 761.4039; Found: 761.4026.

MethylO-((2S,3R,4R,5R,6R)-4,5-bis(benzyloxy)-3-(((benzyloxy)carbonyl)amino)-6-(((triisopropylsilyl)oxy)methyl)tetrahydro-2H-pyran-2-yl)-N-(tert-butoxycarbonyl)-L-threoninate (5a). 5a was prepared from **4a** (2.70 g, 3.55 mmol) following the procedure described for **5**. Purification by flash chromatography (DCM/MeOH = 10:1) gave the title compound (2.1 g, 2.89 mmol, 81%) as a colorless oil. following the procedure described for **5** in 81% yield as a colorless oil. $[\alpha]_D^{25}$ +66.8 (*c* 1.1, $CHCl_3$). IR (film)ν_{max} cm^{-1}: 3346, 3387, 3064, 3033, 2942, 2866, 1745, 1717, 1586, 1500, 1456, 1389, 1366, 1345, 1250, 1166, 1089, 1019, 911, 883, 792, 735, 660, 462. ^{1}H NMR (400 MHz, $CDCl_3$): δ 7.39 – 7.27 (m, 10H), 5.29 (d, *J* = 9.5 Hz, 1H), 4.86 (d, *J* = 5.9 Hz, 1H), 4.84 (d, *J* = 1.8 Hz, 1H), 4.74 (d, *J* = 11.5 Hz, 1H), 4.62 (d, *J* = 11.4 Hz, 1H), 4.55 (d, *J* = 11.5 Hz, 1H), 4.32 (dd, *J* = 9.6, 2.6 Hz, 1H), 4.22 (dq, *J* = 6.4, 2.7 Hz, 1H), 4.02 (d, *J*= 2.7 Hz, 1H), 3.84 – 3.76 (m, 2H), 3.75 (s, 3H), 3.73 (m, 1H), 3.44 (dd, *J* = 10.4, 2.6 Hz, 1H), 3.23 (dd, *J* = 10.5, 3.7 Hz, 1H), 1.47 (s, 9H), 1.30 (d, *J* = 6.4 Hz, 3H), 1.09 – 1.02 (m, 21H). ^{13}C NMR (100 MHz, $CDCl_3$): δ 171.7, 156.1, 138.8, 138.2, 128.6, 128.3, 128.1, 127.9, 127.8, 127.6, 102.2, 81.1, 80.1, 74.7, 72.6, 72.3, 72.0, 62.4, 58.4, 52.7, 51.6, 28.4, 18.5, 18.1, 11.9. HRMS (ESI) m/z: $[M + H]^+$ Calcd for $C_{39}H_{63}O_9N_2Si$ 731.4297; Found: 731.4281.

MethylO-((2S,3R,4R,5R,6R)-3-amino-4,5-bis(benzyloxy)-6-(((triisopropylsilyl)oxy)methyl)tetrahydro-2H-pyran-2-yl)-N-(tert-butoxycarbonyl)-L-allothreoninate (5b). 5b was prepared from **4b** (1.4 g, 1.84 mmol) following the procedure described for **5**. Purification by flash chromatography (DCM/MeOH = 10:1) gave the title compound (1.08g, 1.47mmol, 81%) as a colorless oil. $[\alpha]_D^{19}$ +110.5 (*c* 1.1, $CHCl_3$). IR (film)ν_{max} cm^{-1}: 3371, 3250, 3031, 2942, 2866, 1744, 1710, 1584, 1533, 1457, 1383, 1365, 1320, 1251, 1216, 1163, 1016, 911, 883, 784, 766, 696, 534. ^{1}H NMR (400 MHz, $CDCl_3$): δ 7.41 – 7.19 (m, 10H), 5.56 (d, *J* = 9.1 Hz, 1H), 4.96 (d, *J*=3.7 Hz, 1H), 4.88 (d, *J* = 11.3 Hz, 1H), 4.74 (d, *J* = 11.6 Hz, 1H), 4.65 (d, *J* = 11.3 Hz, 1H), 4.53 (d, *J* = 11.6 Hz, 1H), 4.40 (dd, *J* = 9.4, 3.4 Hz, 1H), 4.08 (d, *J* = 2.4 Hz, 1H), 4.05 – 3.96 (m, 1H), 3.91 – 3.81 (m, 3H), 3.68 (s, 3H), 3.44 (dd, *J* = 10.4, 2.4 Hz, 1H), 3.31 (dd, *J* = 10.4, 3.7 Hz, 1H), 1.44 (s, 9H), 1.25 (d, *J* = 6.4 Hz, 3H), 1.16 – 1.05 (m, 21H). ^{13}C NMR (100 MHz, $CDCl_3$): δ 170.8, 155.4, 138.9, 138.2, 128.6, 128.3, 128.0, 127.9, 127.9, 127.6, 98.4, 81.2, 79.9, 74.7, 72.4, 72.4, 71.9, 61.9,

58.2, 52.1, 51.0, 28.4, 18.1, 16.1, 12.0. HRMS (ESI) m/z: $[M + H]^+$ Calcd for $C_{39}H_{63}O_9N_2Si$ 731.4297; Found: 731.4265.

MethylO-((2S,3R,4R,5R,6R)-4,5-bis(benzyloxy)-3-(((benzyloxy)carbonyl)amino)-6-(((triisopropylsilyl)oxy)methyl)tetrahydro-2H-pyran-2-yl)-N-(tert-butoxycarbonyl)-L-threoninate (6a). 6a was prepared from **5a** (520 mg, 0.71 mmol) following the procedure described for **6**. Purification by flash chromatography (petroleum ether/ethyl acetate = 5:1) gave the title compound (590 mg, 0.68 mmol, 96%) as a colorless oil. $[\alpha]_D^{25}$ +49.7 (*c* 1.05, $CHCl_3$). IR (film)ν_{max} cm^{-1}: 3351, 2942, 2866, 1717, 1518, 1455, 1365, 1335, 1250, 1218, 1168, 1095, 1055, 1024, 911, 883, 780, 736, 697. ^1H NMR (400 MHz, $CDCl_3$): δ 7.40 – 7.21 (m, 15H), 5.19 – 5.07 (m, 3H) 4.96 (d, *J* = 11.5 Hz, 1H), 4.84 (d, *J* = 3.8 Hz, 1H), 4.75 (d, *J* = 9.9 Hz, 1H), 4.70 (d, *J* = 12.1 Hz, 1H), 4.60 (d, *J* = 11.5 Hz, 1H), 4.56 (d, *J* = 12.0 Hz, 1H), 4.41 (td, *J* = 10.4, 3.7 Hz, 1H), 4.31 (dd, *J* = 9.9, 2.4 Hz, 1H), 4.21 – 4.08 (m, 1H), 4.05 – 3.95 (m, 1H), 3.82 – 3.68 (m, 4H), 3.54 (s, 3H), 1.46 (s, 9H), 1.27 (d, *J* = 6.4 Hz, 3H), 1.04 (m, 21H). ^{13}C NMR (100 MHz, $CDCl_3$): δ 171.7, 156.2, 155.9, 138.7, 138.2, 136.7, 128.5, 128.3, 128.3, 128.2, 128.1, 127.8, 127.6, 100.7, 80.3, 77.9, 74.6, 72.8, 72.3, 72.0, 66.8, 62.5, 58.1, 52.5, 51.3, 28.4, 18.2, 18.1, 11.9. HRMS (ESI) m/z: $[M + H]^+$ Calcd for $C_{47}H_{69}O_{11}N_2Si$ 865.4665; Found: 865.4653.

MethylO-((2S,3R,4R,5R,6R)-4,5-bis(benzyloxy)-3-(((benzyloxy)carbonyl)amino)-6-(((triisopropylsilyl)oxy)methyl)tetrahydro-2H-pyran-2-yl)-N-(tert-butoxycarbonyl)-L-allothreoninate (6b). 6b was prepared from **5b** (940 mg, 1.28 mmol) following the procedure described for **6**. Purification by flash chromatography (petroleum ether/ethyl acetate = 5:1) gave the title compound (1.03 g, 1.19 mmol, 93%) as a colorless oil. $[\alpha]_D^{21}$ +68.9 (*c* 1.2, $CHCl_3$). IR (film)ν_{max} cm^{-1}: 3444, 3347, 2942, 2891, 2866, 1718, 1508, 1455, 1388, 1365, 1251, 1211, 1166, 1100, 1056, 1022, 915, 883, 789, 737, 697. ^1H NMR (400 MHz, $CDCl_3$): δ 7.39 – 7.17 (m, 15H), 5.35 (d, *J* = 8.7 Hz, 1H), 5.14 (d, *J* = 12.2 Hz, 1H), 5.07 (d, *J* = 12.2 Hz, 1H), 5.00 – 4.86 (m, 2H), 4.78 – 4.65 (m, 2H), 4.61 (d, *J* = 11.3 Hz, 1H), 4.55 (d, *J* = 12.0 Hz, 1H), 4.47 (td, *J* = 10.3, 3.8 Hz, 1H), 4.41-4.35 (m, 1H), 4.06 – 4.02 (m, 1H), 4.01 - 3.94 (m, 1H), 3.79 (s, 3H), 3.70 – 3.54 (m, 4H), 1.41 (s, 9H), 1.14 (d, *J* = 6.2 Hz, 3H), 1.12 – 1.02 (m, 21H). ^{13}C NMR (100 MHz, $CDCl_3$): δ 170.7, 156.1, 155.3, 138.8, 138.3, 136.7, 128.6, 128.5, 128.4, 128.3, 128.1, 127.7, 127.5, 96.0, 80.0, 78.1, 74.6, 73.8, 72.7, 72.3, 71.9, 66.8, 62.0, 58.0, 52.2, 51.0, 28.3, 18.1, 15.4, 12.0. HRMS (ESI) m/z: $[M + H]^+$ Calcd for $C_{47}H_{69}O_{11}N_2Si$ 865.4665; Found: 865.4625.

MethylO-((2S,3R,4R,5R,6R)-4,5-bis(benzyloxy)-3-(((benzyloxy)carbonyl)amino)-6-(hydroxymethyl)tetrahydro-2H-pyran-2-yl)-N-(tert-butoxycarbonyl)-L-threoninate (7a). 7a was prepared from **6a** (940 mg, 1.08 mmol) following the procedure described for **7**. Purification by flash chromatography (petroleum ether/ethyl acetate = 2:1) gave the title compound (710 mg, 1.00 mmol, 93%) as a white solid. m.p. 37-39 °C. $[\alpha]_D^{21}$+73.6 (*c* 0.5, $CHCl_3$). IR (film)ν_{max} cm^{-1}: 3456, 3063, 3031, 2977, 2932, 1715, 1518, 1454, 1392, 1365, 1336, 1308, 1217, 1166, 1135, 1054, 1026, 908, 776, 738, 698, 596, 476. ^1H NMR (400 MHz, $CDCl_3$): δ 7.42 – 7.17 (m, 15H), 5.16 – 5.04 (m, 3H), 4.98 (d, *J* = 11.7 Hz, 1H), 4.88 (d, *J* = 3.8 Hz, 1H), 4.78 – 4.69 (m, 2H), 4.57 (d, *J* = 11.7 Hz, 1H), 4.55 (d, *J* = 11.9 Hz, 1H), 4.43 (td, *J* = 10.4, 3.7

Hz, 1H), 4.30 (dd, *J* = 9.4, 2.5 Hz, 1H), 4.18 – 4.12 (m, 1H), 3.94 – 3.90 (m, 1H), 3.79 – 3.67 (m, 3H), 3.58 – 3.49 (m, 4H), 1.45 (s, 9H), 1.23 (d, *J* = 6.4 Hz, 3H). ^{13}C NMR (100 MHz, $CDCl_3$): δ 171.7, 156.2, 155.8, 138.2, 138.0, 136.6, 128.6, 128.6, 128.5, 128.3, 128.2, 128.1, 127.9, 127.7, 100.4, 80.4, 77.8, 74.2, 72.6, 72.2, 71.4, 66.8, 62.4, 57.9, 52.6, 51.2, 28.4, 18.1. HRMS (ESI) m/z: $[M + H]^+$ Calcd for $C_{38}H_{49}O_{11}N_2$ 709.3331; Found: 709.3296.

MethylO-((2S,3R,4R,5R,6R)-4,5-bis(benzyloxy)-3-(((benzyloxy)carbonyl)amino)-6-(hydroxymethyl)tetrahydro-2H-pyran-2-yl)-N-(tert-butoxycarbonyl)-L-allothreoninate (7b). 7b was prepared from **6b** (2.34 g, 2.7 mmol) following the procedure described for **7**. Purification by flash chromatography (petroleum ether/ethyl acetate = 2:1) gave the title compound (1.8 g, 2.53 mmol, 93%) as a white solid. m.p. 133-135 ºC, $[\alpha]_D^{19}$ +84.3 (*c* 0.8, $CHCl_3$). IR (film)ν_{max} cm^{-1}: 3455, 3361, 3089, 3065, 3032, 2981, 1743, 1687, 1520, 1454, 1368, 1348, 1301, 1282, 1238, 1211, 1178, 1137, 1211, 1178, 1136, 1096, 1044, 986, 942, 899, 857, 780, 748, 732, 695, 601, 461. ^{1}H NMR (400 MHz, $CDCl_3$): δ 7.39 – 7.17 (m, 15H), 5.64 (d, *J* = 8.8 Hz, 1H), 5.16 (d, *J* = 12.2 Hz, 1H), 5.07 (d, *J* = 12.3 Hz, 1H), 5.02 – 4.87 (m, 2H), 4.76 – 4.56 (m, 3H), 4.52 (d, *J* = 12.0 Hz, 1H), 4.46 (td, *J* = 10.0, 3.8 Hz, 1H), 4.38 (d, *J* = 9.3 Hz, 1H), 4.01 – 3.86 (m, 3H), 3.82 (dd, *J* = 11.5, 6.6 Hz, 1H), 3.72 – 3.64 (m, 3H), 3.60 (dd, *J* = 11.4, 4.5 Hz, 1H), 3.50 (d, *J* = 10.9 Hz, 1H), 2.18 (br, 1H), 1.42 (s, 9H), 1.19 (d, *J* = 6.7 Hz, 3H); ^{13}C NMR (100 MHz, $CDCl_3$): δ 170.6, 156.1, 155.4, 138.2, 137.9, 136.6, 128.6, 128.5, 128.5, 128.3, 128.0, 127.8, 127.5, 98.1, 80.3, 78.0, 76.2, 74.3, 72.7, 72.0, 66.9, 62.8, 58.2, 52.3, 50.9, 28.3, 16.8. HRMS (ESI) m/z: $[M + H]^+$ Calcd for $C_{38}H_{49}O_{11}N_2$ 709.3331; Found: 709.3319.

MethylO-((2S,3R,4R,5R,6S)-4,5-bis(benzyloxy)-3-(((benzyloxy)carbonyl)amino)-6-carbamoyltetrahydro-2H-pyran-2-yl)-N-(tert-butoxycarbonyl)-L-threoninate (8a). 8a was prepared from **7a** (148 mg, 0.208 mmol) following the procedure described for **8**. Purification by flash chromatography (petroleum ether/ethyl acetate = 1:1) gave the title compound (120 mg, 0.166 mmol, 80%) as a white solid. m.p. 59-61 ºC. $[\alpha]_D^{20}$ +80.7 (*c* 1.0, $CHCl_3$). IR (film)ν_{max} cm^{-1}: 3485, 3305, 3174, 2977, 2933, 1707, 1690, 1584, 1513, 1454, 1393, 1365, 1334, 1216, 1055, 1023, 907, 737, 698. ^{1}H NMR (400 MHz, $CDCl_3$): δ 7.41 – 7.11 (m, 15H), 6.51 (s, 1H), 6.08 (s, 1H), 5.19 (d, *J* = 9.5 Hz, 1H), 5.14 – 5.04 (m, 2H), 4.96 (d, *J* = 3.7 Hz, 1H), 4.88 (d, *J* = 11.0 Hz, 1H), 4.74 – 4.66 (m, 2H), 4.61 (d, *J* = 10.9 Hz, 1H), 4.48 (d, *J* = 11.8 Hz, 2H), 4.40 (td, *J* = 10.2, 3.5 Hz, 1H), 4.34 -4.26 (m, 2H), 4.22 – 4.12 (m, 1H), 3.62 (dd, *J* = 10.9, 2.6 Hz, 1H), 3.53 (s, 3H), 1.47 (s, 9H), 1.21 (d, *J* = 6.3 Hz, 3H).^{13}C NMR (100 MHz, $CDCl_3$): δ 171.6, 171.4, 156.2, 155.9, 138.3, 137.8, 136.5, 128.5, 128.5, 128.3, 128.2, 128.1, 127.9, 127.6, 100.3, 80.5, 76.5, 75.1, 74.2, 72.2, 71.5, 66.9, 57.9, 52.6, 50.8, 28.4, 18.0. HRMS (ESI) m/z: $[M + H]^+$ Calcd for $C_{38}H_{48}O_{11}N_3$ 722.3283; Found: 722.3266.

MethylO-((2S,3R,4R,5R,6S)-4,5-bis(benzyloxy)-3-(((benzyloxy)carbonyl)amino)-6-carbamoyltetrahydro-2H-pyran-2-yl)-N-(tert-butoxycarbonyl)-L-allothreoninate (8b). 8b was prepared from **7b** (1.52 g, 2.10 mmol) following the procedure described for **8**. Purification by flash chromatography (petroleum ether/ethyl acetate = 1:1) gave the title compound (1.15 g, 1.59 mmol, 76%) as a white solid. m.p 240-242 ºC; $[\alpha]_D^{21}$ +145.1 (*c* 0.7, DMF). IR (film)ν_{max} cm^{-1}: 3404, 3354, 3199, 2971, 2925, 1744, 1690, 1641, 1522, 1452, 1369,

1349, 1287, 1055, 1023, 934, 794, 732, 695. ^{1}H NMR (400 MHz, DMSO-d_6): δ 7.41 (s, 1H), 7.34 – 7.14 (m, 17H), 7.11 (s, 1H), 5.05 (s, 2H), 4.94 (d, J = 3.8 Hz, 1H), 4.66 (t, J = 11.3 Hz, 2H), 4.50 (t, J = 10.5 Hz, 2H), 4.34 (s, 1H), 4.07 (t, J = 8.0 Hz, 1H), 4.02 – 3.85 (m, 3H), 3.64 (dd, J = 11.2, 2.8 Hz, 1H), 3.56 (s, 3H), 1.34 (s, 9H), 1.01 (d, J = 6.1 Hz, 3H); ^{13}C NMR (100 MHz, DMSO-d$_6$): δ 171.3, 170.5, 156.3, 155.4, 138.8, 138.6, 137.2, 128.3, 128.1, 128.0, 127.7, 127.7, 127.6, 127.5, 127.4, 127.3, 95.1, 78.6, 75.7, 74.4, 74.3, 72.0, 71.4, 71.0, 65.2, 58.3, 51.8, 50.6, 28.1, 15.4. HRMS (ESI) m/z: $[M + H]^+$ Calcd for $C_{38}H_{48}O_{11}N_3$ 722.3283; Found: 722.3264.

O-((2S,3R,4R,5R,6S)-4,5-bis(benzyloxy)-3-(((benzyloxy)carbonyl)amino)-6-carbamoyltetrahydro-2H-pyran-2-yl)-N-(tert-butoxycarbonyl)-L-threonine (9a). 9a (56 mg) was prepared from **8a** (70 mg, 0.097 mmol) following the procedure described for **9** in 82% yield as a white solid. which was used in the next reaction without further purification.

O-((2S,3R,4R,5R,6S)-4,5-bis(benzyloxy)-3-(((benzyloxy)carbonyl)amino)-6-carbamoyltetrahydro-2H-pyran-2-yl)-N-(tert-butoxycarbonyl)-L-allothreonine (9b). 9b (941 mg) was prepared from **8b** (1.2 g, 1.66 mmol) following the procedure described for **9** in 80% yield as a white solid. which was used in the next reaction without further purification.

Benzyl(6R,9S,12S)-9-(2-(benzyloxy)-2-oxoethyl)-6-((R)-1-(((2S,3R,4R,5R,6S)-4,5-bis(benzyloxy)-3-(((benzyloxy)carbonyl)amino)-6-carbamoyltetrahydro-2H-pyran-2-yl)oxy)ethyl)-12-(4-methoxybenzyl)-2,2-dimethyl-4,7,10-trioxo-3-oxa-5,8,11-triazatridecan-13-oate (30a). 30a was prepared from **9** (65 mg, 0.091 mmol) following the procedure described for **30**. Purification by flash chromatography (DCM/MeOH = 97:3) gave the title compound (75 mg, 0.063 mmol, 71%) as a white solid. m.p. 216-218 ^{o}C, $[\alpha]_D^{15}$+8.7 (c 0.5, DMF). IR (film)ν_{max} cm^{-1}: 3317, 3206, 3063, 3033, 2980, 2927, 1734, 1692, 1651, 1538, 1514, 1454, 1391, 1284, 1247, 1170, 1137, 1058, 1019, 843, 738, 697, 558. ^{1}H NMR (600 MHz, DMSO-d_6): δ 8.53 (d, J = 7.6 Hz, 1H), 8.29 (d, J = 8.0 Hz, 1H), 7.48 (s, 1H), 7.38 – 7.15 (m, 25H), 7.11 (d, J = 8.7 Hz, 2H), 7.02 (d, J = 10.2 Hz, 1H), 6.88 (d, J = 8.8 Hz, 1H), 6.79 (d, J = 8.7 Hz, 2H), 5.17 (d, J = 12.8 Hz, 1H), 5.08 – 4.98 (m, 5H), 4.93 (d, J = 12.9 Hz, 1H), 4.80 – 4.75 (m, 1H), 4.68 (dd, J = 11.6, 5.1 Hz, 2H), 4.56 – 4.43 (m, 4H), 4.35 (dd, J = 8.9, 3.3 Hz, 1H), 4.16 – 4.09 (m, 2H), 3.98 – 3.93 (m, 1H), 3.79 (d, J = 12.8 Hz, 1H), 3.68 (s, 3H), 2.94 (dd, J = 7.7, 2.6 Hz, 2H), 2.71 (dd, J = 16.5, 4.9 Hz, 1H), 2.56 – 2.50 (m, 1H), 1.37 (s, 9H), 1.02 (d, J = 6.5 Hz, 3H); ^{13}C NMR (150 MHz, DMSO-d$_6$) δ 171.0, 170.5, 170.3, 169.6, 168.4, 158.0, 156.2, 155.7, 138.9, 138.7, 137.1, 135.8, 135.6, 130.1, 128.6, 128.4, 128.3, 128.3, 128.2, 128.2, 128.1, 128.0, 128.0, 127.9, 127.9, 127.8, 127.6, 127.4, 127.2, 127.2, 127.2, 127.1, 127.0, 113.7, 99.2, 78.8, 77.3, 76.9, 74.7, 74.2, 71.3, 71.1, 65.9, 65.8, 65.2, 58.2, 54.9, 54.3, 53.6, 50.7, 48.9, 41.8, 36.6, 35.7, 28.1, 16.3; HRMS (ESI) m/z: $[M + H]^+$ Calcd for $C_{65}H_{74}O_{16}N_5$ 1180.5125; Found: 1180.5136.

Benzyl(6S,9R,12S)-9-(2-(benzyloxy)-2-oxoethyl)-6-((R)-1-(((2S,3R,4R,5R,6S)-4,5-bis(benzyloxy)-3-(((benzyloxy)carbonyl)amino)-6-carbamoyltetrahydro-2H-pyran-2-yl)oxy)ethyl)-12-(4-methoxybenzyl)-2,2-dimethyl-4,7,10-trioxo-3-oxa-5,8,11-triazatridecan-13-oate (30b). 30b was prepared from **9a** (56 mg, 0.079 mmol) following the

procedure described for **30**. Purification by flash chromatography (DCM/MeOH = 97:3) gave the title compound (65 mg, 0.055 mmol, 70%) as a white solid. m.p 72-74 ºC, $[\alpha]_D^{20}$ +80.4 (*c* 0.5, $CHCl_3$). IR (film)ν_{max} cm^{-1}: 3475, 3337, 3063, 3033, 2977, 2934, 1681, 1513, 1455, 1388, 1364, 1248, 1168, 1056, 1025, 913, 845, 739, 698, 559; ^{1}H NMR (600 MHz, DMSO-d_6): δ 8.46 (d, *J* = 7.6 Hz, 1H), 8.17 (d, *J* = 7.6 Hz, 1H), 7.47 (s, 1H), 7.40 – 7.15 (m, 25H), 7.12 (d, *J* = 9.2 Hz, 1H), 7.02 (d, *J* = 8.4 Hz, 2H), 6.88 (d, *J* = 8.6 Hz, 1H), 6.74 (d, *J* = 8.5 Hz, 2H), 5.11 (d, *J* = 12.6 Hz, 1H), 5.04 (dd, *J* = 19.0, 6.5 Hz, 4H), 4.91 (d, *J* = 3.0 Hz, 1H), 4.88 (d, *J* = 12.7 Hz, 1H), 4.73 (q, *J* = 7.6 Hz, 1H), 4.67 (t, *J* = 11.4 Hz, 2H), 4.57 – 4.48 (m, 3H), 4.41 (s, 1H), 4.19 (d, *J* = 8.5 Hz, 1H), 4.16 – 4.12 (m, 1H), 4.02 (td, *J* = 10.6, 3.2 Hz, 2H), 3.83 – 3.79 (m, 1H), 3.64 (s, 3H), 2.94 (dd, *J* = 13.6, 6.0 Hz, 1H), 2.83 (dd, *J* = 13.6, 8.4 Hz, 1H), 2.66 (d, *J* = 4.7 Hz, 1H), 2.55 (dd, *J* = 16.3, 7.8 Hz, 1H), 1.41 (s, 9H), 1.08 (d, *J* = 6.2 Hz, 3H); ^{13}C NMR (150 MHz, DMSO-d_6): δ 170.9, 170.5, 169.9, 169.7, 169.3, 158.0, 156.2, 155.5, 138.8, 138.7, 137.2, 135.9, 135.6, 130.1, 128.4, 128.3, 128.2, 128.1, 128.0, 127.9, 127.9, 127.8, 127.6, 127.3, 127.2, 127.1, 113.6, 99.7, 78.5, 76.7, 76.4, 74.7, 74.1, 71.2, 66.0, 65.7, 65.3, 58.0, 54.9, 53.8, 50.8, 49.1, 45.8, 38.2, 36.2, 36.1, 28.2, 17.5. HRMS (ESI) m/z: $[M + H]^+$ Calcd for $C_{65}H_{74}O_{16}N_5$ 1180.5125; Found: 1180.5110.

Benzyl(6S,9R,12S)-9-(2-(benzyloxy)-2-oxoethyl)-6-((S)-1-(((2S,3R,4R,5R,6S)-4,5-bis(benzyloxy)-3-(((benzyloxy)carbonyl)amino)-6-carbamoyltetrahydro-2H-pyran-2-yl)oxy)ethyl)-12-(4-methoxybenzyl)-2,2-dimethyl-4,7,10-trioxo-3-oxa-5,8,11-triazatridecan-13-oate (30c). 30c was prepared from **9b** (235 mg, 0.33 mmol) following the procedure described for **30**. Purification by flash chromatography (DCM/MeOH = 97:3) gave the title compound (306 mg, 0.26 mmol, 79%) as a white solid. m.p 78-80 ºC, $[\alpha]_D^{21}$ +52.3 (*c* 1.05, $CHCl_3$). IR (film)ν_{max} cm^{-1}: 3476, 3331, 3063, 3033, 2971, 2933, 1732, 1690, 1666, 1536, 1514, 1454, 1388, 1366, 1352, 1302, 1283, 1247, 1174, 1132, 1057, 1025, 920, 824, 736, 697, 532; ^{1}H NMR (400 MHz, DMSO-d_6): δ 8.63 (d, *J* = 8.1 Hz, 1H), 7.99 (d, *J* = 8.1 Hz, 1H), 7.47 (s, 1H), 7.42 – 7.20 (m, 25H), 7.16 – 7.06 (m, 3H), 6.97 (d, *J* = 8.0 Hz, 2H), 6.69 (d, *J* = 8.1 Hz, 2H), 5.15 – 5.00 (m, 5H), 4.97 – 4.87 (m, 2H), 4.84 – 4.64 (m, 4H), 4.58 (d, *J* = 11.3 Hz, 2H), 4.44 – 4.38 (m, 2H), 4.16 – 3.98 (m, 3H), 3.91 – 3.82 (m, 1H), 3.62 (s, 3H), 2.95 (dd, *J* = 13.9, 5.9 Hz, 1H), 2.82 (dd, *J* = 13.7, 8.9 Hz, 1H), 2.72 – 2.67 (m, 1H), 2.50 – 2.44 (m, 1H), 1.40 (s, 9H), 1.02 (d, *J* = 6.4 Hz, 3H); ^{13}C NMR (100 MHz, DMSO-d_6): δ 170.9, 170.4, 169.6, 168.6, 164.6, 158.0, 156.3, 155.1, 138.9, 137.4, 135.9, 135.6, 130.2, 128.5, 128.4, 128.2, 128.1, 128.0, 127.9, 127.8, 127.6, 127.5, 127.4, 127.3, 127.2, 113.5, 94.5, 78.8, 76.0, 75.1, 74.3, 71.9, 71.4, 66.0, 65.8, 65.1, 59.3, 54.9, 53.5, 50.7, 49.1, 38.2, 36.2, 28.1, 14.7. HRMS (ESI) m/z: $[M + H]^+$ Calcd for $C_{65}H_{74}O_{16}N_5$ 1180.5125; Found:1180.5135.

Benzyl(6S,9S,12S)-9-(2-(benzyloxy)-2-oxoethyl)-6-((S)-1-(((2S,3R,4R,5R,6S)-4,5-bis(benzyloxy)-3-(((benzyloxy)carbonyl)amino)-6-carbamoyltetrahydro-2H-pyran-2-yl)oxy)ethyl)-12-(4-methoxybenzyl)-2,2-dimethyl-4,7,10-trioxo-3-oxa-5,8,11-triazatridecan-13-oate (30d). **30d** was prepared from **9b** (200 mg, 0.28 mmol) following the procedure described for **30**. Purification by flash chromatography (DCM/MeOH = 97:3) gave the title compound (253 mg, 0.21 mmol, 76%) as a white solid. m.p 161-163 ºC; $[\alpha]_D^{22}$ +73.0 (*c* 0.78, $CHCl_3$). IR (film)ν_{max} cm^{-1}: 3473, 3444, 3281, 3063, 3033, 2975, 2934, 1741, 1678, 1612, 1512, 1454, 1389, 1343, 1301, 1248, 1172, 1057, 1025, 907, 738, 698, 550. ^{1}H

NMR (400 MHz, DMSO-d_6): δ 8.62 (d, J = 6.8 Hz, 1H), 8.17 (d, J = 7.9 Hz, 1H), 7.44 (s, 1H), 7.40 – 7.18 (m, 23H), 7.12 (dd, J = 9.4, 4.0 Hz, 4H), 7.00 (d, J = 9.4 Hz, 1H), 6.90 (s, 1H), 6.76 (d, J = 8.7 Hz, 2H), 5.12 – 4.91 (m, 7H), 4.85 – 4.76 (m, 1H), 4.69 (dd, J = 11.4, 5.5 Hz, 2H), 4.61 – 4.50 (m, 3H), 4.45 (s, 1H), 4.26 – 3.99 (m, 4H), 3.92 – 3.83 (m, 1H), 3.68 (s, 3H), 3.01 (dd, J = 13.7, 7.1 Hz, 1H), 2.89 (dd, J = 13.8, 7.8 Hz, 1H), 2.70 (dd, J = 16.0, 4.7 Hz, 1H), 2.59 (dd, J = 15.9, 9.5 Hz, 1H), 1.38 (s, 9H), 1.02 (d, J = 6.2 Hz, 3H); ^{13}C NMR (100 MHz, DMSO-d6): δ 171.2, 170.9, 170.4, 169.7, 169.3, 158.0, 156.1, 155.2, 138.9, 137.1, 135.8, 135.6, 130.1, 128.5, 128.4, 128.3, 128.2, 128.1, 128.1, 128.0, 127.7, 127.6, 127.4, 127.2, 113.7, 94.5, 78.5, 75.9, 75.0, 74.4, 71.8, 71.4, 70.9, 65.8, 65.4, 58.6, 54.9, 54.4, 50.6, 49.1, 36.8, 35.8, 28.1, 14.6. HRMS (ESI) m/z: $[M + H]^+$ Calcd for $C_{65}H_{74}O_{16}N_5$ 1180.5125; Found: 1180.5161.

Benzyl(S)-3-((2R,3R)-2-amino-3-(((2S,3R,4R,5R,6S)-4,5-bis(benzyloxy)-3-(((benzyloxy)carbonyl)amino)-6-carbamoyltetrahydro-2H-pyran-2-yl)oxy)butanamido)-4-(((S)-1-(benzyloxy)-3-(4-methoxyphenyl)-1-oxopropan-2-yl)amino)-4-oxobutanoate (31a). 31a was prepared from **30a** (200 mg, 0.168 mmol) following the procedure described for **31**. Purification by flash chromatography (DCM/MeOH = 95:5) gave the title compound (154 mg, 0.142 mmol, 85%) as a white solid. m.p.195 -198 ºC; $[\alpha]_D^{18}$ +65.7 (c 1.0, $CHCl_3$). IR (film)ν_{max} cm^{-1}: 3328, 3063, 3033, 2926, 1736, 1686, 1645, 1539, 1515, 1454, 1380, 1354, 1285, 1251, 1173, 1138, 1056, 1025, 911, 825, 737, 697. ^{1}H NMR (600 MHz, DMSO-d_6): δ 8.47 (d, J = 7.2 Hz, 1H), 8.17 (s, 1H), 7.49 (s, 1H), 7.42 (d, J = 9.3 Hz, 1H), 7.39 – 7.17 (m, 25H), 7.10 (d, J = 8.5 Hz, 2H), 6.79 (d, J = 8.6 Hz, 2H), 5.14 – 4.95 (m, 7H), 4.75 - 4.68 (m, 3H), 4.55 (dd, J = 11.3, 5.6 Hz, 2H), 4.50 – 4.42 (m, 2H), 4.14 (s, 1H), 4.04 (td, J = 11.4, 3.6 Hz, 1H), 3.93 – 3.88 (m, 1H), 3.83 (dd, J = 11.1, 2.4 Hz, 1H), 3.69 (s, 3H), 3.43 (s, 1H), 2.96 (dd, J = 13.8, 6.1 Hz, 1H), 2.89 (dd, J = 13.6, 8.7 Hz, 1H), 2.73 – 2.67 (m, 1H), 2.60 (dd, J = 16.0, 9.1 Hz, 1H), 1.79 (br., 2H), 0.92 (d, J = 6.4 Hz, 3H). ^{13}C NMR (150 MHz, DMSO-d_6): δ 171.0, 170.6, 170.4, 169.8, 158.0, 156.3, 138.8, 138.7, 137.1, 135.9, 135.6, 130.1, 128.6, 128.4, 128.3, 128.1, 128.0, 128.0, 127.9, 127.9, 127.7, 127.6, 127.4, 127.3, 113.7, 97.6, 76.3, 74.7, 74.2, 71.2, 66.0, 65.7, 65.3, 57.6, 54.9, 54.1, 50.9, 48.8, 40.1, 39.9, 39.8, 39.7, 39.5, 39.4, 39.2, 39.1, 36.5, 35.7, 14.9. HRMS (ESI) m/z: $[M + H]^+$ Calcd for $C_{60}H_{66}O_{14}N_5$ 1080.4601; Found: 1080.4599.

Benzyl(R)-3-((2S,3R)-2-amino-3-(((2S,3R,4R,5R,6S)-4,5-bis(benzyloxy)-3-(((benzyloxy)carbonyl)amino)-6-carbamoyltetrahydro-2H-pyran-2-yl)oxy)butanamido)-4-(((S)-1-(benzyloxy)-3-(4-methoxyphenyl)-1-oxopropan-2-yl)amino)-4-oxobutanoate (31b). 31b was prepared from **30b** (160 mg, 0.135 mmol) following the procedure described for **31**. Purification by flash chromatography (DCM/MeOH = 95:5) gave the title compound (128 mg, 0.118 mmol, 87%) as a white solid. m.p.188-190 ºC; $[\alpha]_D^{20}$ +74.9 (c 1.16, $CHCl_3$). IR (film)ν_{max} cm^{-1}: 3307, 3064, 3033, 2930, 1736, 1684, 1649, 1537, 1513, 1454, 1383, 1350, 1286, 1248, 1170, 1137, 1056, 1025, 916, 734, 696. ^{1}H NMR (400 MHz, DMSO-d_6): δ 8.49 (d, J = 7.9 Hz, 1H), 8.16 (s, 1H), 7.47 (s, 1H), 7.43 – 7.17 (m, 27H), 7.04 (d, J = 8.6 Hz, 2H), 6.75 (d, J = 8.6 Hz, 2H), 5.14 – 4.99 (m, 5H), 4.99 – 4.91 (m, 2H), 4.75 (br, 1H), 4.66 (t, J = 10.5 Hz, 2H), 4.59 – 4.47 (m, 3H), 4.42 (s, 1H), 4.14 (s, 1H), 4.01 (td, J = 10.5 , 3.5 Hz, 1H), 3.78 (dd, J = 11.2, 2.7 Hz, 1H), 3.74 – 3.67 (m, 1H), 3.64 (s, 3H), 3.19 (d, J = 5.0 Hz, 1H), 2.96 (dd, J = 13.8, 5.9 Hz, 1H), 2.83 (dd, J = 13.8, 8.6 Hz, 1H), 2.65 (dd, J = 16.3, 4.7 Hz, 1H), 2.60

– 2.52 (m, 1H), 1.93 (br., 2H), 1.04 (d, J = 6.2 Hz, 3H); ^{13}C NMR (100 MHz, DMSO-d_6): δ 172.2, 171.1, 170.7, 170.2, 169.9, 158.1, 156.3, 138.9, 138.7, 137.3, 136.0, 135.7, 130.2, 128.5, 128.4, 128.3, 128.3, 128.2, 128.1, 128.0, 127.9, 127.7, 127.5, 127.4, 127.3, 113.6, 99.8, 79.4, 76.4, 74.6, 74.2, 71.2, 66.1, 65.8, 65.3, 59.2, 54.9, 53.8, 51.1, 48.9, 36.5, 36.1, 17.0. HRMS (ESI) m/z: $[M + H]^+$ Calcd for $C_{60}H_{66}O_{14}N_5$ 1080.4601; Found: 1080.4564.

Benzyl(R)-3-((2S,3S)-2-amino-3-(((2S,3R,4R,5R,6S)-4,5-bis(benzyloxy)-3-(((benzyloxy)carbonyl)amino)-6-carbamoyltetrahydro-2H-pyran-2-yl)oxy)butanamido)-4-(((S)-1-(benzyloxy)-3-(4-methoxyphenyl)-1-oxopropan-2-yl)amino)-4-oxobutanoate (31c). 31c was prepared from **30c** (386 mg, 0.327 mmol) following the procedure described for **31**. Purification by flash chromatography (DCM/MeOH = 95:5) gave the title compound (308 mg, 0.285 mmol, 87%) as a white solid. m.p 206-208 ºC. $[\alpha]_D^{22}$ +68.4 (c 0.86, $CHCl_3$). IR (film)ν_{max} cm^{-1}: 3394, 3334, 3063, 3032, 2934, 1737, 1693, 1668, 1640, 1535, 1514, 1453, 1380, 1281, 1247, 1174, 1134, 1056, 924, 878, 825, 778, 737, 697. ^{1}H NMR (400 MHz, DMSO-d_6) δ 8.47 (d, J = 7.9 Hz, 1H), 8.19 (br, 1H), 7.50 (s, 1H), 7.43 – 7.17 (m, 27H), 7.06 (d, J = 8.2 Hz, 2H), 6.77 (d, J = 8.3 Hz, 2H), 5.05 (m, 7H), 4.73 (d, J = 11.2 Hz, 3H), 4.57 (d, J = 11.7 Hz, 3H), 4.45 (s, 1H), 4.29 (s, 1H), 4.08 (m, 1H), 3.91 (m, 2H), 3.67 (s, 3H), 3.41 (m, 1H), 2.98 (dd, J = 13.8, 6.1 Hz, 1H), 2.86 (dd, J = 14.0, 8.5 Hz, 1H), 2.70 - 2.58 (m, 2H), 1.87 (br., 2H), 0.94 (d, J = 6.3 Hz, 3H). ^{13}C NMR (100 MHz, DMSO-d_6): δ 172.2, 171.1, 170.8, 170.2, 169.8, 158.0, 156.3, 138.9, 138.8, 137.2, 135.9, 135.7, 130.2, 128.5, 128.4, 128.3, 128.3, 128.1, 128.1, 128.0, 127.9, 127.7, 127.5, 127.5, 127.4, 127.3, 127.3, 113.6, 94.8, 76.3, 74.7, 74.3, 73.2, 71.4, 71.3, 66.1, 65.7, 65.2, 59.0, 54.9, 53.8, 50.8, 48.8, 36.4, 36.0, 12.6. HRMS (ESI) m/z: $[M + H]^+$ Calcd for $C_{60}H_{66}O_{14}N_5$ 1080.4601; Found: 1080.4609.

Benzyl(S)-3-((2S,3S)-2-amino-3-(((2S,3R,4R,5R,6S)-4,5-bis(benzyloxy)-3-(((benzyloxy)carbonyl)amino)-6-carbamoyltetrahydro-2H-pyran-2-yl)oxy)butanamido)-4-(((S)-1-(benzyloxy)-3-(4-methoxyphenyl)-1-oxopropan-2-yl)amino)-4-oxobutanoate (31d). 31d was prepared from **30d** (180 mg, 0.152 mmol) following the procedure described for **31**. Purification by flash chromatography (DCM/MeOH = 95:5) gave the title compound (135 mg, 0.125 mmol, 82%) as a white solid. m.p 196-198 ºC; $[\alpha]_D^{22}$ +76.3 (c 0.35, $CHCl_3$). IR (film)ν_{max} cm^{-1}: 3331, 3063, 3032, 2933, 1735, 1691, 1642, 1536, 1514, 1453, 1281, 1249, 1174, 1133, 1056, 924, 822, 806, 734, 696. ^{1}H NMR (500 MHz, DMSO-d_6): δ 8.53 (d, J = 7.2 Hz, 1H), 8.19 (br, 1H), 7.48 (s, 1H), 7.39 – 7.24 (m, 27H), 7.13 (d, J = 8.1 Hz, 2H), 6.80 (d, J = 8.1 Hz, 2H), 5.11 – 5.00 (m, 6H), 4.96 (d, J = 3.7 Hz, 1H), 4.78 – 4.68 (m, 3H), 4.56 (dd, J = 11.4, 3.1 Hz, 2H), 4.52 – 4.43 (m, 2H), 4.21 (s, 1H), 4.05 (td, J = 10.3, 3.6 Hz, 1H), 3.96 – 3.87 (m, 2H), 3.69 (s, 3H), 3.45 (s, 1H), 2.99 – 2.91 (m, 2H), 2.76 – 2.61 (m, 2H), 1.89 (br., 2H), 0.91 (d, J = 6.2 Hz, 3H). ^{13}C NMR (125 MHz, DMSO-d6): δ 172.0, 171.3, 170.9, 170.4, 170.0, 158.1, 156.3, 138.9, 138.8, 137.2, 136.0, 135.7, 130.2, 128.7, 128.4, 128.4, 128.3, 128.2, 128.1, 128.1, 128.0, 127.9, 127.8, 127.6, 127.5, 127.5, 127.4, 127.4, 127.3, 127.3, 113.7, 95.0, 76.2, 74.7, 74.4, 73.2, 71.4, 71.1, 66.0, 65.8, 65.3, 59.0, 55.0, 54.4, 50.7, 48.5, 36.7, 35.7, 12.7. HRMS (ESI) m/z: $[M + H]^+$ Calcd for $C_{60}H_{66}O_{14}N_5$ 1080.4601; Found: 1080.4571.

Benzyl(5S,9R,12S,15S)-12-(2-(benzyloxy)-2-oxoethyl)-9-((R)-1-(((2S,3R,4R,5R,6S)-4,5-bis(benzyloxy)-3-(((benzyloxy)carbonyl)amino)-6-carbamoyltetrahydro-2H-pyran-2-

yl)oxy)ethyl)-5-(7-((2S,5S,6R)-5,6-dimethyltetrahydro-2H-pyran-2-yl)heptyl)-15-(4-methoxybenzyl)-3,7,10,13-tetraoxo-1-phenyl-2-oxa-4,8,11,14-tetraazahexadecan-16-oate (32a). 32a was prepared from **31a** (170 mg, 0.157 mmol) following the procedure described for **32**. Purification by flash chromatography (DCM/MeOH = 95:3) gave the title compound (181 mg, 0.121 mmol, 77%) as a white solid. m.p. 242 -244 ºC; $[\alpha]_D^{22}$ +43.3 (*c* 0.45, DMF). ^{1}H NMR (600 MHz, DMSO-d_6): δ 8.66 (d, *J* = 8.1 Hz, 1H), 8.54 (d, *J* = 7.1 Hz, 1H), 7.91 (d, *J* = 8.7 Hz, 1H), 7.49 (s, 1H), 7.40 – 7.10 (m, 30H), 7.08 (d, *J* = 8.4 Hz, 2H), 6.78 (d, *J* = 8.2 Hz, 2H), 5.15 (d, *J* = 12.9 Hz, 1H), 5.11 – 4.99 (m, 6H), 4.89 (dd, *J* = 20.2, 12.7 Hz, 2H), 4.80 – 4.68 (m, 4H), 4.60 (d, *J* = 11.7 Hz, 1H), 4.53 (d, *J* = 11.1 Hz, 1H), 4.45 – 4.40 (m, 2H), 4.15 – 4.09 (m, 2H), 3.98 (s, 1H), 3.76 (d, *J* = 9.8 Hz, 2H), 3.67 (s, 3H), 3.18 – 3.05 (m, 2H), 2.98 – 2.94 (m, 1H), 2.68 (s, 2H), 2.41 – 2.37 (m, 2H), 2.17 (d, *J* = 10.3 Hz, 1H), 2.00 – 1.95 (m, 2H), 1.67 – 1.64 (m, 1H), 1.47 – 1.44 (m, 1H), 1.31 – 1.05 (m, 18H), 1.04 (d, *J* = 6.1 Hz, 3H), 0.91 (d, *J* = 5.9 Hz, 3H), 0.74 (d, *J* = 4.2 Hz, 3H). ^{13}C NMR (150 MHz, DMSO-d_6): δ 170.9, 170.7, 170.3, 169.6, 167.8, 162.3, 158.0, 156.4, 138.9, 137.4, 137.1, 135.8, 135.6, 130.1, 129.6, 129.3, 128.7, 128.4, 128.3, 128.2, 128.1, 128.0, 127.8, 127.6, 127.5, 127.4, 127.2, 127.1, 127.0, 113.7, 99.8, 78.6, 77.1, 76.6, 74.3, 71.5, 66.0, 65.8, 65.3, 65.0, 55.8, 54.2, 50.9, 48.9, 36.9, 35.1, 35.0, 32.4, 31.8, 31.3, 30.8, 29.0, 28.7, 28.6, 26.5, 25.2, 19.7, 17.8, 15.4. HRMS (ESI) m/z: $[M + H]^+$ Calcd for $C_{85}H_{103}O_{18}N_6$ 1495.7323; Found: 1495.7296.

Benzyl(5S,9S,12R,15S)-12-(2-(benzyloxy)-2-oxoethyl)-9-((R)-1-(((2S,3R,4R,5R,6S)-4,5-bis(benzyloxy)-3-(((benzyloxy)carbonyl)amino)-6-carbamoyltetrahydro-2H-pyran-2-yl)oxy)ethyl)-5-(7-((2S,5S,6R)-5,6-dimethyltetrahydro-2H-pyran-2-yl)heptyl)-15-(4-methoxybenzyl)-3,7,10,13-tetraoxo-1-phenyl-2-oxa-4,8,11,14-tetraazahexadecan-16-oate (32b). 32b was prepared from **31b** (150 mg, 0.138 mmol) following the procedure described for **32**. Purification by flash chromatography (DCM/MeOH = 95:3) gave the title compound (148 mg, 0.099 mmol, 72%) as a white solid. m.p.232-234 ºC; $[\alpha]_D^{23}$ +38.9 (*c* 0.20, $CHCl_3$). IR (film)ν_{max} cm^{-1}: 3315, 3064, 3033, 2928, 2853, 1733, 1695, 1632, 1540, 1512, 1454, 1378, 1356, 1285, 1252, 1177, 1140, 1056, 1012, 960, 922, 843, 736, 697, 605. ^{1}H NMR (600 MHz, DMSO-d$_6$): ^{1}H NMR (600 MHz, DMSO-d$_6$) δ 8.47 (d, *J* = 7.9 Hz, 1H), 8.34 (d, *J* = 8.2 Hz, 1H), 7.98 (d, *J* = 8.1 Hz, 1H), 7.51 (s, 1H), 7.41 – 7.19 (m, 30H), 7.16 (d, *J* = 6.9 Hz, 3H), 7.04 (d, *J* = 8.4 Hz, 2H), 6.74 (d, *J* = 8.4 Hz, 2H), 5.13 (dd, *J* = 12.7, 5.4 Hz, 2H), 5.10 – 5.01 (m, 4H), 4.96 – 4.90 (m, 3H), 4.82 – 4.75 (m, 1H), 4.67 (d, *J* = 11.2 Hz, 1H), 4.62 (d, *J* = 11.5 Hz, 1H), 4.55 – 4.46 (m, 4H), 4.42 (s, 1H), 4.16 (s, 1H), 4.06 (td, *J* = 10.4, 3.8 Hz, 1H), 3.91 – 3.83 (m, 2H), 3.80 (d, *J* = 12.3 Hz, 1H), 3.63 (s, 3H), 3.18 – 3.10 (m, 1H), 2.99 – 2.91 (m, 2H), 2.90 – 2.84 (m, 1H), 2.72 – 2.65 (m, 1H), 2.46 – 2.37 (m, 1H), 2.35 – 2.28 (m, 1H), 1.71 – 1.64 (m, 1H), 1.55 – 1.47 (m, 1H), 1.44 – 1.12 (m, 18H), 1.08 (d, *J* = 6.4 Hz, 3H), 1.05 (d, *J* = 6.1 Hz, 3H), 0.75 (d, *J* = 5.6 Hz, 3H). ^{13}C NMR (150 MHz, DMSO-d$_6$): δ 171.1, 170.6, 170.3, 170.1, 169.9, 168.9, 158.0, 156.2, 155.6, 138.8, 138.6, 137.4, 137.1, 135.9, 135.6, 130.2, 128.6, 128.4, 128.4, 128.3, 128.3, 128.2, 128.2, 128.0, 128.0, 127.9, 127.9, 127.8, 127.7, 127.6, 127.5, 127.4, 127.3, 127.3, 127.1, 126.9, 113.6, 99.9, 78.6, 76.9, 76.8, 76.7, 76.6, 74.6, 74.2, 72.8, 71.2, 66.0, 65.9, 65.4, 65.0, 56.4, 54.9, 54.0, 53.6, 50.9, 49.0, 48.3, 41.2, 36.9, 36.4, 36.1, 36.1, 36.0, 34.2, 33.0, 32.4, 31.8, 30.9, 29.1, 29.1, 28.9, 25.4, 25.1, 25.1, 23.3, 22.2, 19.8, 17.8, 17.1. HRMS (ESI) m/z: $[M + H]^+$ Calcd for $C_{85}H_{103}O_{18}N_6$ 1495.7323; Found: 1495.7330.

Benzyl(5S,9S,12R,15S)-12-(2-(benzyloxy)-2-oxoethyl)-9-((S)-1-(((2S,3R,4R,5R,6S)-4,5-bis(benzyloxy)-3-(((benzyloxy)carbonyl)amino)-6-carbamoyltetrahydro-2H-pyran-2-yl)oxy)ethyl)-5-(7-((2S,5S,6R)-5,6-dimethyltetrahydro-2H-pyran-2-yl)heptyl)-15-(4-methoxybenzyl)-3,7,10,13-tetraoxo-1-phenyl-2-oxa-4,8,11,14-tetraazahexadecan-16-oate (32c). 32c was prepared from **31c** (160 mg, 0.148 mmol) following the procedure described for **32**. Purification by flash chromatography (DCM/MeOH = 95:3) gave the title compound (166 mg, 0.111 mmol, 75%) as a white solid. m.p. 214-216 °C; $[\alpha]_D^{22}$ +45.0 (*c* 0.18, $CHCl_3$), IR (film)ν_{max} cm^{-1}: 3479, 3293, 3064, 3034, 2928, 2854, 1732, 1689, 1666, 1642, 1538, 1513, 1453, 1377, 1283, 1247, 1175, 1056, 1026, 913, 822, 734, 696. ^{1}H NMR (400 MHz, DMSO-d_6): δ 8.38 (dd, *J* = 12.5, 7.7 Hz, 2H), 8.23 (d, *J* = 8.1 Hz, 1H), 7.46 (d, *J* = 9.5 Hz, 1H), 7.36 – 7.23 (m, 30H), 7.18 – 7.09 (m, 2H), 7.06 (d, *J* = 8.1 Hz, 2H), 6.93 (d, *J* = 9.4 Hz, 1H), 6.76 (d, *J* = 8.2 Hz, 2H), 5.13 – 4.90 (m, 9H), 4.73 – 4.63 (m, 3H), 4.58 – 4.44 (m, 4H), 4.41 – 4.33 (m, 1H), 4.23 (d, *J* = 13.5 Hz, 1H), 4.17 – 4.03 (m, 1H), 3.97 – 3.80 (m, 3H), 3.66 (s, 3H), 3.24 – 3.09 (m, 1H), 3.01 – 2.88 (m, 3H), 2.75 – 2.55 (m, 2H), 2.39 – 2.22 (m, 2H), 1.67 (d, *J* = 7.5 Hz, 1H), 1.57 – 1.46 (m, 1H), 1.43 – 1.13 (m, 16H), 1.12 – 1.09 (m, 1H), 1.07 (d, *J* = 6.4 Hz, 6H), 0.76 (d, *J* = 5.3 Hz, 3H). ^{13}C NMR (100 MHz, DMSO-d_6): δ 171.0, 170.6, 170.1, 169.8, 169.7, 158.0, 156.1, 155.5, 138.8, 138.5, 137.4, 137.0, 135.8, 135.6, 130.1, 128.6, 128.3, 128.3, 128.3, 128.2, 128.1, 128.0, 127.8, 127.8, 127.7, 127.6, 127.5, 127.4, 127.3, 127.2, 113.6, 93.9, 78.6, 76.7, 76.6, 76.5, 74.4, 74.2, 72.8, 71.3, 71.1, 70.7, 65.9, 65.7, 65.4, 64.9, 57.4, 54.8, 54.0, 50.5, 49.1, 48.2, 41.3, 36.9, 36.1, 35.9, 34.0, 33.0, 32.3, 31.7, 30.8, 29.1, 29.0, 28.8, 25.3, 25.1, 23.2, 22.1, 19.7, 17.7, 14.5. HRMS (ESI) m/z: $[M + H]^+$ Calcd for $C_{85}H_{103}O_{18}N_6$ 1495.7323; found: 1495.7316.

Benzyl(5S,9S,12S,15S)-12-(2-(benzyloxy)-2-oxoethyl)-9-((S)-1-(((2S,3R,4R,5R,6S)-4,5-bis(benzyloxy)-3-(((benzyloxy)carbonyl)amino)-6-carbamoyltetrahydro-2H-pyran-2-yl)oxy)ethyl)-5-(7-((2S,5S,6R)-5,6-dimethyltetrahydro-2H-pyran-2-yl)heptyl)-15-(4-methoxybenzyl)-3,7,10,13-tetraoxo-1-phenyl-2-oxa-4,8,11,14-tetraazahexadecan-16-oate (32d). 32d was prepared from **31d** (120 mg, 0.111 mmol) following the procedure described for **32**. Purification by flash chromatography (DCM/MeOH = 95:3) gave the title compound (123 mg, 0.082 mmol, 74%) as a white solid. m.p. 194-196 °C, $[\alpha]_D^{22}$ +43.5 (*c* 0.13, $CHCl_3$), IR (film)ν_{max} cm^{-1}: 3474, 3264, 3064, 3033, 2930, 2854, 1687, 1649, 1612, 1546, 1513, 1454, 1344, 1248, 1173, 1057, 1028, 913, 738, 697. ^{1}H NMR (600 MHz, DMSO-d_6): δ 8.50 (d, *J* = 6.6 Hz, 1H), 8.19 (dd, *J* = 13.0, 7.7 Hz, 2H), 7.43 (s, 1H), 7.38 – 7.18 (m, 30H), 7.14 (d, *J* = 8.4 Hz, 3H), 7.08 (d, *J* = 8.2 Hz, 2H), 6.93 (d, *J* = 9.0 Hz, 1H), 6.75 (d, *J* = 8.4 Hz, 2H), 5.11 – 4.98 (m, 6H), 4.97 – 4.88 (m, 3H), 4.76 (td, *J* = 8.6, 4.4 Hz, 1H), 4.67 – 4.45 (m, 6H), 4.40 (t, *J* = 7.7 Hz, 1H), 4.12 (s, 1H), 4.10 – 4.00 (m, 2H), 3.95 – 3.82 (m, 2H), 3.67 (s, 3H), 3.19 – 3.10 (m, 1H), 3.06 (dd, *J* = 13.7, 6.5 Hz, 1H), 2.96 – 2.83 (m, 2H), 2.73 (dd, *J* = 16.2, 4.5 Hz, 1H), 2.62 (dd, *J* = 16.2, 9.6 Hz, 1H), 2.34 (dt, *J* = 14.1, 6.9 Hz, 1H), 2.26 (dd, *J* = 14.1, 6.4 Hz, 1H), 1.74 – 1.63 (m, 1H), 1.55 – 1.45 (m, 1H), 1.44 – 1.08 (m, 18H), 1.06 (d, J = 6.1 Hz, 1H), 1.00 (d, *J* = 6.1 Hz, 3H), 0.76 (d, *J* = 5.8 Hz, 3H).^{13}C NMR (150MHz, DMSO-d_6): δ 171.3, 170.9, 170.7, 170.4, 169.7, 169.7, 158.0, 156.1, 155.6, 139.0, 138.9, 137.4, 137.1, 135.9, 135.6, 130.2, 128.5, 128.4, 128.3, 128.3, 128.2, 128.2, 128.1, 128.0, 128.0, 127.9, 127.9, 127.8, 127.7, 127.7, 127.6, 127.4, 127.3, 127.2, 127.2, 127.1, 113.6, 94.1, 78.6, 76.8, 76.7, 76.3, 75.0, 74.4, 72.9, 71.4, 71.0, 70.8, 65.9, 65.7, 65.4, 65.0, 57.1, 54.9, 54.7, 50.6, 49.2, 48.4, 41.5, 36.9, 36.5,

36.1, 36.0, 34.2, 33.0, 32.4, 31.8, 30.9, 29.1, 29.0, 28.9, 25.4, 25.1, 25.1, 23.3, 22.2, 19.8, 17.8, 14.4. HRMS (ESI) m/z: $[M + H]^+$ Calcd for $C_{85}H_{103}O_{18}N_6$ 1495.7323; Found: 1495.7299.

(S)-3-((2R,3R)-2-((S)-3-amino-10-((2S,5S,6R)-5,6-dimethyltetrahydro-2H-pyran-2-yl)decanamido)-3-(((2S,3R,4R,5R,6S)-3-amino-6-carbamoyl-4,5-dihydroxytetrahydro-2H-pyran-2-yl)oxy)butanamido)-4-(((S)-1-carboxy-2-(4-methoxyphenyl)ethyl)amino)-4-oxobutanoic acid (1a). 1a (11 mg) was prepared from **32a** (24 mg, 0.016 mmol) following the procedure described for **1** in 77% yield as a white solid (The purification method is the same as **1**). m.p. 205-207 ºC; $[\alpha]_D^{22}$ +35.9 (*c* 0.21,CH_3OH). IR (film)ν_{max} cm^{-1}: 3290, 3070, 2924, 2851, 1670, 1545, 1514, 1421, 1249, 1202, 1185, 1140, 1089, 1041, 838, 801, 722, 613. ^1H NMR (600 MHz, MeOD-d_4): δ 7.15 (d, *J* = 8.6 Hz, 2H), 6.84 (d, *J* = 8.6 Hz, 2H), 5.41 (d, *J* = 3.7 Hz, 1H), 4.76 (dd, *J* = 10.1, 3.8 Hz, 1H), 4.61 (dd, *J* = 8.3, 5.2 Hz, 1H), 4.42 (d, *J* = 5.2 Hz, 1H), 4.26 (d, *J* = 1.4 Hz, 1H), 4.23 (dd, *J* = 2.8, 1.4 Hz, 1H), 4.19 (quint, *J* = 6.3 Hz, 1H), 3.97 (dd, *J* = 10.8, 3.0 Hz, 1H), 3.76 (s, 3H), 3.54-3.46 (m, 2H), 3.28 – 3.21 (m, 1H), 3.14 (dd, *J* = 14.0, 5.2 Hz, 1H), 3.03 (dq, *J* = 8.3, 6.2 Hz, 1H), 2.96 (dd, *J* = 14.0, 8.4 Hz, 1H), 2.87 (dd, *J* = 17.2, 3.8 Hz, 1H), 2.78 (dd, *J* = 16.3, 3.8 Hz, 1H), 2.66 (dd, J = 16.4, 9.2 Hz, 1H), 2.56 (dd, *J* = 16.3, 9.0 Hz, 1H), 1.76 – 1.74 (m, 1H), 1.67 – 1.59 (m, 3H), 1.50 - 1.30 (m, 15H), 1.30 (d, *J* = 6.3 Hz, 3H), 1.21 – 1.18 (m, 2H), 1.15 (d, *J* = 6.2 Hz, 3H), 0.83 (d, *J* = 6.0 Hz, 3H). ^{13}C NMR (150 MHz, MeOD-d_4): δ 174.4, 174.1, 173.4, 173.0, 172.4, 171.3, 160.1, 131.4, 130.1, 114.9, 98.4, 81.1, 79.3, 77.6, 73.5, 70.0, 67.9, 59.0, 55.7, 55.4, 52.3, 51.3, 50.3, 40.4, 38.7, 37.6, 37.5, 37.4, 36.5, 34.0, 33.9, 33.4, 30.8, 30.7, 30.4, 30.3, 26.7, 26.2, 20.0, 18.4, 18.2. HRMS (ESI) m/z: $[M + H]^+$ Calcd for $C_{41}H_{67}O_{14}N_6$ 867.4710; Found: 867.4691.

(R)-3-((2S,3R)-2-((S)-3-amino-10-((2S,5S,6R)-5,6-dimethyltetrahydro-2H-pyran-2-yl)decanamido)-3-(((2S,3R,4R,5R,6S)-3-amino-6-carbamoyl-4,5-dihydroxytetrahydro-2H-pyran-2-yl)oxy)butanamido)-4-(((S)-1-carboxy-2-(4-methoxyphenyl)ethyl)amino)-4-oxobutanoic acid (1b). 1b (10 mg) was prepared from **32b** (22 mg, 0.015 mmol) following the procedure described for **1** in 74% yield as a white solid (The purification method is the same as **1**). m.p 176-179℃. $[\alpha]_D^{19}$ +44.3 (*c* 0.55, CH_3OH), IR (film)ν_{max} cm^{-1}: 3263, 3069, 2930, 2855, 1669, 1544, 1514, 1432, 1259, 1202, 1138, 1091, 1037, 801, 722, 601.^1H NMR (600 MHz, MeOD-d_4): δ 7.12 (d, *J* = 8.5 Hz, 2H), 6.84 (d, *J* = 8.5 Hz, 2H), 5.19 (d, *J* = 3.6 Hz, 1H), 4.69 (dd, *J* = 8.4, 4.9 Hz, 1H), 4.63 (dd, *J* = 8.5, 5.2 Hz, 1H), 4.52 (d, *J* = 1.6 Hz, 1H), 4.37 (q, *J* = 5.9 Hz, 1H), 4.30 – 4.23 (m, 2H), 4.03 (dd, *J* = 10.8, 2.7 Hz, 1H), 3.76 (s, 3H), 3.57 – 3.50 (m, 1H), 3.46 (dd, *J* = 10.8, 3.7 Hz, 1H), 3.28 – 3.22 (m, 1H), 3.16 (dd, *J* = 13.9, 5.1 Hz, 1H), 3.03 (dq, *J* = 8.7, 6.2 Hz, 1H), 2.92 (dd, *J* = 14.0, 8.7 Hz, 1H), 2.85 – 2.80 (m, 1H), 2.71 – 2.65 (m, 1H), 2.62 – 2.56 (m, 1H), 1.77 – 1.73 (m, 1H), 1.69 – 1.59 (m, 3H), 1.50 – 1.28 (m, 15H), 1.25 (d, *J* = 6.4 Hz, 3H), 1.21 – 1.18 (m, 2H), 1.15 (d, *J* = 6.2 Hz, 3H), 0.83 (d, *J* = 5.9 Hz, 3H). ^{13}C NMR (150 MHz, MeOD-d_4): δ 174.4, 173.3, 172.9, 172.4, 160.1, 131.4, 130.0, 114.9, 98.4, 81.1, 79.3, 77.3, 73.4, 70.0, 67.9, 58.7, 55.7, 55.4, 52.3, 51.5, 50.3, 38.7, 37.6, 37.4, 36.8, 33.9, 33.4, 30.7, 30.4, 30.3, 26.7, 26.2, 20.0, 19.3, 18.2. HRMS (ESI) m/z: $[M + H]^+$ Calcd for $C_{41}H_{67}O_{14}N_6$ 867.4710; found: 867.4683.

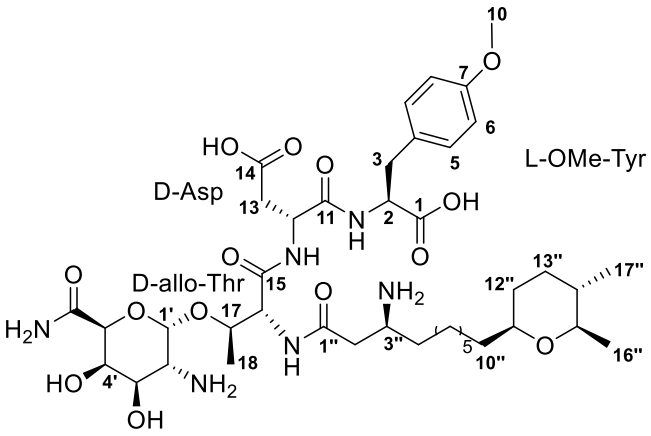
(R)-3-((2S,3S)-2-((S)-3-amino-10-((2S,5S,6R)-5,6-dimethyltetrahydro-2H-pyran-2-yl)decanamido)-3-(((2S,3R,4R,5R,6S)-3-amino-6-carbamoyl-4,5-dihydroxytetrahydro-

2H-pyran-2-yl)oxy)butanamido)-4-(((S)-1-carboxy-2-(4-methoxyphenyl)ethyl)amino)-4-oxobutanoic (1c). 1c (15 mg) was prepared from **32c** (35 mg, 0.023 mmol) following the procedure described for **1** in 75% yield as a white solid (The purification method is the same as **1**). m.p 194-196℃, $[\alpha]^{22.3}_{D}$ +59.0 (*c* 0.12, CH_3OH), IR (film)ν_{max} cm^{-1}： 3268, 3067, 2931, 2864, 1674, 1547, 1514, 1430, 1249, 1200, 1141, 1086, 1044, 879, 838, 800, 723, 601, 521. ^1H NMR (600 MHz, MeOD-d_4): δ 7.12 (d, *J* = 8.3 Hz, 2H), 6.84 (d, *J* = 8.3 Hz, 2H), 5.34 (d, *J* = 3.9 Hz, 1H), 4.71 (dd, *J* = 8.6, 4.8 Hz, 1H), 4.62 (dd, *J* = 8.2, 5.3 Hz, 1H), 4.52 (d, *J* = 5.9 Hz, 1H), 4.40 (d, *J* = 1.4 Hz,1H), 4.25 (dd, *J* = 3.1, 1.4 Hz, 1H), 4.20 (quint, *J* = 6.3 Hz, 1H), 4.01 (dd, *J* = 10.8, 3.0 Hz, 1H), 3.76 (s, 3H), 3.53-3.45 (m, 2H), 3.30 – 3.21 (m, 1H), 3.14 (dd, *J* = 14.0, 5.2 Hz, 1H), 3.03 (dq, *J* = 8.4, 6.1 Hz, 1H), 2.92 (dd, *J* = 14.0, 8.2 Hz, 1H), 2.70-2.64 (m, 2H), 2.57 (dd, *J* = 17.0, 8.6 Hz, 1H), 2.51 (dd, *J* = 16.6, 9.2 Hz, 1H), 1.78 – 1.74 (m, 1H), 1.67 – 1.59 (m, 3H), 1.49 – 1.30 (m, 15H), 1.27 (d, *J* = 6.4 Hz, 3H), 1.21 – 1.18 (m, 2H), 1.15 (d, *J* = 6.2 Hz, 3H), 0.83 (d, *J* = 5.7 Hz, 3H).^{13}C NMR (150 MHz, MeOD-d_4): δ 174.4, 174.0, 173.7, 172.6, 172.1, 171.2, 160.1, 131.5, 130.0, 114.9, 95.1, 81.1, 79.3, 74.2, 73.7, 70.0, 67.9, 59.0, 55.7, 55.3, 51.8, 51.1, 50.3, 38.7, 37.8, 37.4, 36.8, 33.9, 33.4, 30.7, 30.4, 30.4, 26.7, 26.2, 20.0, 18.2, 15.5. HRMS (ESI) m/z: $[M + H]^+$ Calcd for $C_{41}H_{67}O_{14}N_6$ 867.4710; Found: 867.4687.

(S)-3-((2S,3S)-2-((S)-3-amino-10-((2S,5S,6R)-5,6-dimethyltetrahydro-2H-pyran-2-yl)decanamido)-3-(((2S,3R,4R,5R,6S)-3-amino-6-carbamoyl-4,5-dihydroxytetrahydro-2H-pyran-2-yl)oxy)butanamido)-4-(((S)-1-carboxy-2-(4-methoxyphenyl)ethyl)amino)-4-oxobutanoic acid (1d). 1d (19 mg) was prepared from **32d** (45 mg, 0.030 mmol) following the procedure described for **1** in 74% yield as a white solid (The purification method is the same as **1**). m.p188-190℃, $[\alpha]_D^{22}$ +40.3 (*c* 0.1, MeOH), IR (film)ν_{max} cm^{-1}： 3289, 3066, 2931, 2855, 1669, 1537, 1514, 1438, 1248, 1202, 1140, 1086, 1038, 839, 800, 722, 599, 530. ^1H NMR (600 MHz, MeOD-d_4) δ 7.17 (d, *J* = 8.7 Hz, 2H), 6.84 (d, *J*=8.7Hz, 2H), 5.36 (d, *J* = 3.8 Hz, 1H), 4.73 (dd, *J* = 8.3, 4.9 Hz, 1H), 4.63 – 4.54 (m, 2H), 4.31 (d, *J*=1.4Hz, 1H), 4.22 (dd, *J* = 3.1, 1.4 Hz, 1H), 4.18 (quint, *J* = 6.3 Hz, 1H), 3.96 (dd, *J* = 10.7, 3.1 Hz, 1H), 3.76 (s, 3H), 3.49 (dd, *J* = 10.8, 3.9 Hz, 2H), 3.28-3.22 (m, 1H), 3.09 (dd, *J* = 14.0, 5.9 Hz, 1H), 3.06 – 2.97 (m, 2H), 2.83 (dd, *J* = 17.1, 4.9 Hz, 1H), 2.73 (dd, *J* = 17.2, 8.3 Hz, 1H), 2.69 (dd, *J* = 16.5, 3.9 Hz, 1H), 2.56 (dd, *J* = 16.6, 9.0 Hz, 1H), 1.77-1.72 (m , 1H), 1.68 – 1.59 (m, 3H), 1.50 – 1.30 (m, 15H), 1.28 (d, *J* = 6.2 Hz, 3H), 1.20 – 1.18 (m, 2H), 1.15 (d, *J* = 6.2 Hz, 3H), 0.83 (d, *J* = 6.1 Hz, 3H). ^{13}C NMR (150MHz, MeOD-d_4) δ 174.5, 173.7, 173.6, 172.7, 172.5, 171.2, 160.1, 131.4, 129.9, 114.9, 94.9, 81.1, 79.3, 74.3, 73.7, 70.0, 67.9, 59.0, 55.7, 55.7, 51.9, 51.1, 50.3, 38.7, 37.4, 37.3, 37.3, 37.0, 33.9, 33.8, 33.4, 30.7, 30.4, 30.4, 26.7, 26.2, 20.0, 18.2, 15.4. HRMS (ESI) m/z: $[M + H]^+$ Calcd for $C_{41}H_{67}O_{14}N_6$ 867.4710; Found: 867.4683.

3. The comparison of data of the synthetic compound 1-1d and reported natural Characellide B

After finishing the synthesis of the proposed Characellide B, we compared their data. To our surprise, the NMR data of compound **1** did not match with the data reported for the natural product[1] (Table 1). The detection of a signal at 2.0 ppm in the ^{1}H-NMR spectrum of the natural Characellide B indicated that trace HOAc might exist in the system. To investigate the influence of the presence of acids on the NMR spectra, we added 0.01μL acetic acid to 140μL CD_3OD and found that ^{1}H-NMR spectra did not change (page 74-75 in the SI). Furthermore, when 0.01μL TFA was added to 140μL CD_3OD, the splitting of signals in ^{1}H-NMR became clear, yet the ^{13}C-NMR remained the same (page 75-76 in the SI). Next, we synthesized its four stereoisomers **1a-1d**, focusing on the D-Asp-D-*allo*-Thr fragment to determine the actual structure of characellide B. Upon comparison of the data of the isomers with that of the natural product (Table 2), we found that replacement of the D-Asp-D-*allo*-Thr fragment with L-Asp-L-*allo*-Thr fragment resulted in the NMR data for the 12, 13 and 16 -position to appear similar to that of the natural product. However, the ^{13}C-NMR data for the 17, 18 and 1' -position were different from those of the natural product.



Structure of compound **1**

Table 1: the comparison of ^{1}H and ^{13}C NMR data of compound 1 and reported natural Characellide B

residue	No.	NMR solvent: MeOH-d_4				NMR solvent: DMSO-d_6			
		δ_H(J in Hz)		δ_C		δ_H(J in Hz)		δ_C	
		Natural characellide B[1]	Compd. **1**	Natural Characellide B[1]	Compd. **1**	Natural Characellide B[1]	Compd. **1**	Natural Characellide B[1]	Compd. **1**
O-Me-tyrosine	1			175.1	175.2			172.8	172.6
	2	4.57, dd (8.5, 5.4)	4.58, m	55.7	55.7	4.38, td (8.0, 5.6)	4.40, m	53.8	53.8
	3	3.12, dd	3.16, dd	37.6	37.7	2.94, dd (13.9,	3.00, dd (13.8,	36.1	36.1

		(14.0, 5.4)	(13.8, 5.4)			5.6)	4.8)		
		2.93, dd (14.0, 8.5)	2.93, dd (13.5, 8.4)			2.81, dd (13.9, 8.2)	2.81, dd (13.8, 7.2)		
	4			130.2	130.3			129.2	129.1
	5/9	7.15, d (8.6)	7.15, d (7.8)	131.3	131.4	7.12, d (8.3)	7.12, d (8.4)	130.2	130.2
	6/8	6.84, d (8.8)	6.84, d (8.4)	114.9	114.9	6.82, d (8.3)	6.82, d (8.4)	113.6	113.6
	7			160.1	160.1			157.9	157.9
	10	3.76, s	3.76, s	55.7	55.7	3.71, s	3.71, s	55.0	55.0
	NH					8.30, d (7.9)	8.23, d (7.2)		
Aspartic acid	11			171.8	171.8			169.0	171.8
	12	4.66, dd (8.0, 4.3)	4.66, d （7.2）	50.6	51.6	4.53, td (7.3, 5.3)	4.56, m	48.7	49.4
	13	2.84, dd (16.1, 7.9)	2.60, m	37.3	37.4	2.63, dd (16.2, 5.1)	2.45, m	36.1	36.0
		2.77, dd (16.2, 4.2)	2.60, m			2.58, dd (16.2, 7.0)	2.38, m		
	14			174.8	172.8			172.6	171.4
	NH					8.35, d (7.5)	8.29, s		
threonine	15			171.5	171.8			167.9	168.4
	16	4.53, d (7.2)	4.44, m	58.1	58.8	4.69, dd (8.5, 3.9)	4.49, m	55.6	56.1
	17	4.20, quint (6.5)	4.16, m	76.9	76.5	4.09, dq (6.2, 4.4)	4.06, m	76.1	75.4
	18	1.27, d (6.4)	1.26, d (6.0)	18.1	18.2	1.10, d (6.3)	1.12, d (6.6)	16.3	16.9
	NH					8.60, d (8.4)	8.54, d (7.8)		
Sugar unit	1’	5.37, d (3.8)	5.31, s	97.7	97.6	5.28, d (3.5)	5.24, d (4.8)	95.9	95.5
	2’	3.48, dd (10.8, 3.7)	3.48, dd (10.8, 3.6)	52.1	52.1	3.32, m	3.30	50.3	50.3
	3’	3.95, dd (10.8, 3.1)	3.97, d (10.8)	68.0	68.0	3.69, (10.5, 2.8)	3.71	66.5	66.8
	4’	4.24, dd (3.1, 1.4)	4.24, d (2.4)	70.0	70.0	4.04, bs	4.05, m	68.3	68.4
	5’	4.29, d (1.4)	4.29, d (2.4)	73.1	73.5	4.02, d (1.7)	4.03, m	71.9	71.8
	6’			173.3	173.4			170.0	170.1
	NH					7.89, bs	7.86, bs		
Alkyl chain	1”			172.5	172.8			170.5	170.5
	2”a	2.72, dd (16.6, 4.1)	2.73, m	37.7	37.7	2.65, dd (16.1, 5.9)	2.61, m	37.4	37.4
	2”b	2.56, dd (16.5, 8.5)	2.58, dd (16.5, 8.4)			2.50, m	2.50		
	3”	3.54, m	3.53, m	50.1	50.2	3.38, m	3.39	48.0	48.0
	4”a	1.67, m	1.67, m	33.9	33.9	1.51, m	1.55, m	32.3	32.4

	4”b	1.62, m	1.63, m			1.47, m	1.47, m		
	5”a	1.41, m	1.42, m	26.2	26.2	1.32, m	1.30, m	24.3	24.5
	5”b					1.27, m			
	6”	1.32, m	2H	30.4	30.4	1.22, m	1.23, m	28.9	29.1
	7”		2H						
	8”	1.30, m	2H	30.7	30.7	1.23, m	1.23, m	28.8	28.8
	9”a	1.33, m	1H	26.7	26.7	1.32, m	1H	25.1	25.1
	9”b		1H			1.23, m	1H		
	10”a	1.48, m	1.48, m	37.4	37.4	1.37, m	1.37, m	35.9	35.9
	10”b	1.37, m	1.37, m			1.29, m	1.29, m		
	11”	3.26, m	3.25, m	79.3	79.3	3.16, m	3.16, m	76.7	76.7
	12”a	1.60, m	1.61, m	33.4	33.4	1.54, m	1.53, m	31.8	31.8
	12”b	1.21, m	1.20, m			1.12, m	1.12, m		
	13”a	1.75, m	1.76, m	33.9	33.9	1.68, m	1.68, m	32.3	32.2
	13”b	1.20, m	1.20, m			1.10, m	1.11		
	14”	1.19, m	1.19, m	38.7	38.7	1.11, m	1.11	36.9	36.9
	15”	3.04, dq (8.7, 6.2)	3.04, m	81.1	81.2	2.94, m	2.94, m	78.6	78.6
	16”	1.16, d (6.2)	1.16, d (6.0)	20.0	20.0	1.06, d (6.1)	1.06, d (6.0)	19.8	19.8
	17”	0.83, d (5.9)	0.83, d (6.0)	18.2	18.2	0.77, d (5.2)	0.77, d (5.4)	17.8	17.8
	NH_2					7.89, bs	7.86, bs		

1.Afoullouss, S.; Calabro, K.; Genta-Jouve, G.; Gegunde, S.; Alfonso, A.; Nesbitt, R.; Morrow, C.; Alonso, E.; Botana, L. M.; Allcock, A. L.; Thomas, O. P., Treasures from the Deep: Characellides as Anti-Inflammatory Lipoglycotripeptides from the Sponge Characella pachastrelloides. *Org. Lett.,* 2019, *21* (1), 246-251.

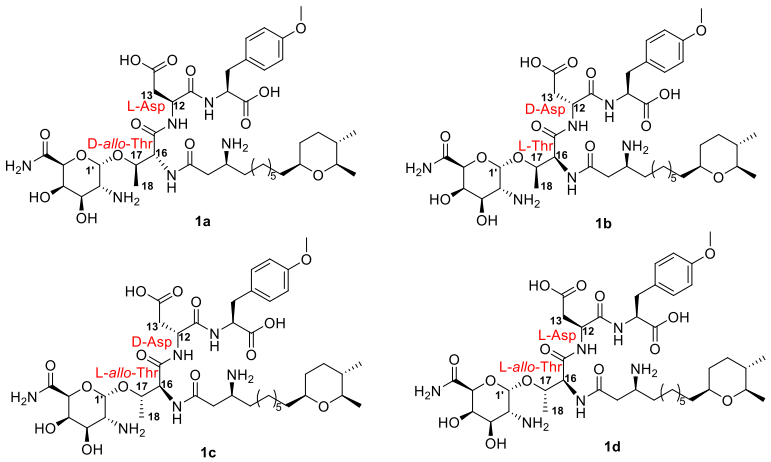
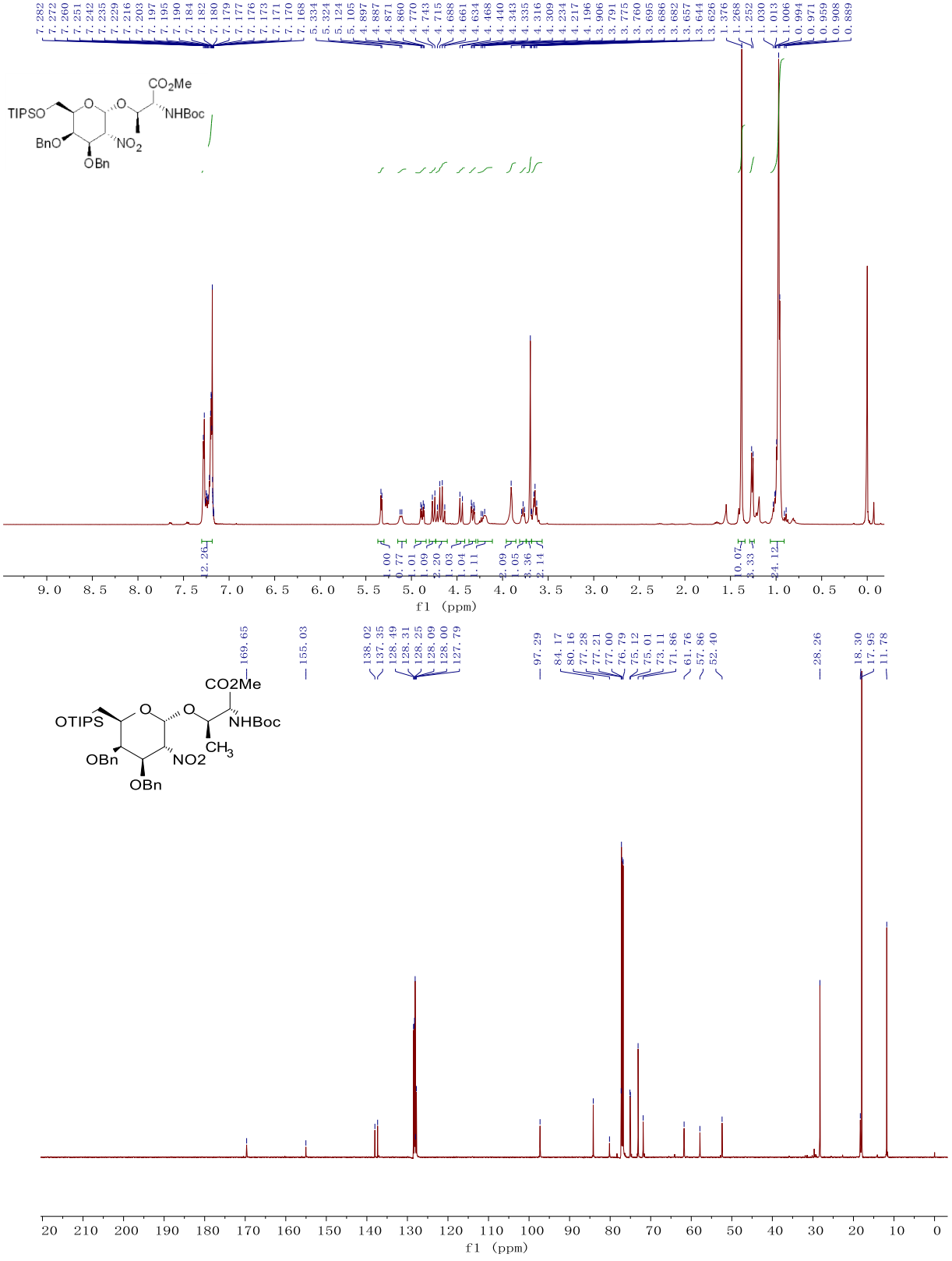


Table 2 the comparison of ^{1}H and ^{13}C NMR data of compound 1-1d in 12, 13, 16, 17, 18 and 1′-position and reported natural Characellide B

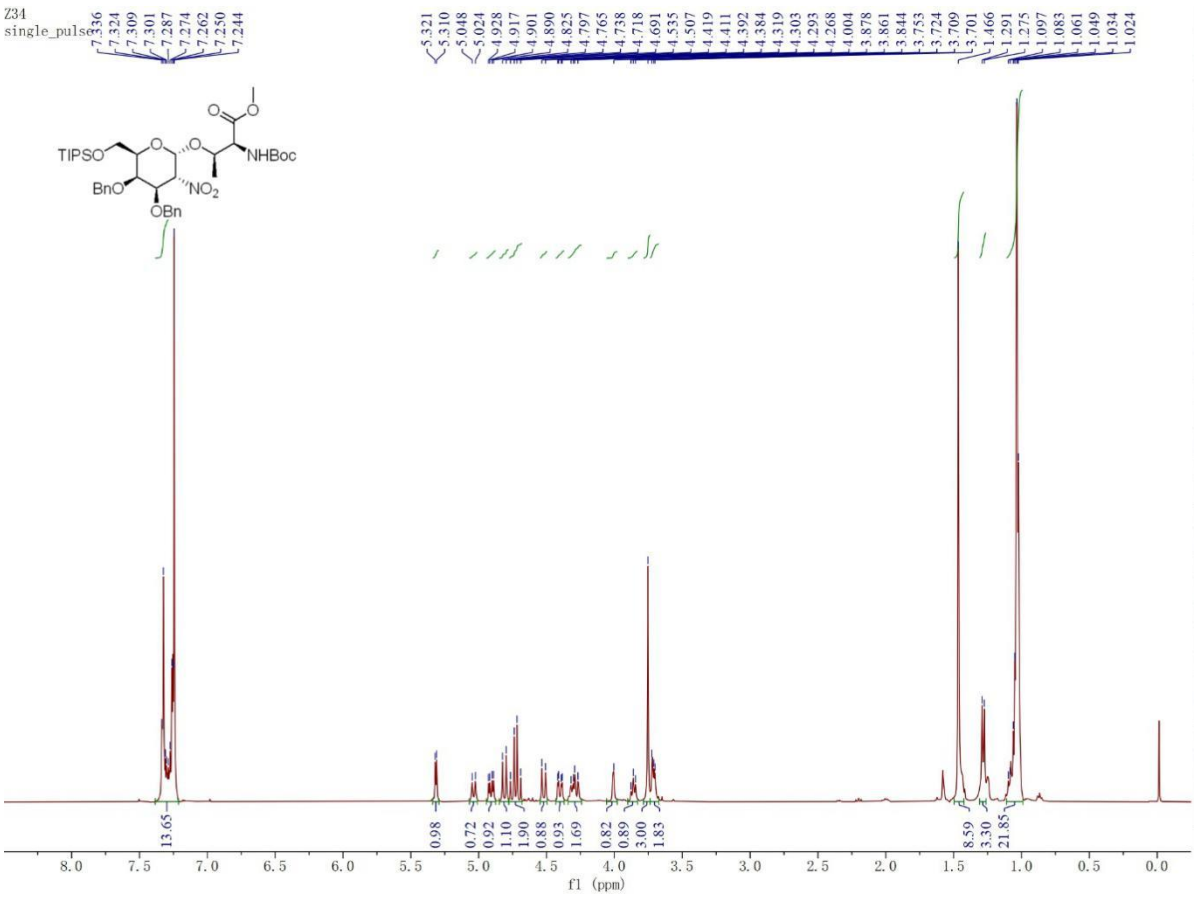
position		Characellide B	**1**	**1a**	**1b**	**1c**	**1d**
12	δ_H (ppm)	4.66, dd (8.0, 4.3)	4.66, d (7.2)	4.76, dd (10.1, 3.8)	4.69, dd (8.4, 4.9)	4.71, dd (8.6, 4.8)	4.73, dd (8.3, 4.9)
	δ_C (ppm)	50.6	51.6	50.3	51.5	51.1	51.1
13	δ_H (ppm)	2.77, dd (16.2, 4.2); 2.84, dd (16.1, 7.9)	2.60，m	2.56, dd (16.3, 9.0); 2.78, dd (16.3, 3.8)	2.60，m	2.66，m	2.73, dd (17.2, 8.3); 2.83, dd (17.1, 4.9)
	δ_C (ppm)	37.3	37.4	37.4	37.4	37.4	37.4
16	δ_H (ppm)	4.53, d (7.2)	4.44，m	4.42, d (5.2)	4.52, d (1.2)	4.52, d (5.9)	4.57, d (6.6)
	δ_C (ppm)	58.1	58.8	59.0	58.7	59.0	59.0
17	δ_H (ppm)	4.20	4.16	4.19	4.36	4.20	4.18
	δ_C (ppm)	76.9	76.5	77.6	77.3	73.7	74.3
18	δ_H (ppm)	1.27	1.26	1.30	1.25	1.27	1.28
	δ_C (ppm)	18.1	18.2	18.2	19.3	15.5	15.4
1’	δ_H (ppm)	5.37, d (3.7)	5.31, s	5.41, d (3.7)	5.19, d (3.6)	5.34, d (3.9)	5.36, d (3.8)
	δ_C (ppm)	97.7	97.6	98.4	98.4	95.1	94.9

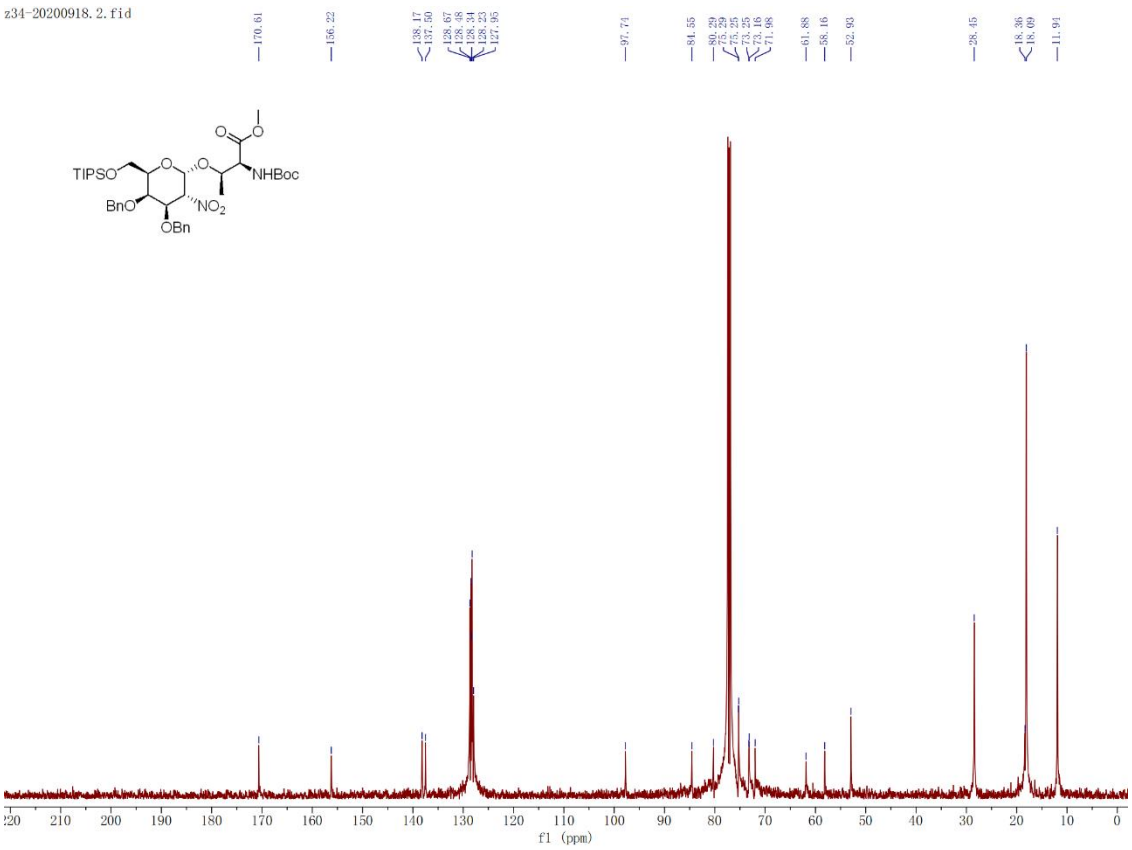
4. ^{1}H, ^{13}C, and 2D-NMR Spectral Copies

(1) ^{1}H NMR (400 MHz) and ^{13}C NMR (100 MHz) Spectra of compound 4 in $CDCl_3$

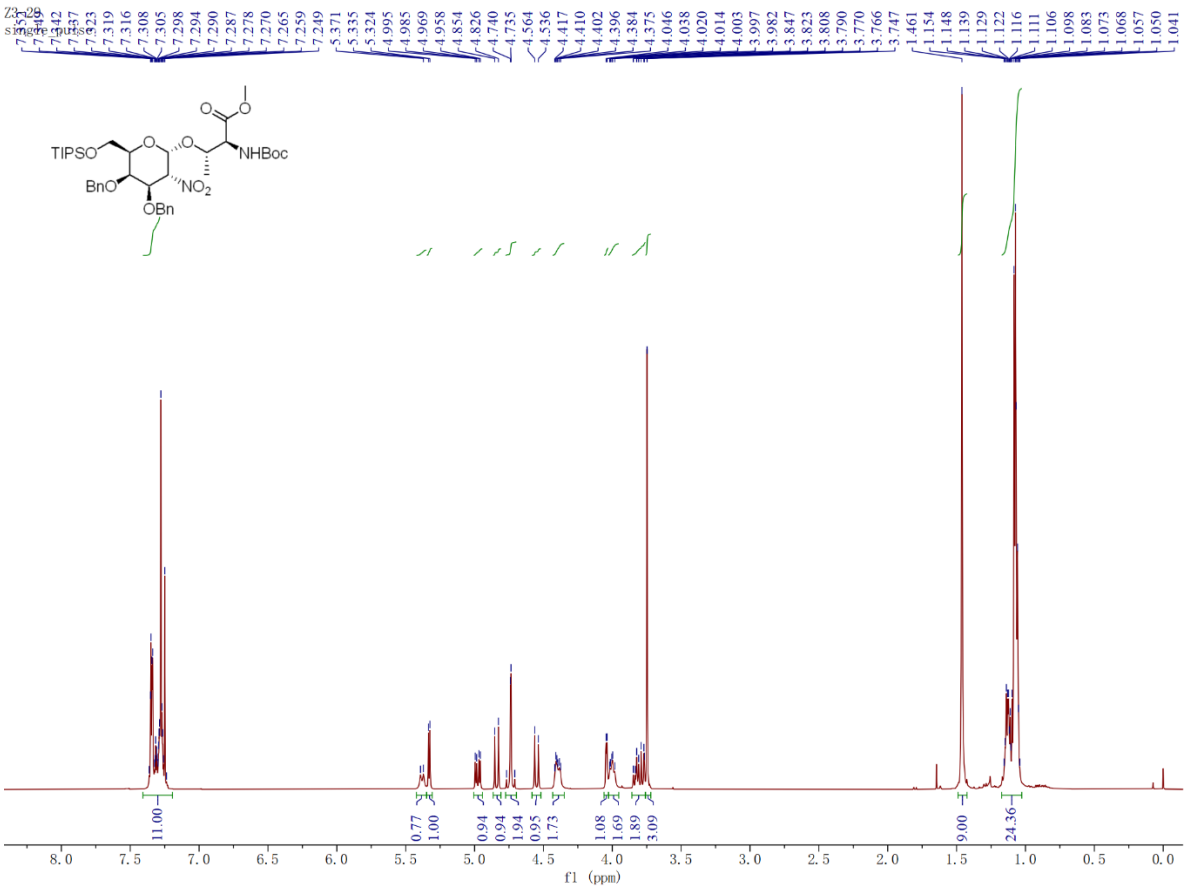


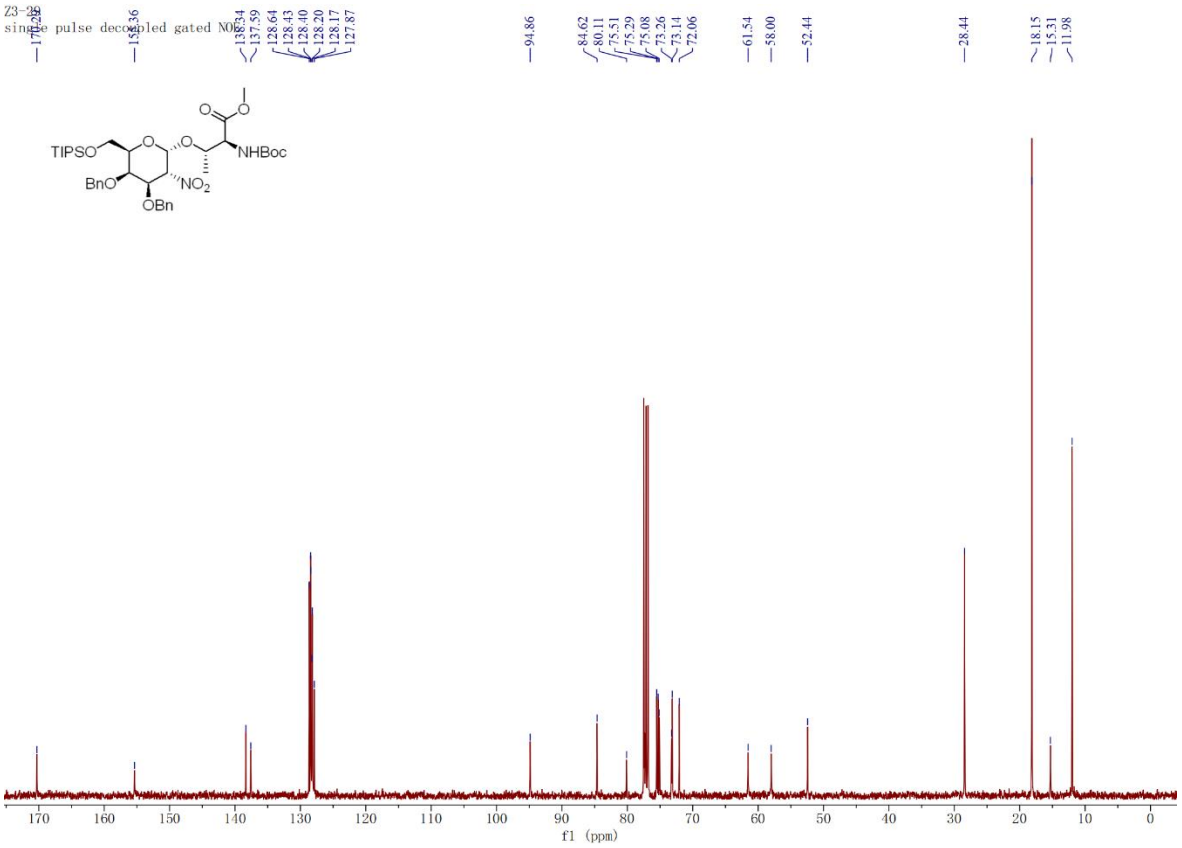
(2) ^{1}H NMR (400 MHz) and ^{13}C NMR (100 MHz) Spectra of compound 4a in $CDCl_3$



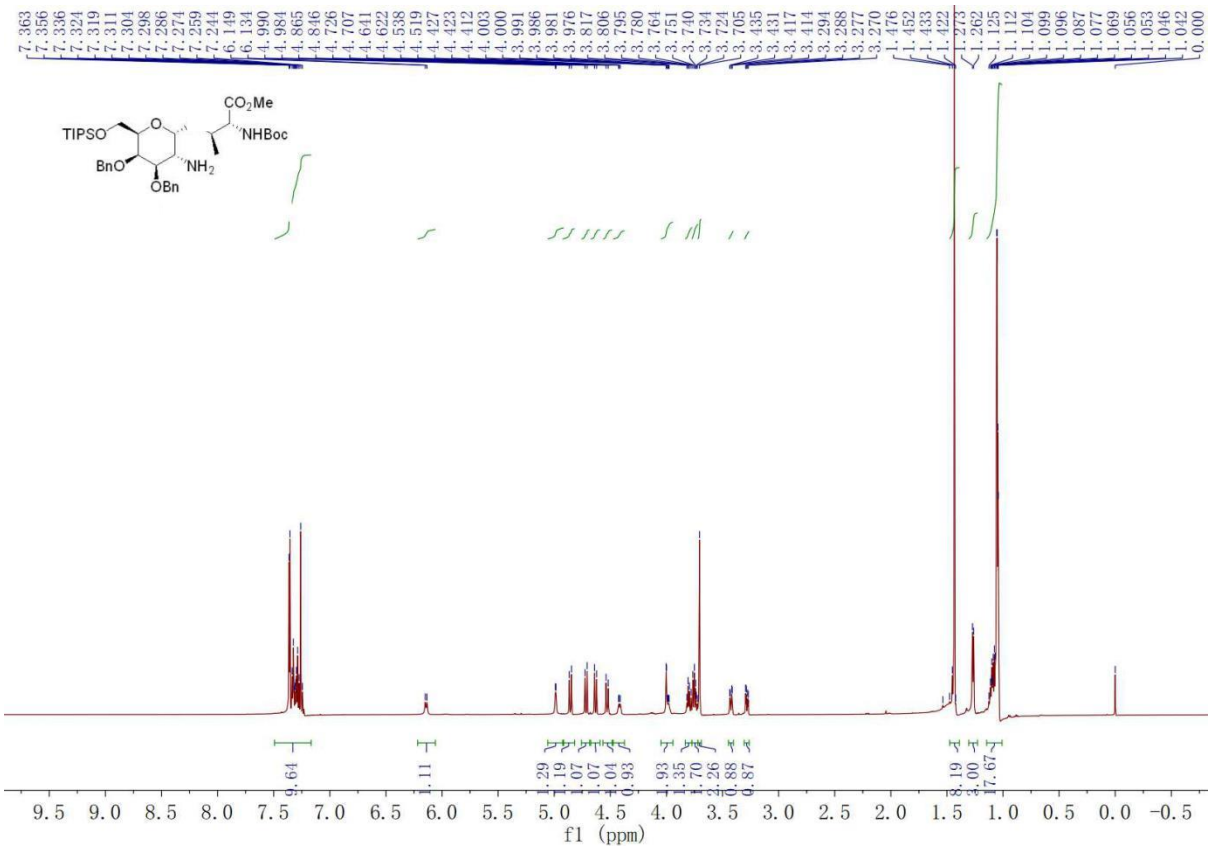


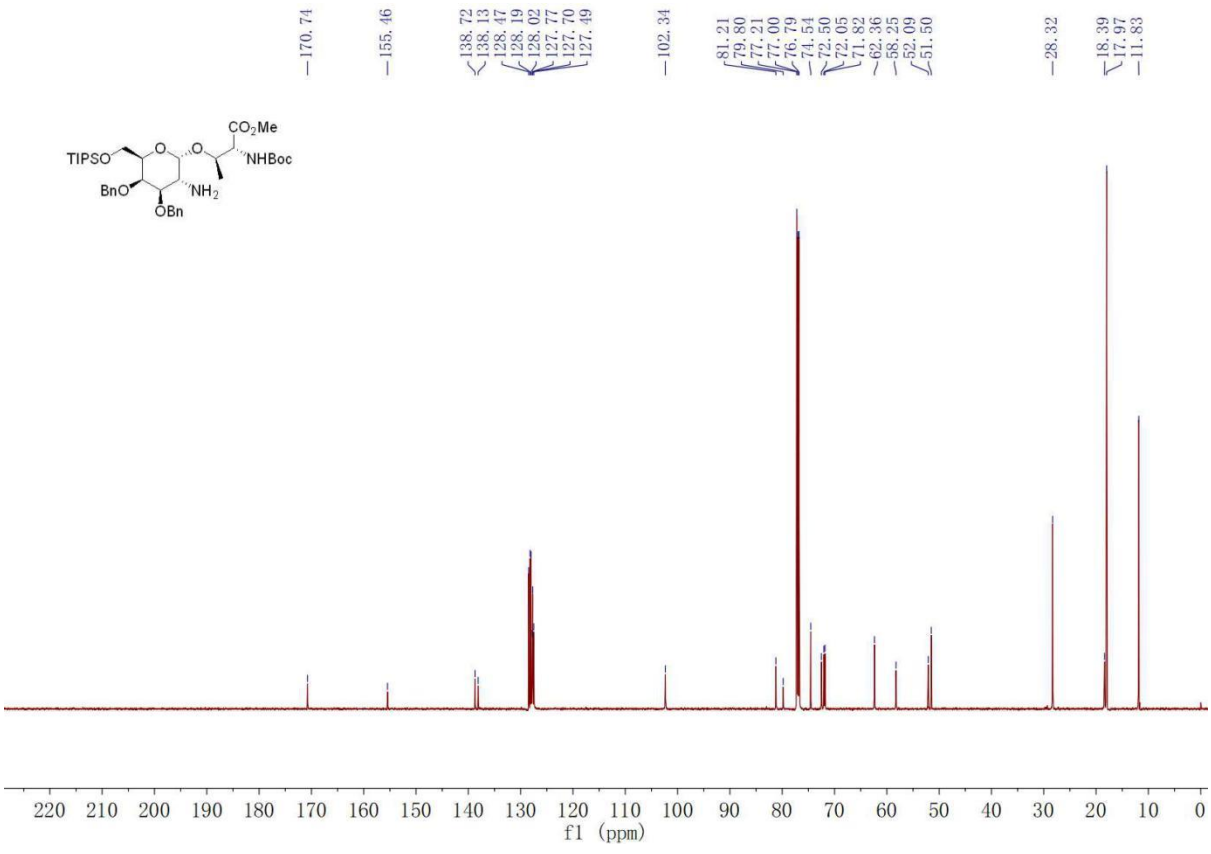
(3) ^{1}H NMR (400 MHz) and ^{13}C NMR (100 MHz) Spectra of compound 4b in $CDCl_3$



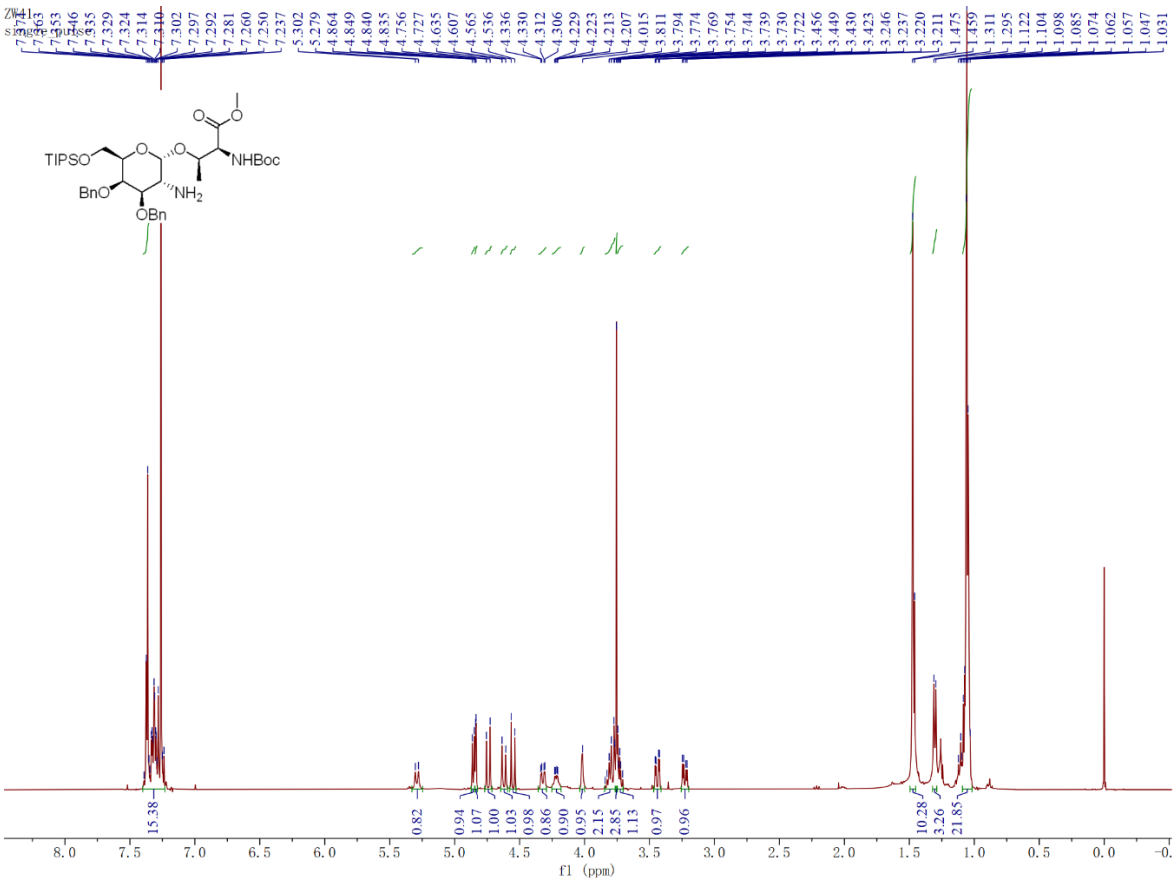


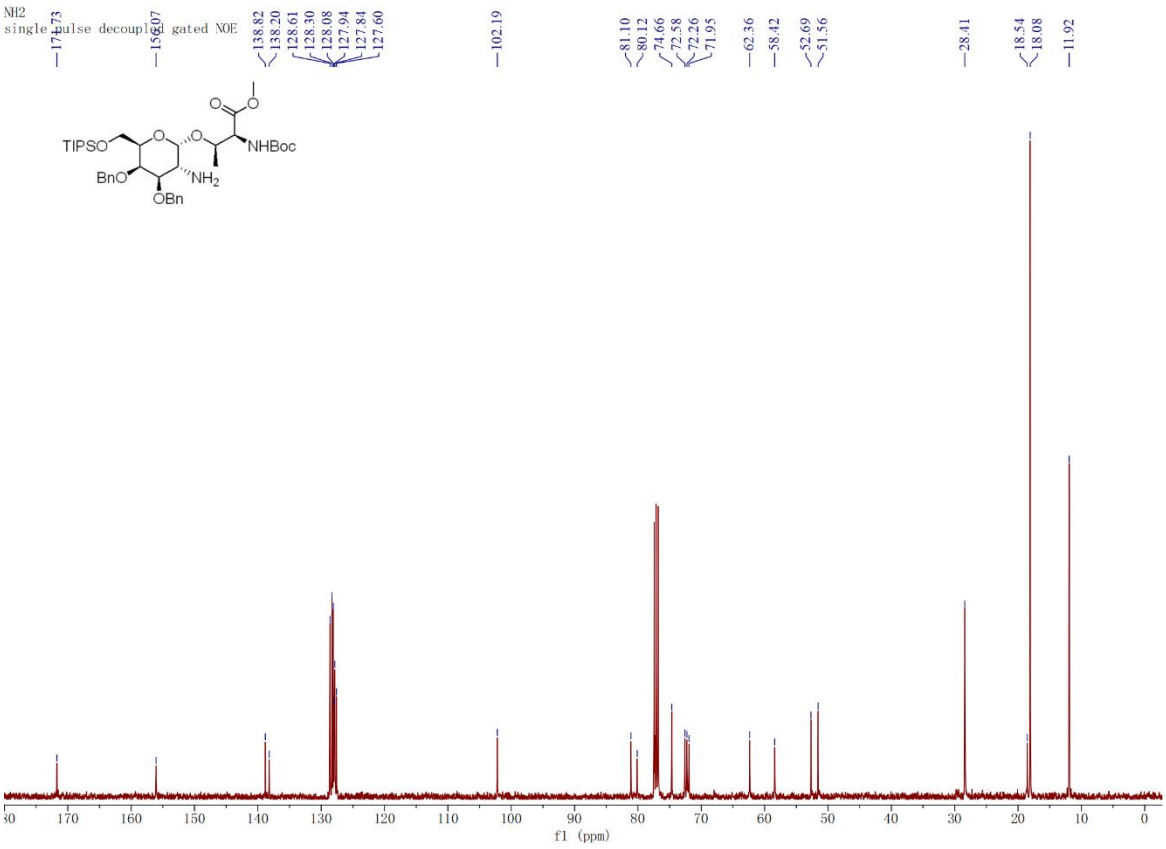
(4) ^{1}H NMR (600 MHz) and ^{13}C NMR (150 MHz) Spectra of compound 5 in $CDCl_3$



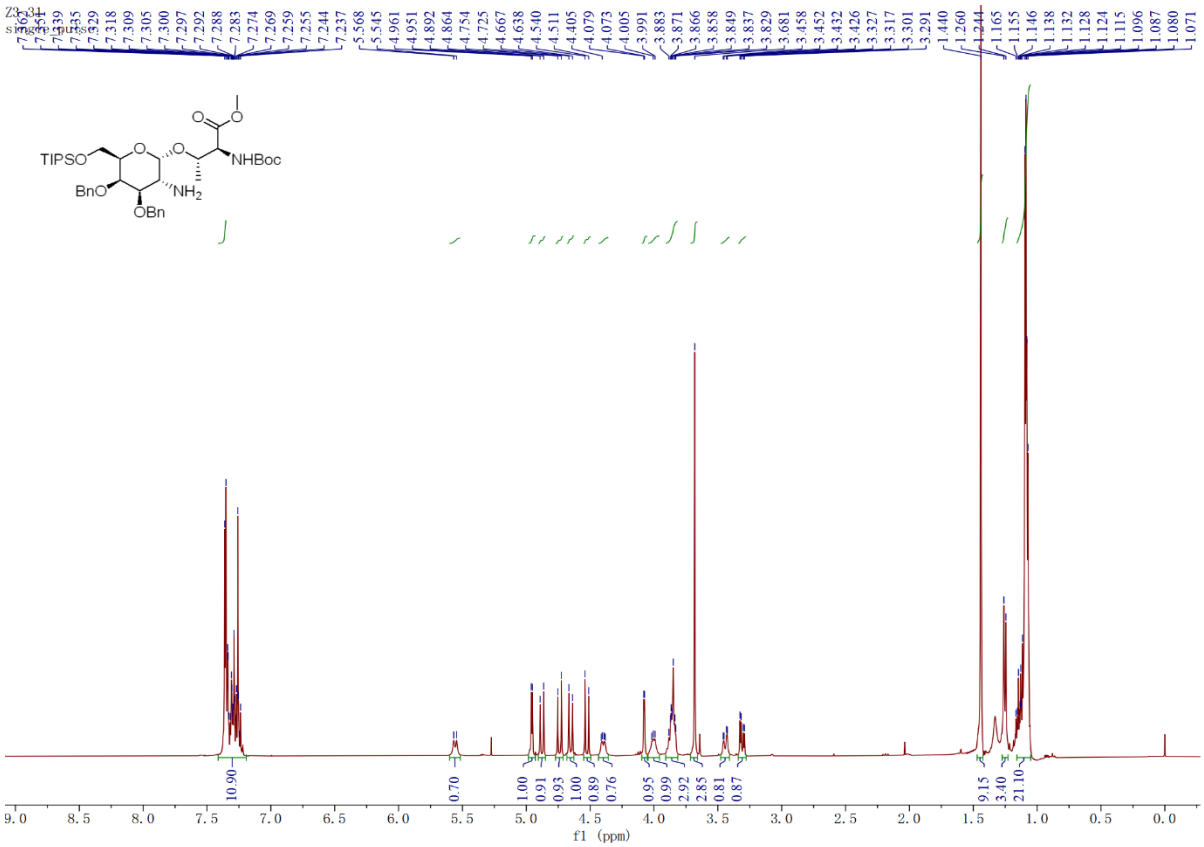


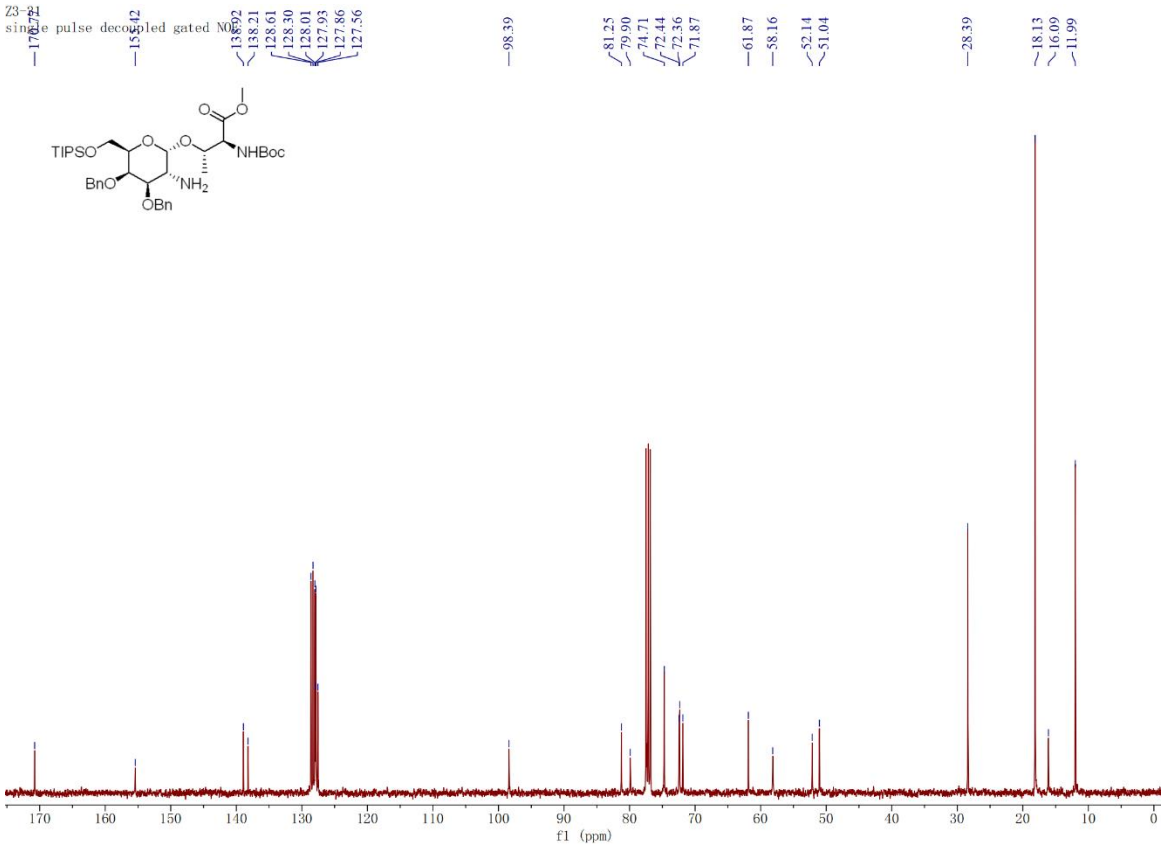
(5) ^{1}H NMR (400 MHz) and ^{13}C NMR (100 MHz) Spectra of compound 5a in $CDCl_3$



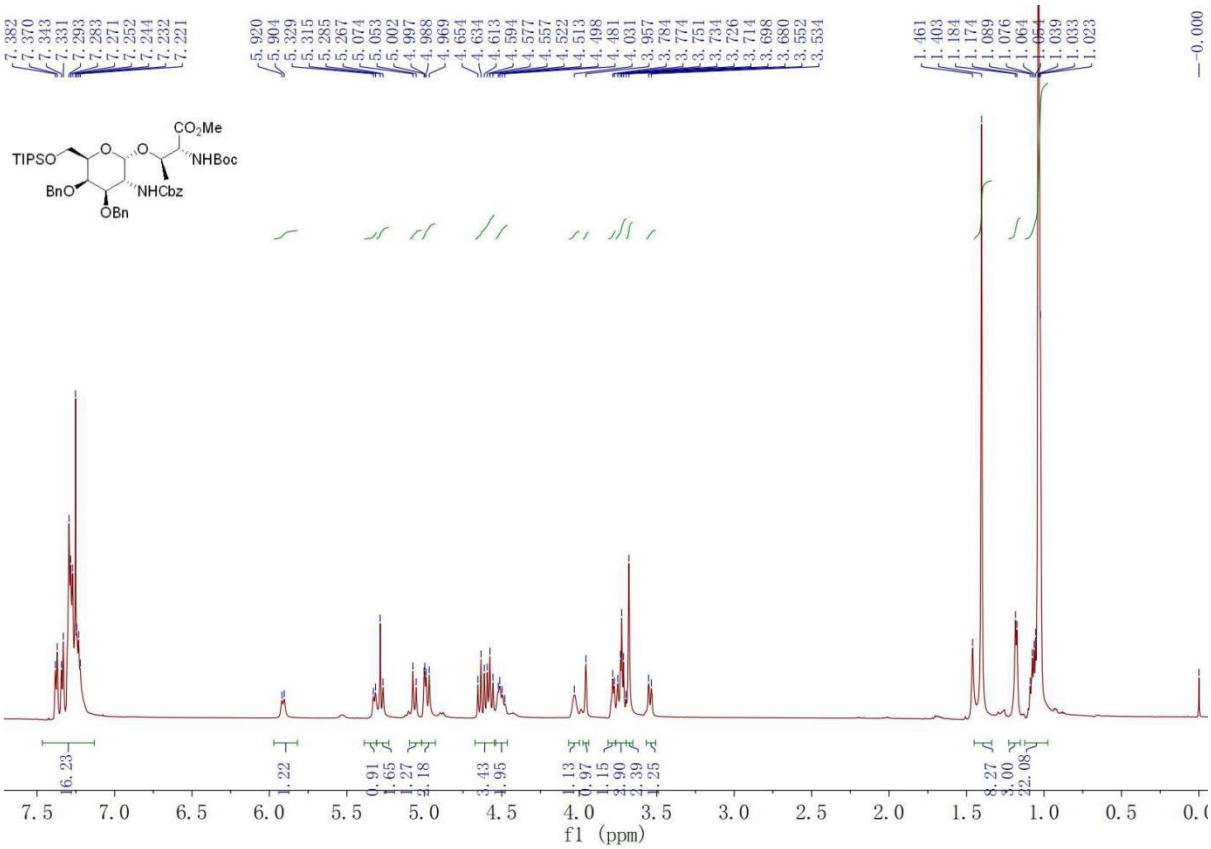


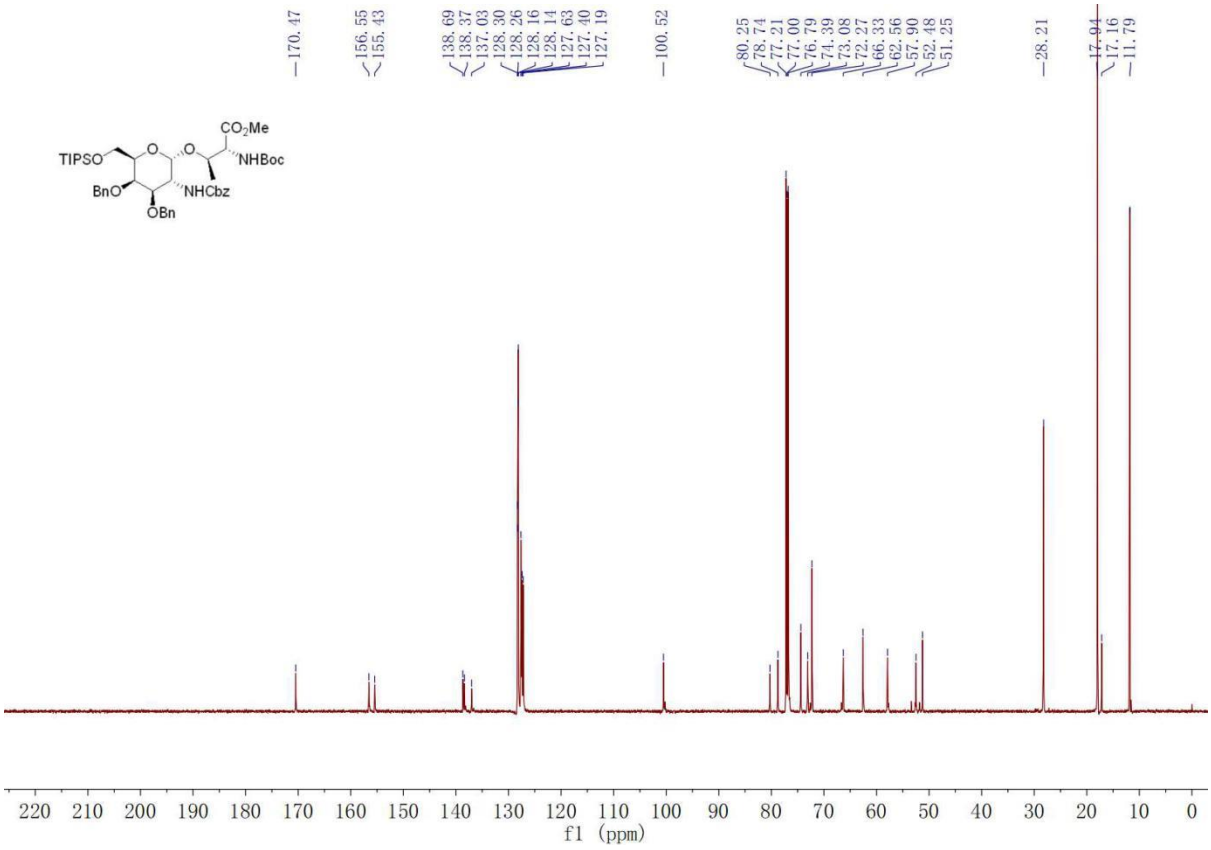
(6) ^{1}H NMR (400 MHz) and ^{13}C NMR (100 MHz) Spectra of compound 5b in $CDCl_3$



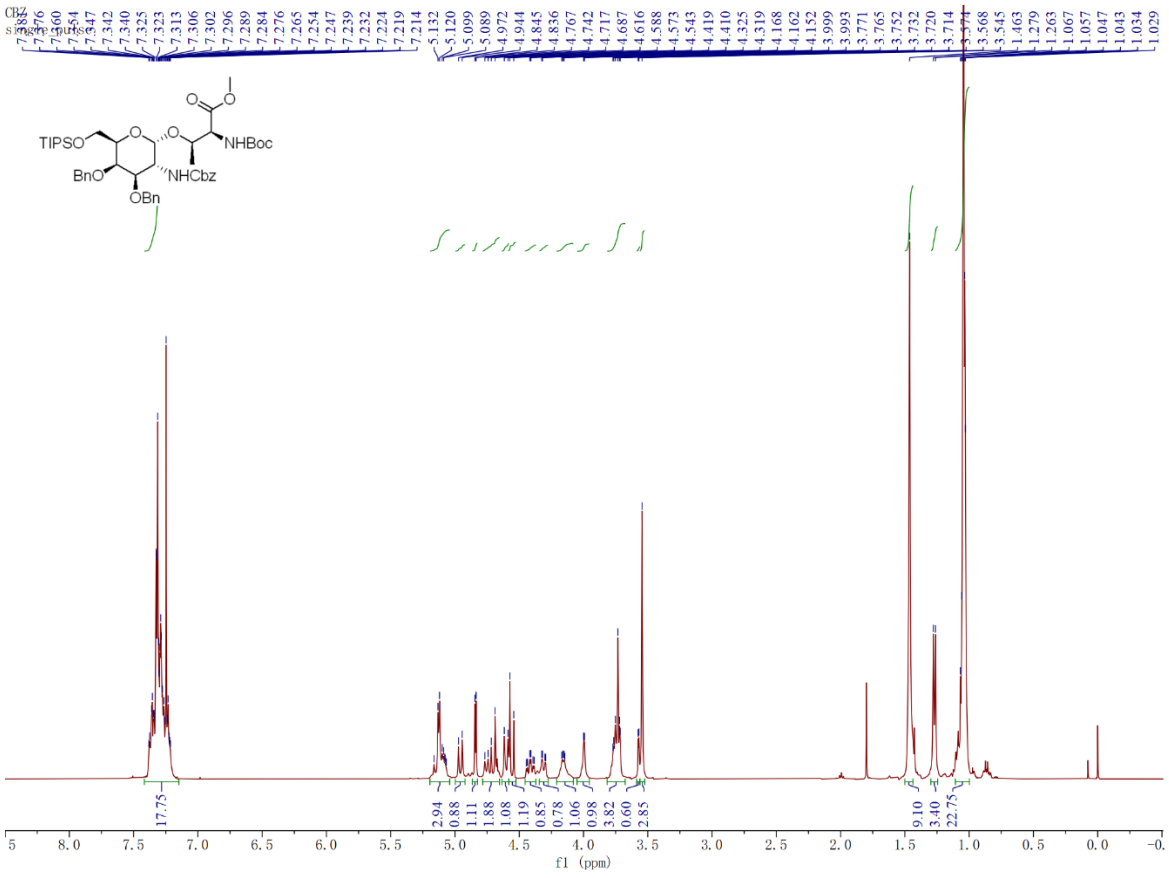


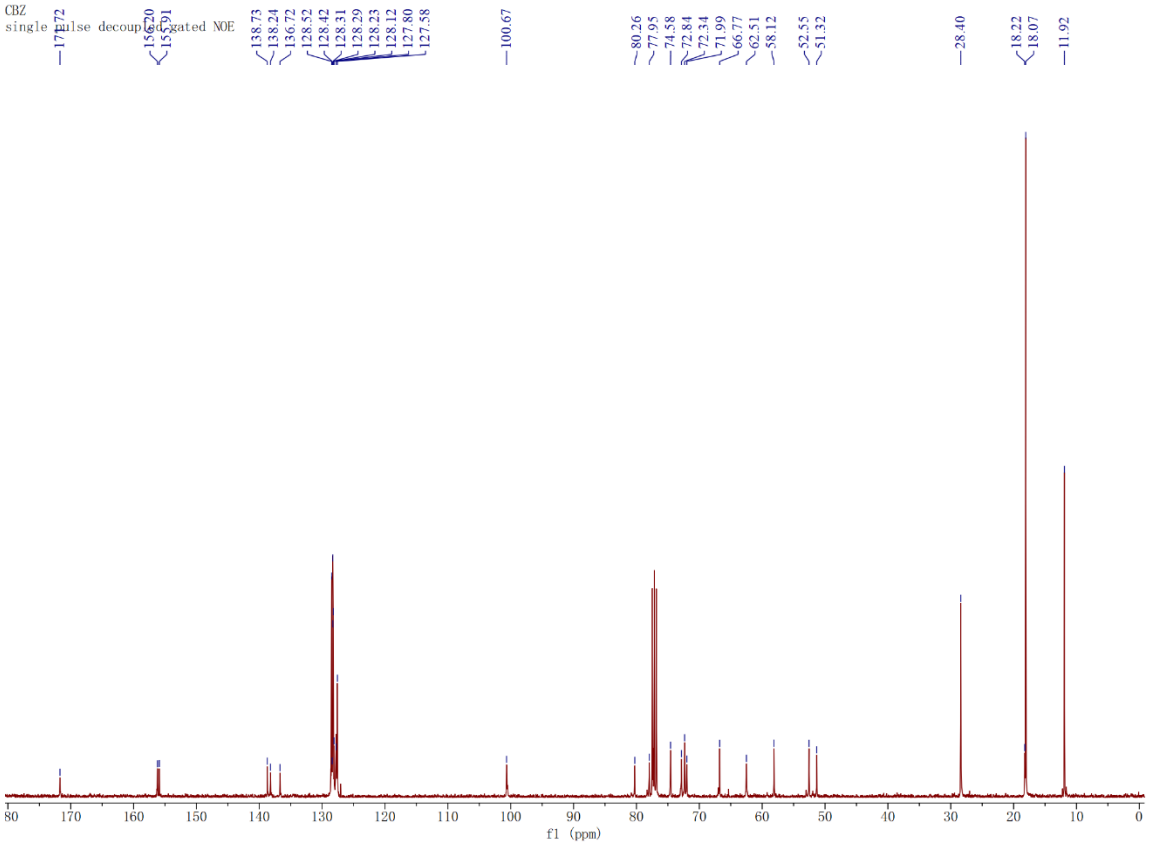
(7) ^{1}H NMR (600 MHz) and ^{13}C NMR (150 MHz) Spectra of compound 6 in $CDCl_3$



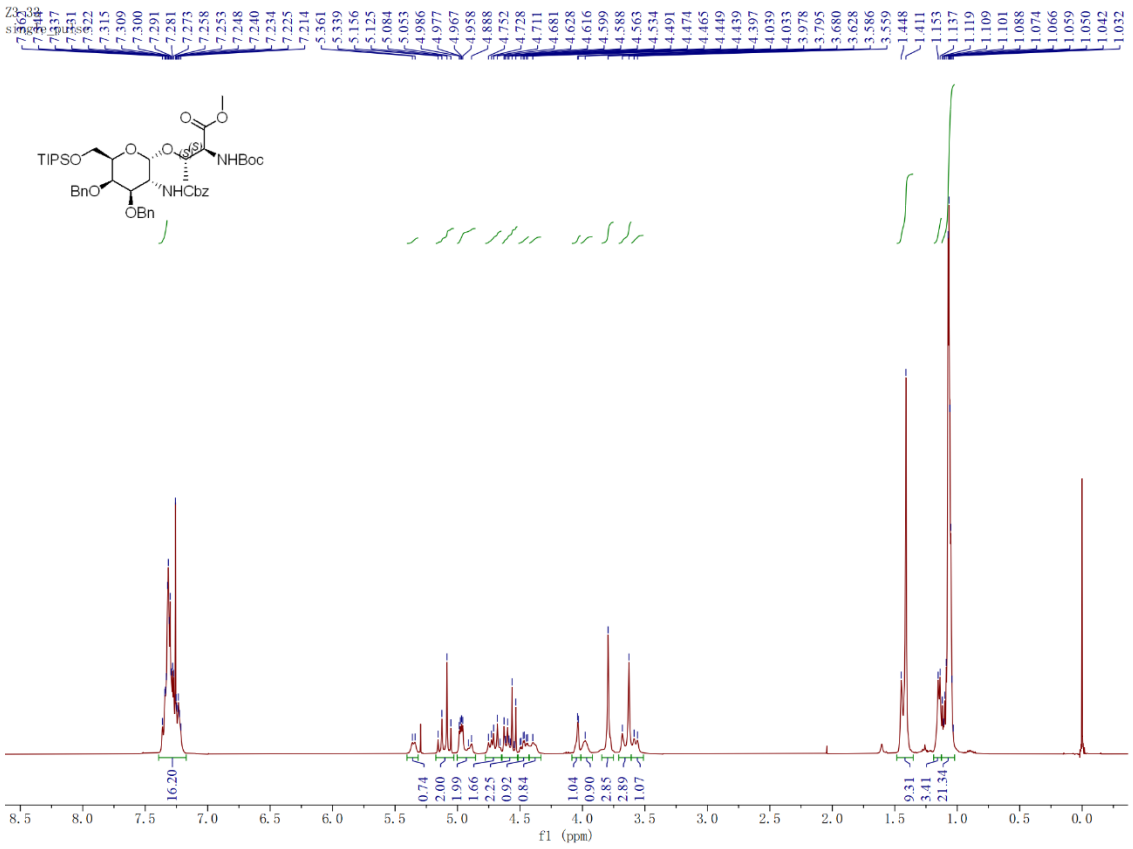


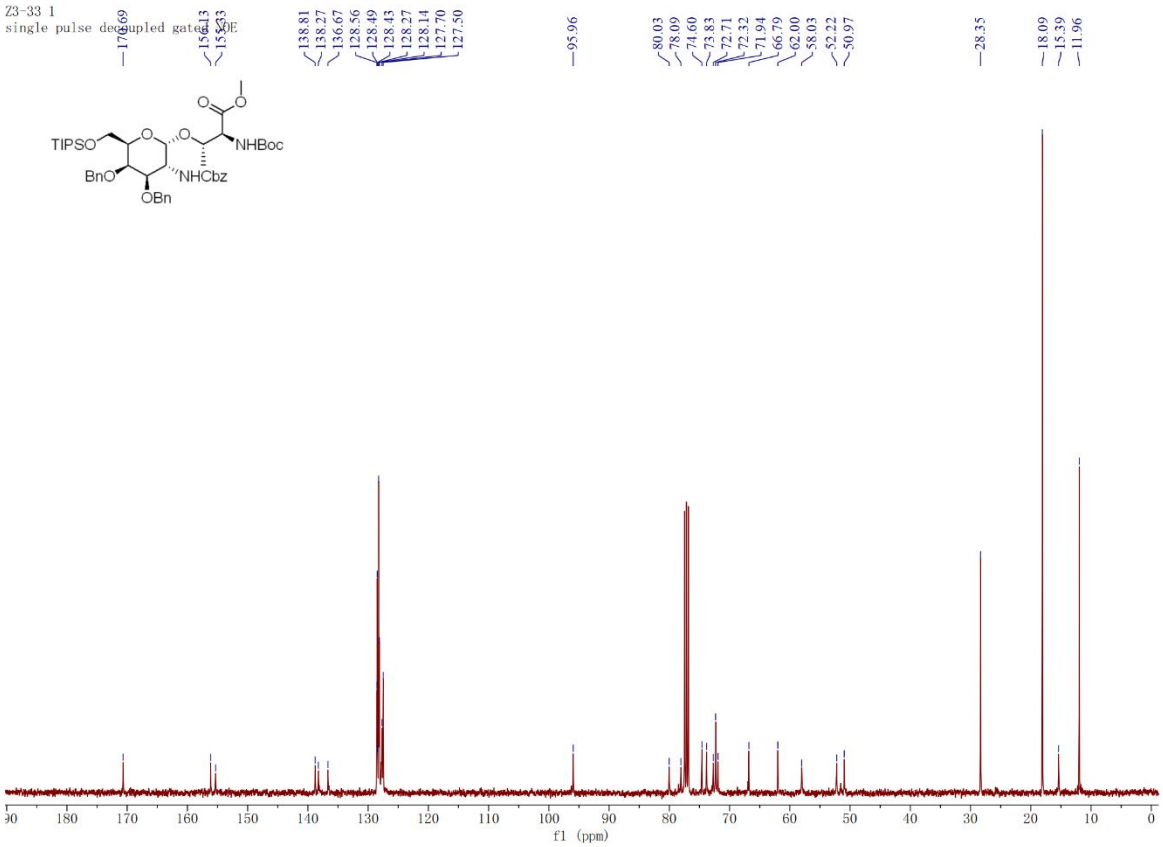
(8) ^{1}H NMR (400 MHz) and ^{13}C NMR (100 MHz) Spectra of compound 6a in $CDCl_3$



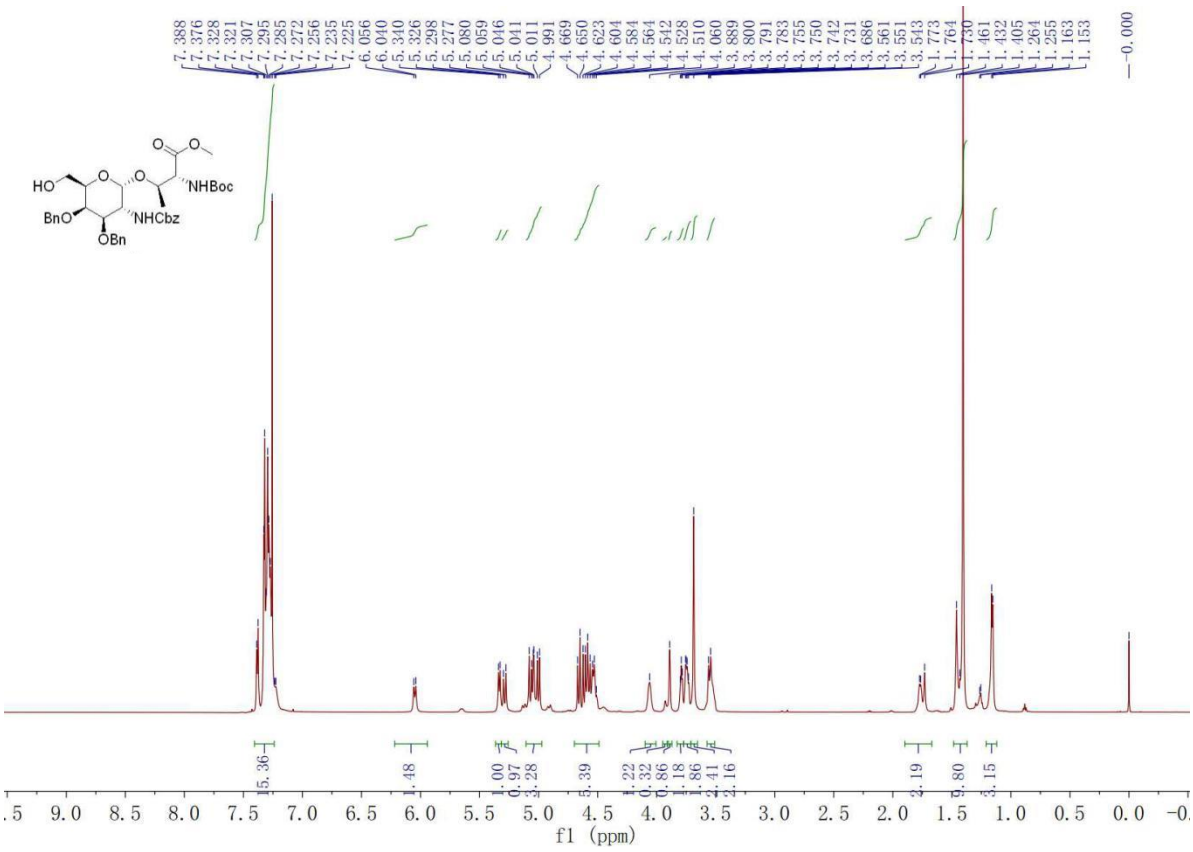


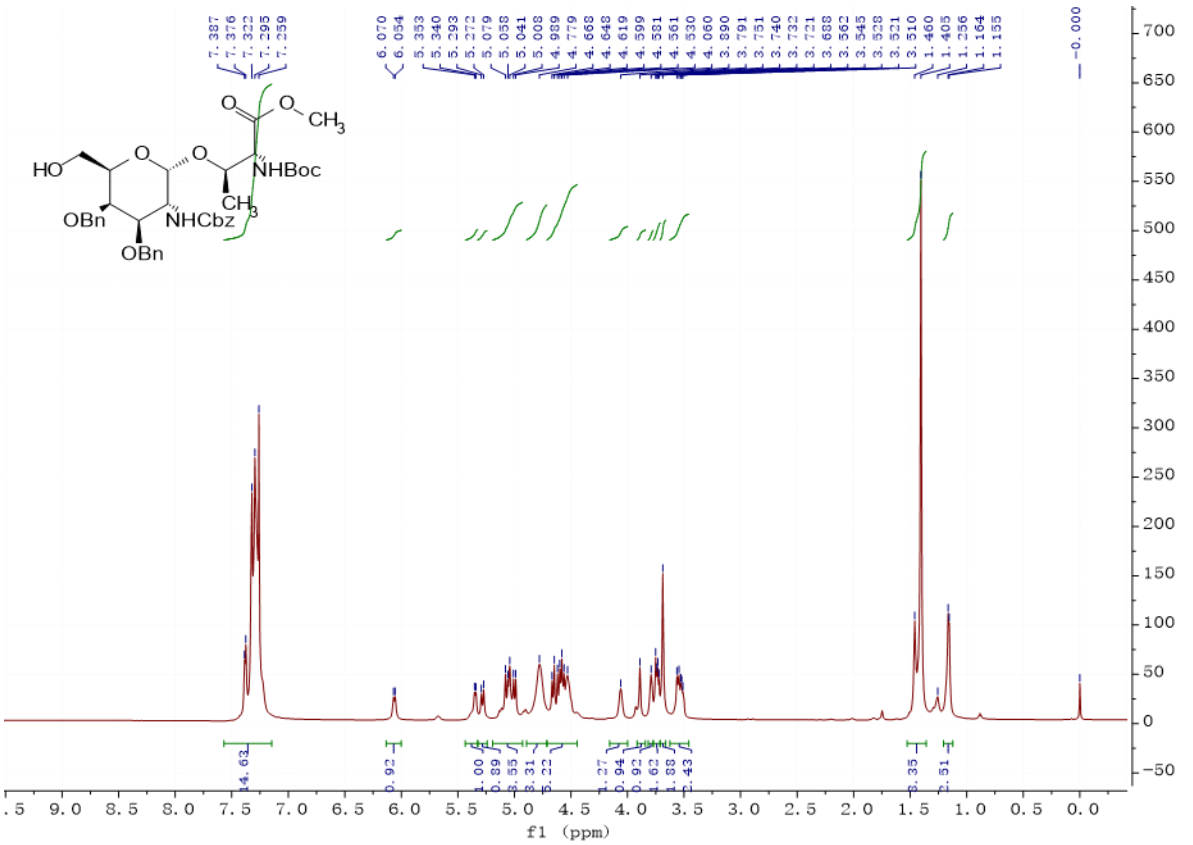
(9) ^{1}H NMR (400 MHz) and ^{13}C NMR (100 MHz) Spectra of compound 6b in $CDCl_3$

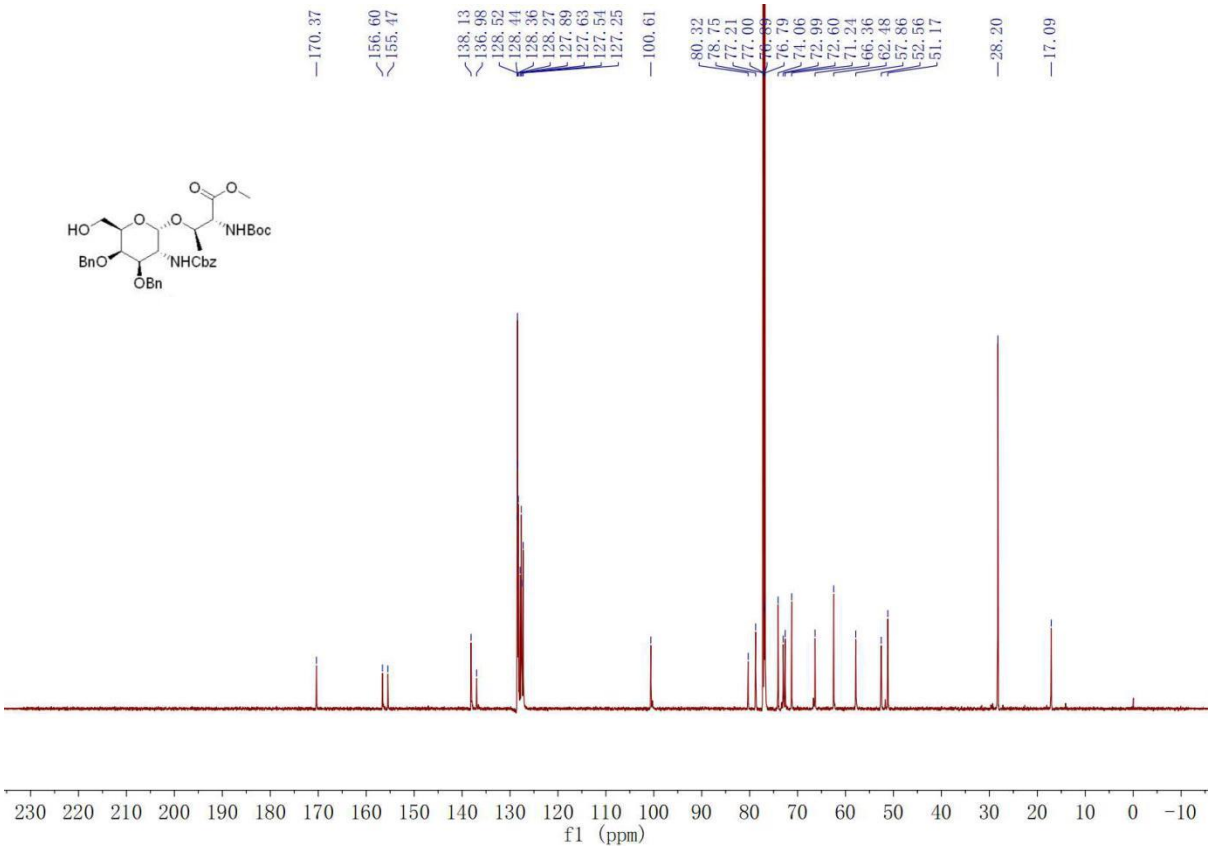




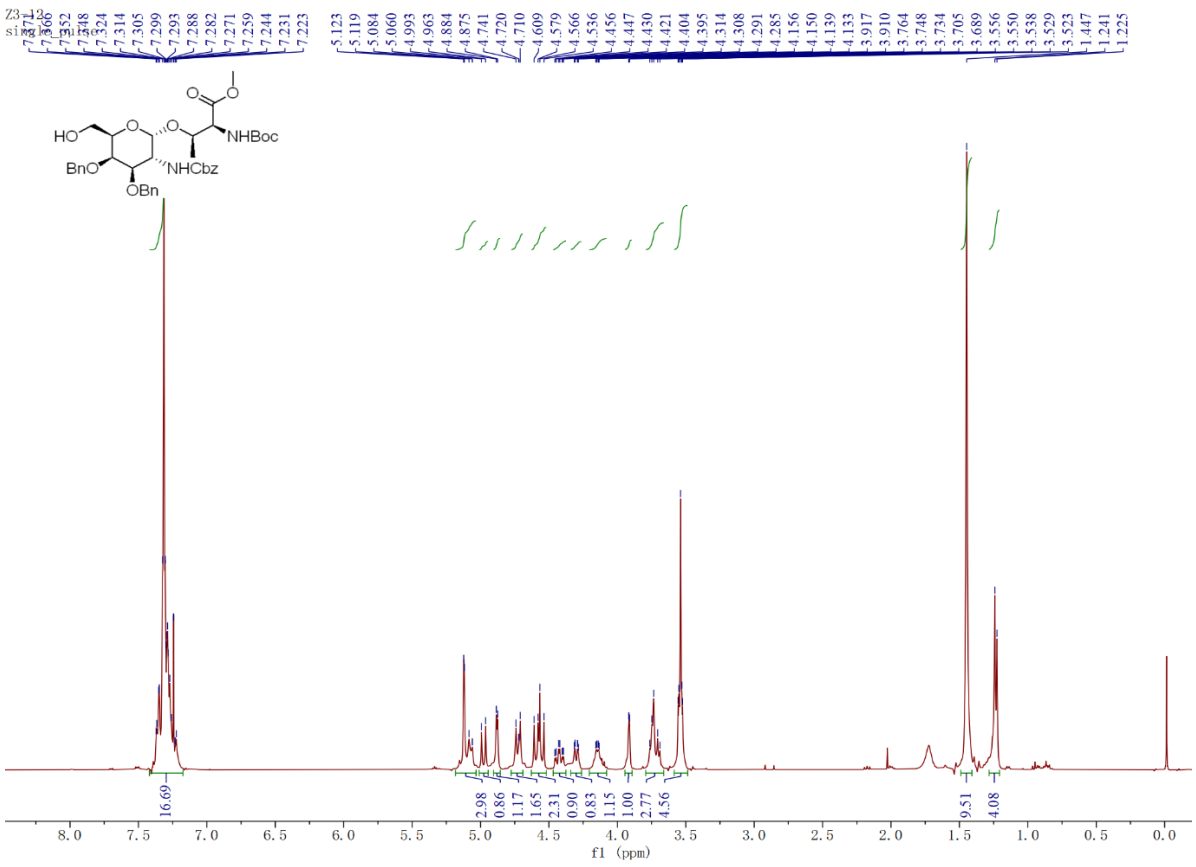
(1) ^{1}H NMR (600 MHz without and with D_2O) and ^{13}C NMR (150 MHz) Spectra of compound 7 in $CDCl_3$

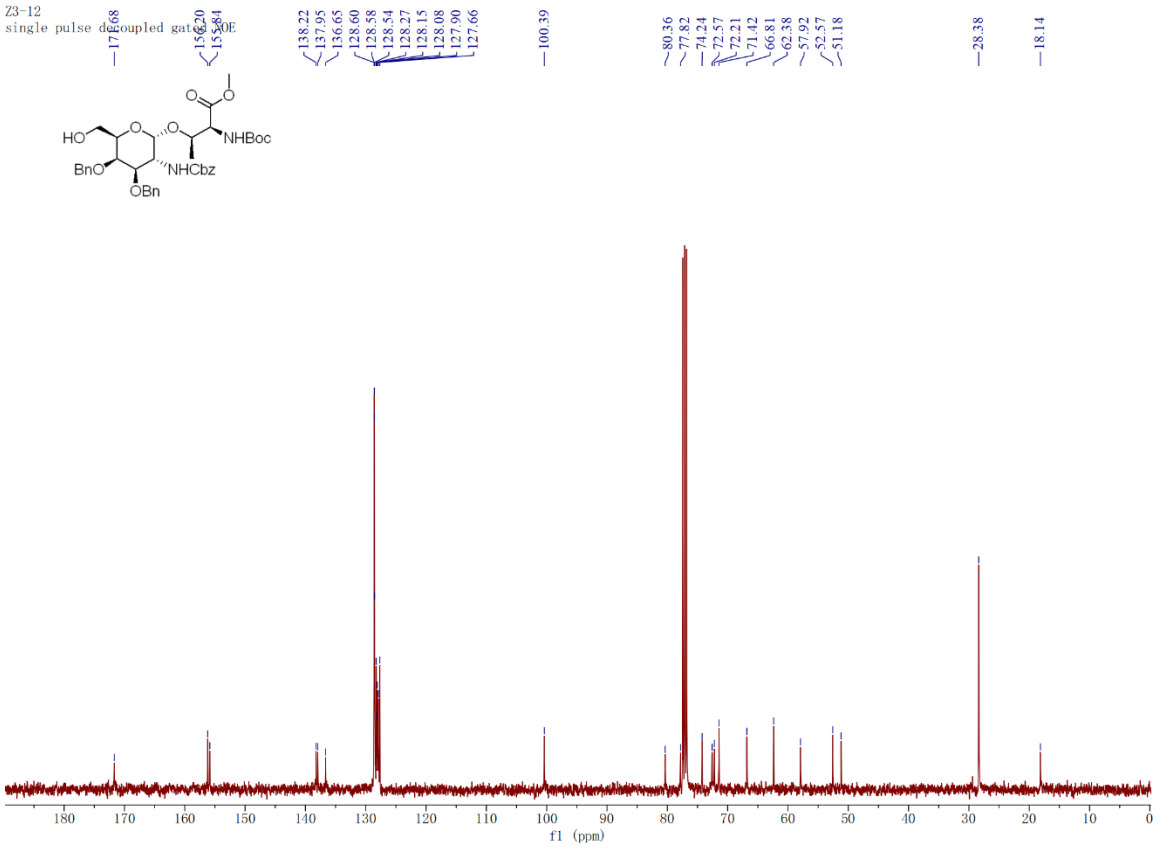




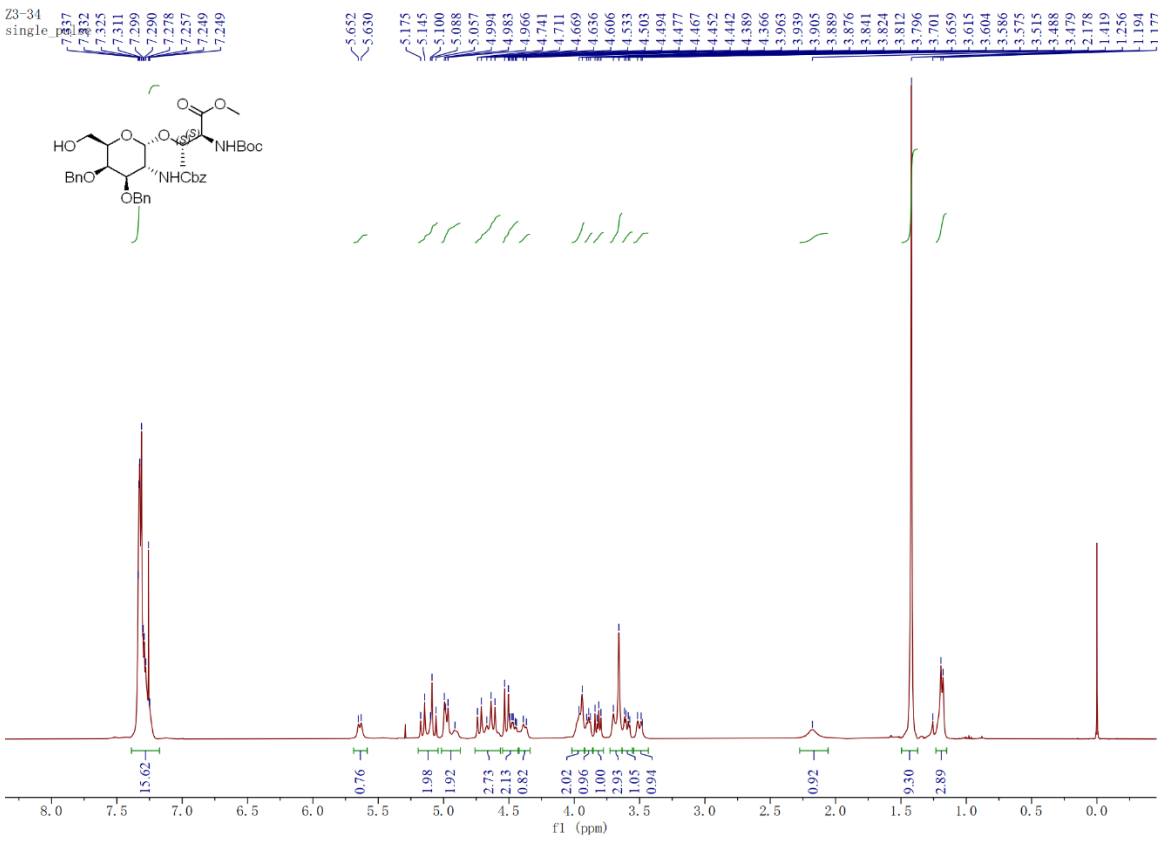


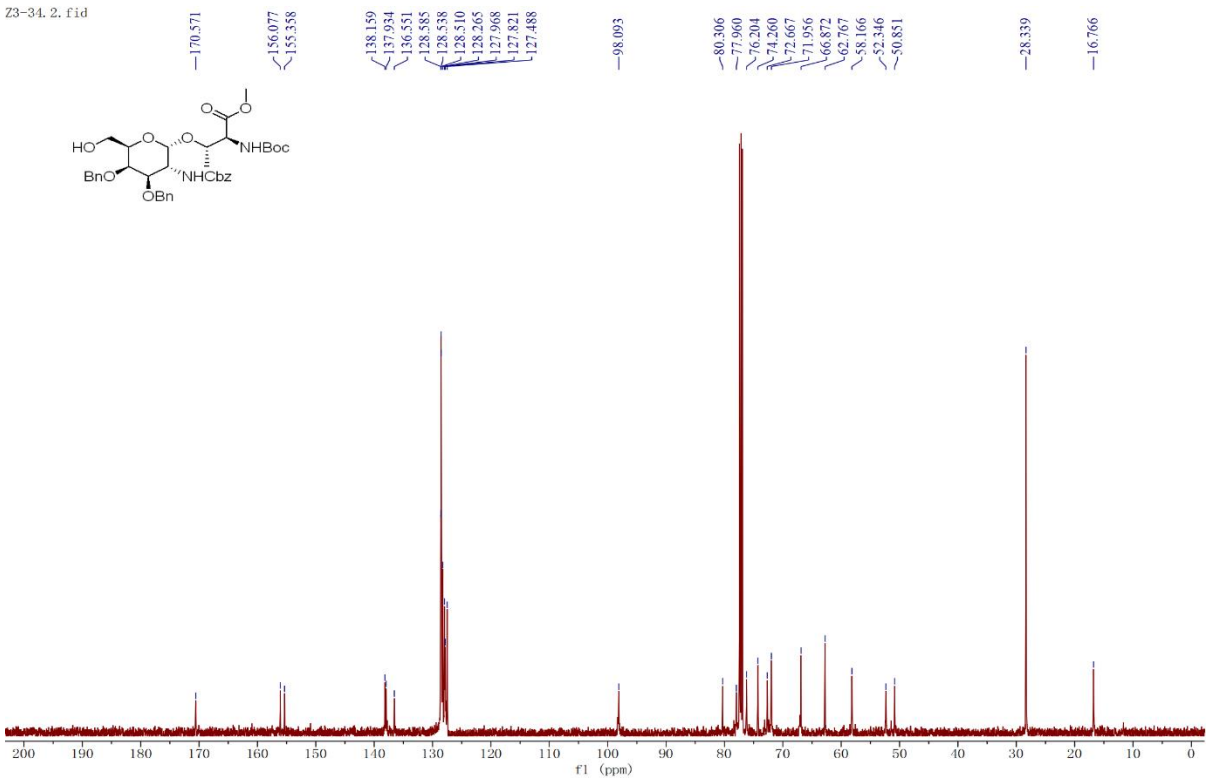
(2) ^{1}H NMR (400 MHz) and ^{13}C NMR (100 MHz) Spectra of compound 7a in $CDCl_3$



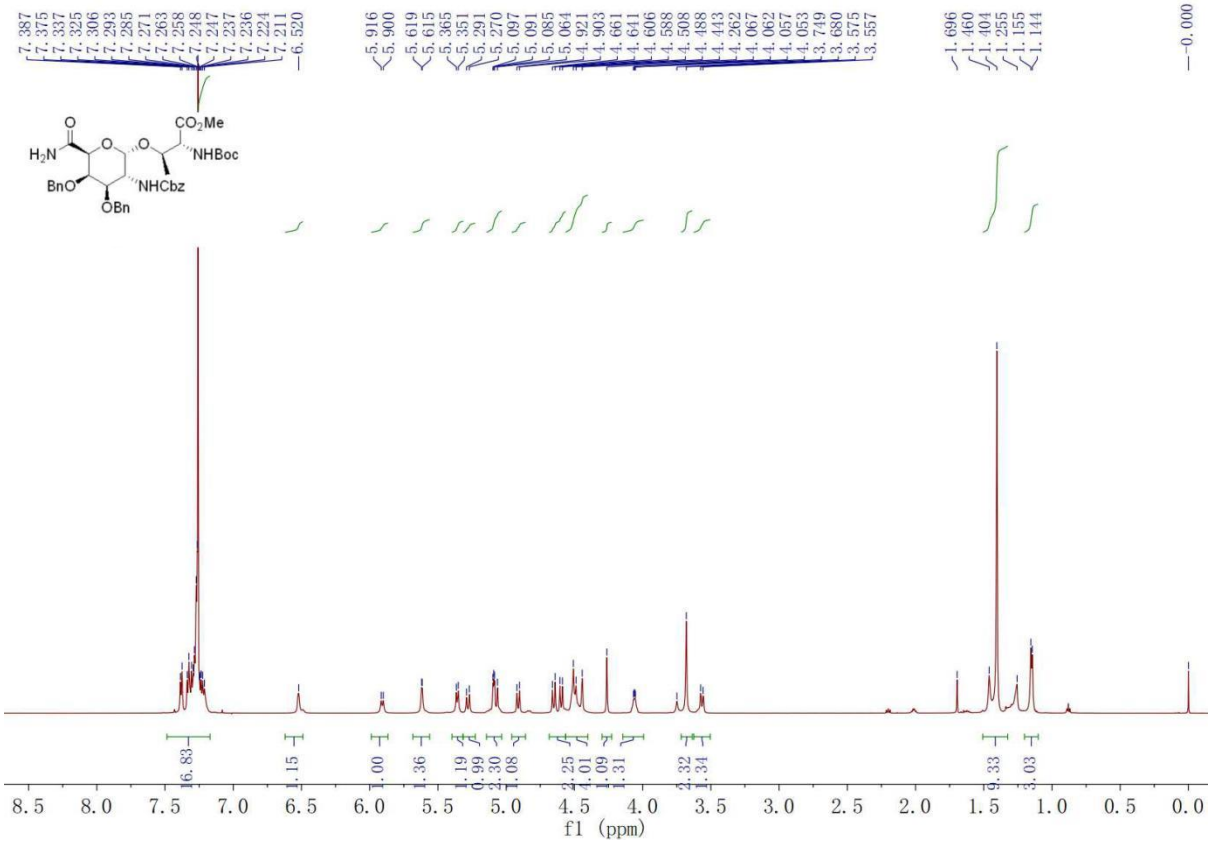


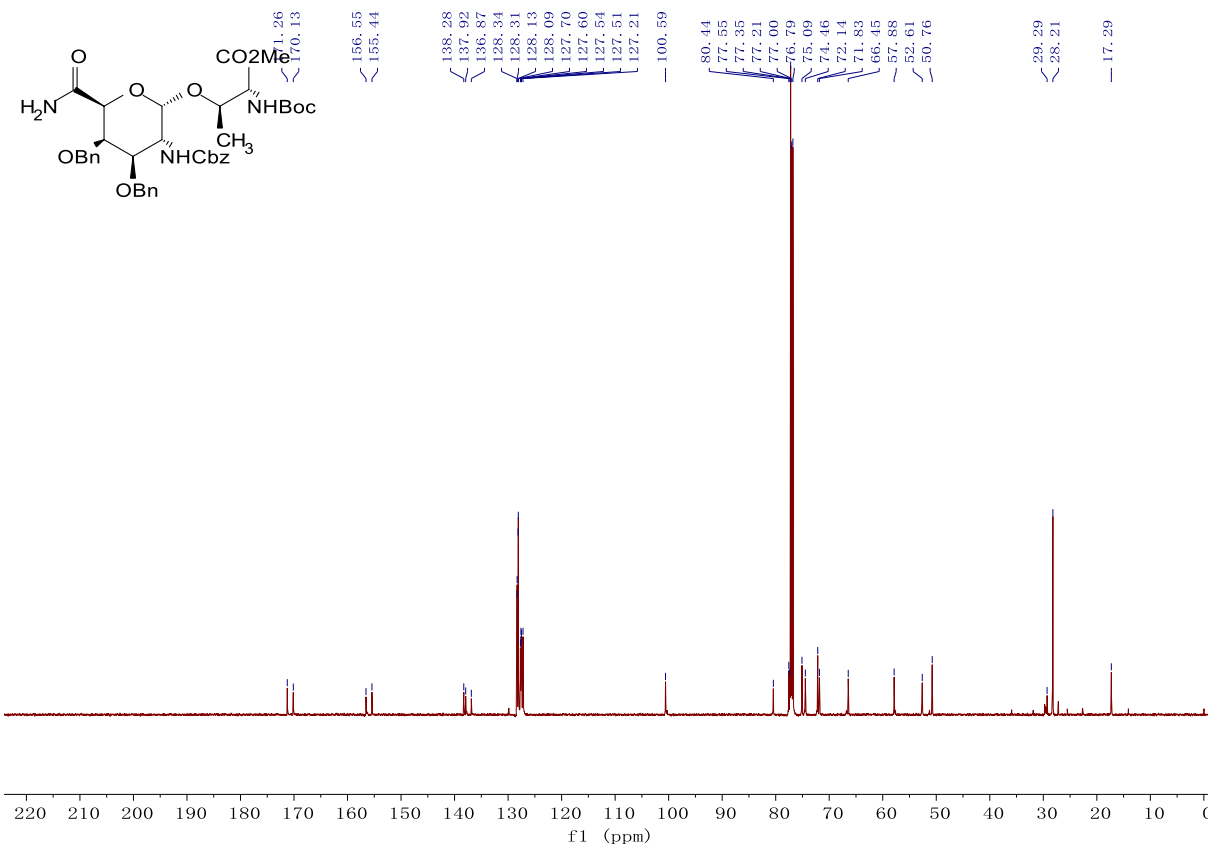
(3) ^{1}H NMR (400 MHz) and ^{13}C NMR (100 MHz) Spectra of compound 7b in $CDCl_3$



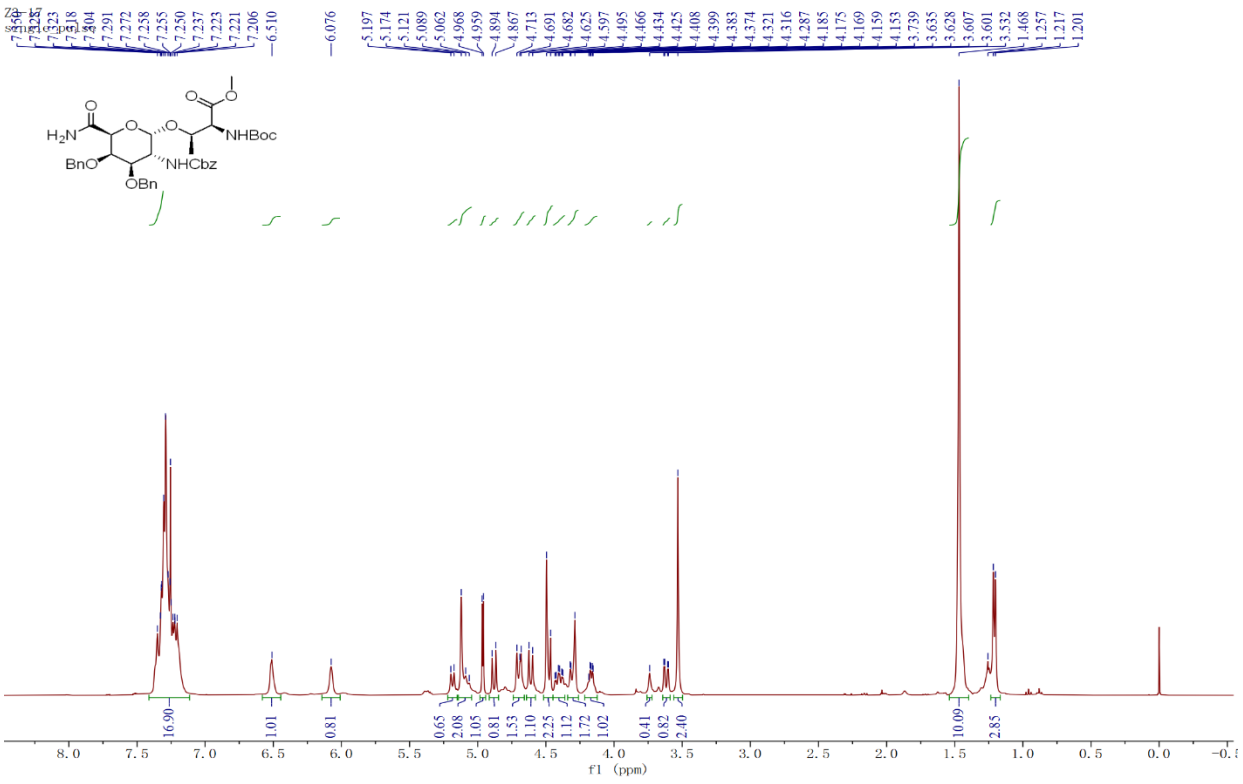


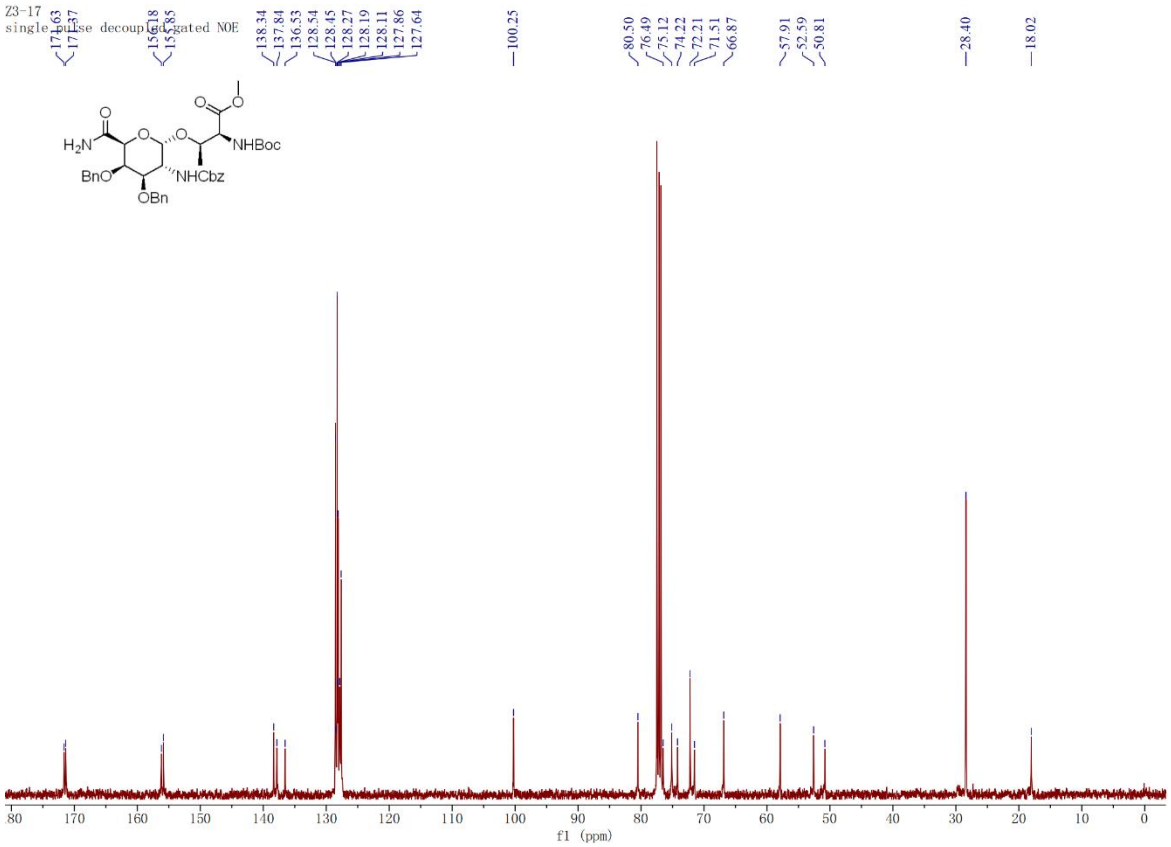
(4) ^{1}H NMR (600 MHz) and ^{13}C NMR (150 MHz) Spectra of compound 8 in $CDCl_3$



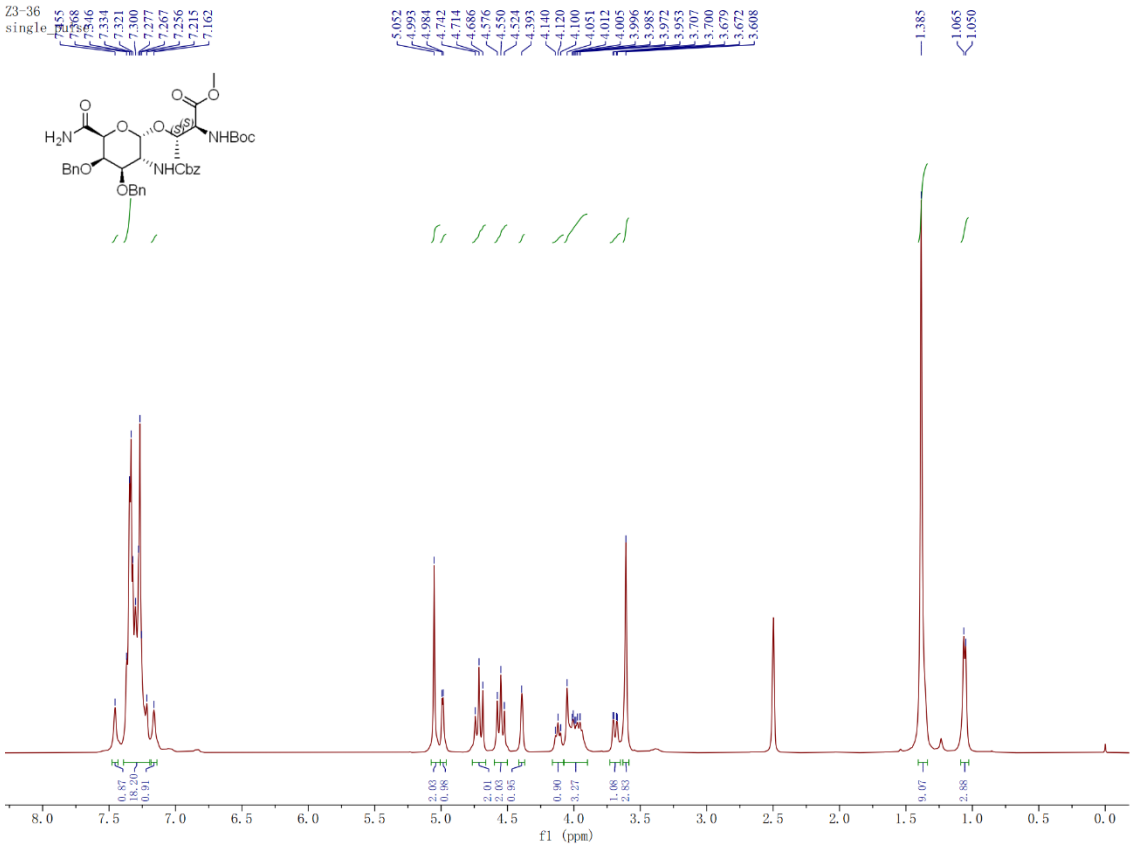


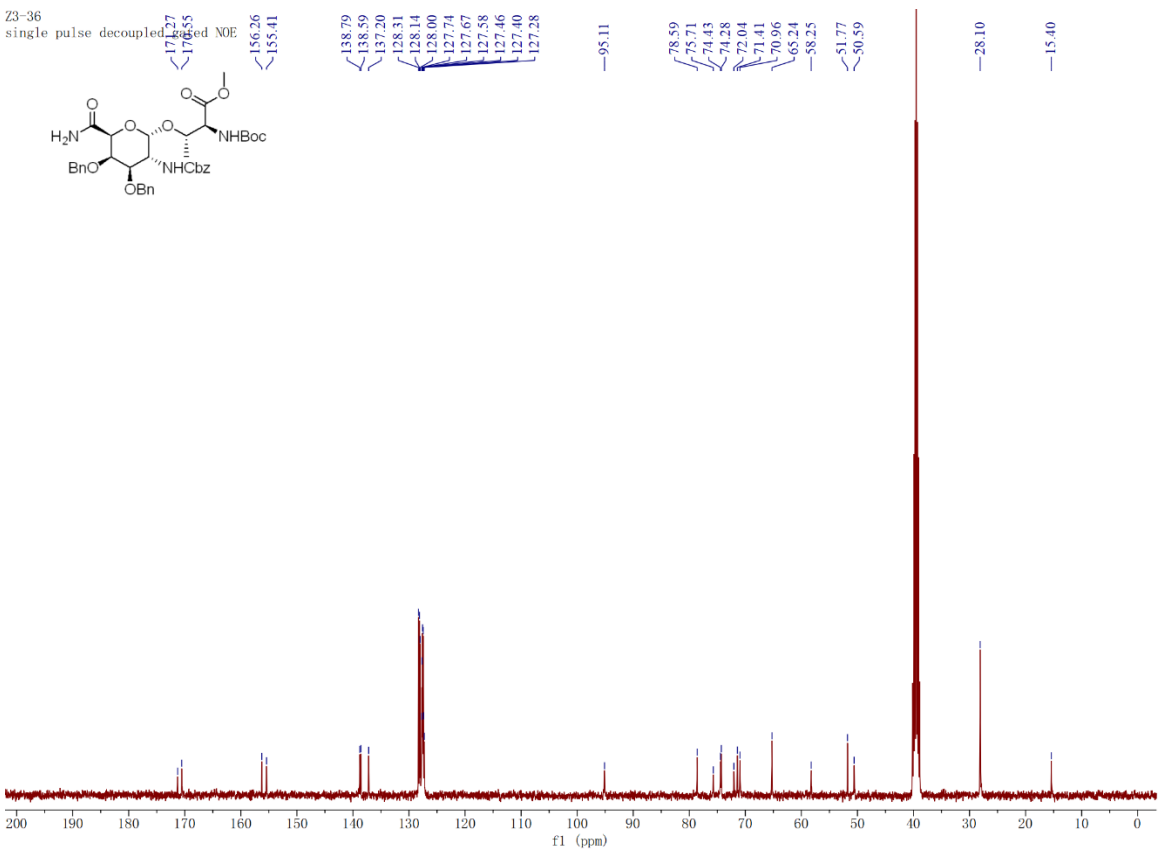
(5) ^{1}H NMR (400 MHz) and ^{13}C NMR (100 MHz) Spectra of compound 8a in $CDCl_3$



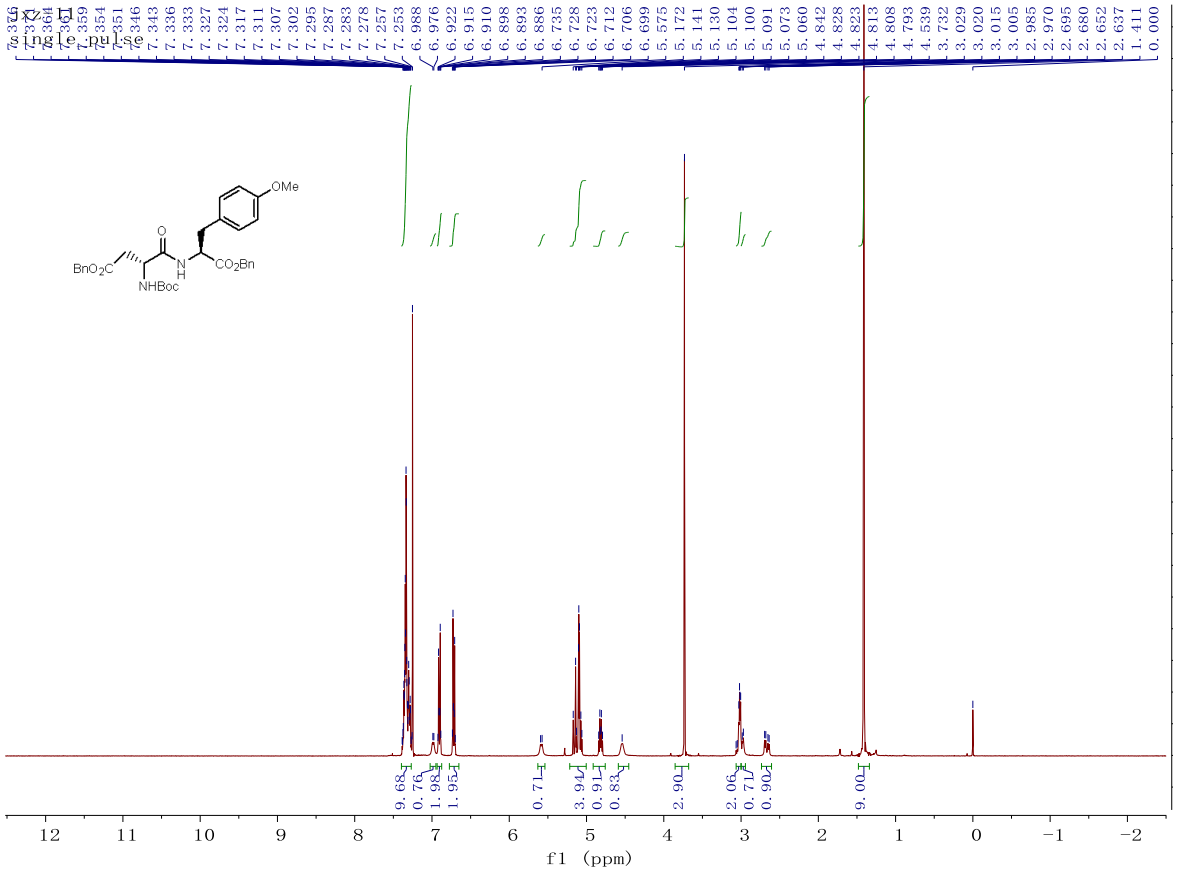


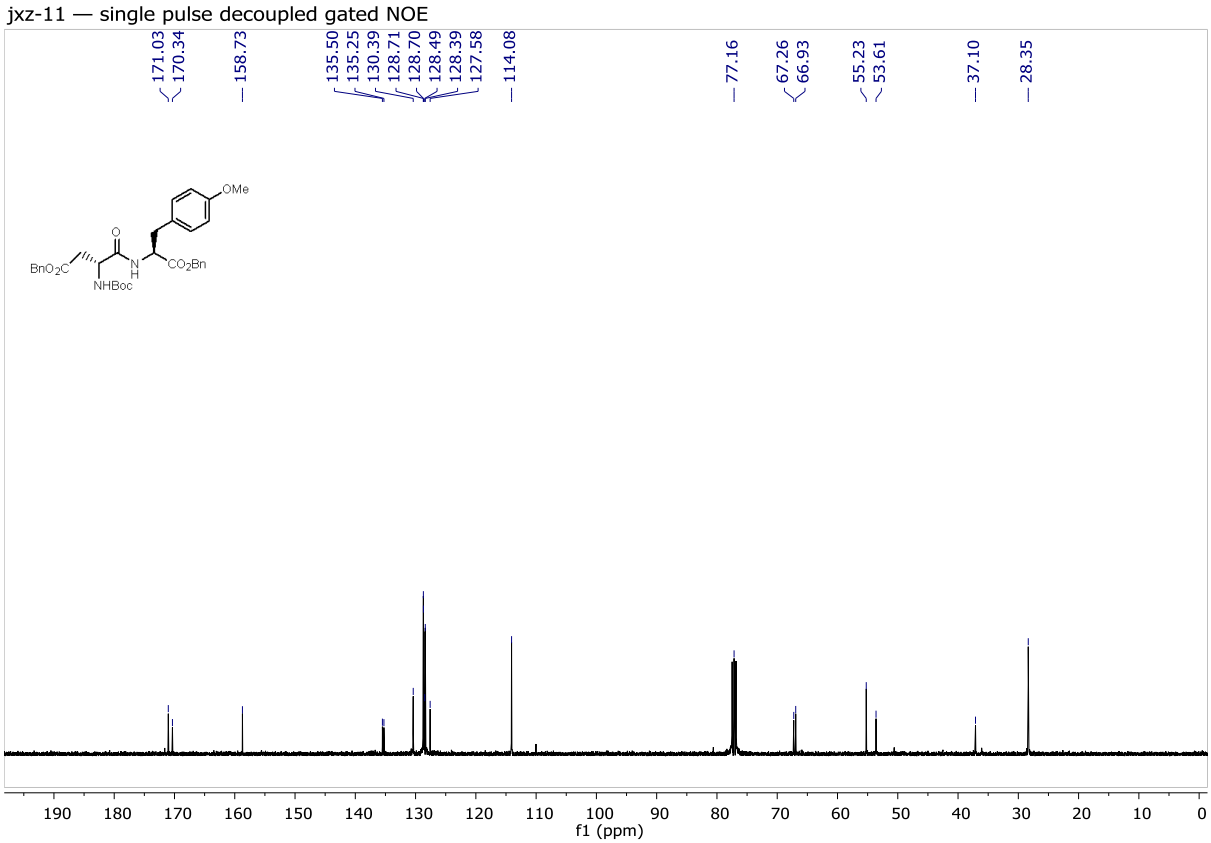
(6) ^{1}H NMR (400 MHz) and ^{13}C NMR (100 MHz) Spectra of compound 8b in DMSO-d$_6$



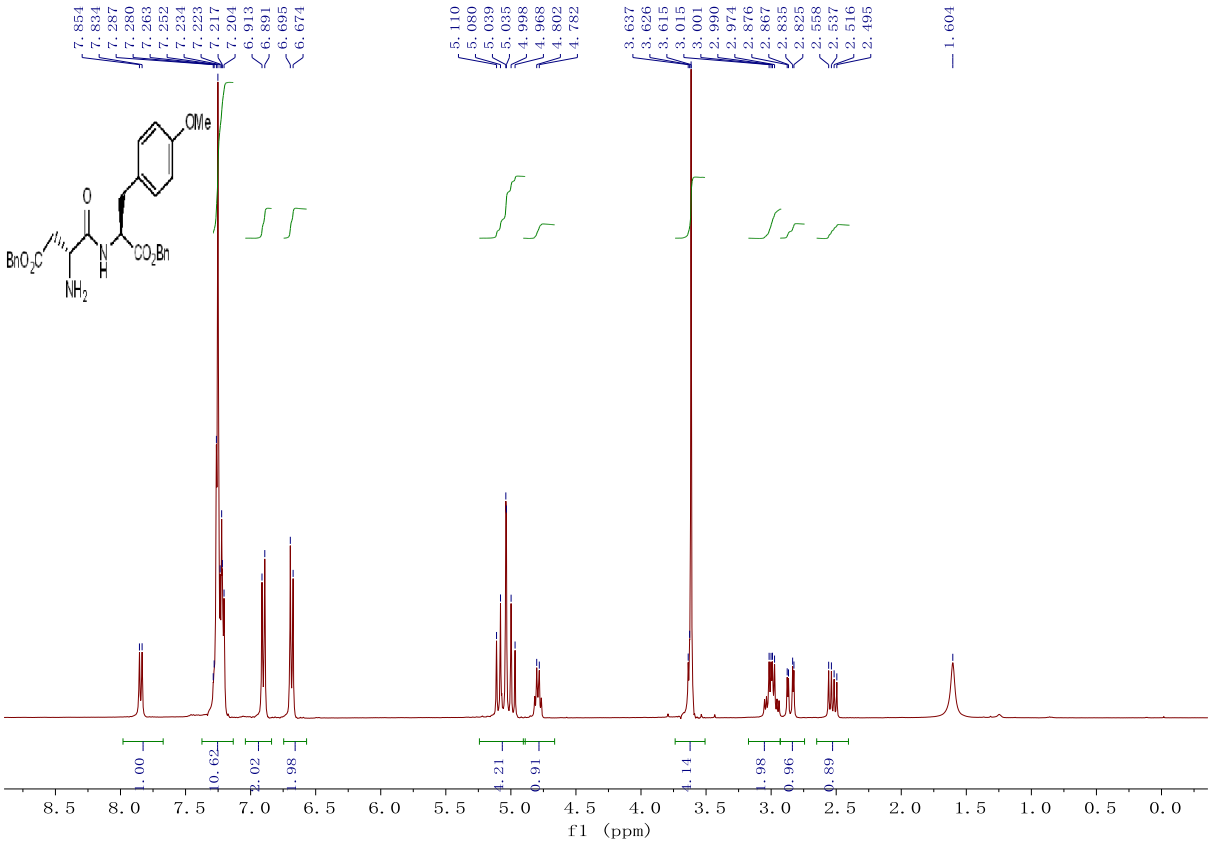


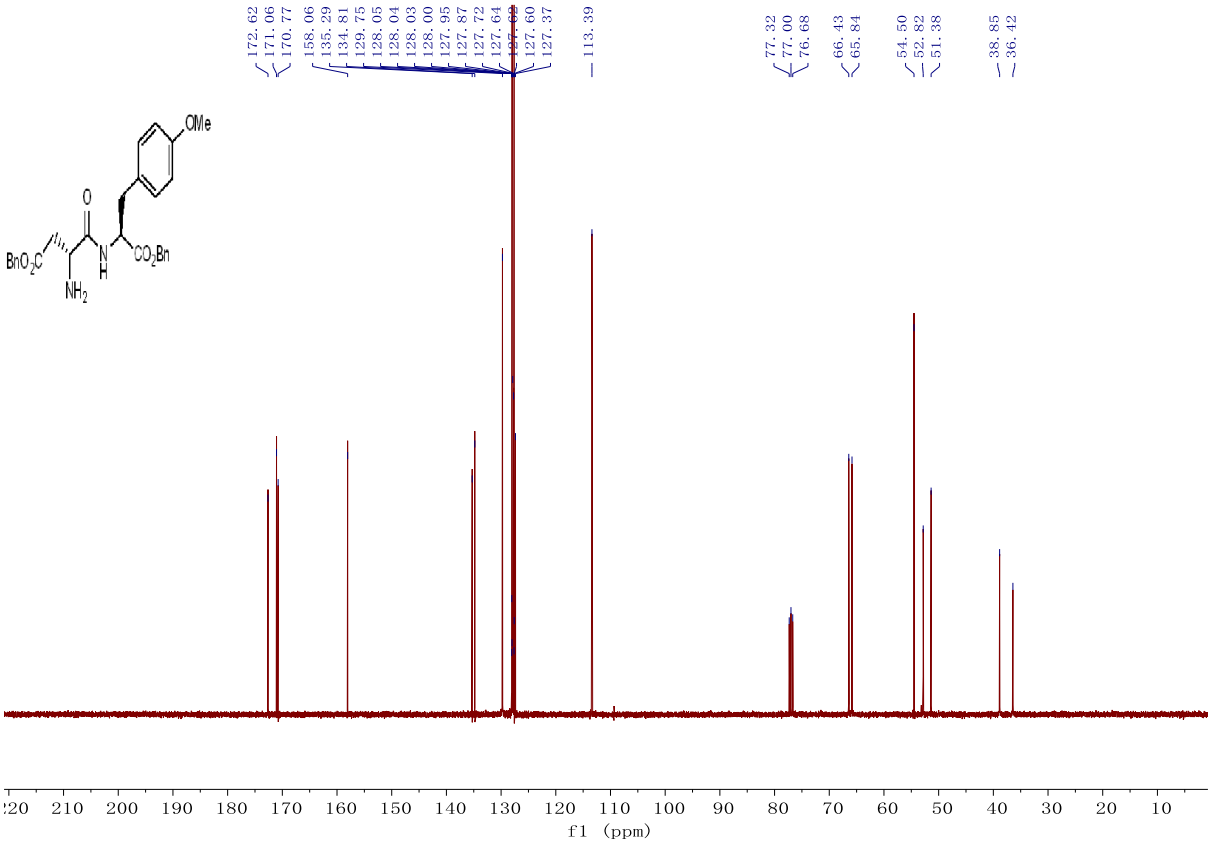
(7) ^{1}H NMR (400 MHz) and ^{13}C NMR (100 MHz) Spectra of compound 11 in $CDCl_3$



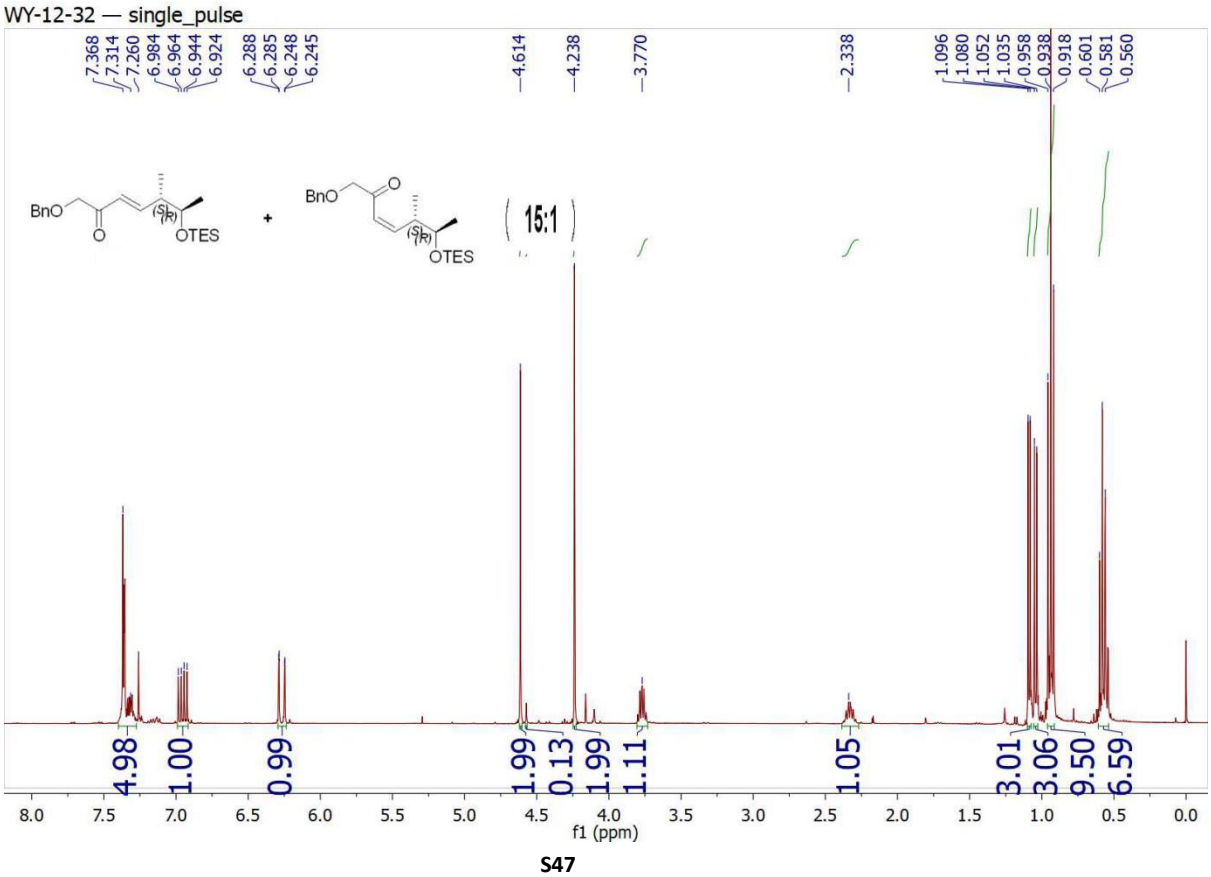


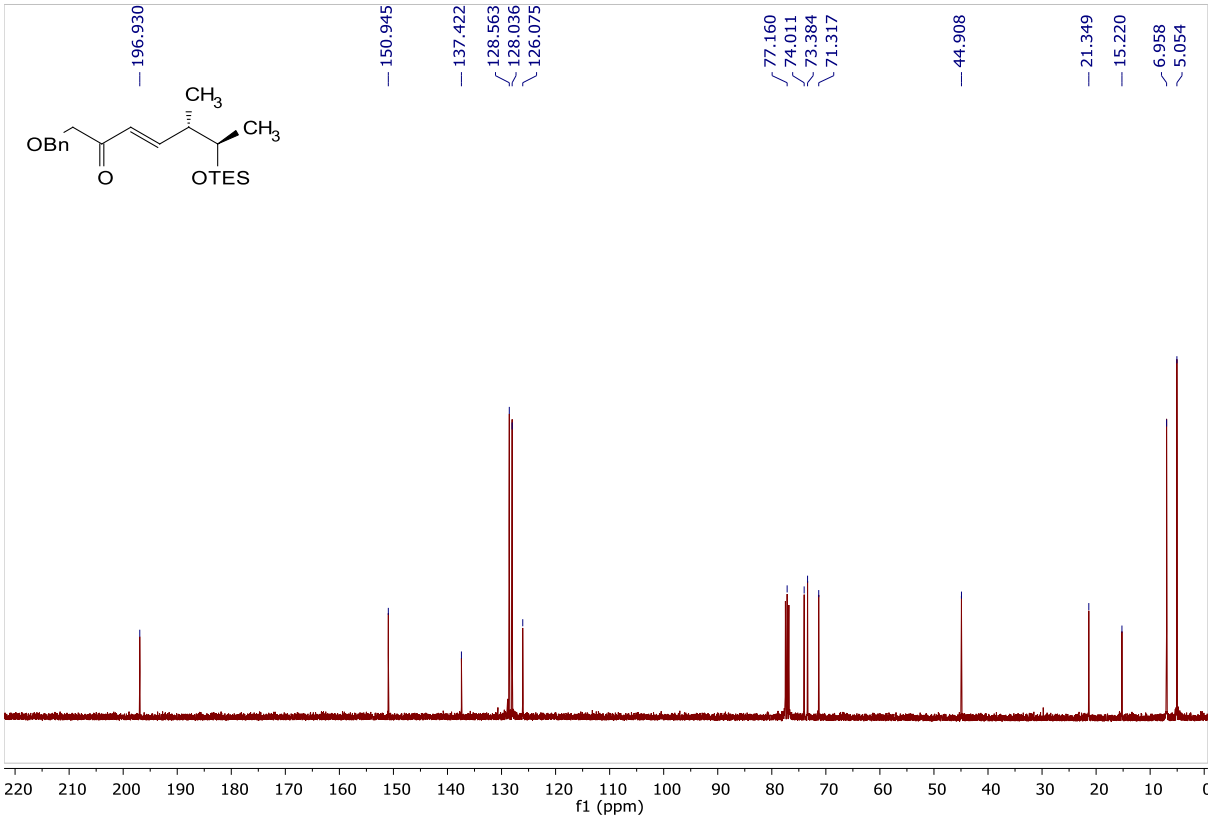
(8) ^{1}H NMR (400 MHz) and ^{13}C NMR (100 MHz) Spectra of compound 12 in $CDCl_3$



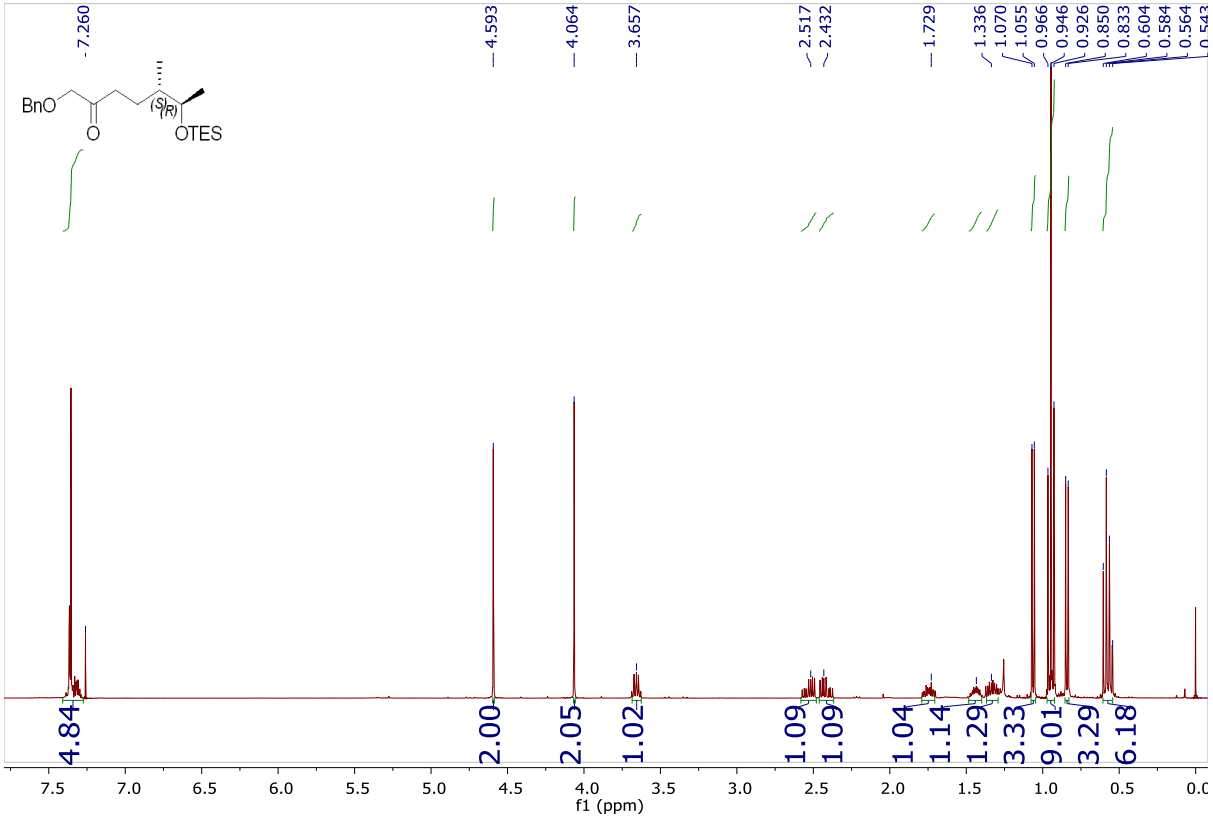


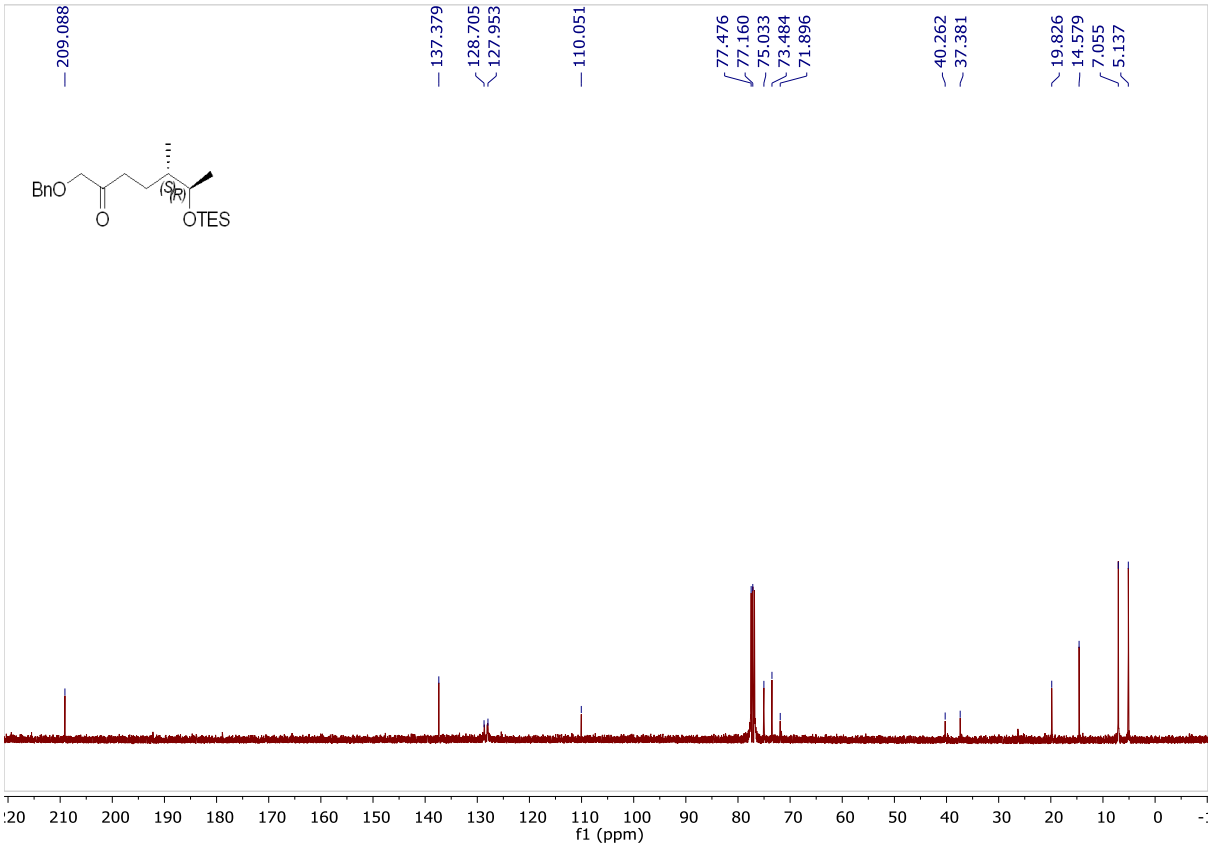
(9) ^{1}H NMR (400 MHz) and ^{13}C NMR (100 MHz) Spectra of compound 16 in $CDCl_3$



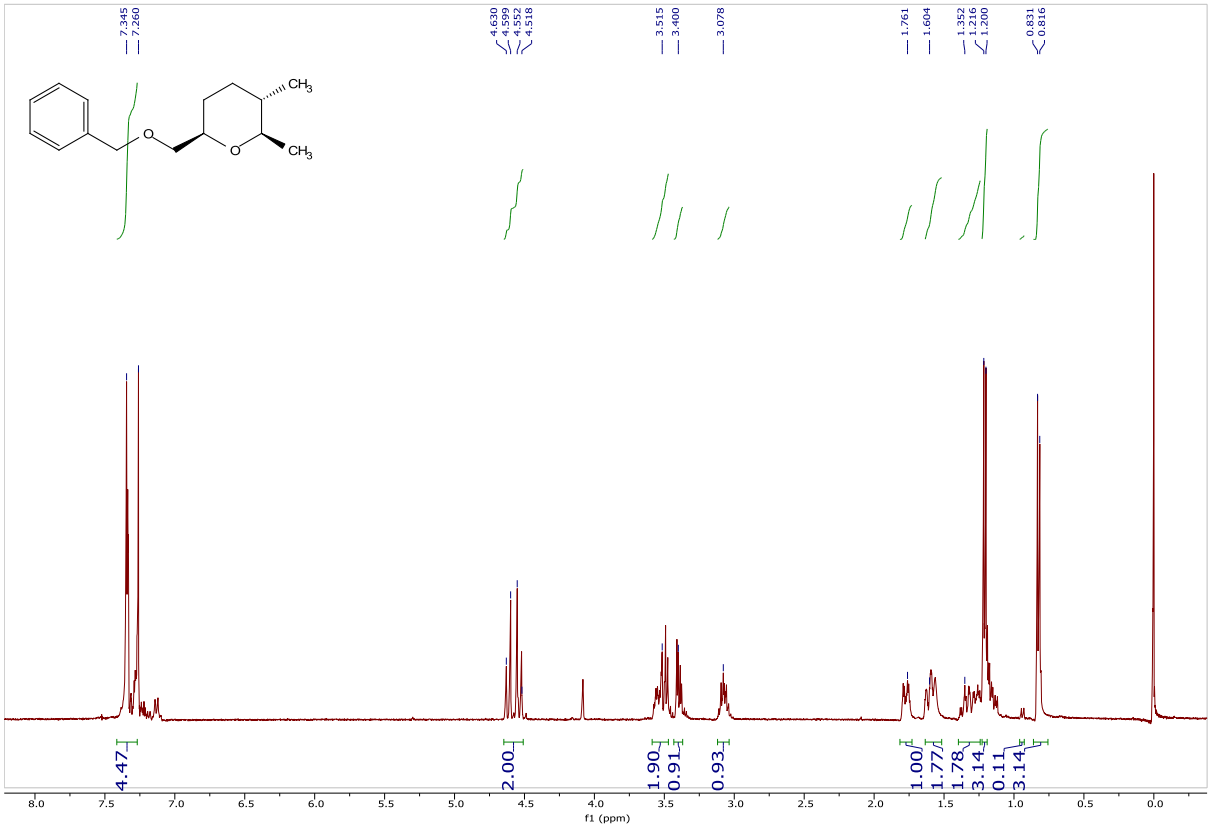


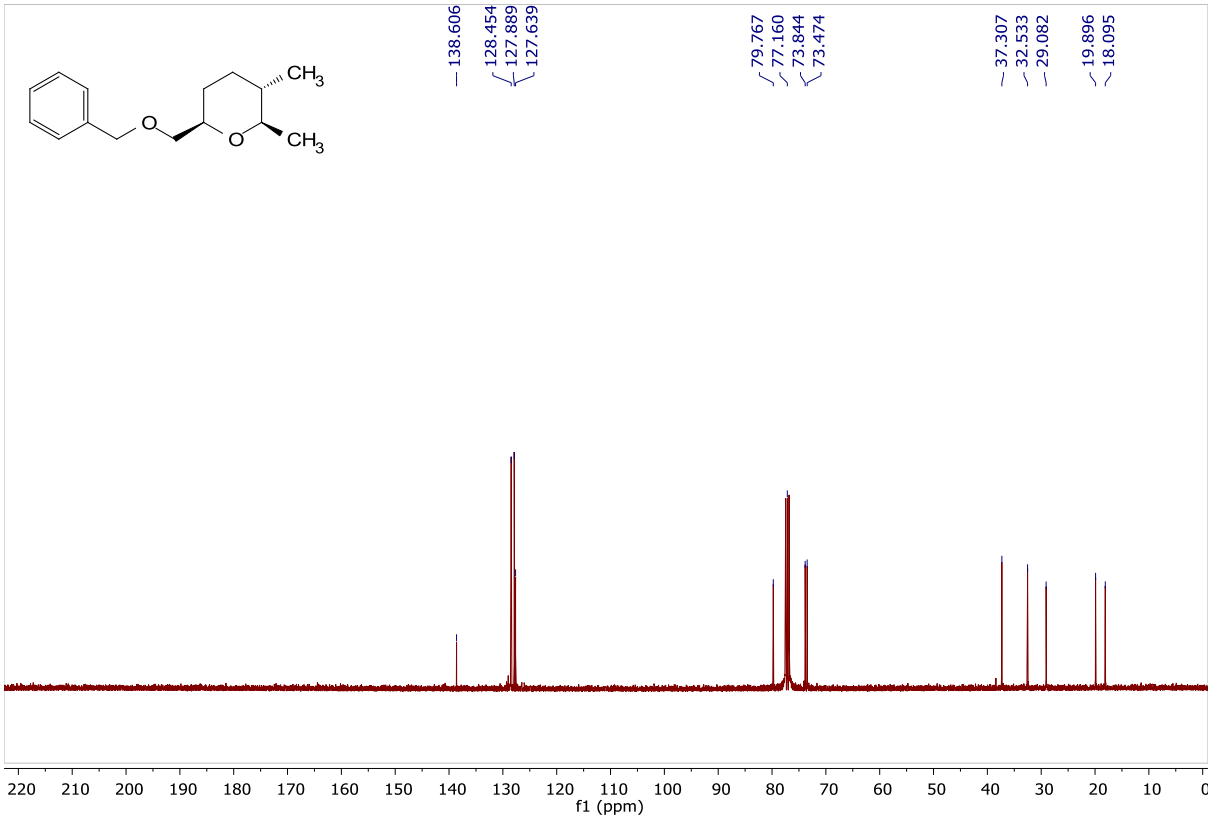
(10) ^{1}H NMR (400 MHz) and ^{13}C NMR (100 MHz) Spectra of compound 17 in $CDCl_3$



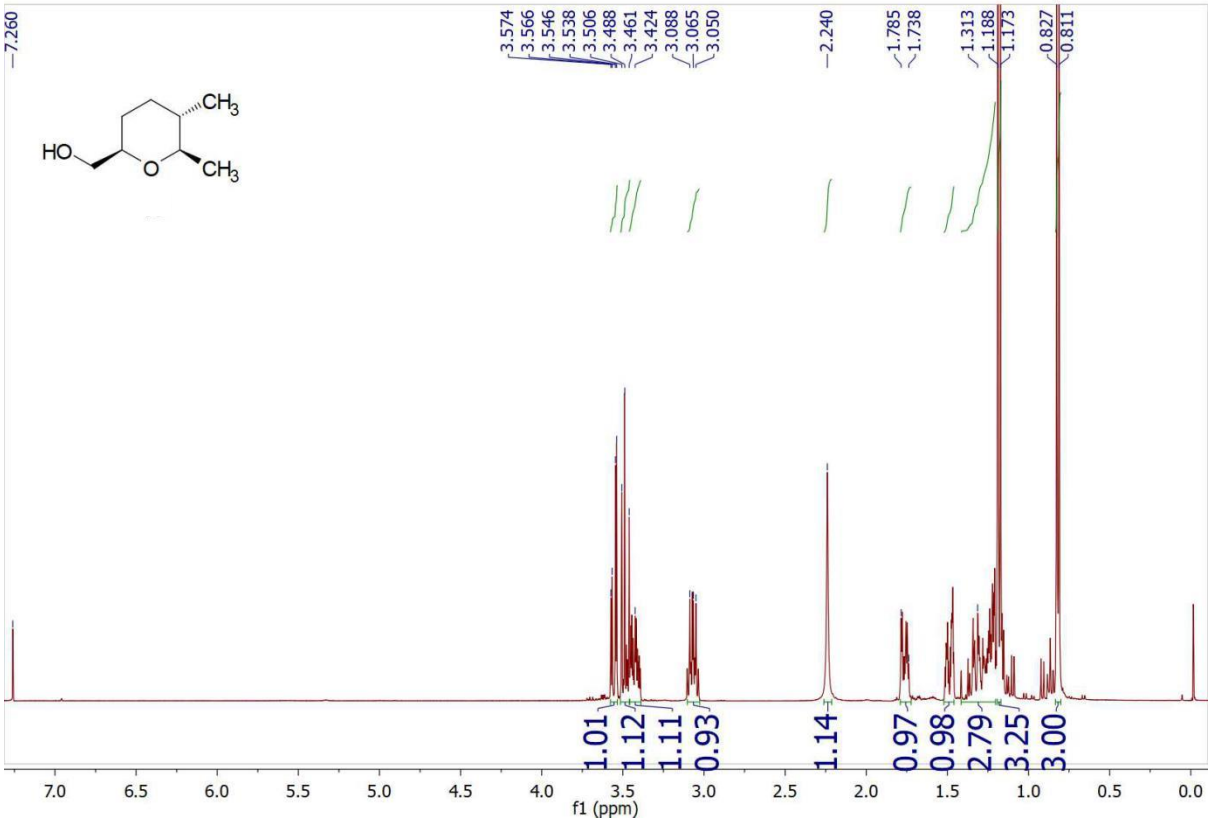


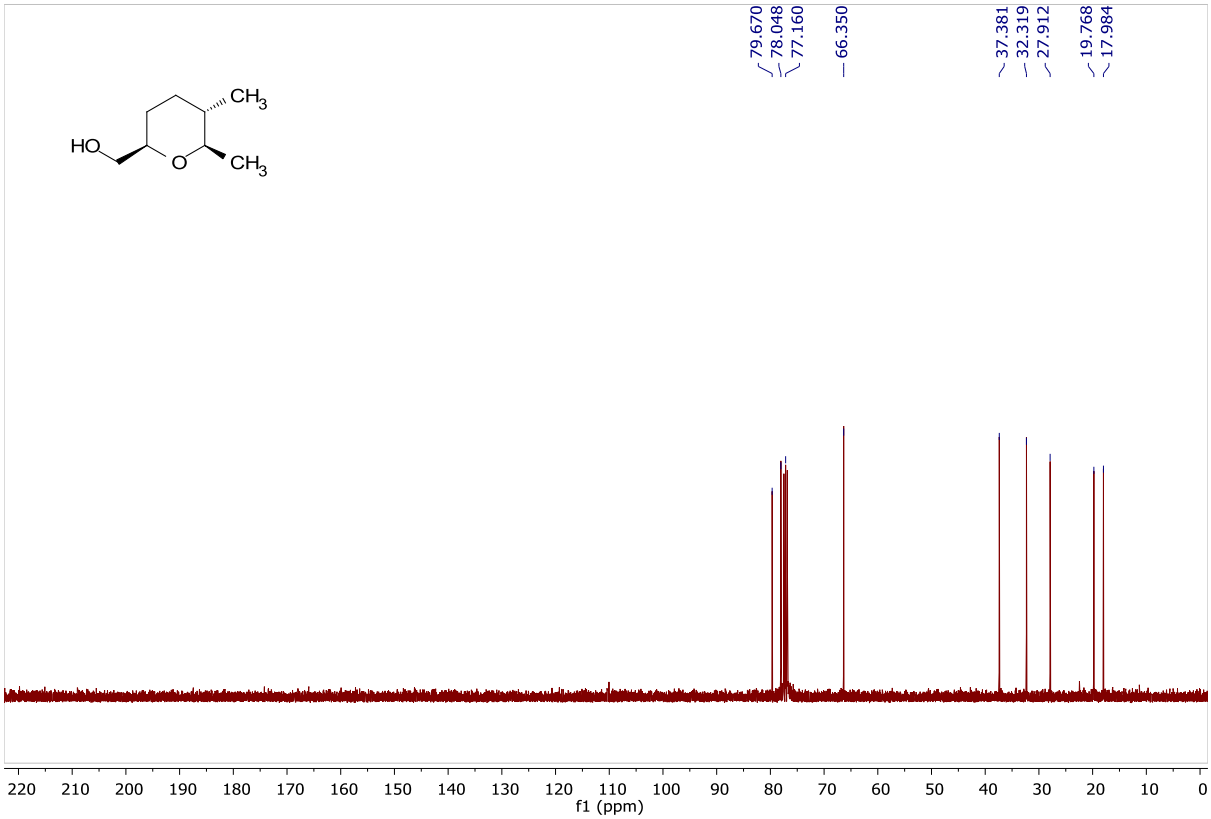
(11) ^{1}H NMR (400 MHz) and ^{13}C NMR (100 MHz) Spectra of compound 18 in $CDCl_3$



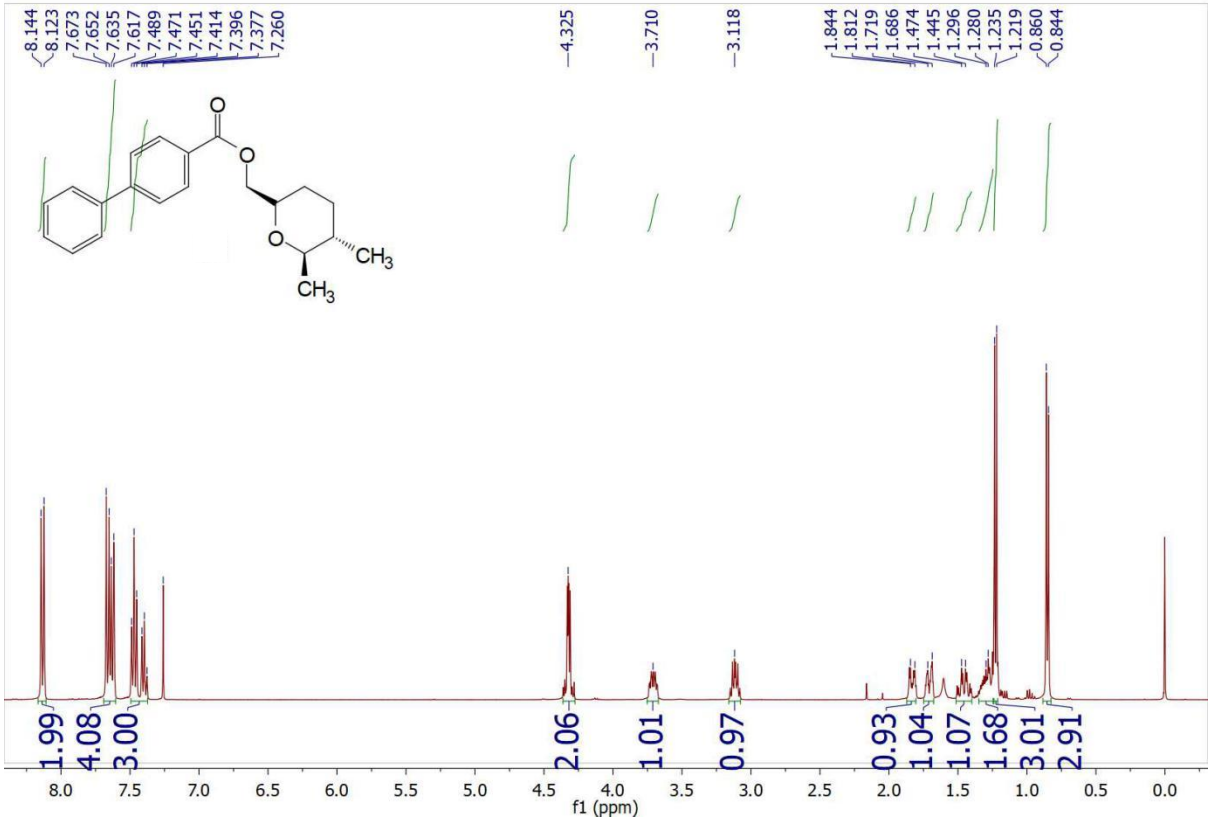


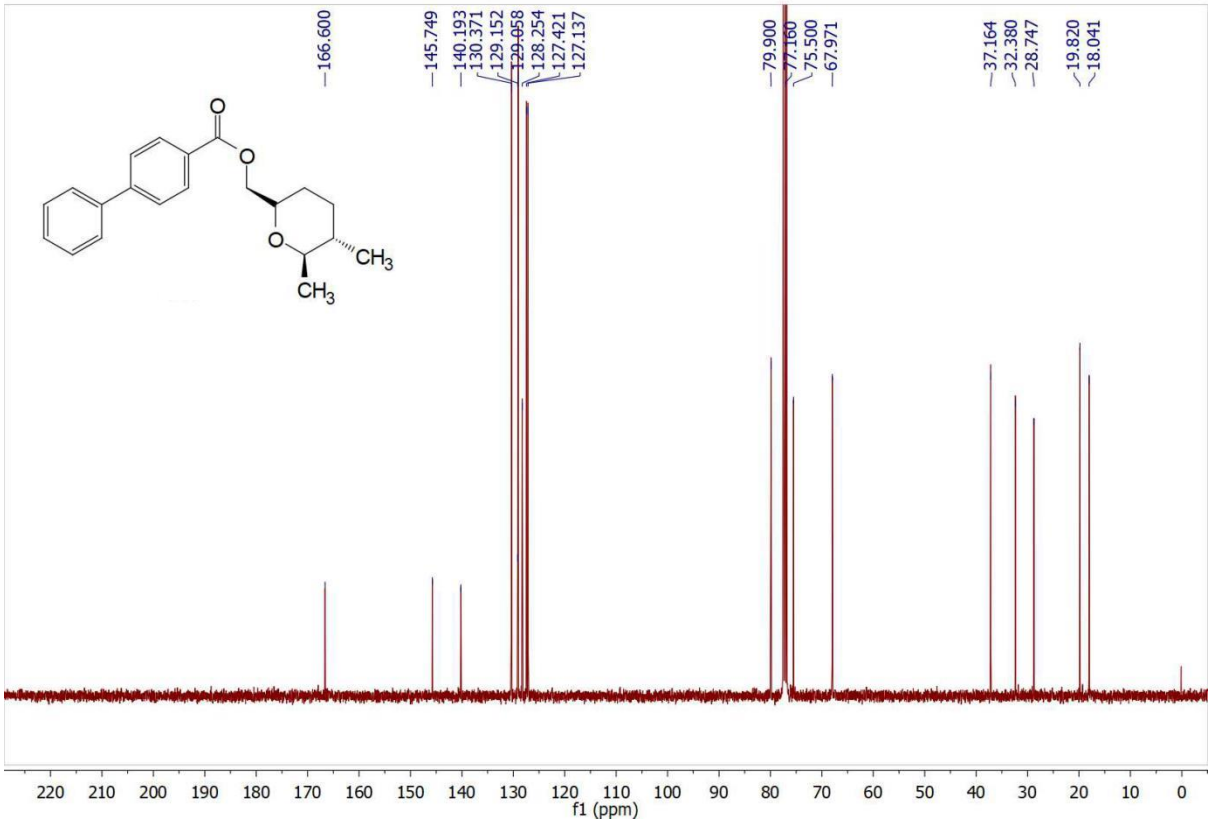
(12) ^{1}H NMR (400 MHz) and ^{13}C NMR (100 MHz) Spectra of compound 19 in $CDCl_3$



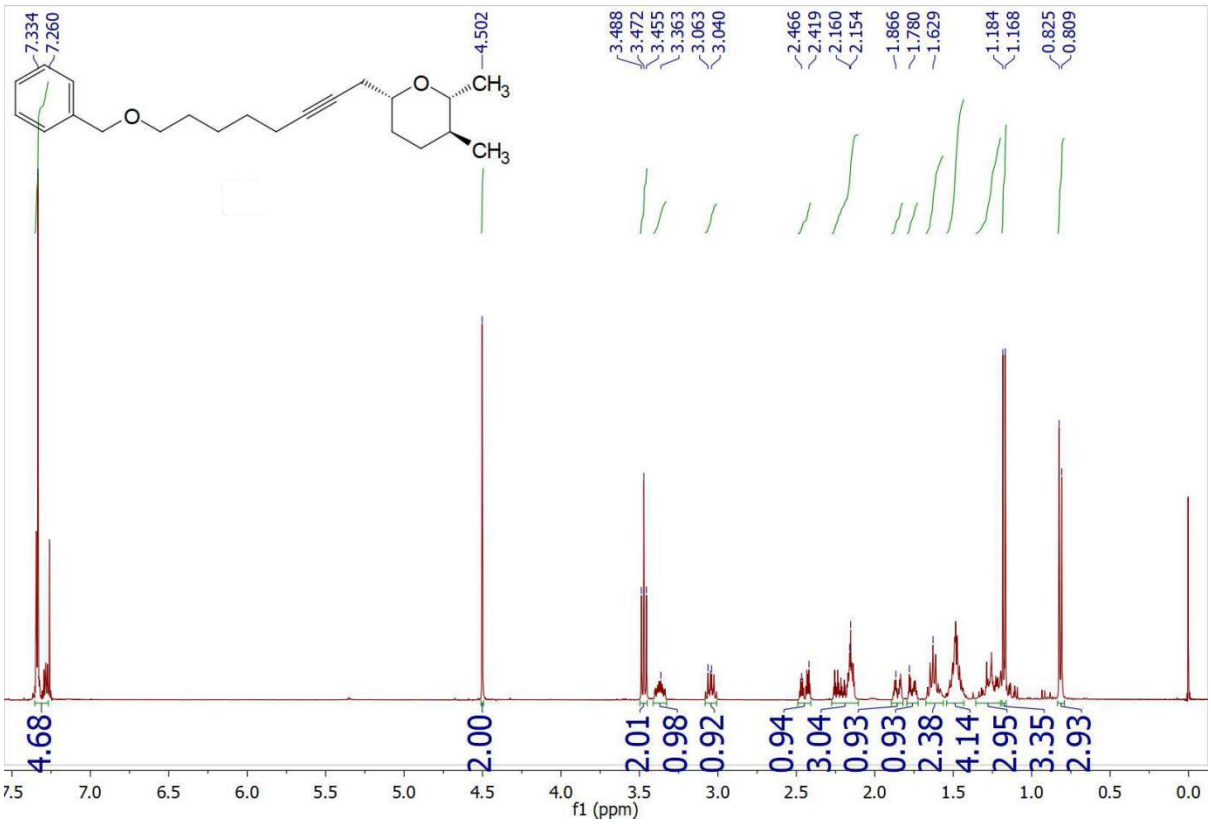


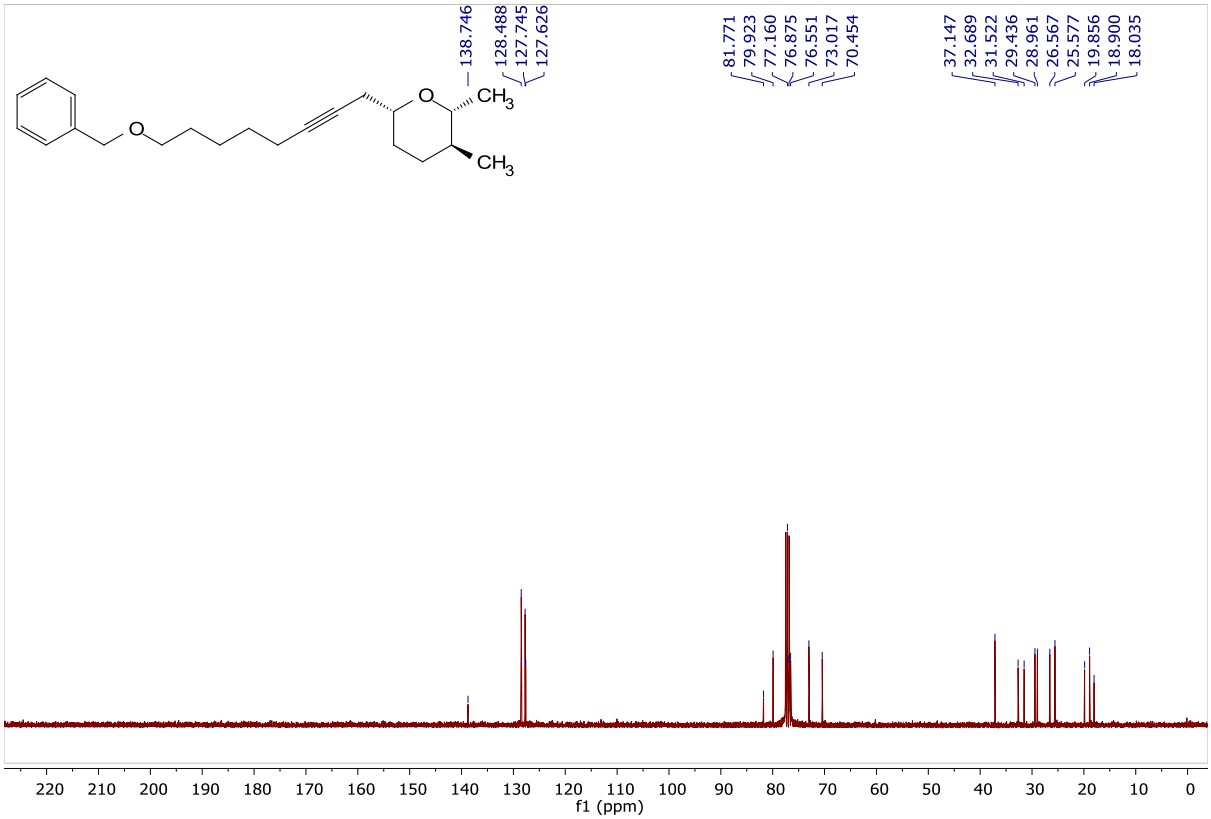
(13) ^{1}H NMR (400 MHz) and ^{13}C NMR (100 MHz) Spectra of compound 20 in $CDCl_3$



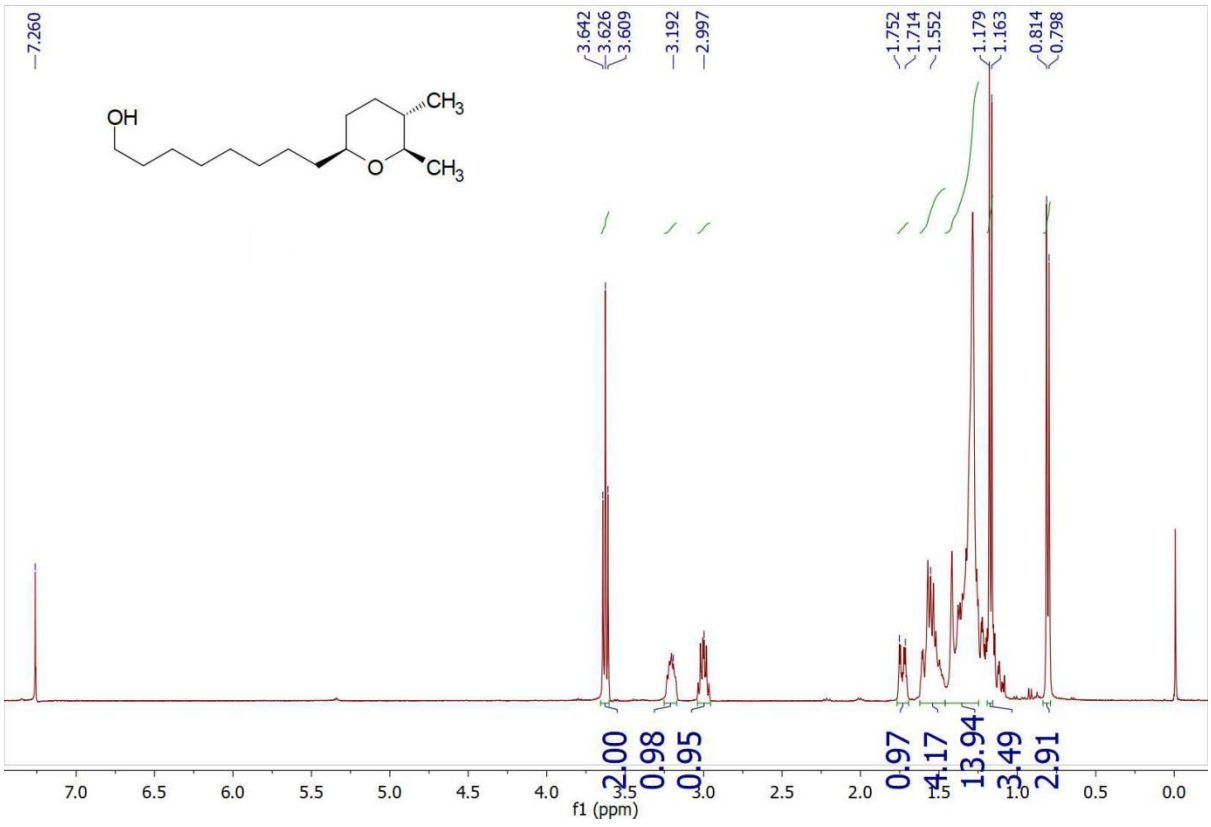


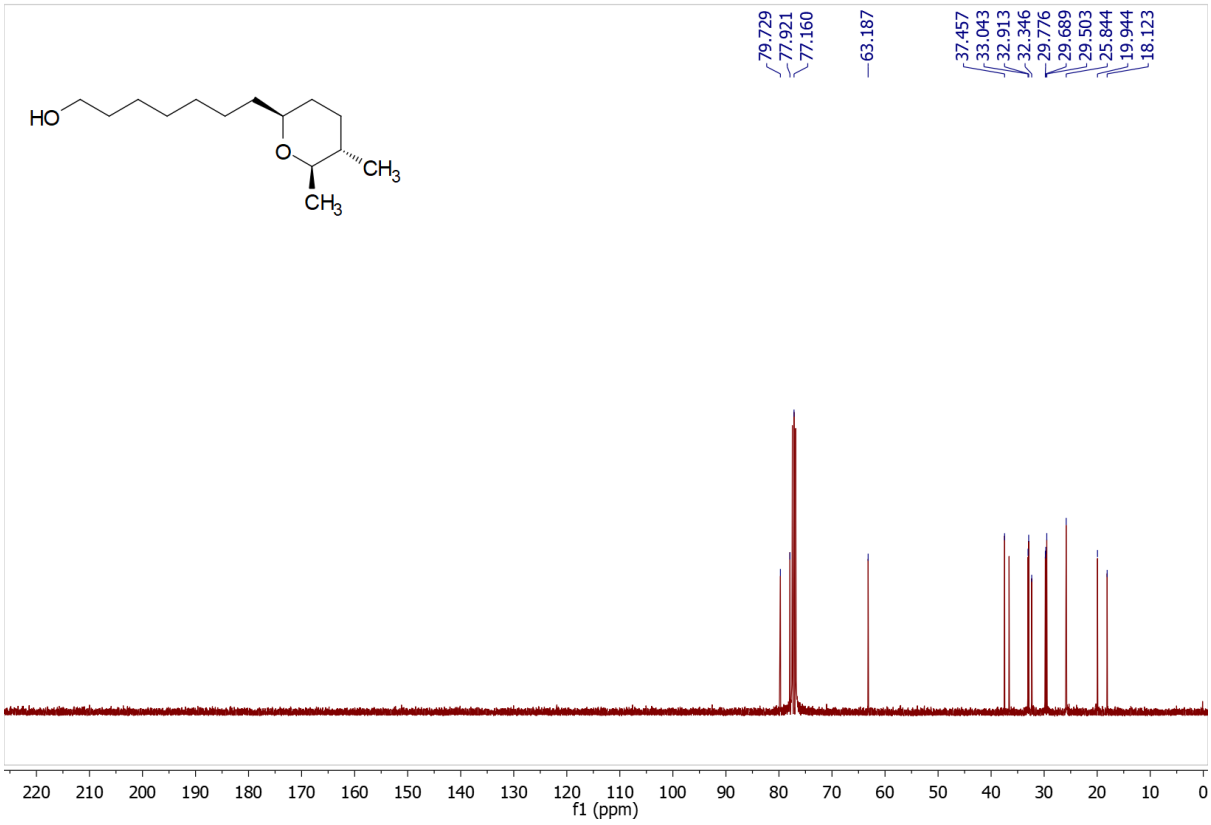
(14) ^{1}H NMR (400 MHz) and ^{13}C NMR (100 MHz) Spectra of compound 23 in $CDCl_3$



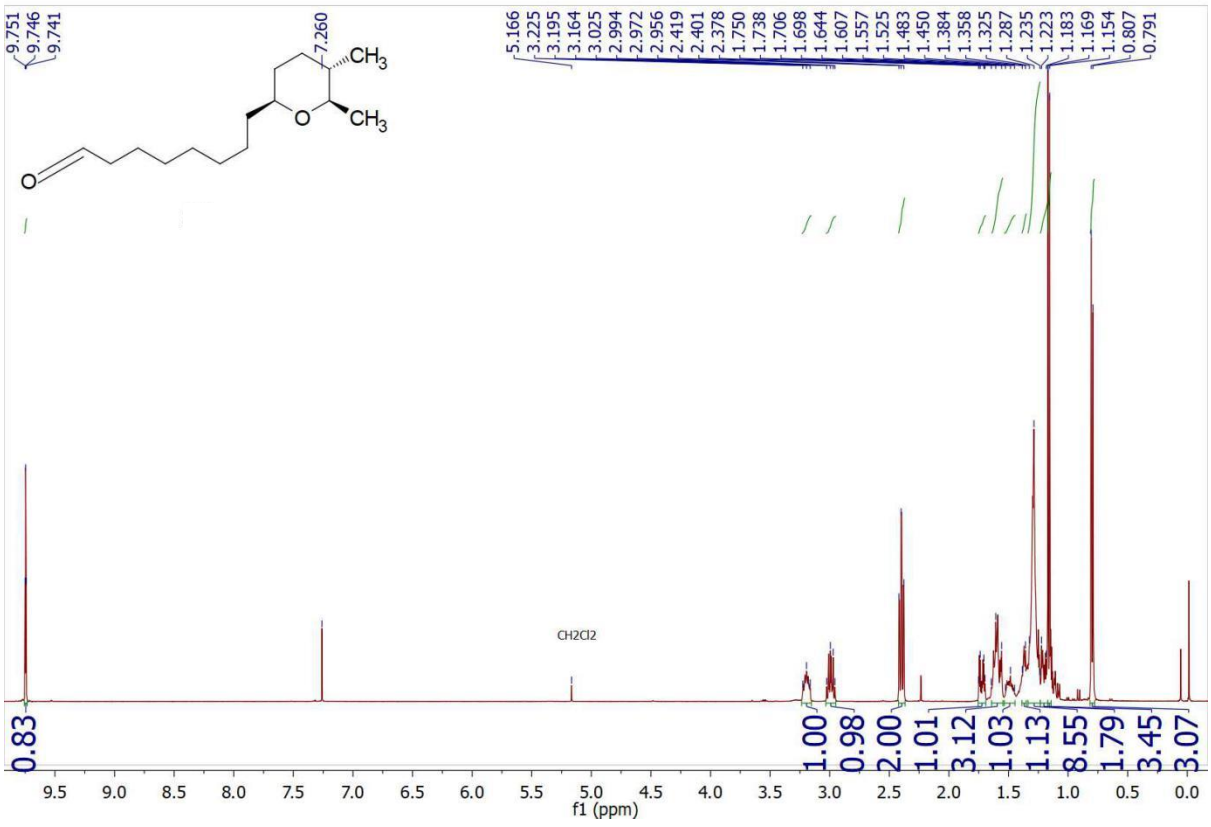


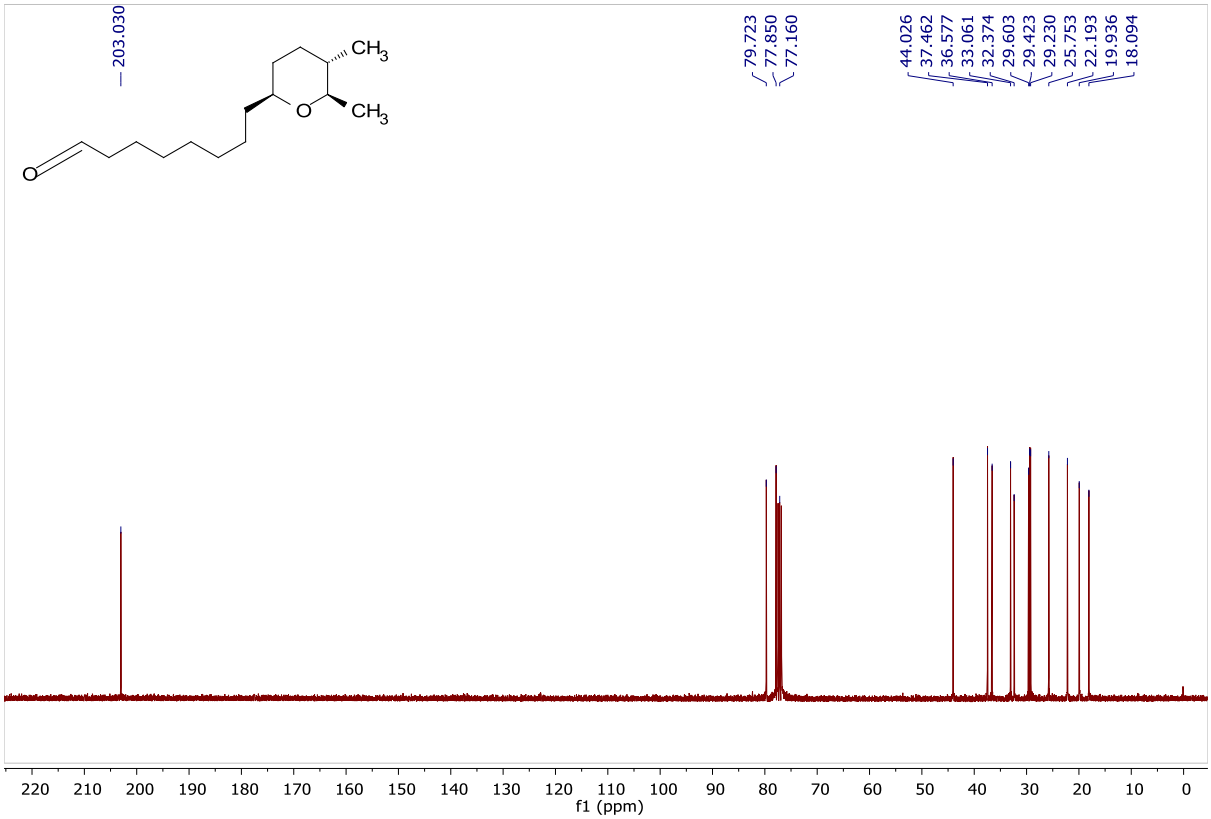
(15) ^{1}H NMR (400 MHz) and ^{13}C NMR (100 MHz) Spectra of compound 24 in $CDCl_3$



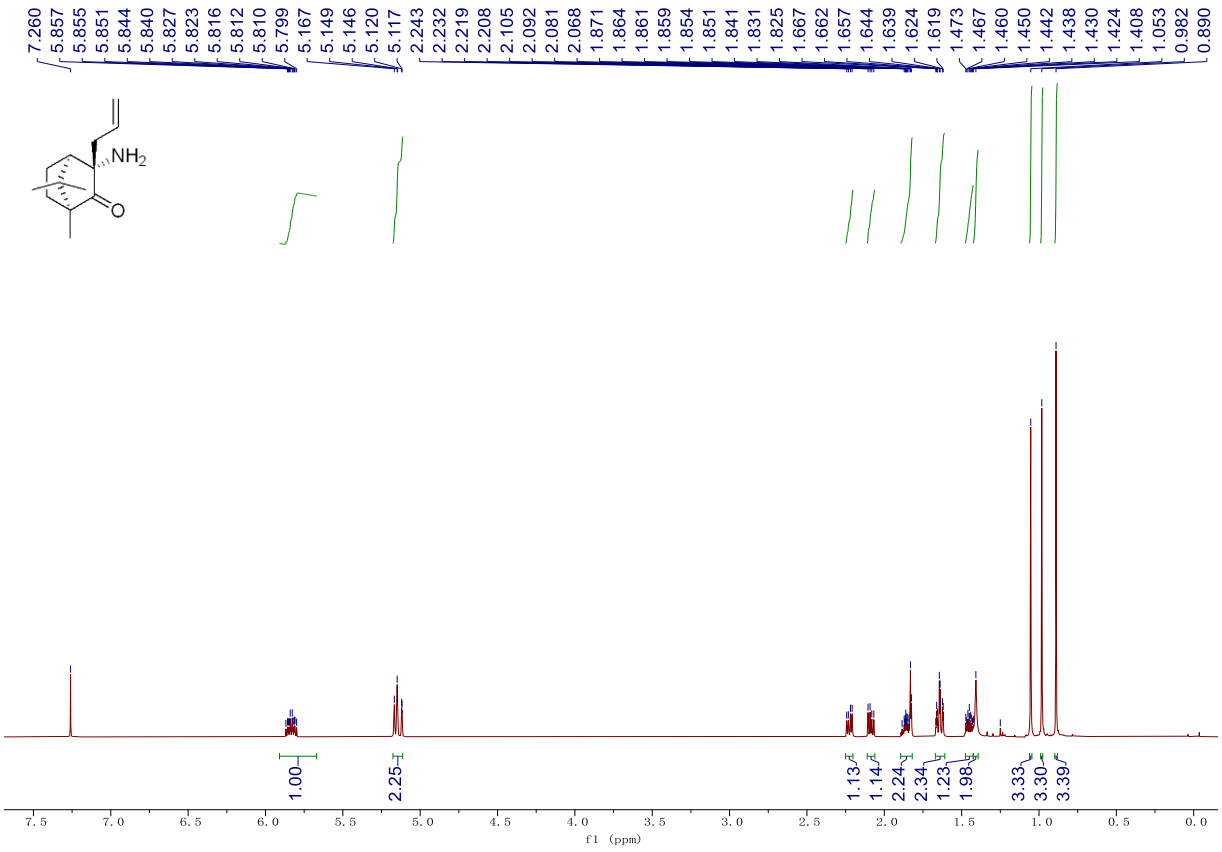


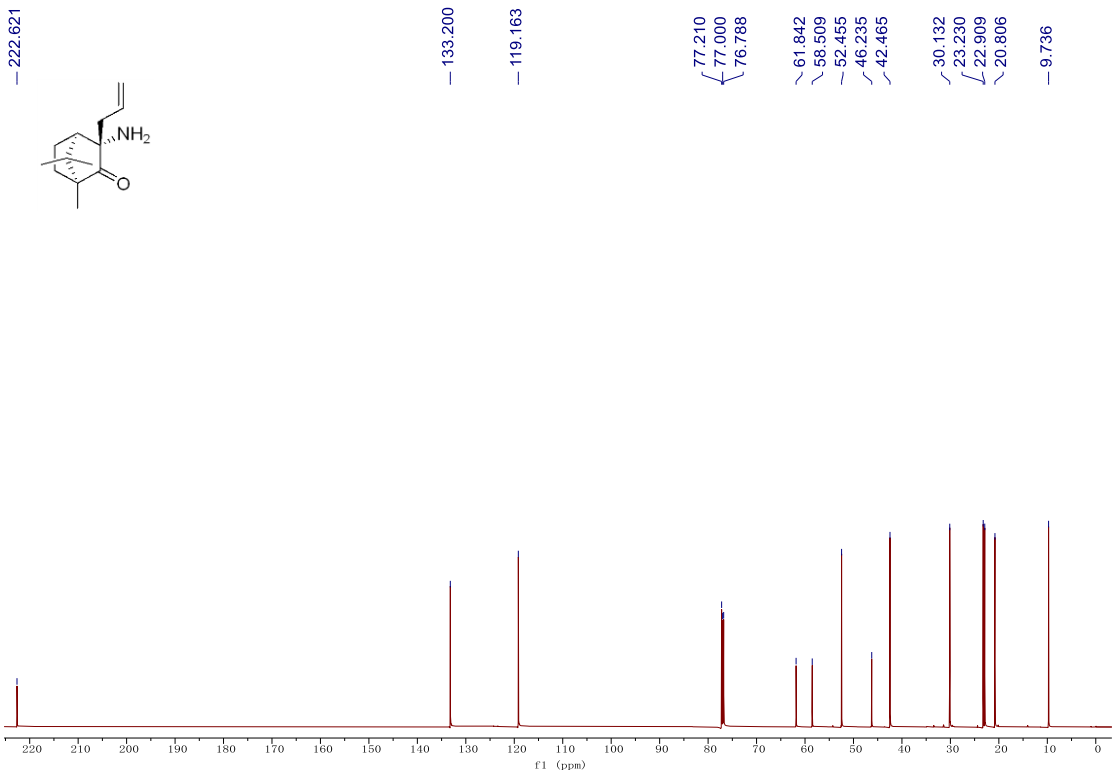
(16) ^{1}H NMR (400 MHz) and ^{13}C NMR (100 MHz) Spectra of compound 25 in $CDCl_3$



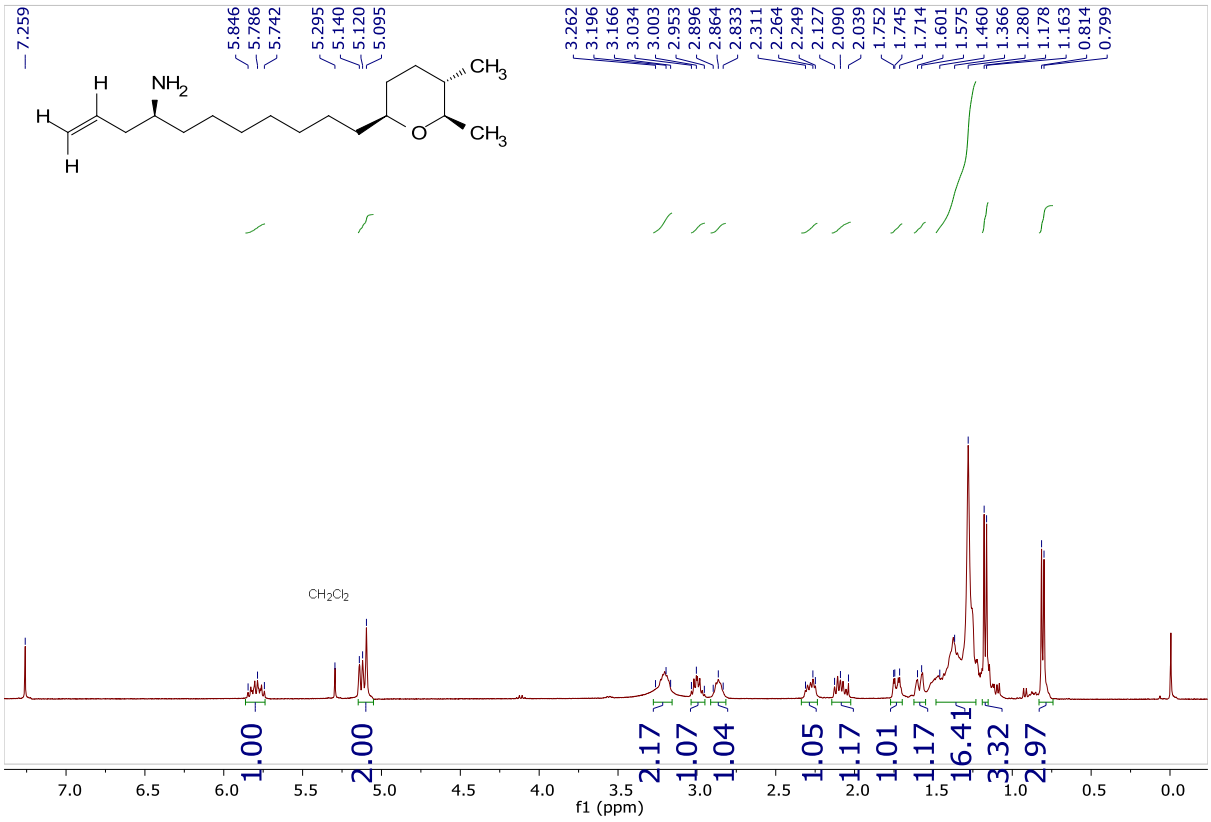


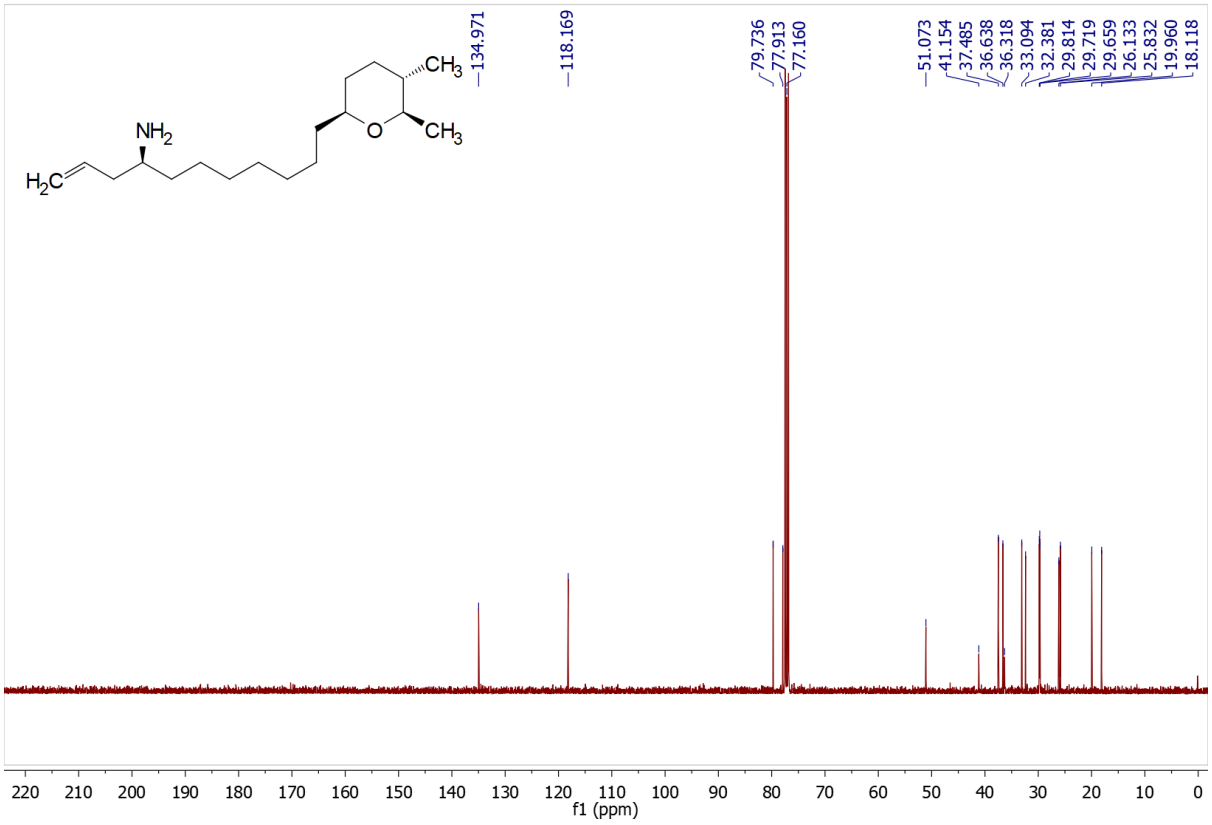
(17) ^{1}H NMR (600 MHz) and ^{13}C NMR (150 MHz) Spectra of compound 26 in $CDCl_3$



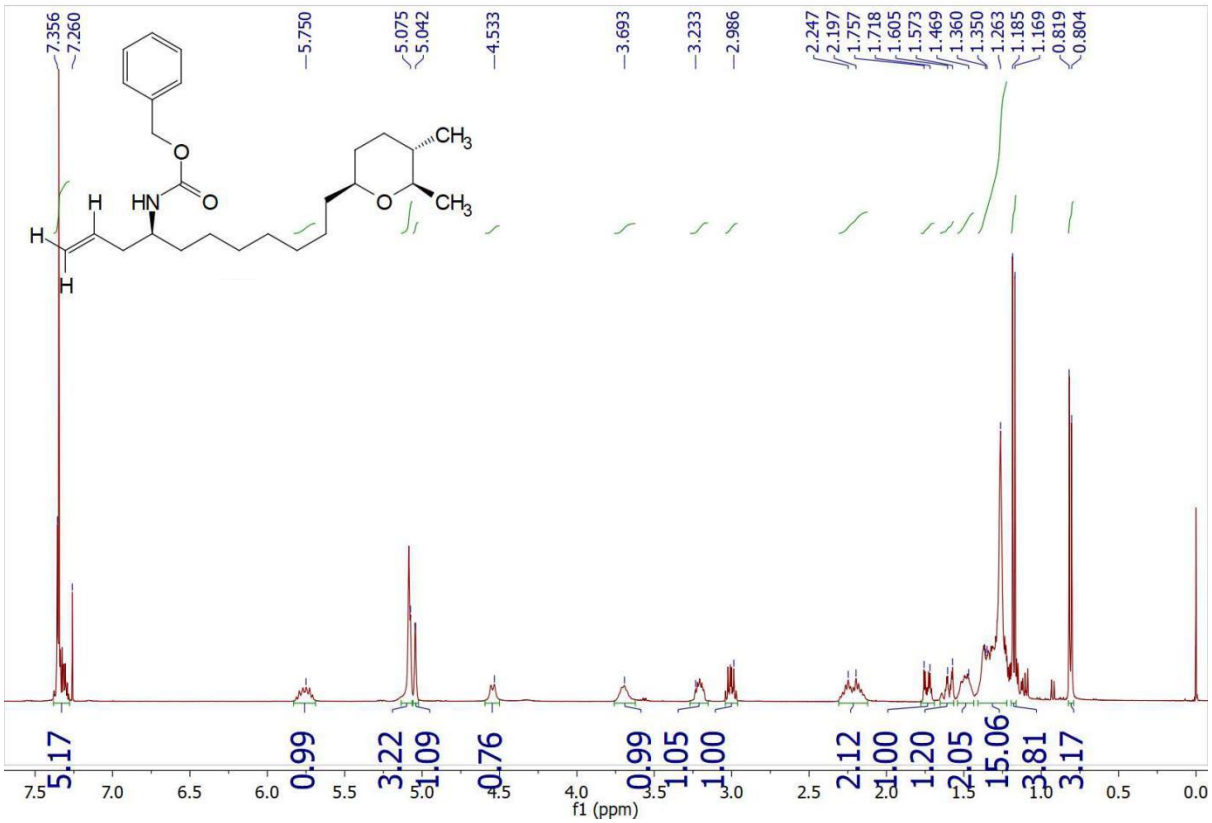


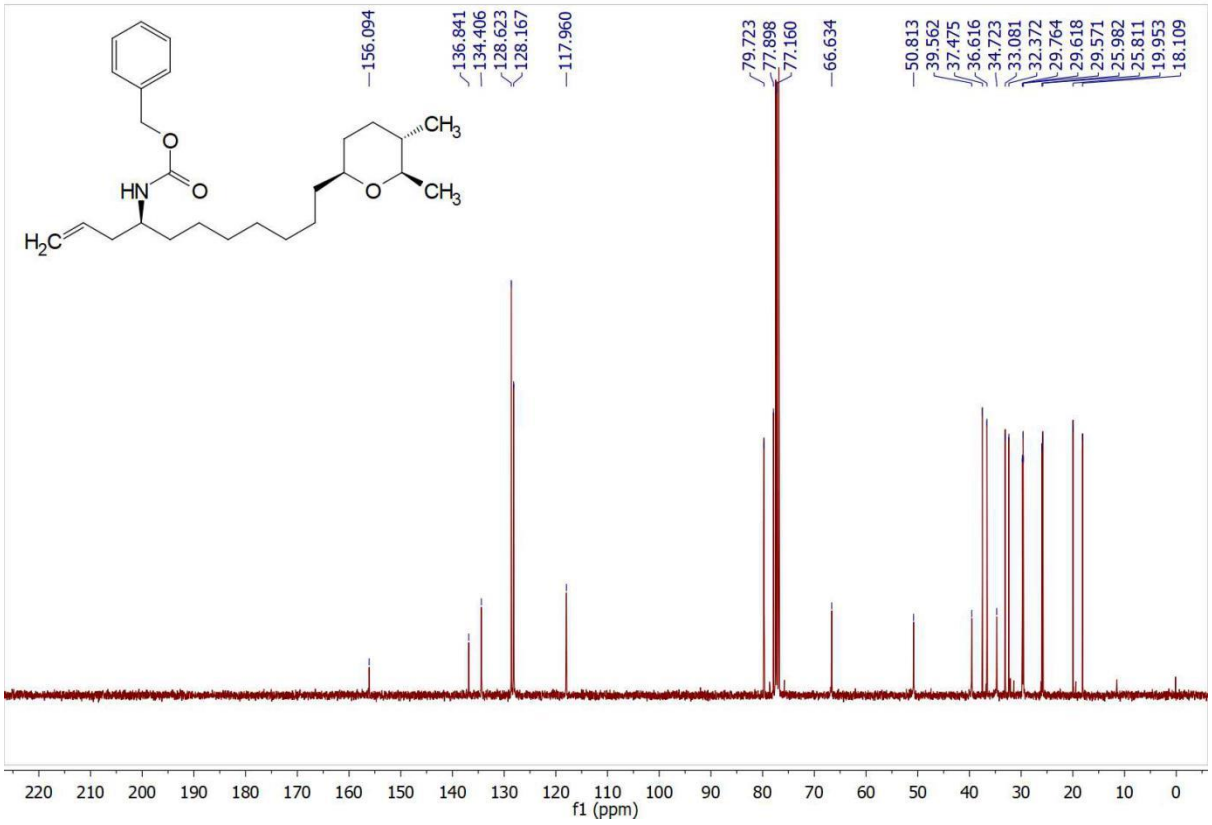
(18) ^{1}H NMR (400 MHz) and ^{13}C NMR (100 MHz) Spectra of compound 27 in $CDCl_3$



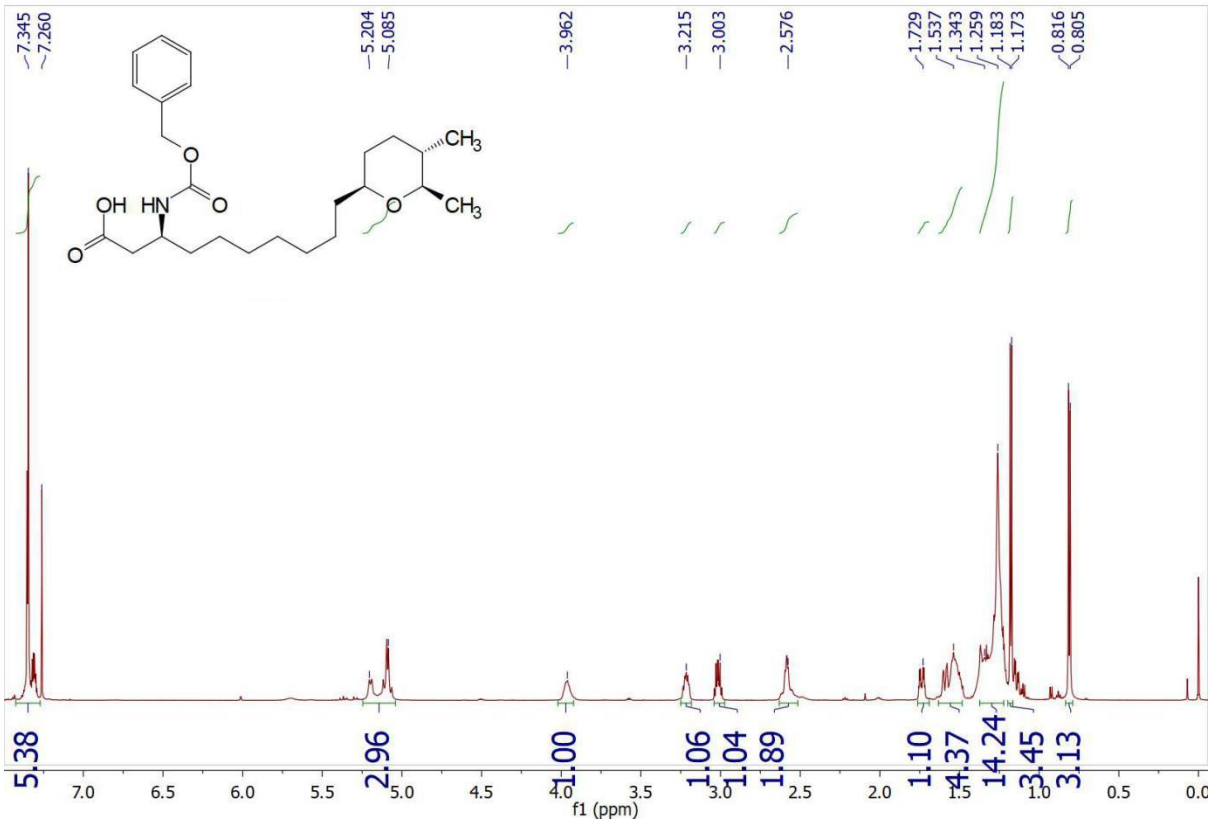


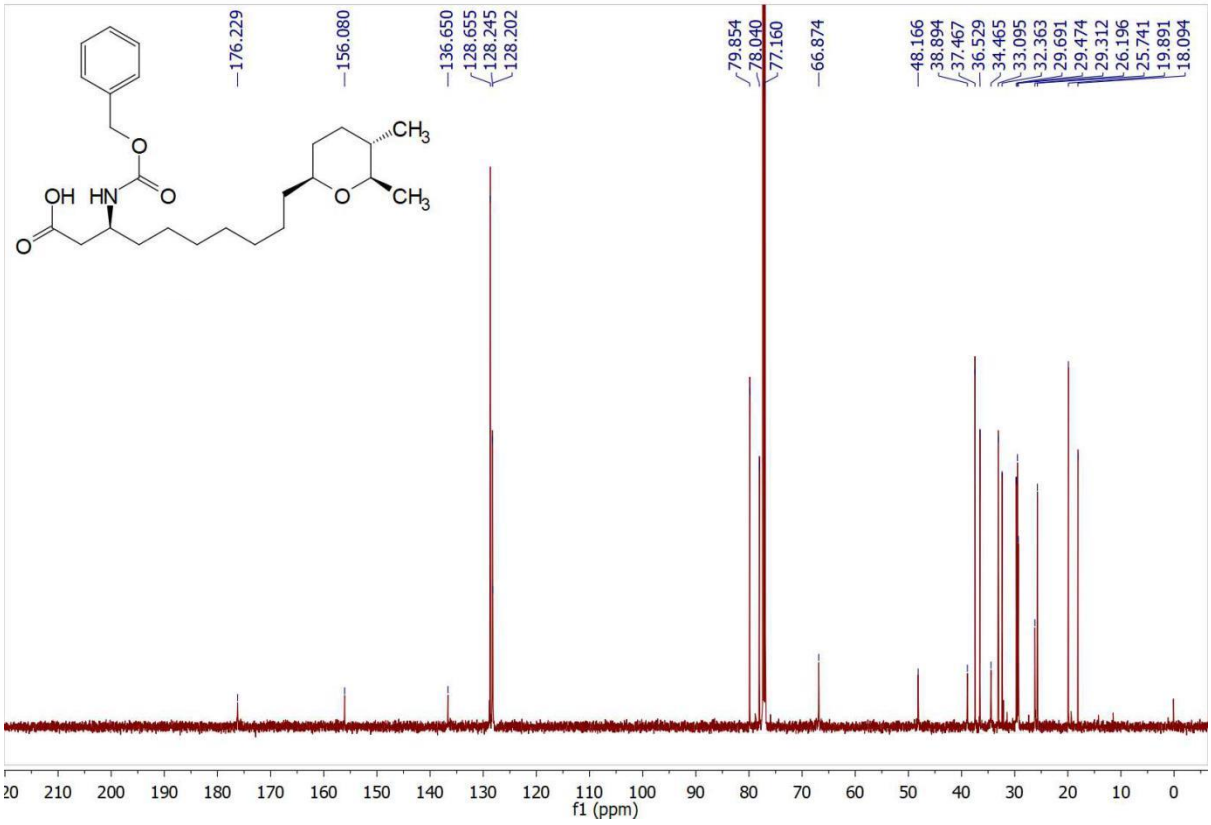
(19) ^{1}H NMR (400 MHz) and ^{13}C NMR (100 MHz) Spectra of compound 28 in $CDCl_3$



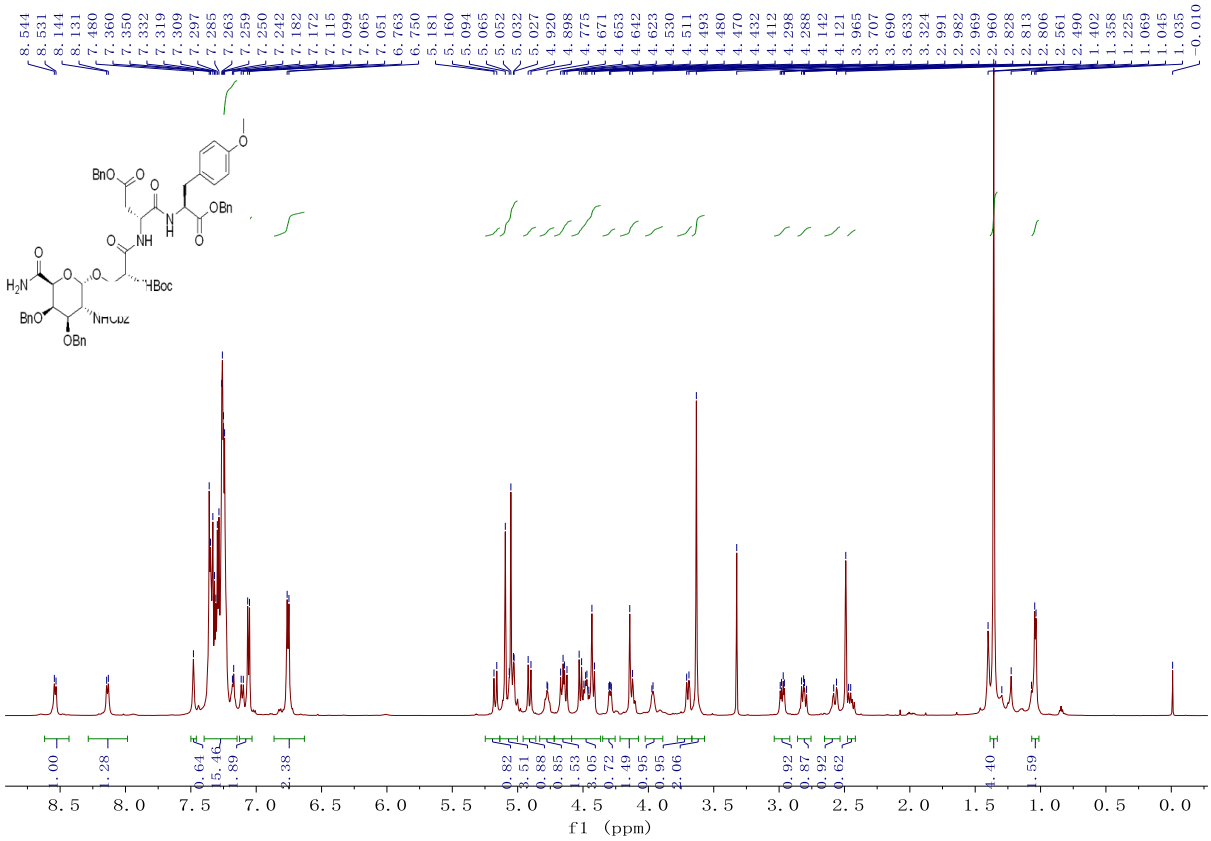


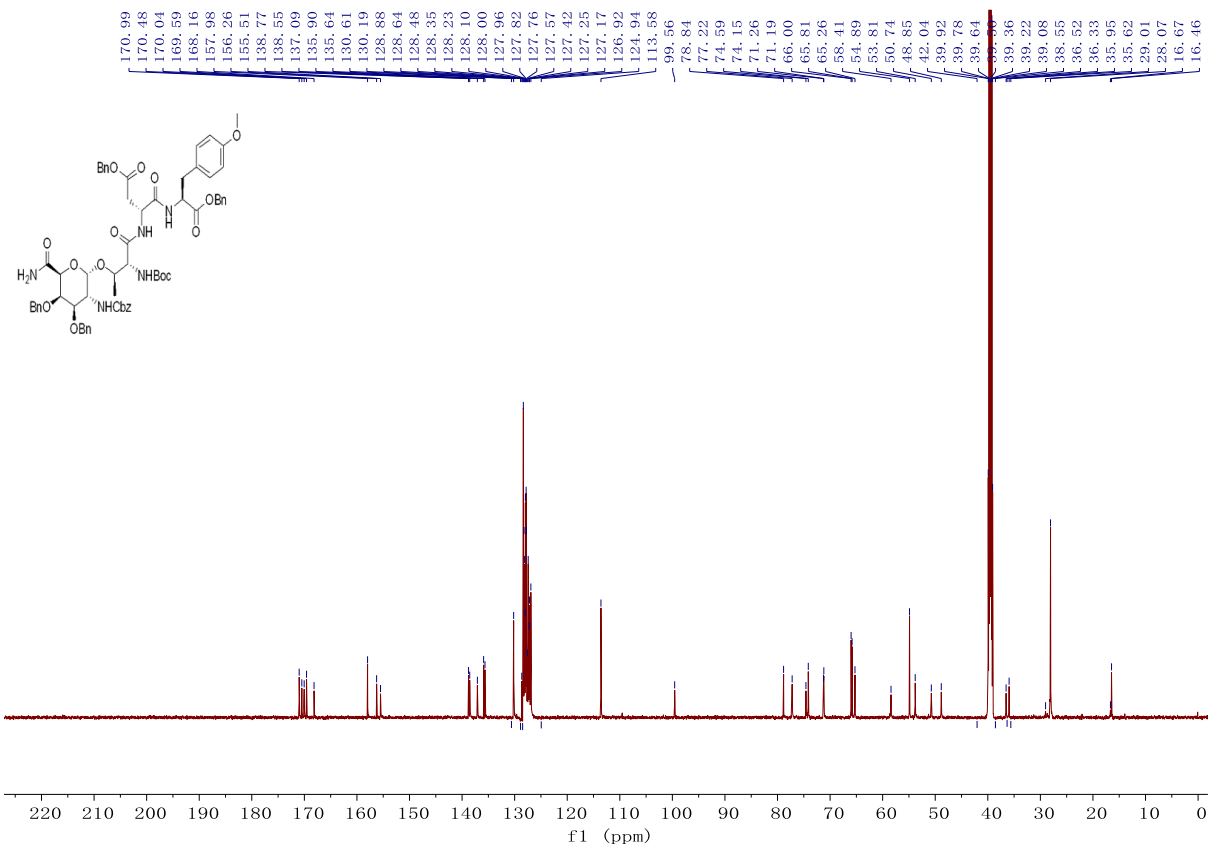
(20) ^{1}H NMR (600 MHz) and ^{13}C NMR (150 MHz) Spectra of compound 29 in $CDCl_3$



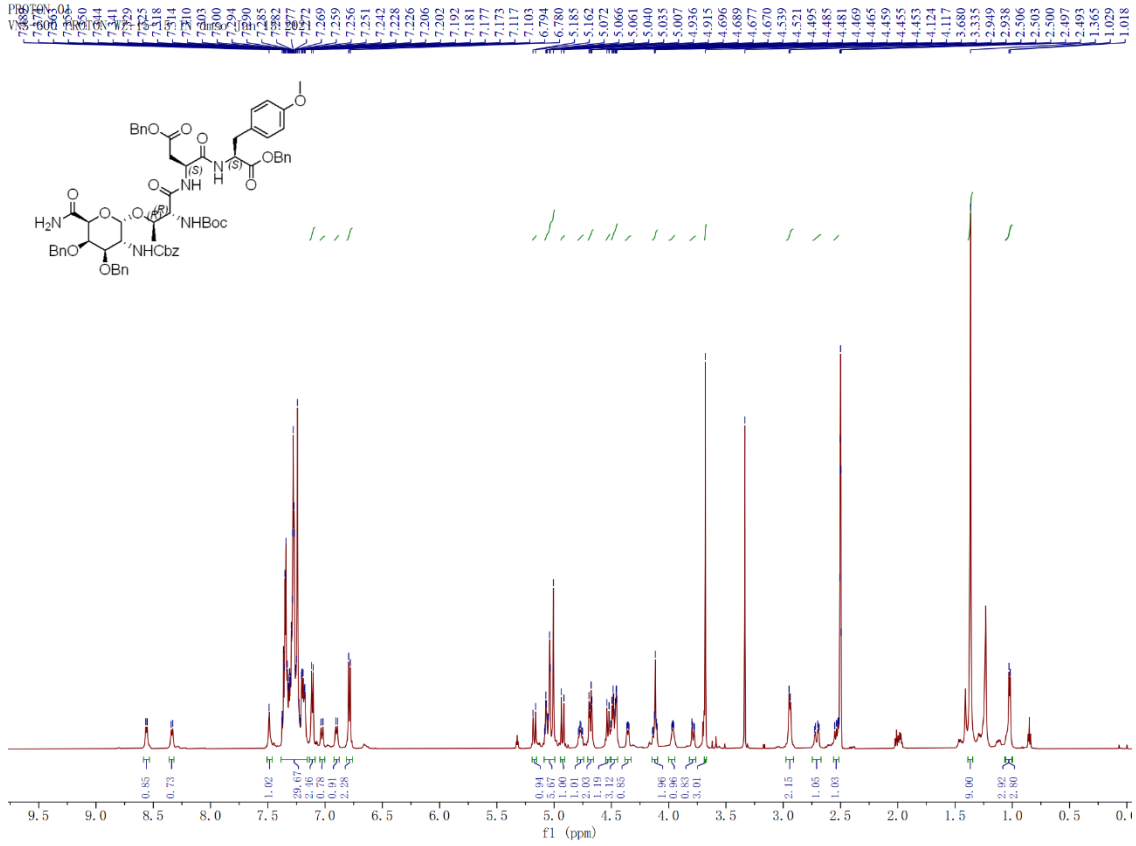


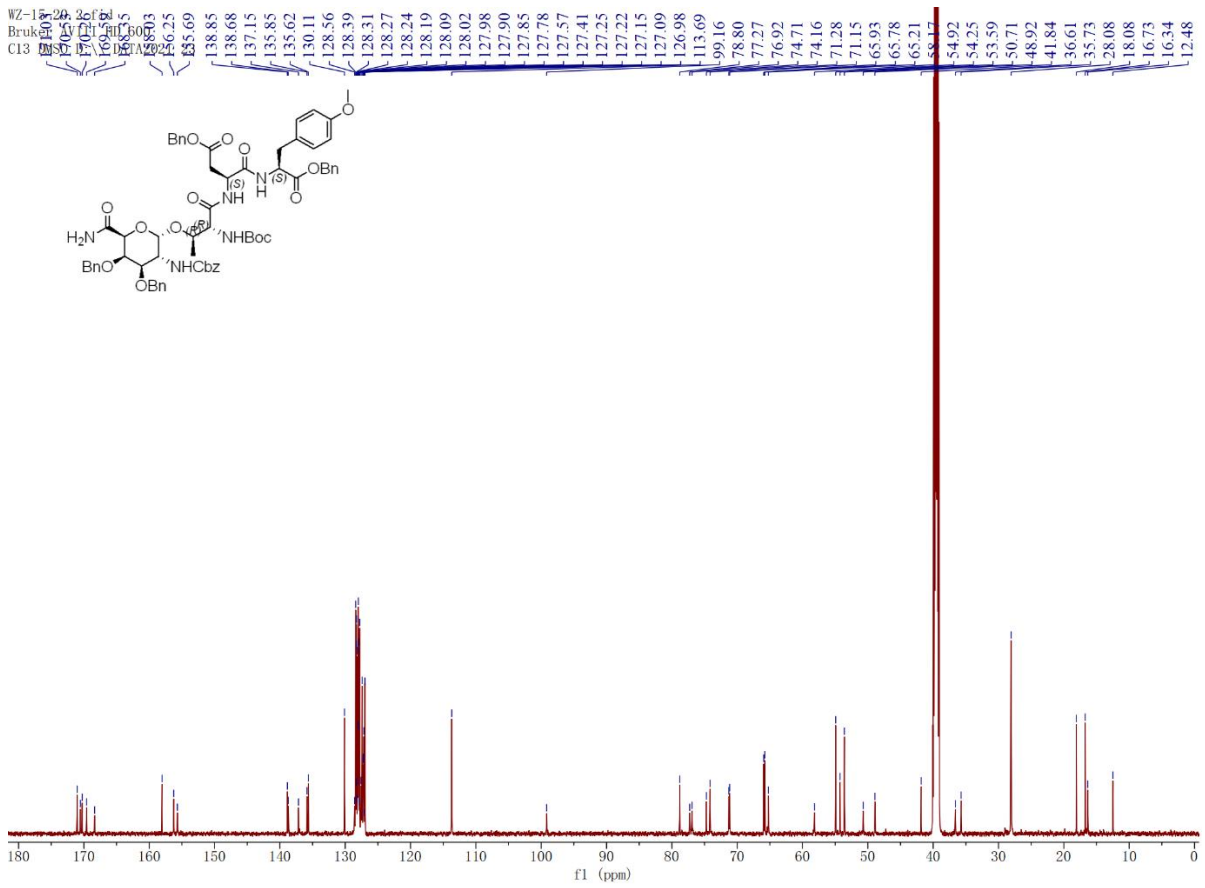
(21) ^{1}H NMR (600 MHz) and ^{13}C NMR (150 MHz) Spectra of compound 30 in DMSO-d_6



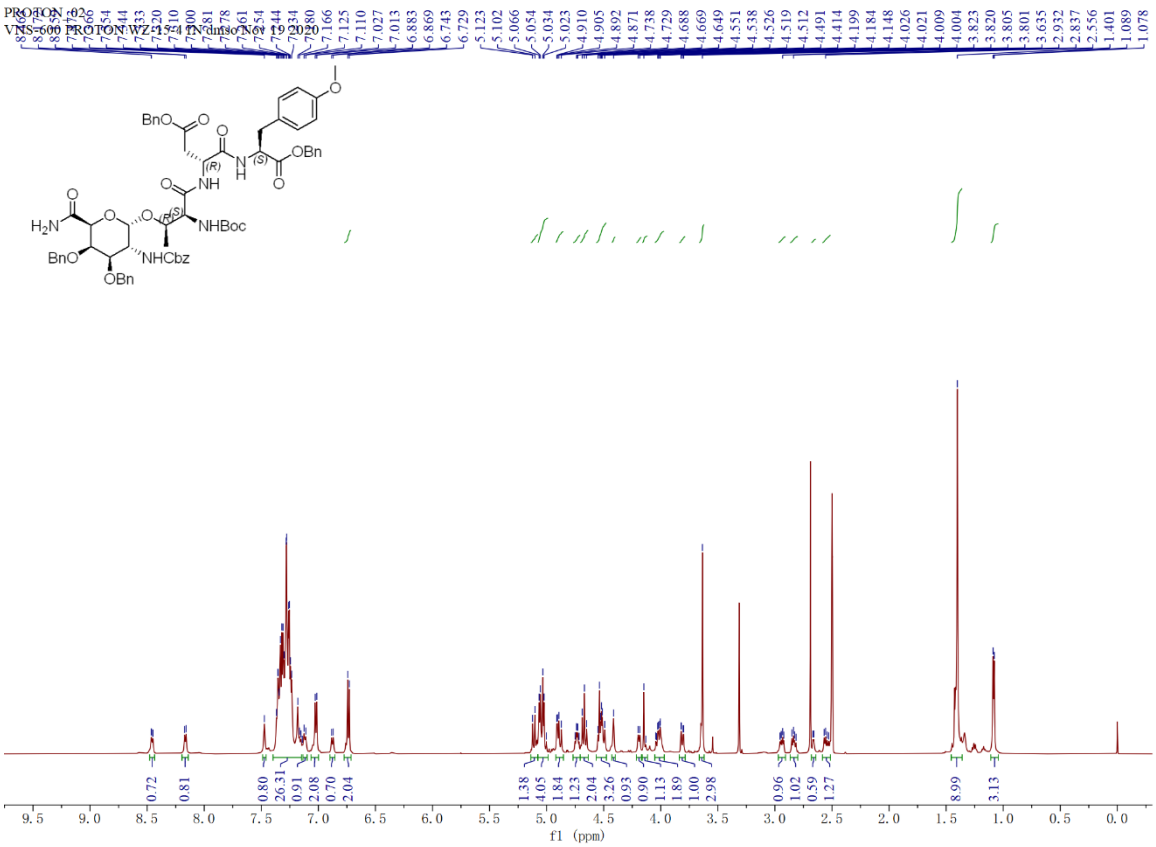


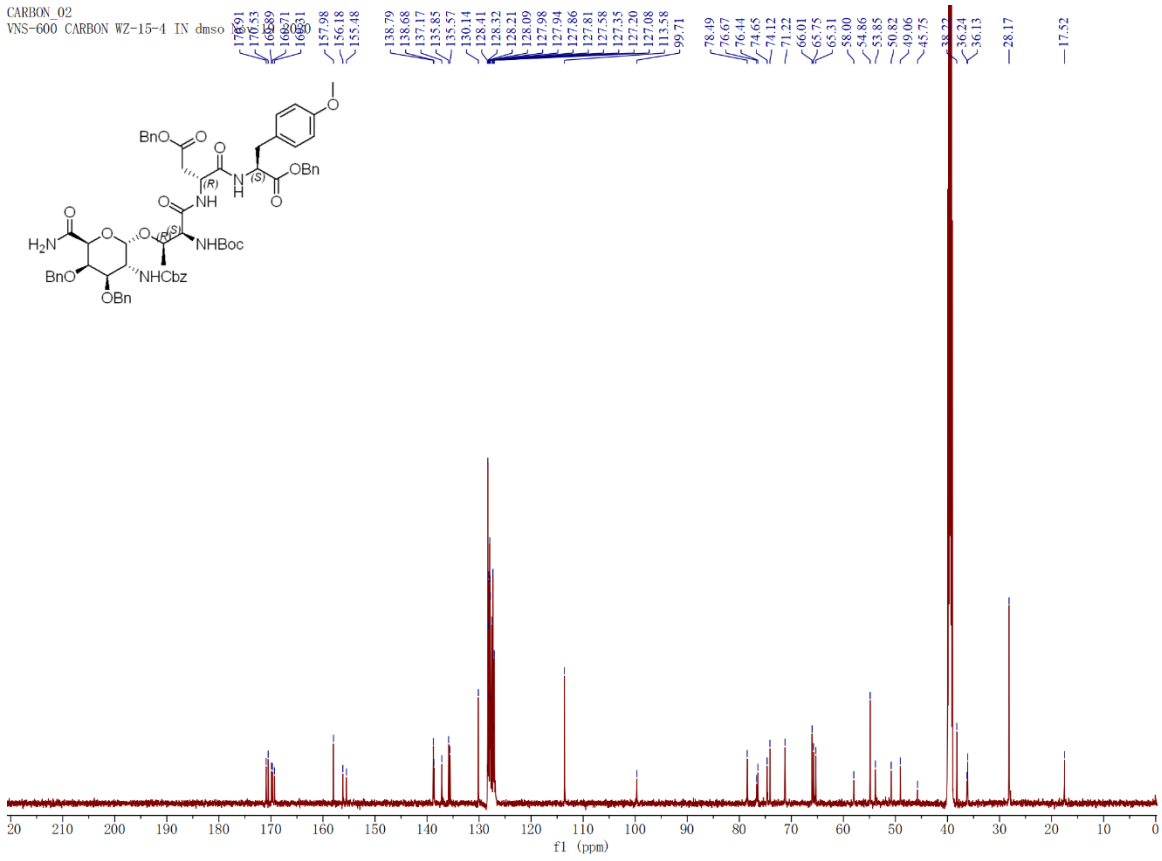
(22) ^{1}H NMR (600 MHz) and ^{13}C NMR (150 MHz) Spectra of compound 30a in DMSO-d$_6$



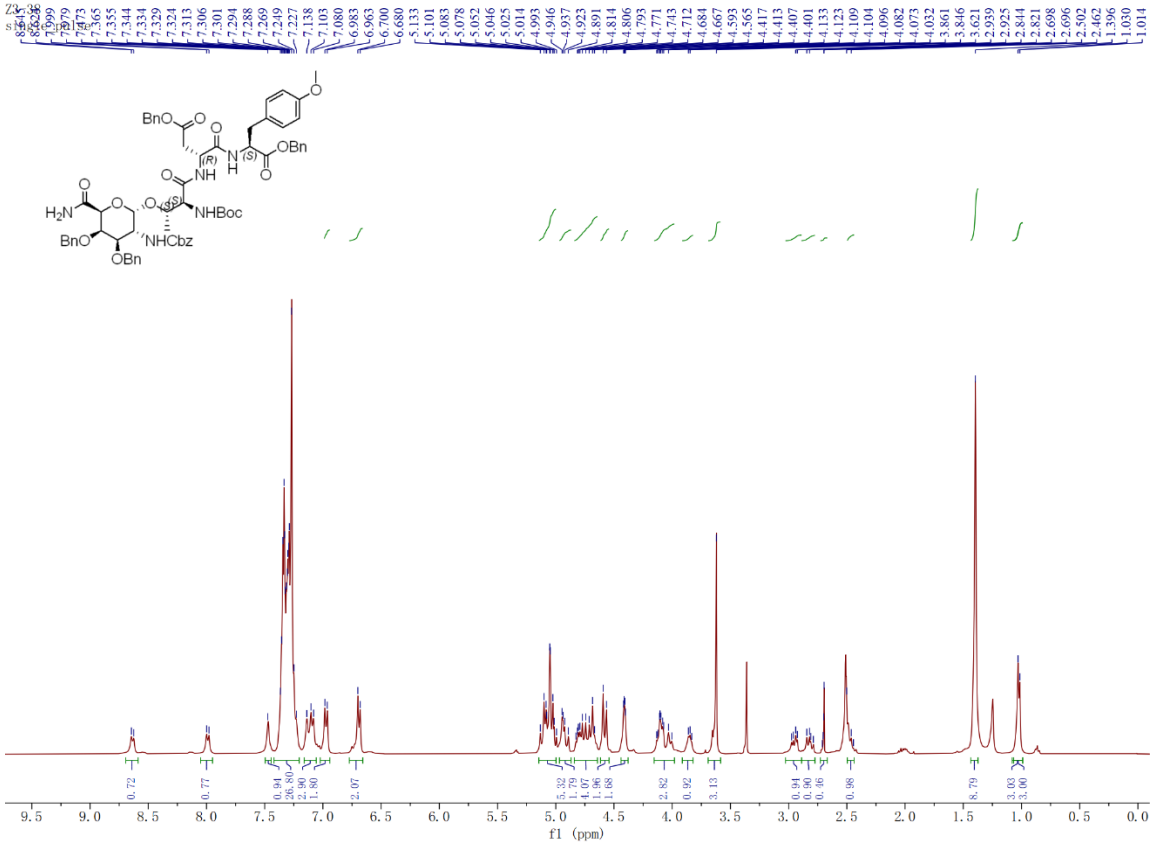


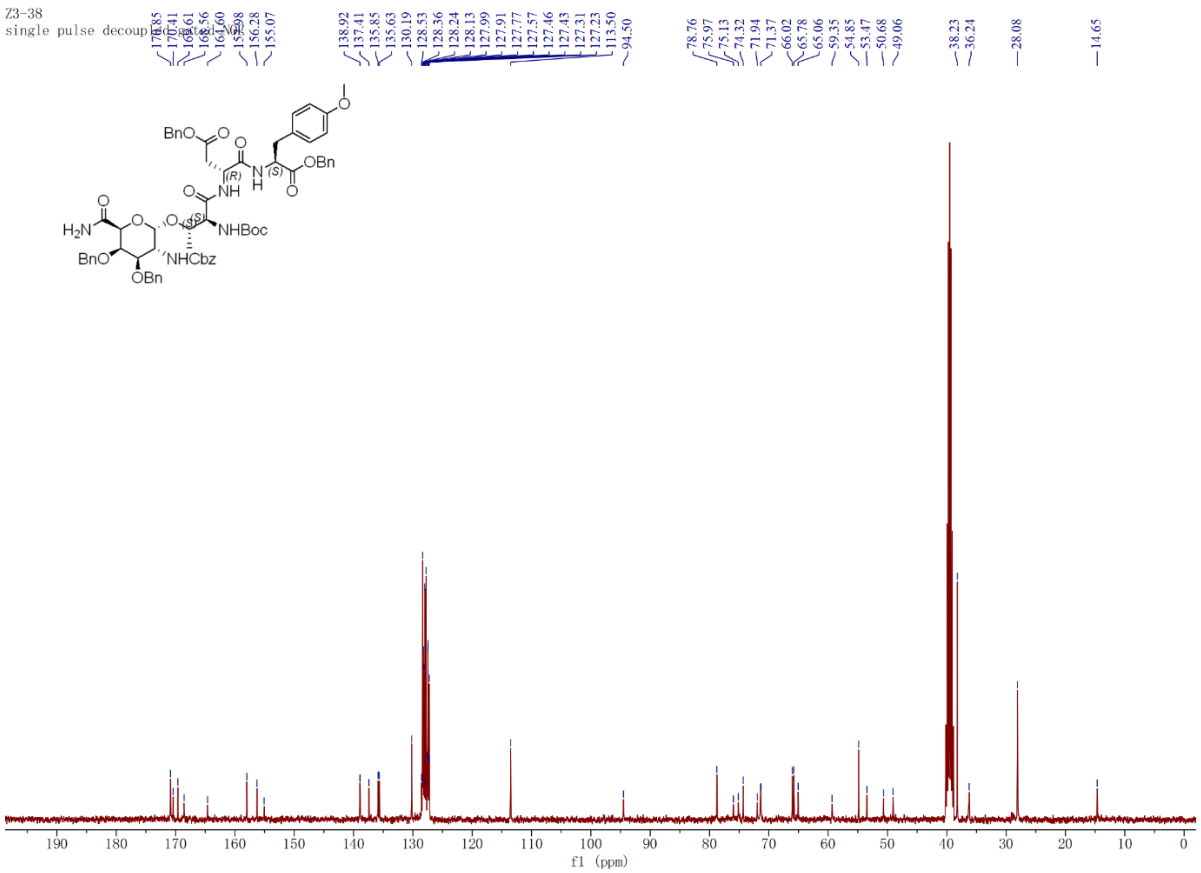
(23) ^{1}H NMR (600 MHz) and ^{13}C NMR (150 MHz) Spectra of compound 30b in DMSO-d$_6$



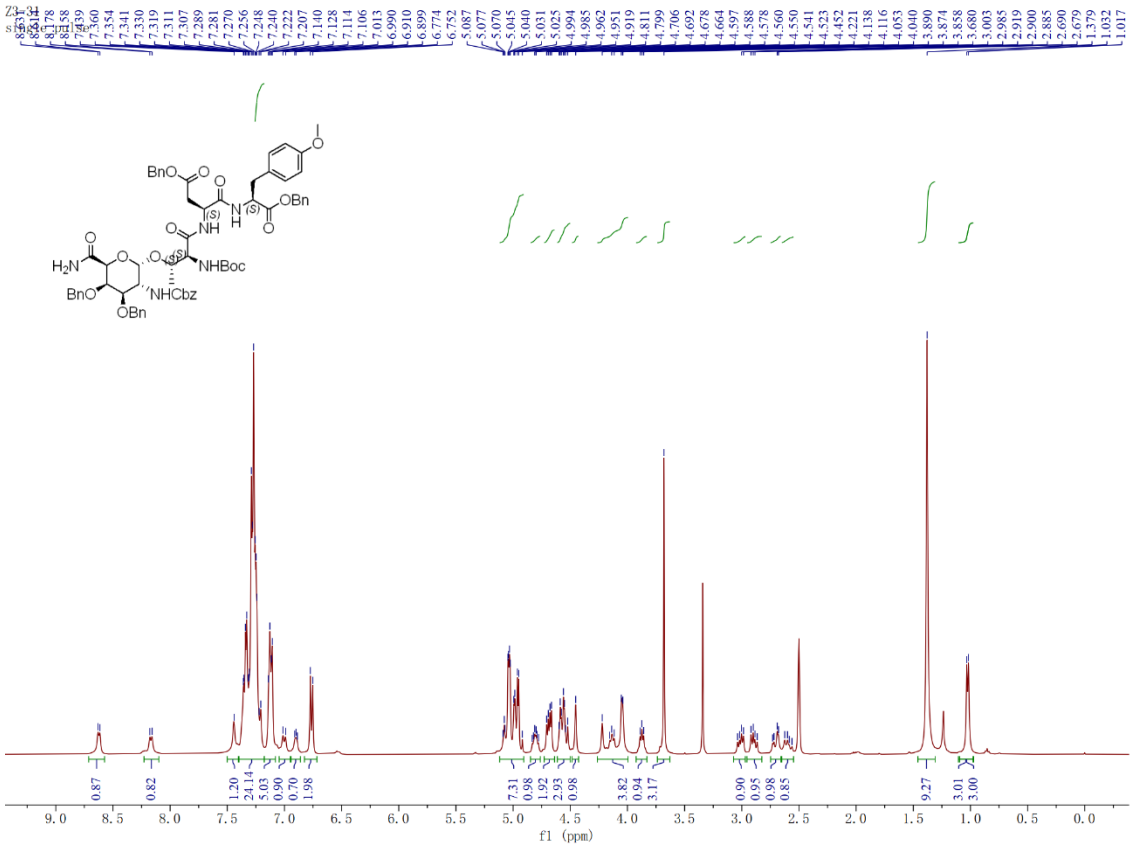


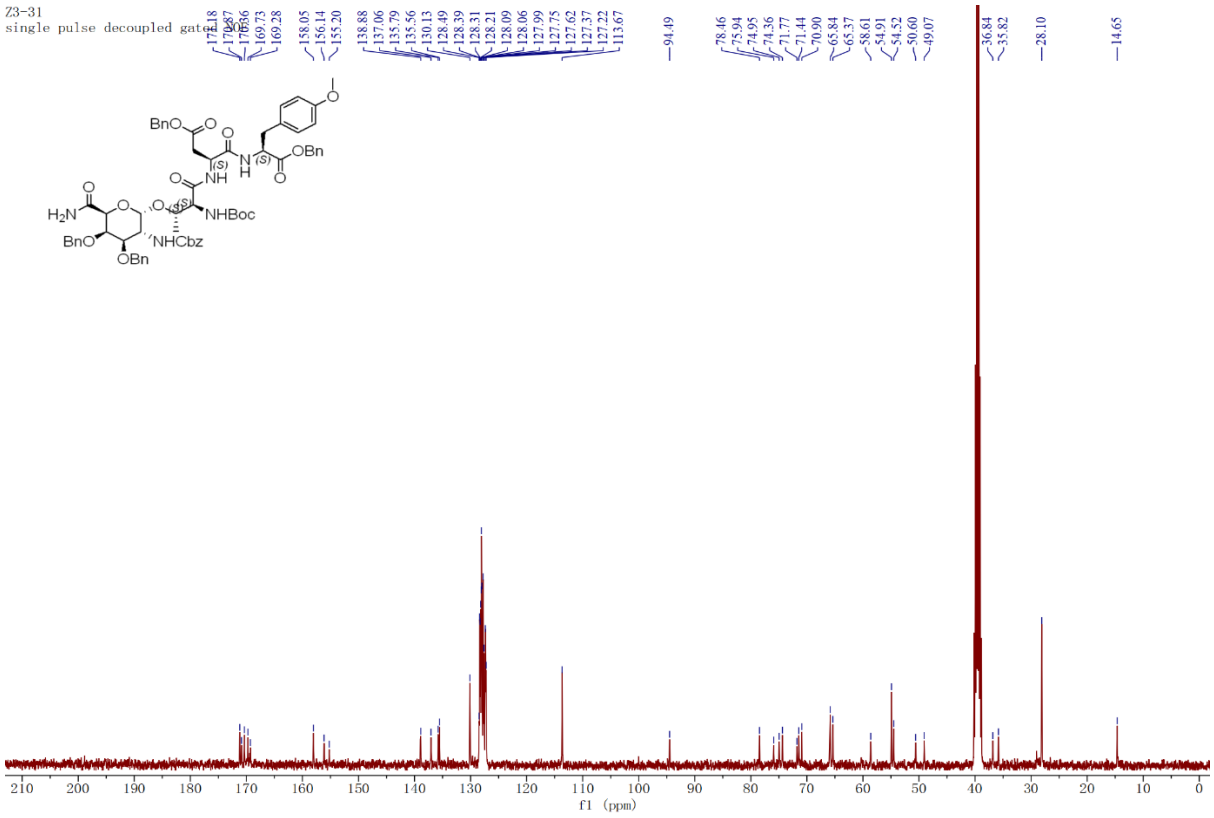
(24) ^{1}H NMR (400 MHz) and ^{13}C NMR (100 MHz) Spectra of compound 30c in DMSO-d$_6$



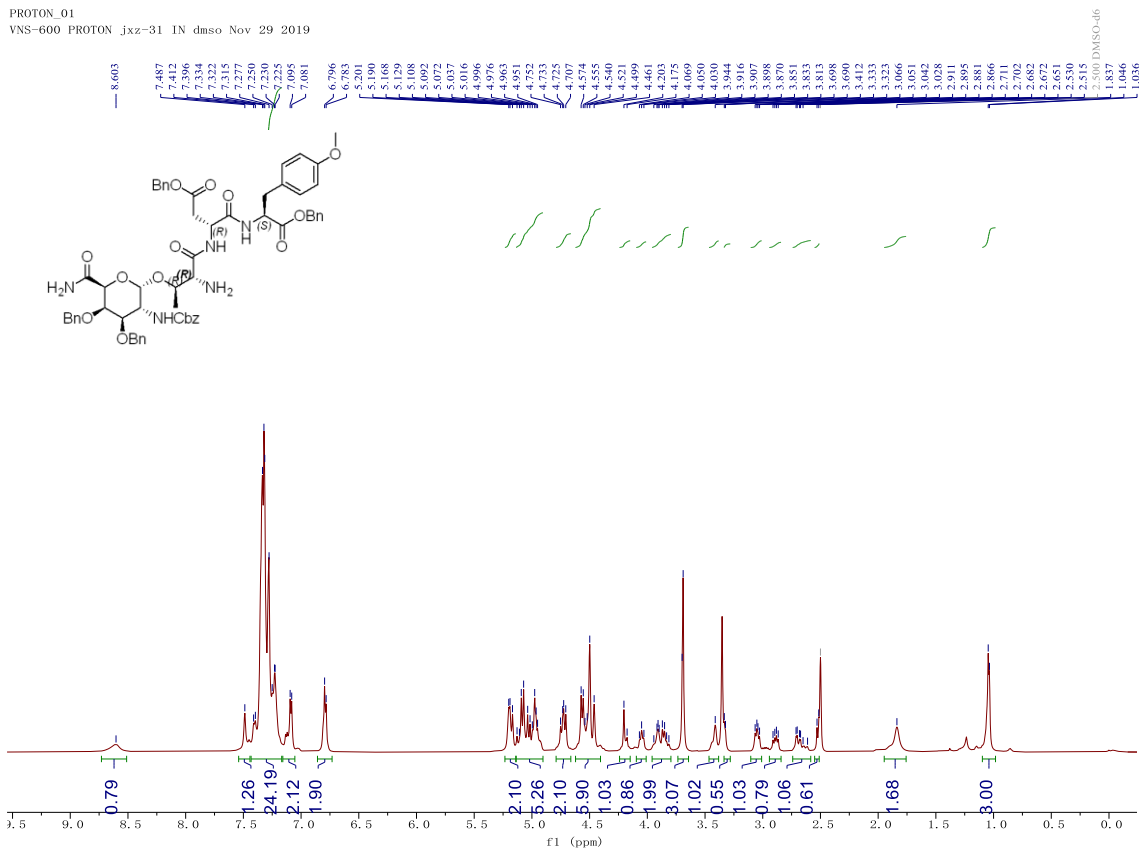


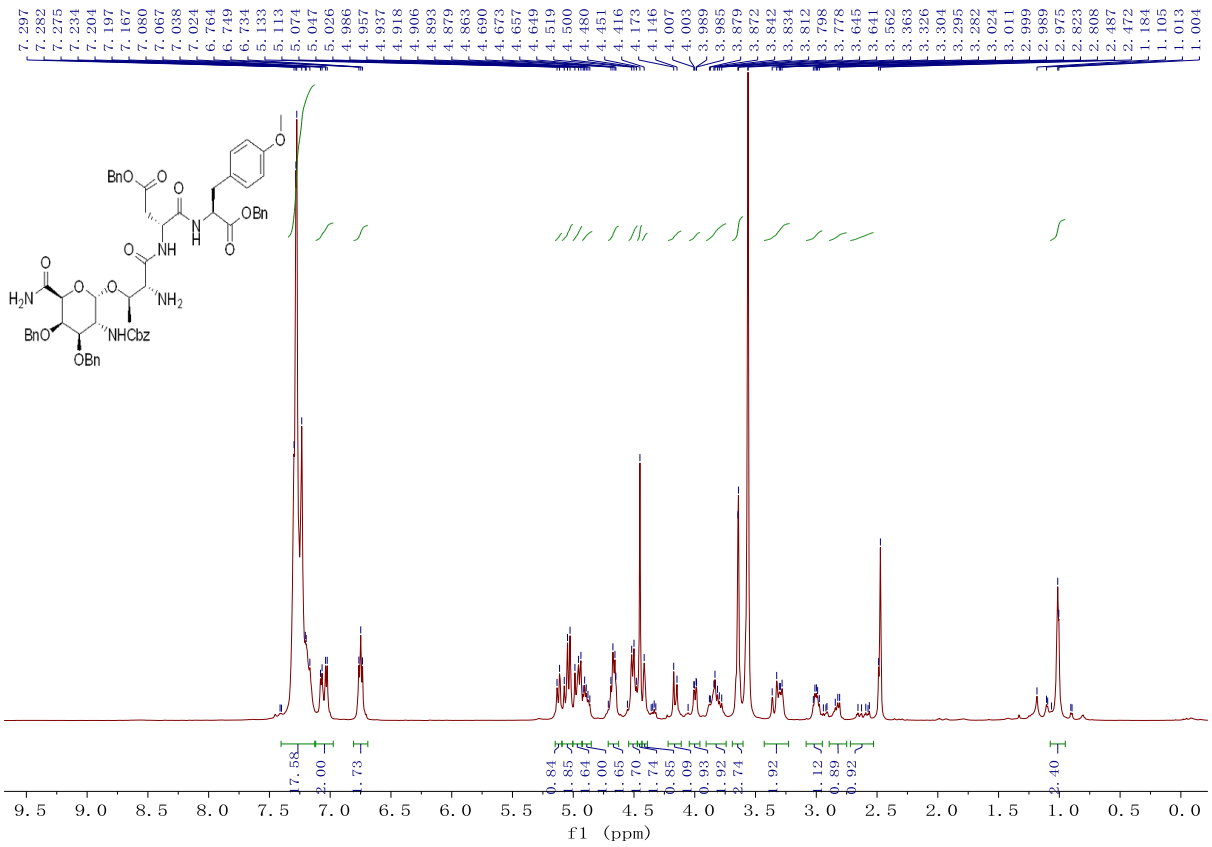
(25) ^{1}H NMR (400 MHz) and ^{13}C NMR (100 MHz) Spectra of compound 30d in DMSO-d$_6$



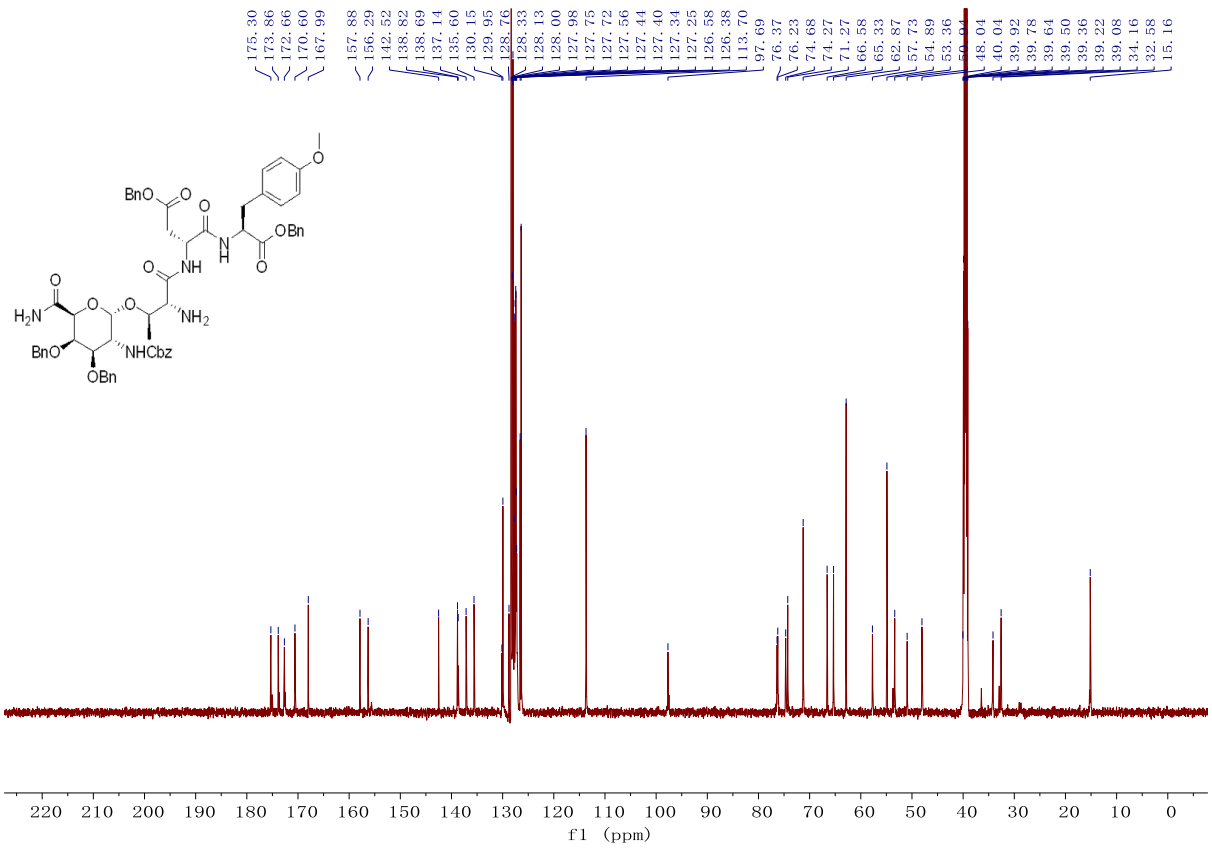


(26) ^{1}H NMR (600 MHz) and ^{13}C NMR (150 MHz) Spectra of compound 31 in DMSO-d_6

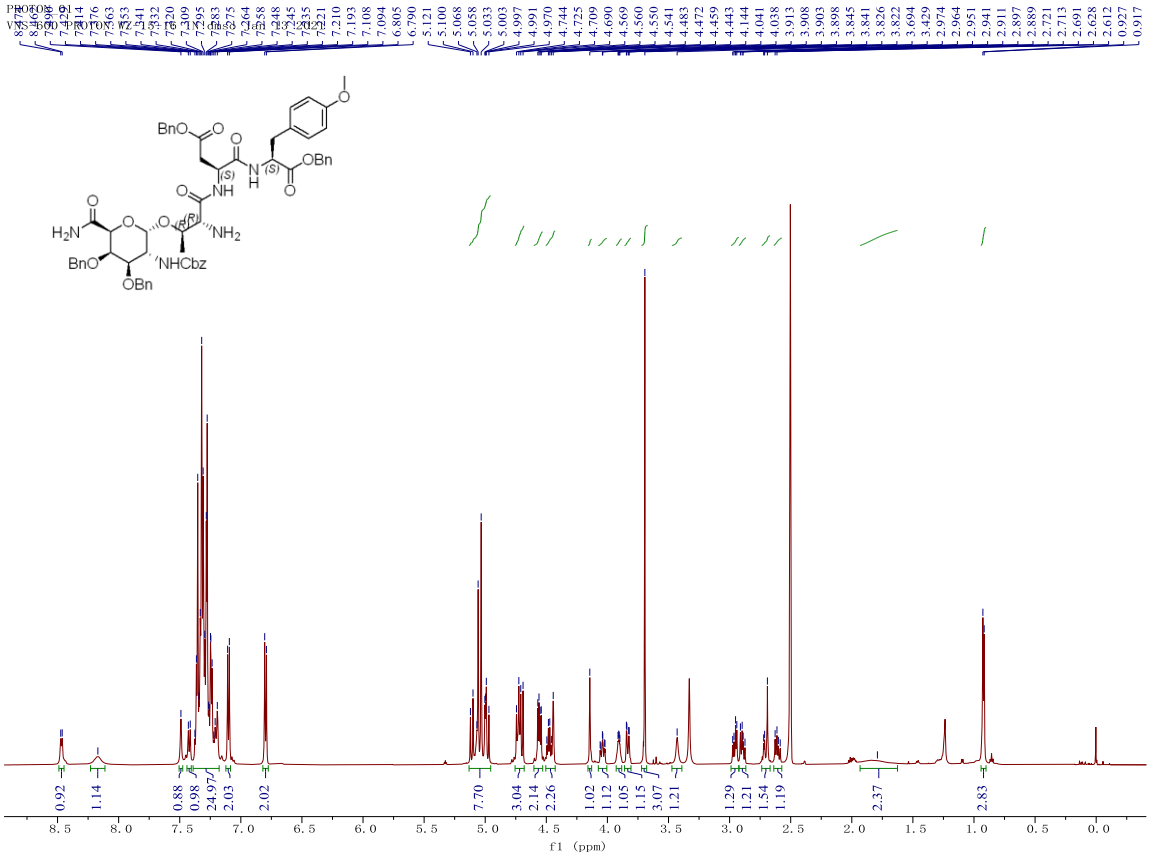


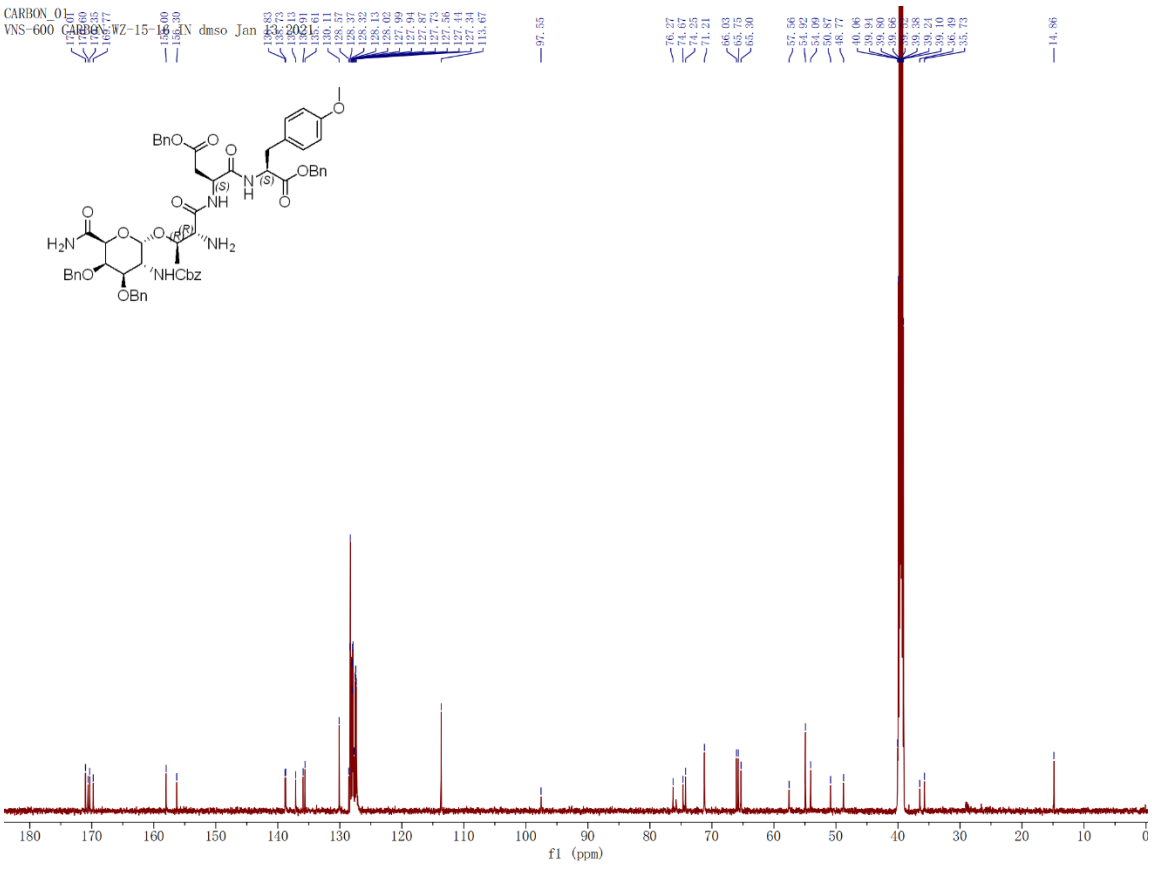


DMSO-d_6+D_2O

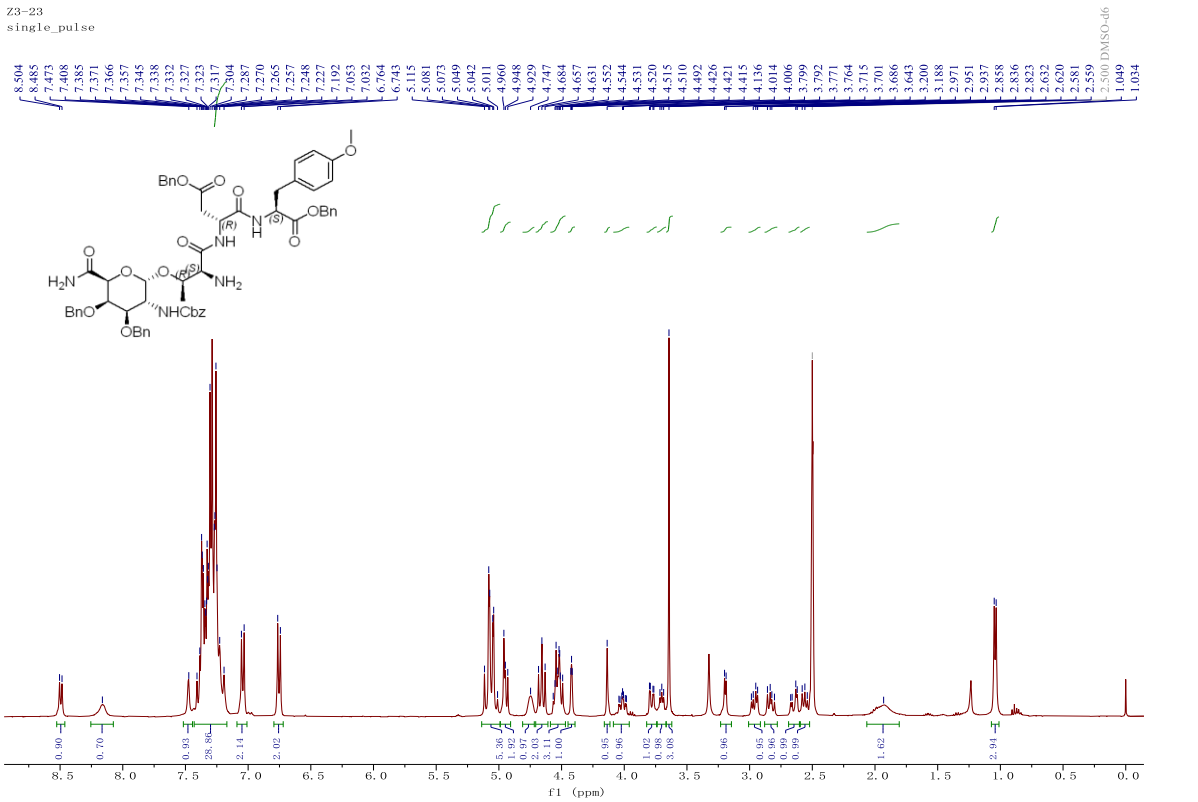


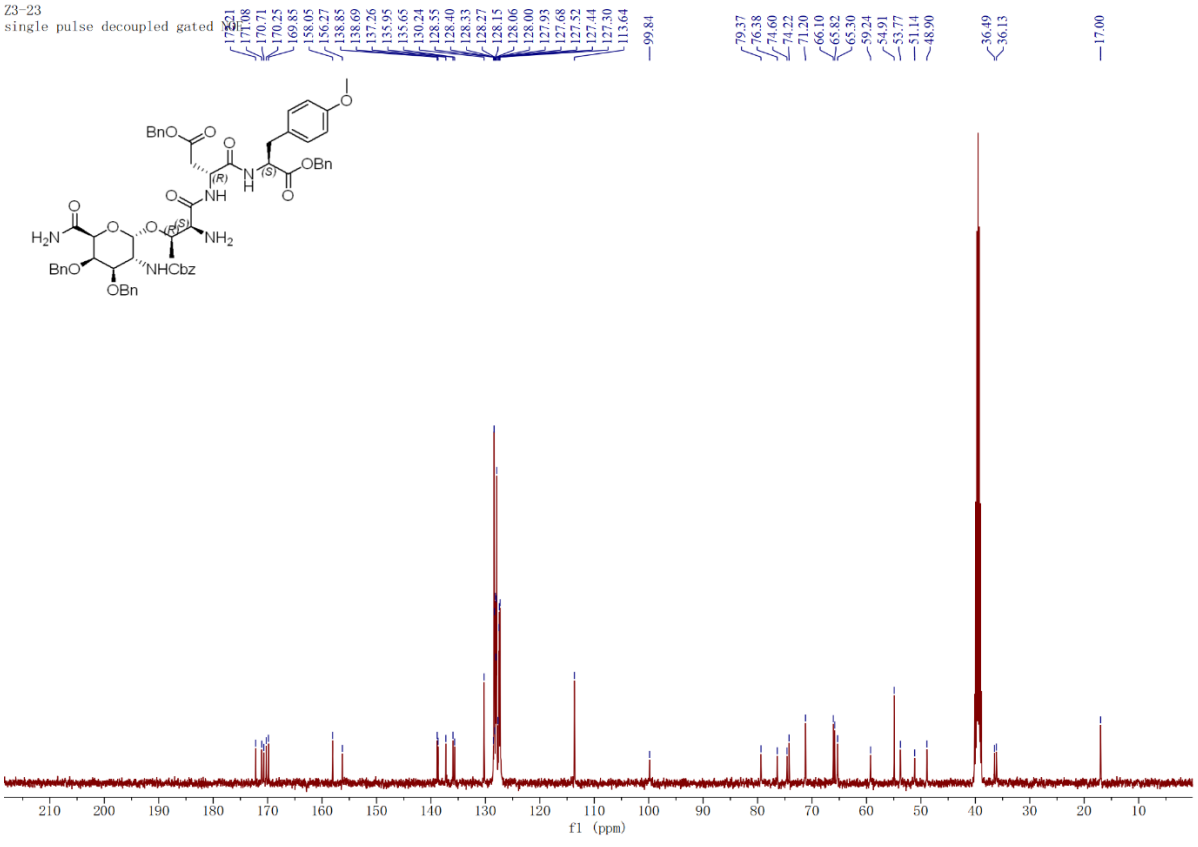
(27) ^{1}H NMR (600 MHz) and ^{13}C NMR (150 MHz) Spectra of compound 31a in DMSO-d$_6$



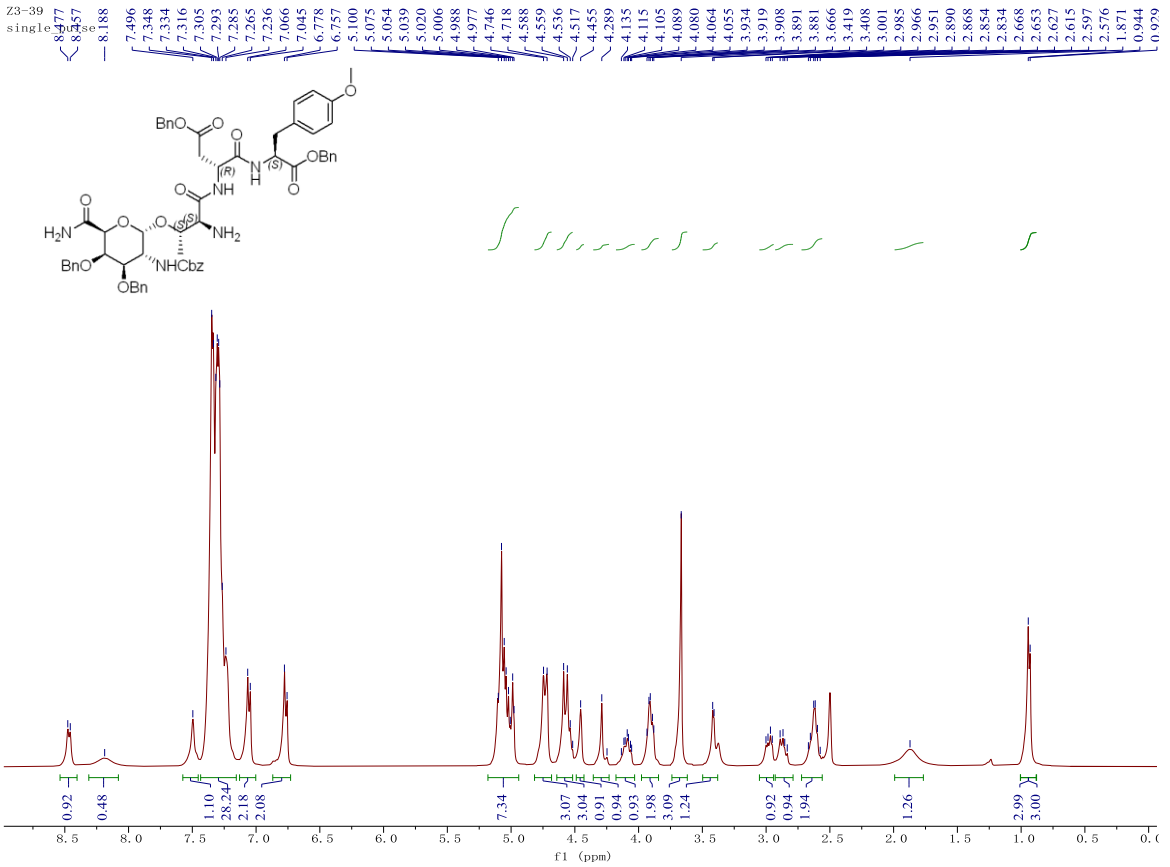


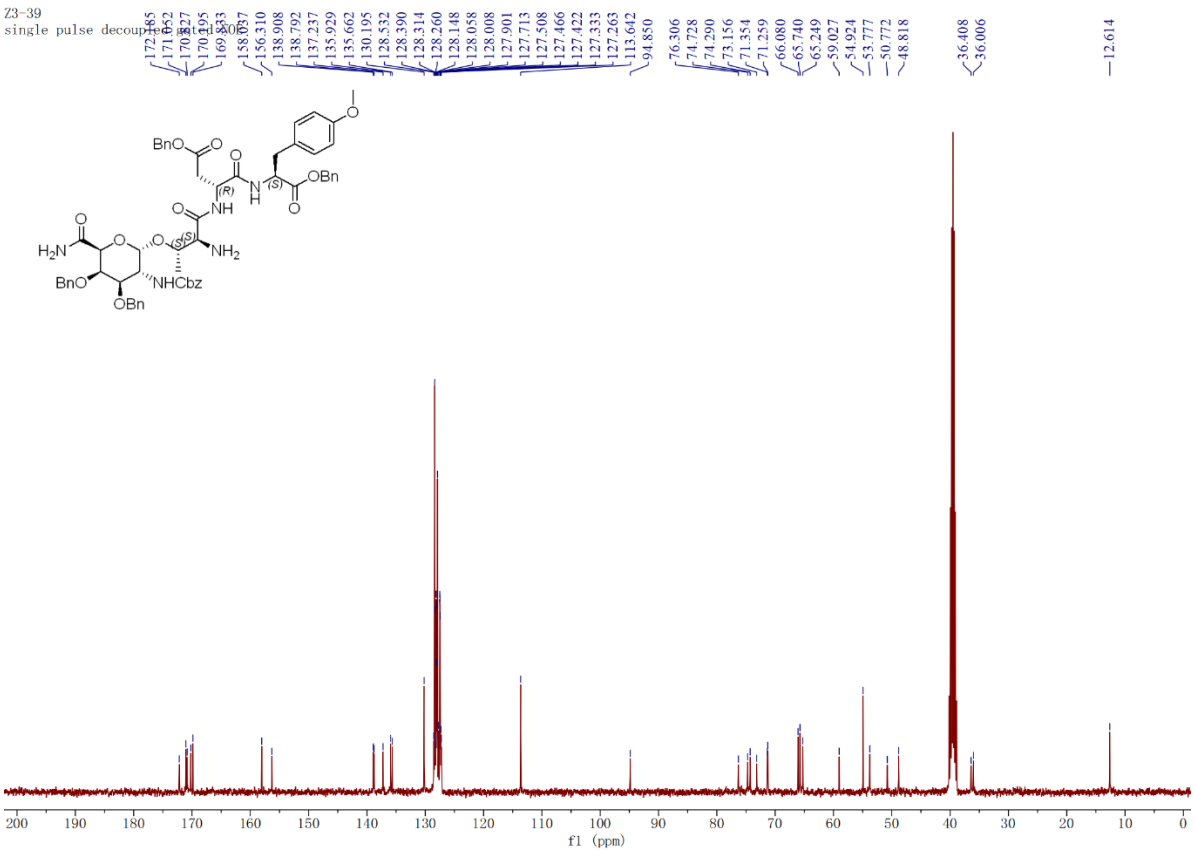
(28) ^{1}H NMR (400 MHz) and ^{13}C NMR (100 MHz) Spectra of compound 31b in DMSO-d$_6$



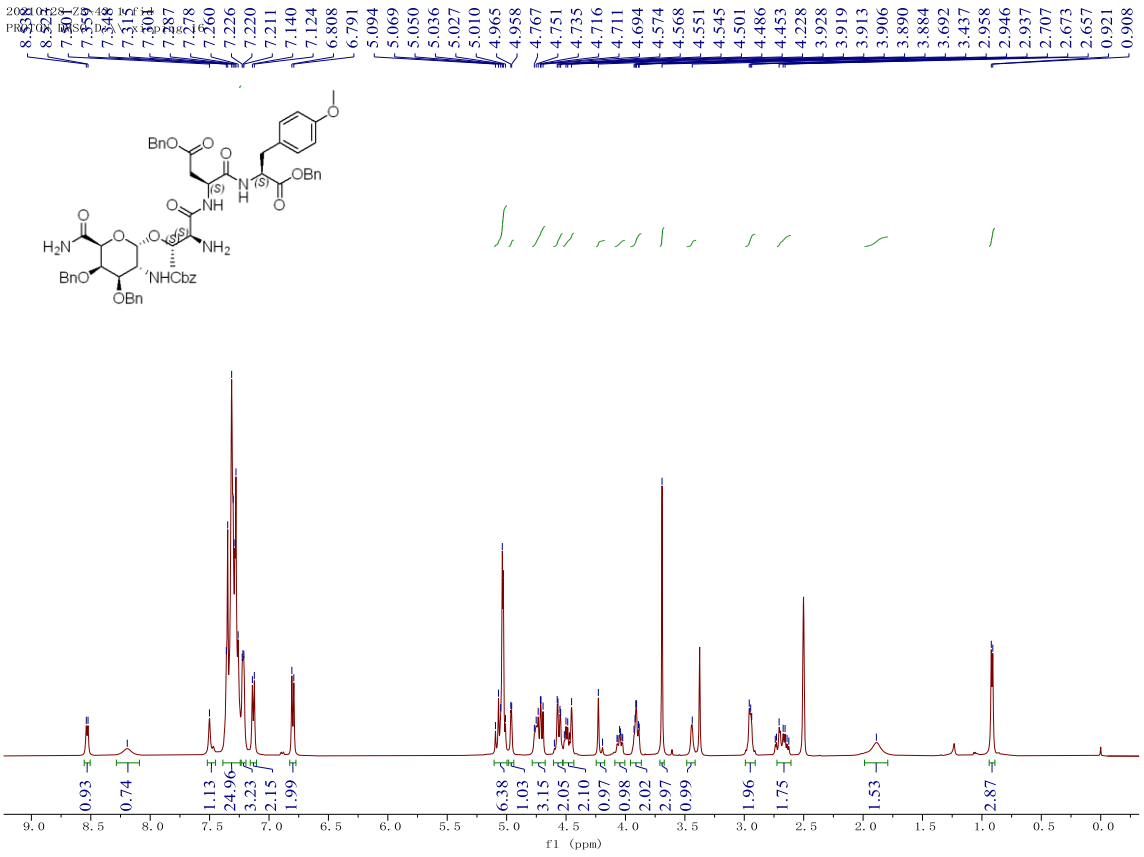


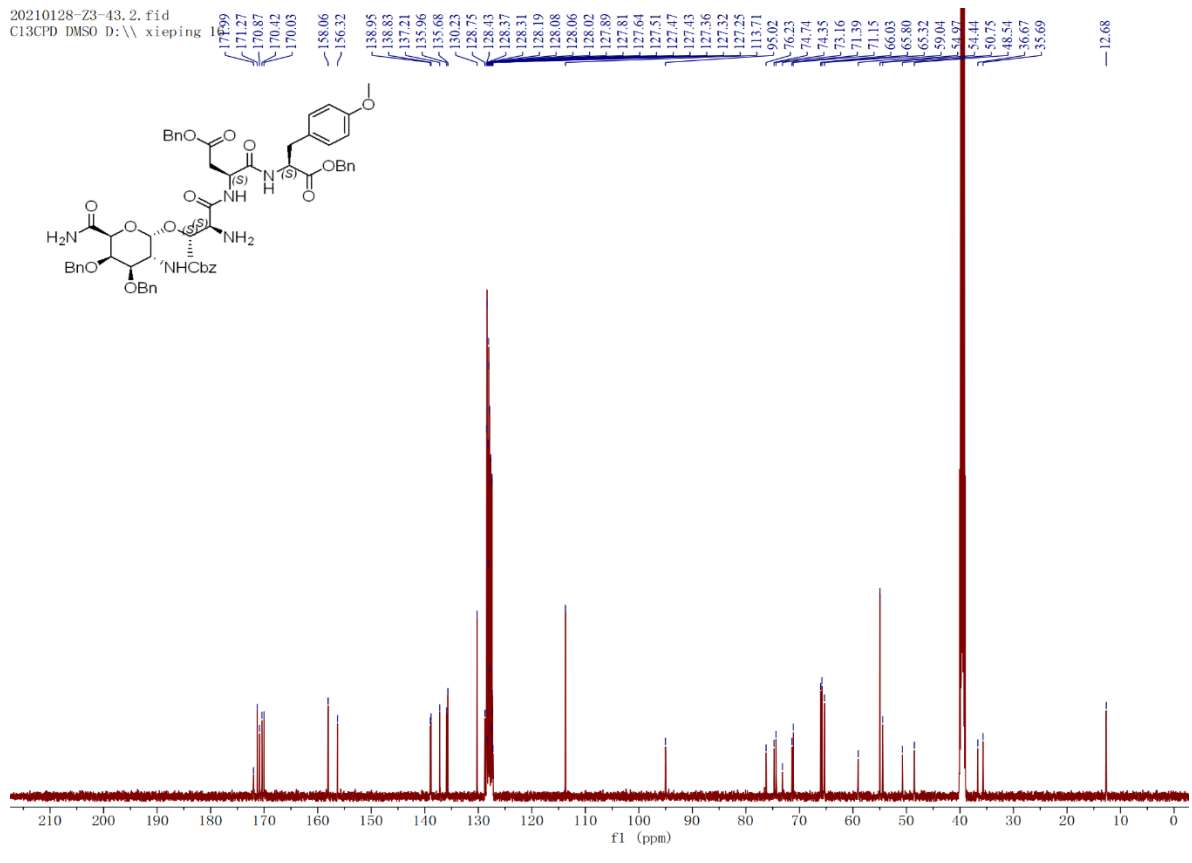
(29) ^{1}H NMR (400 MHz) and ^{13}C NMR (100 MHz) Spectra of compound 31c in DMSO-d$_6$



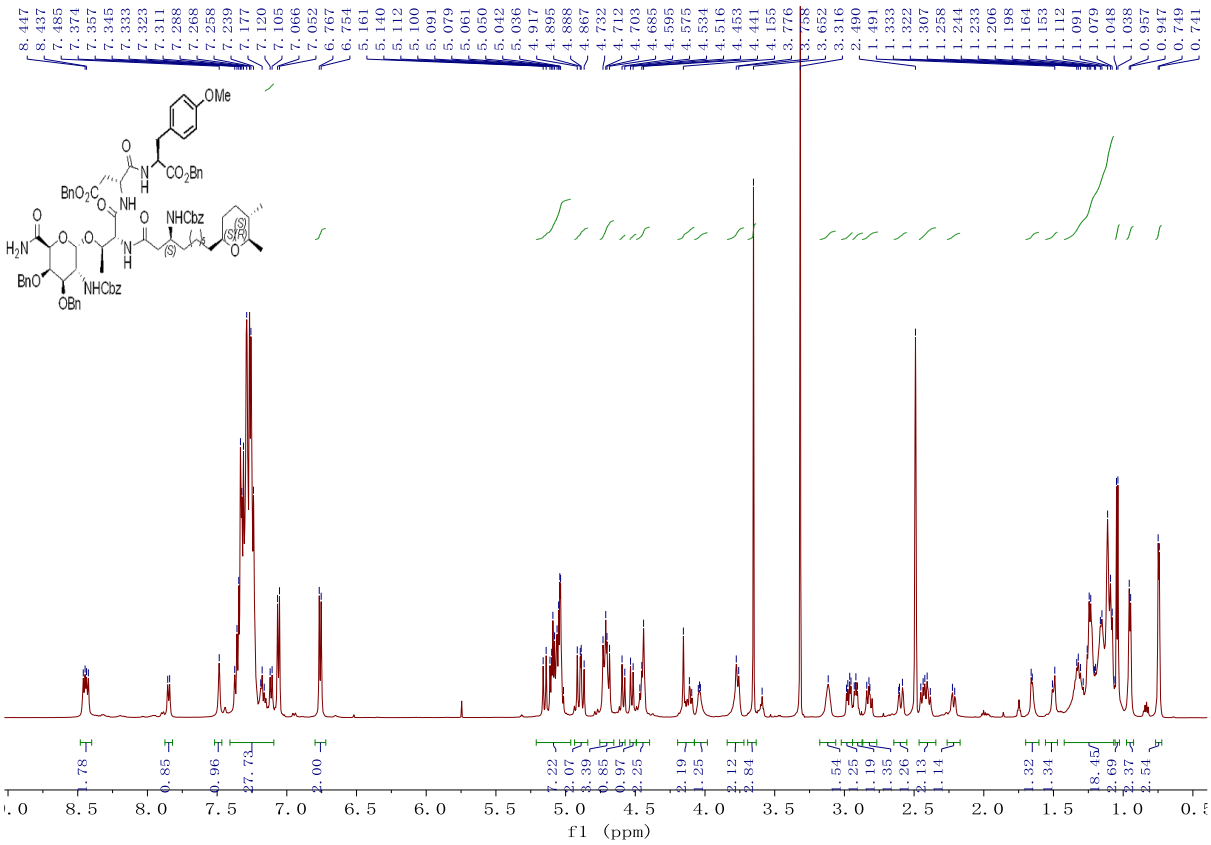


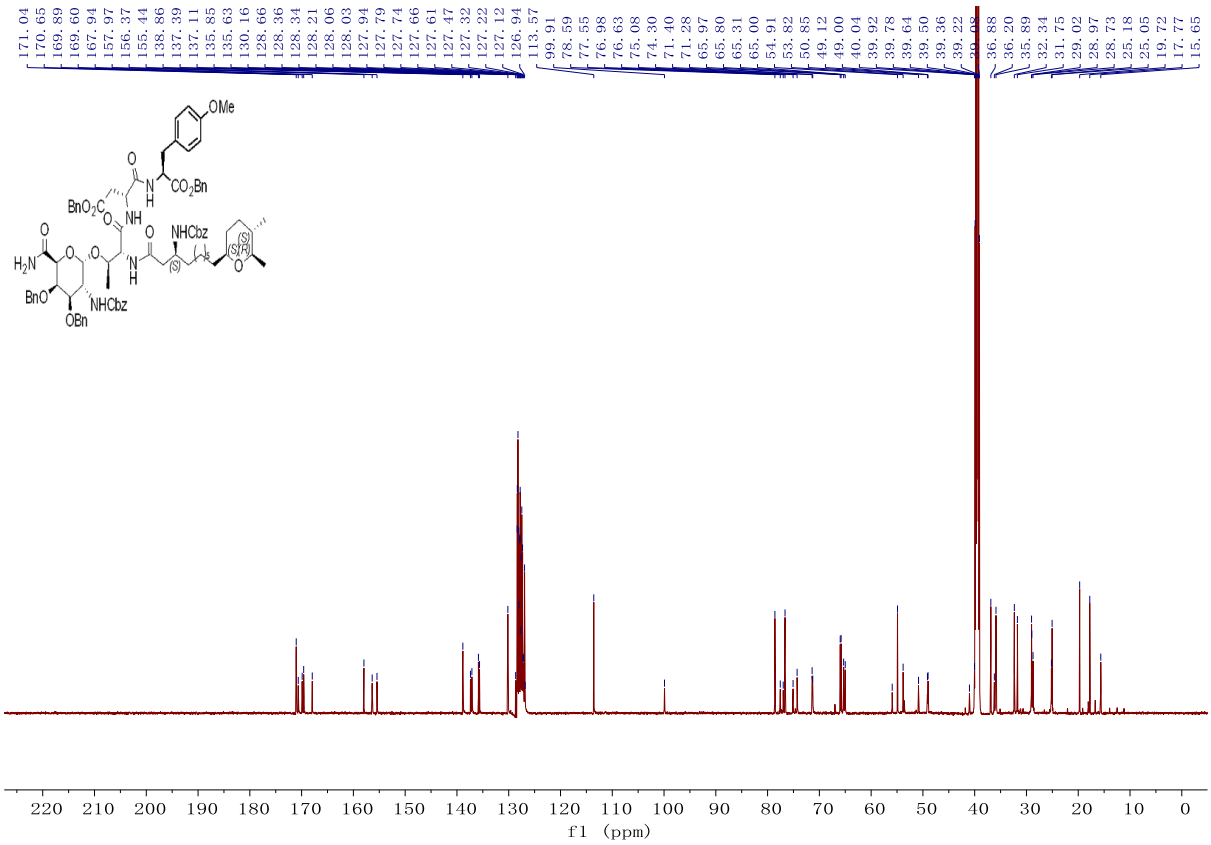
(30) ^{1}H NMR (500 MHz) and ^{13}C NMR (125 MHz) Spectra of compound 31d in DMSO-d$_6$



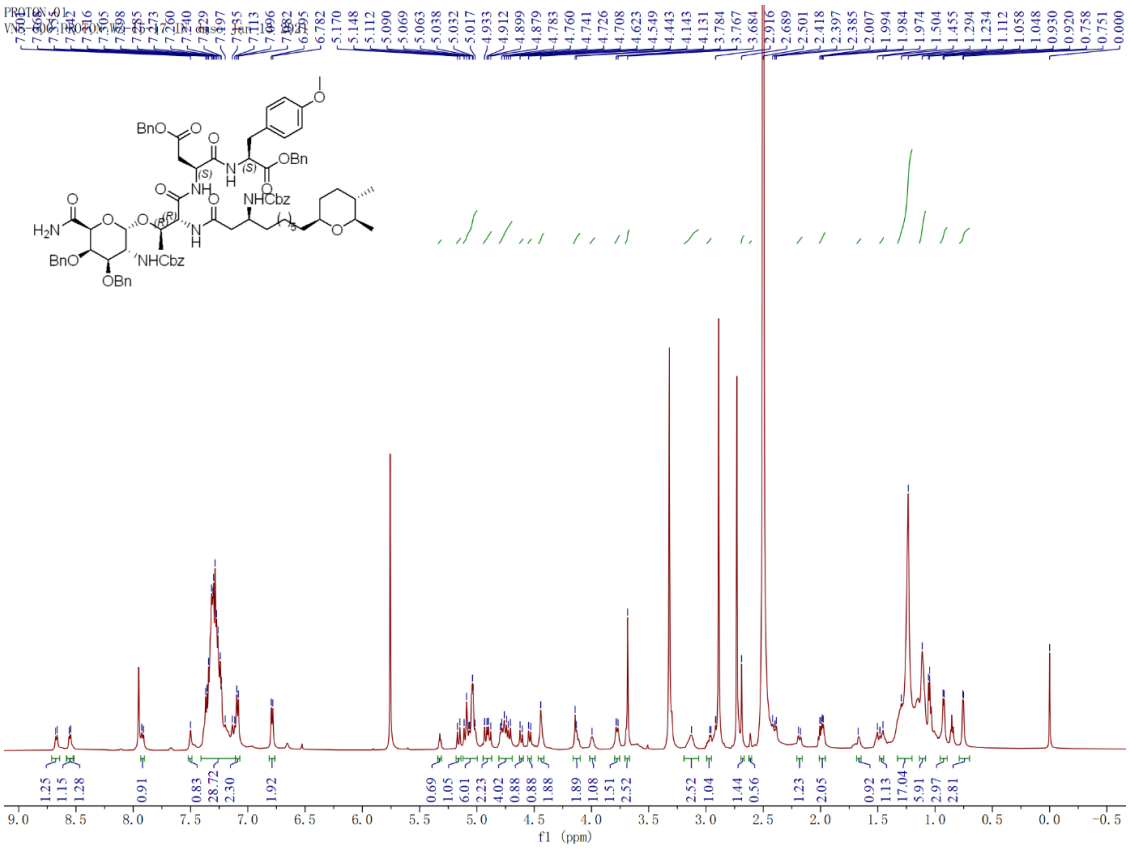


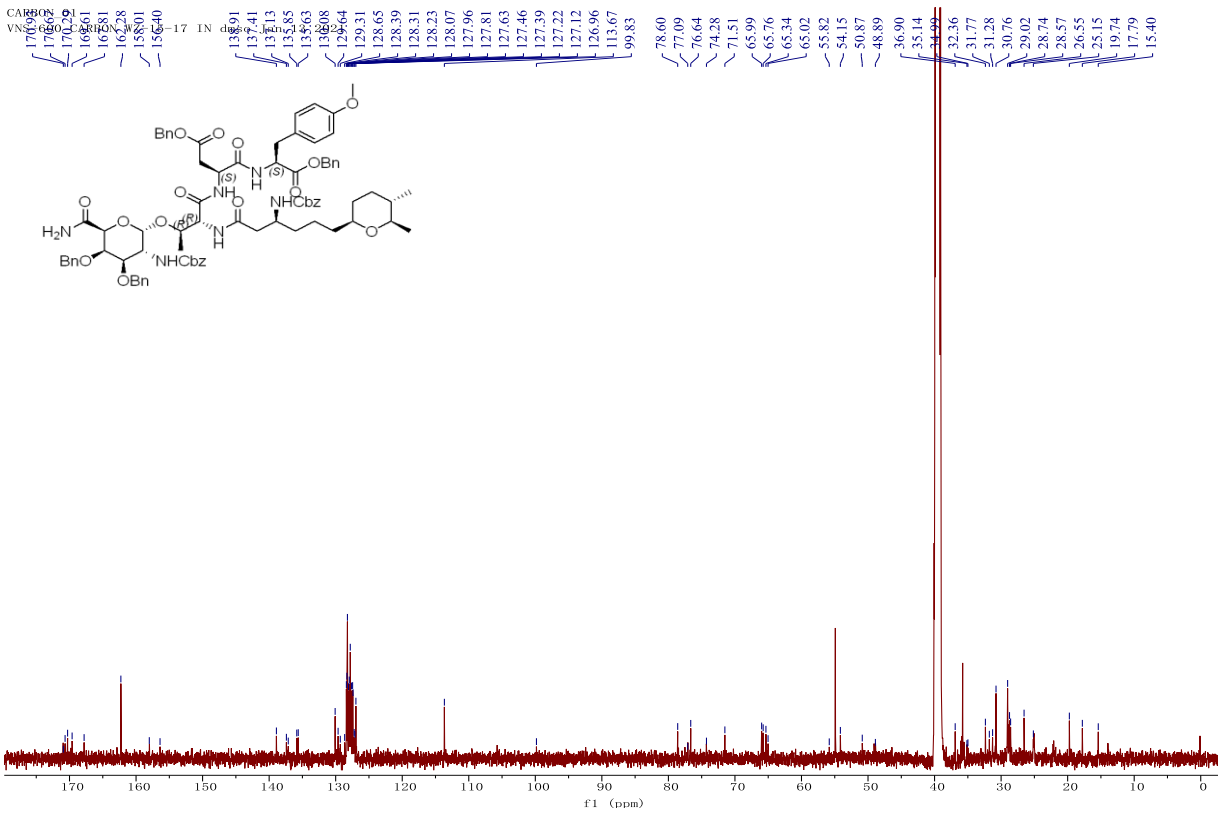
(31) ^{1}H NMR (600 MHz) and ^{13}C NMR (150 MHz) Spectra of compound 32 in DMSO-d_6



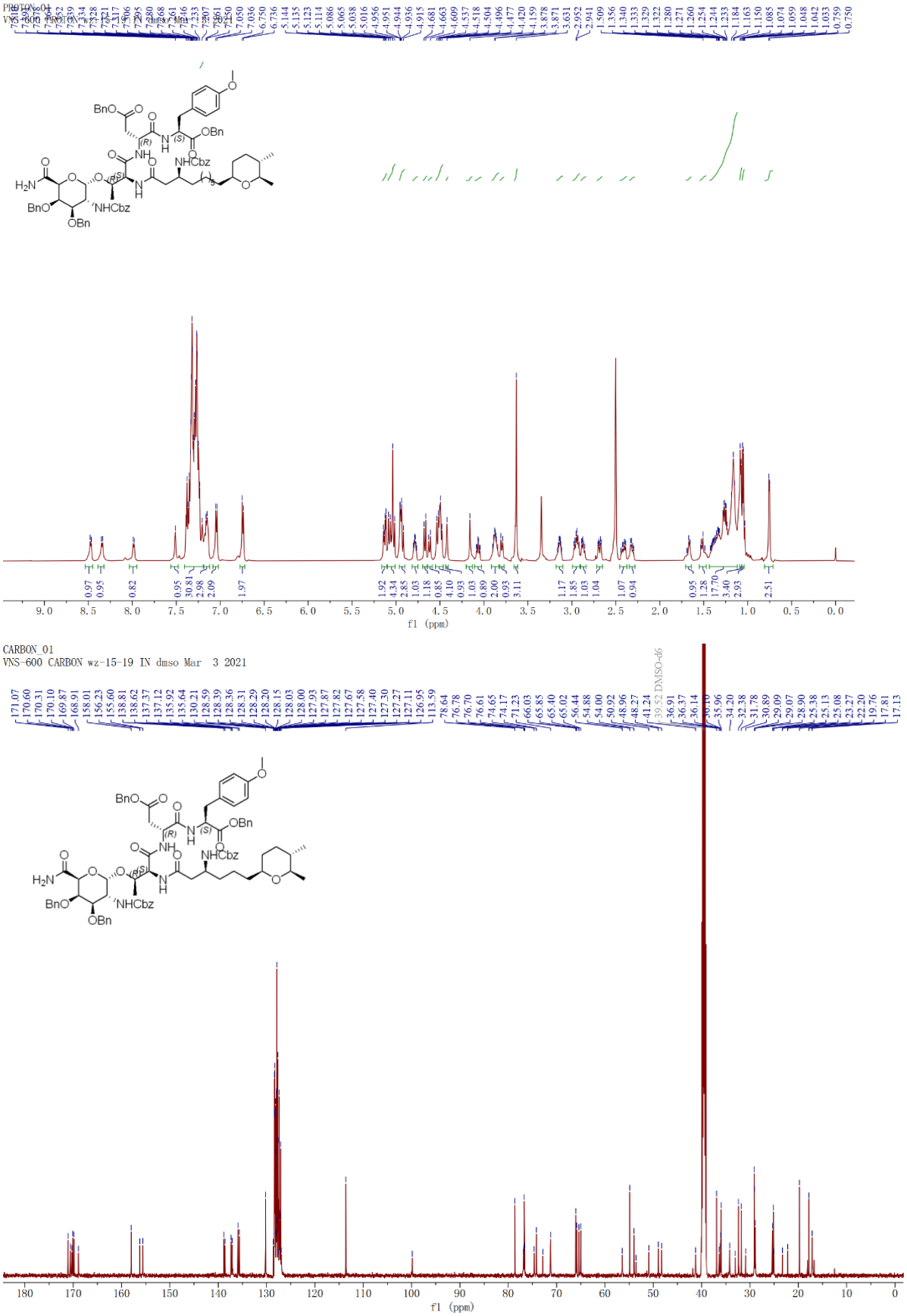


(32) ^{1}H NMR (600 MHz) and ^{13}C NMR (150 MHz) Spectra of compound 32a in DMSO-d$_6$

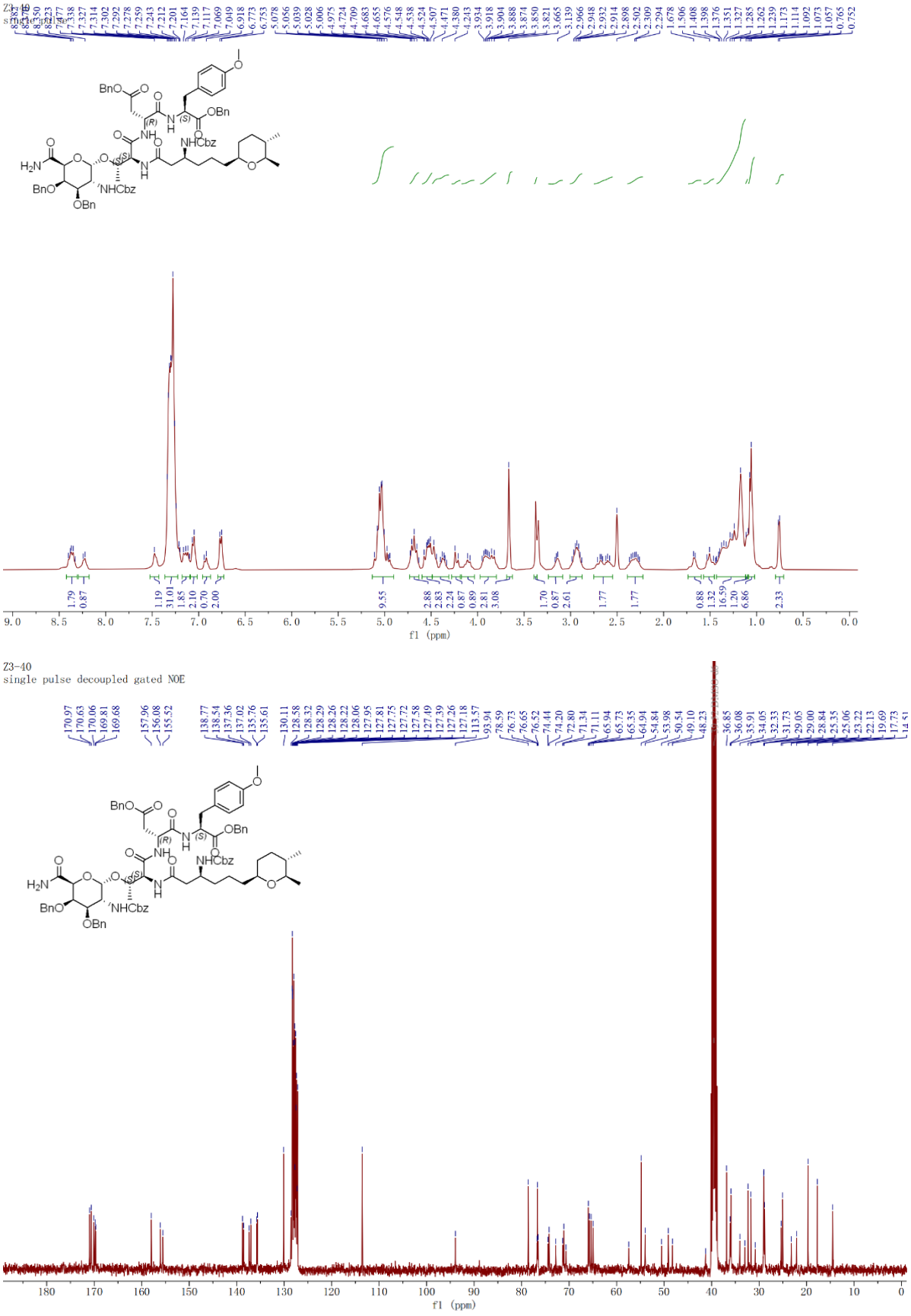




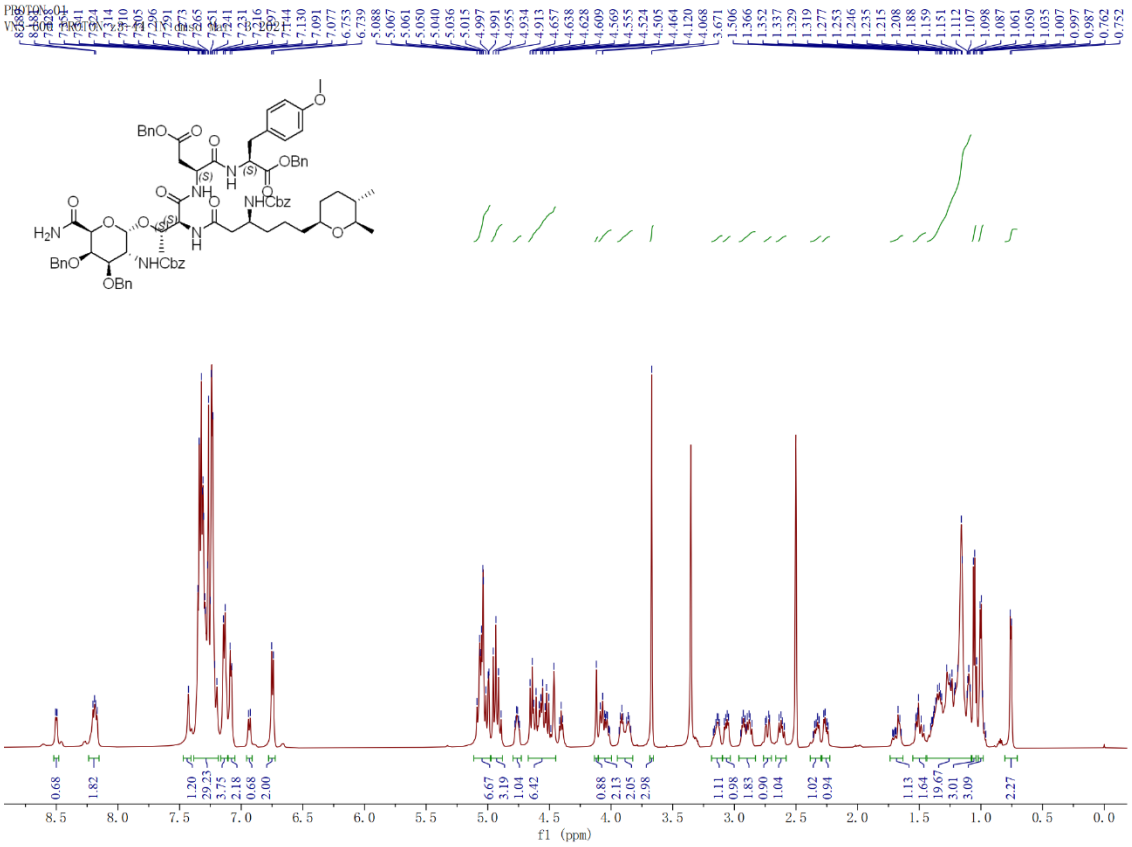
(33) ^{1}H NMR (600 MHz) and ^{13}C NMR (150 MHz) Spectra of compound 32b in DMSO-d$_6$

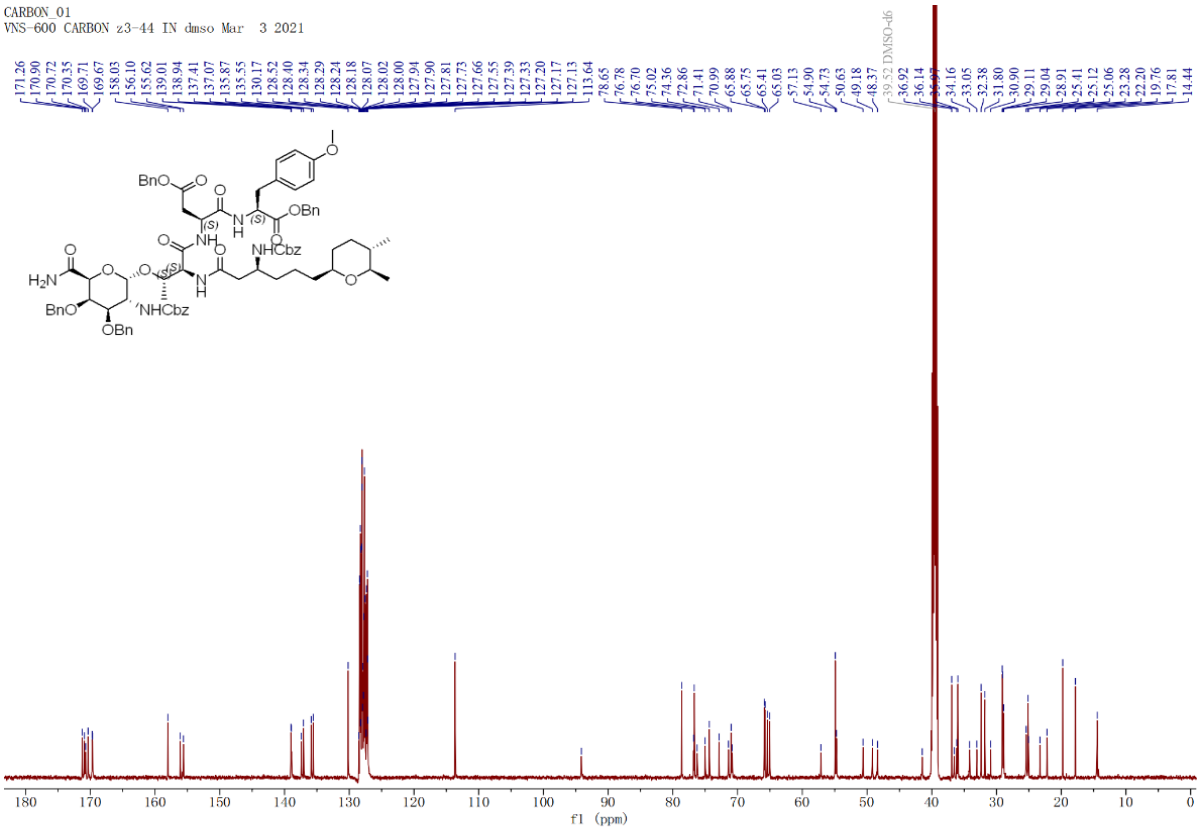


(34) ^{1}H NMR (400 MHz) and ^{13}C NMR (100 MHz) Spectra of compound 32c in DMSO-d$_6$

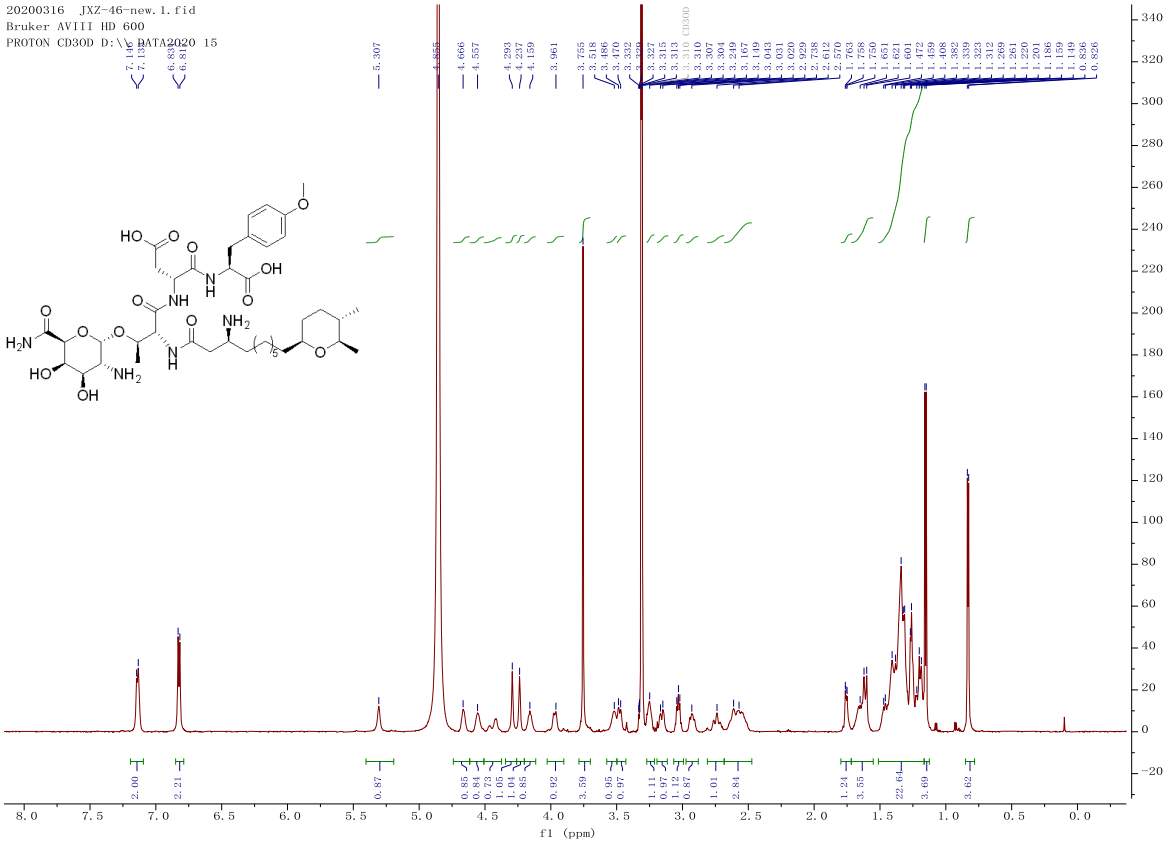


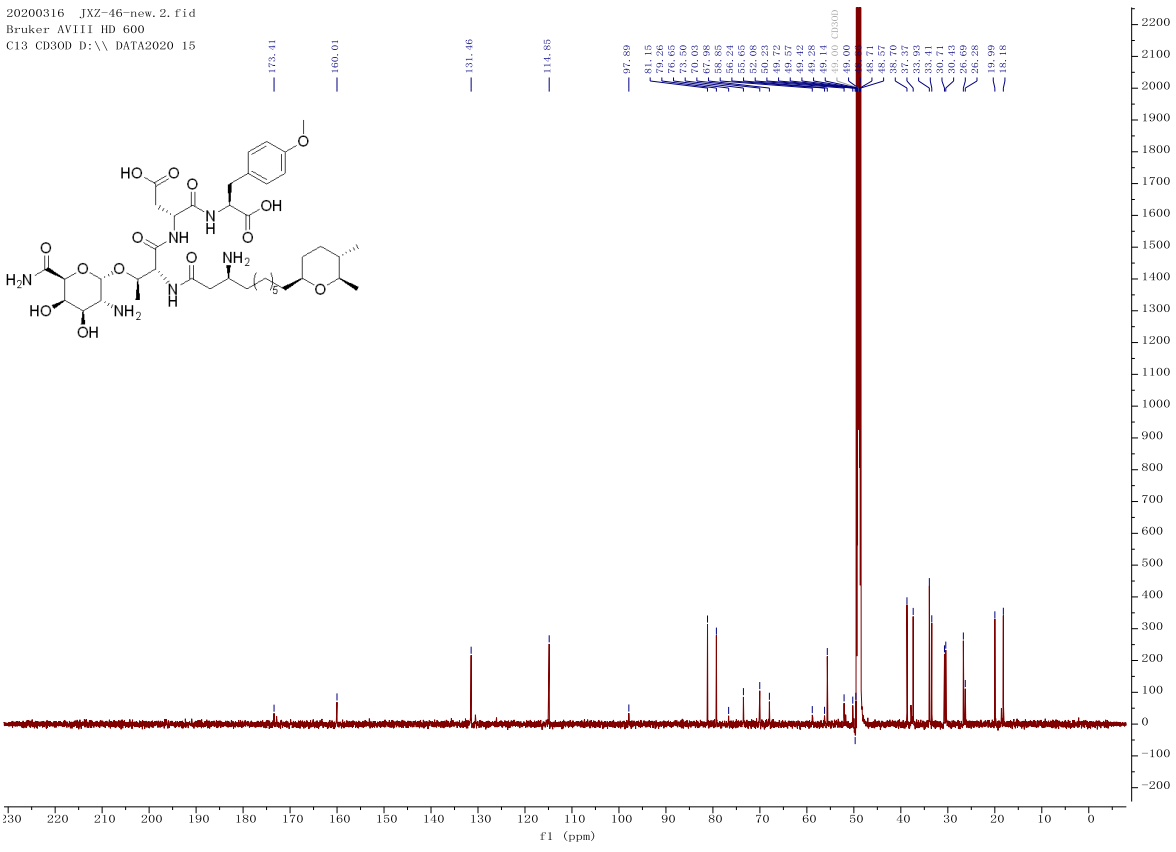
(35) ^{1}H NMR (600 MHz) and ^{13}C NMR (150 MHz) Spectra of compound 32d in DMSO-d$_6$

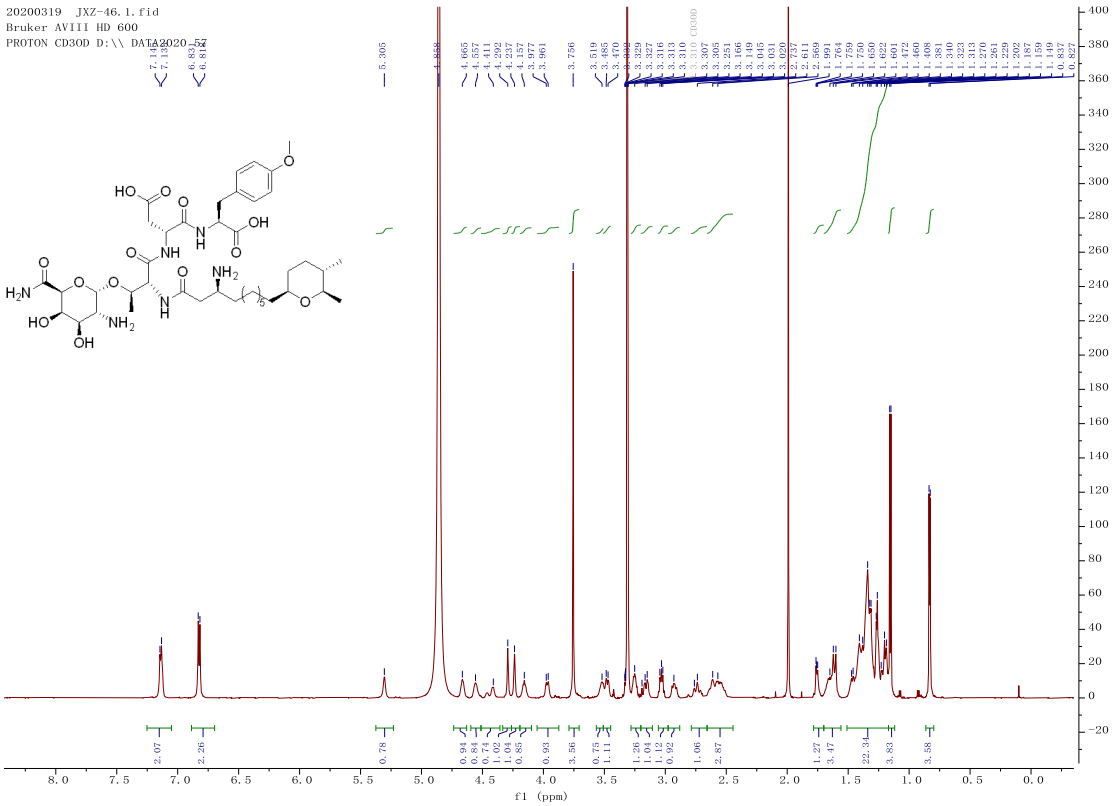




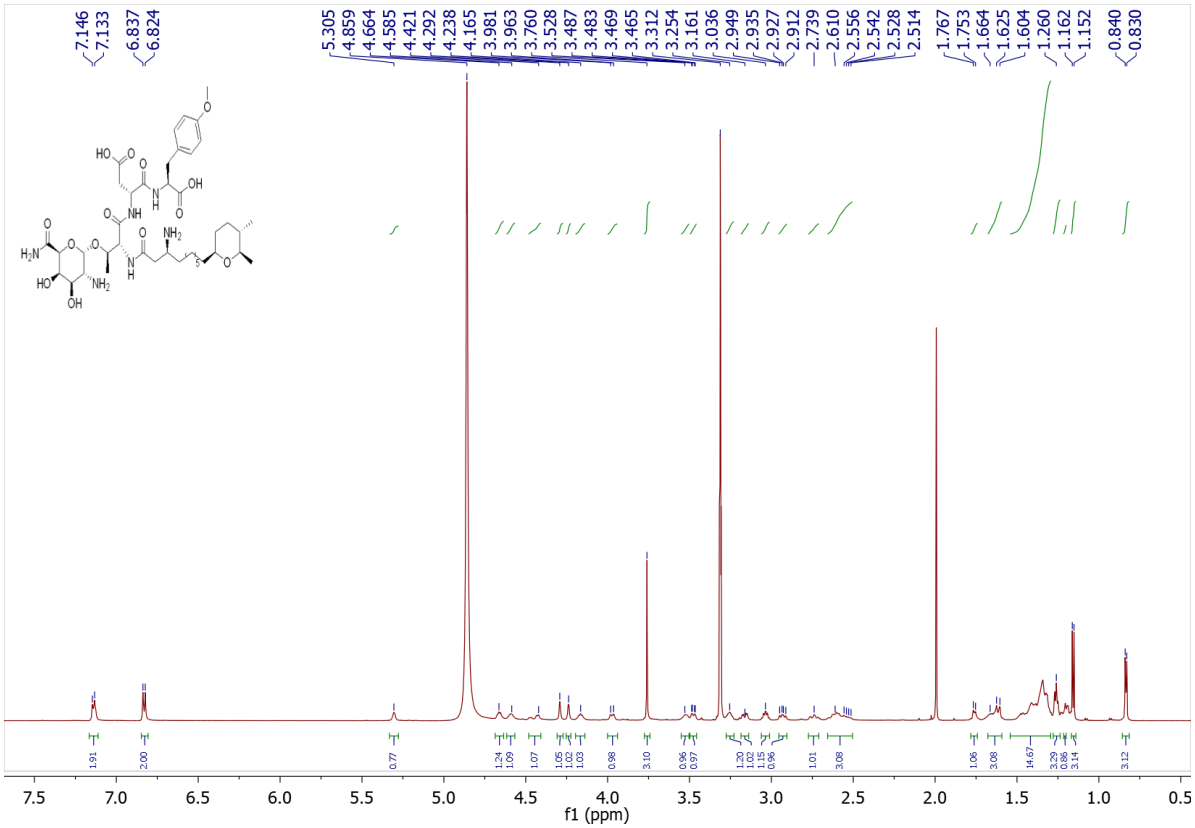
(36) ^{1}H NMR (600 MHz) and ^{13}C NMR (150 MHz) Spectra of compound 1 in CD_3OD



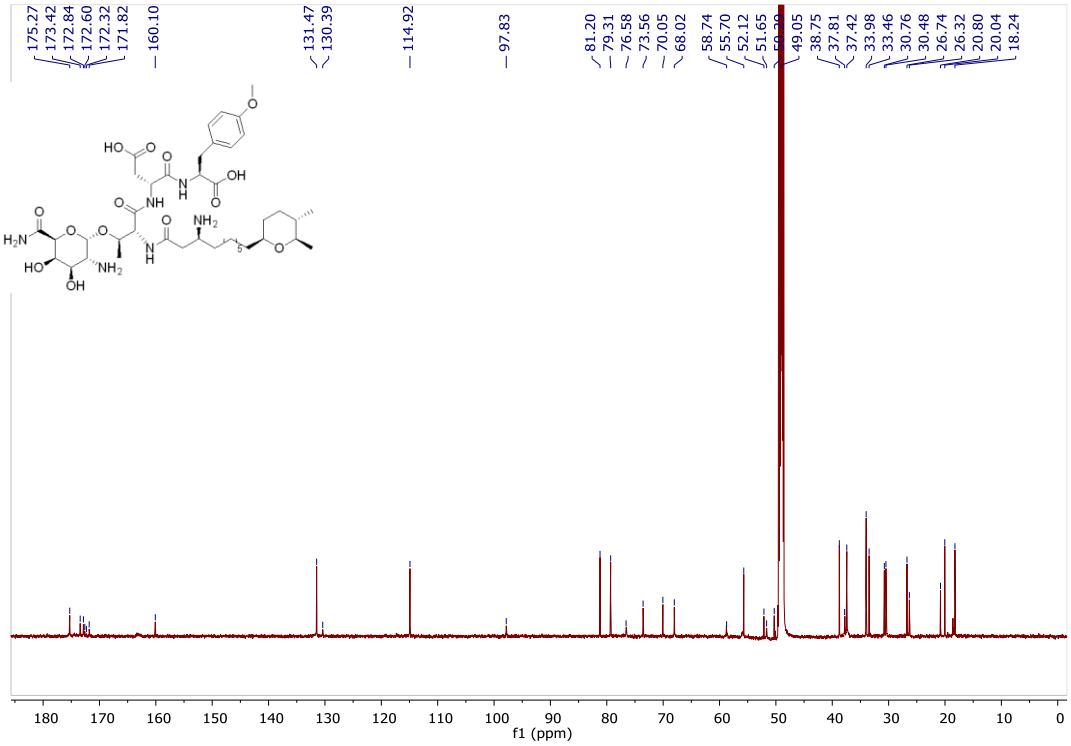




^{1}H NMR **(600 MHz)** and Spectra of compound 1 in CD_3OD (140 μ L+0.01 μ L HOAc)

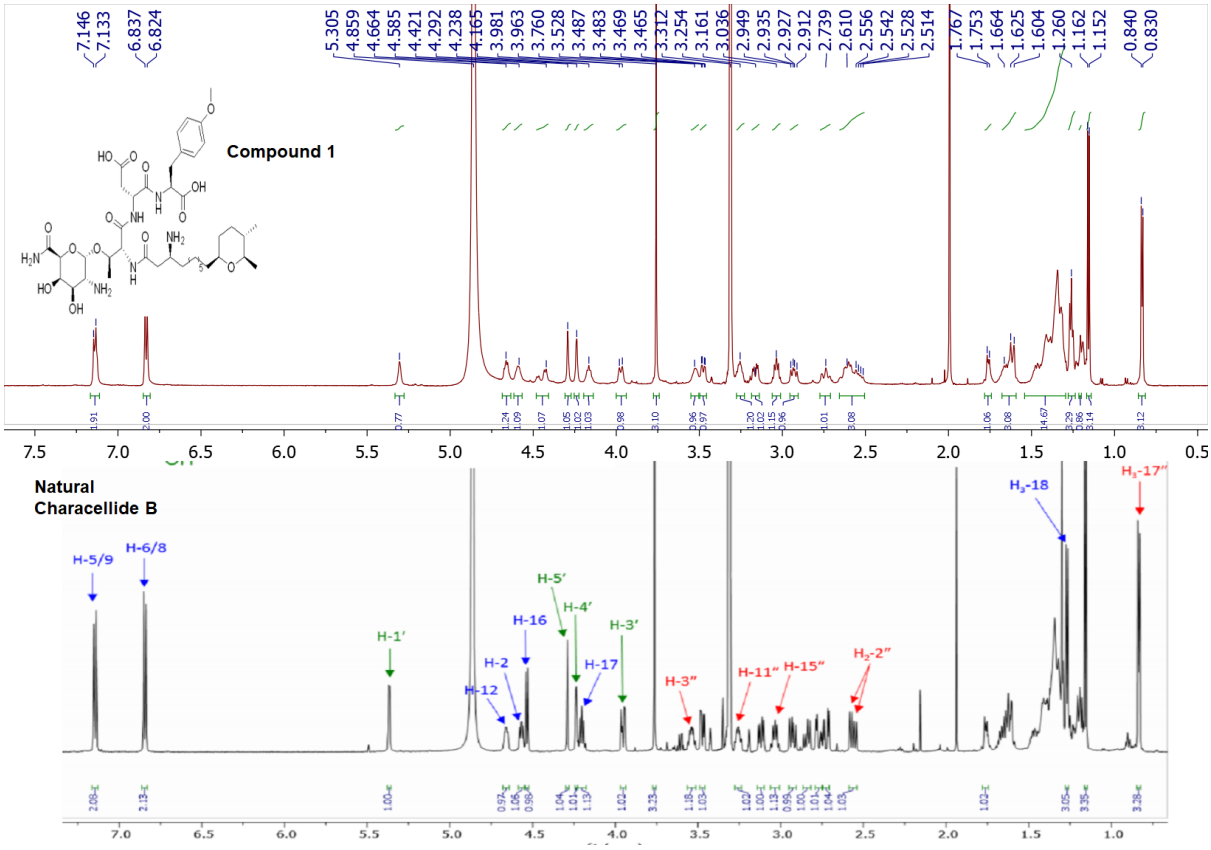


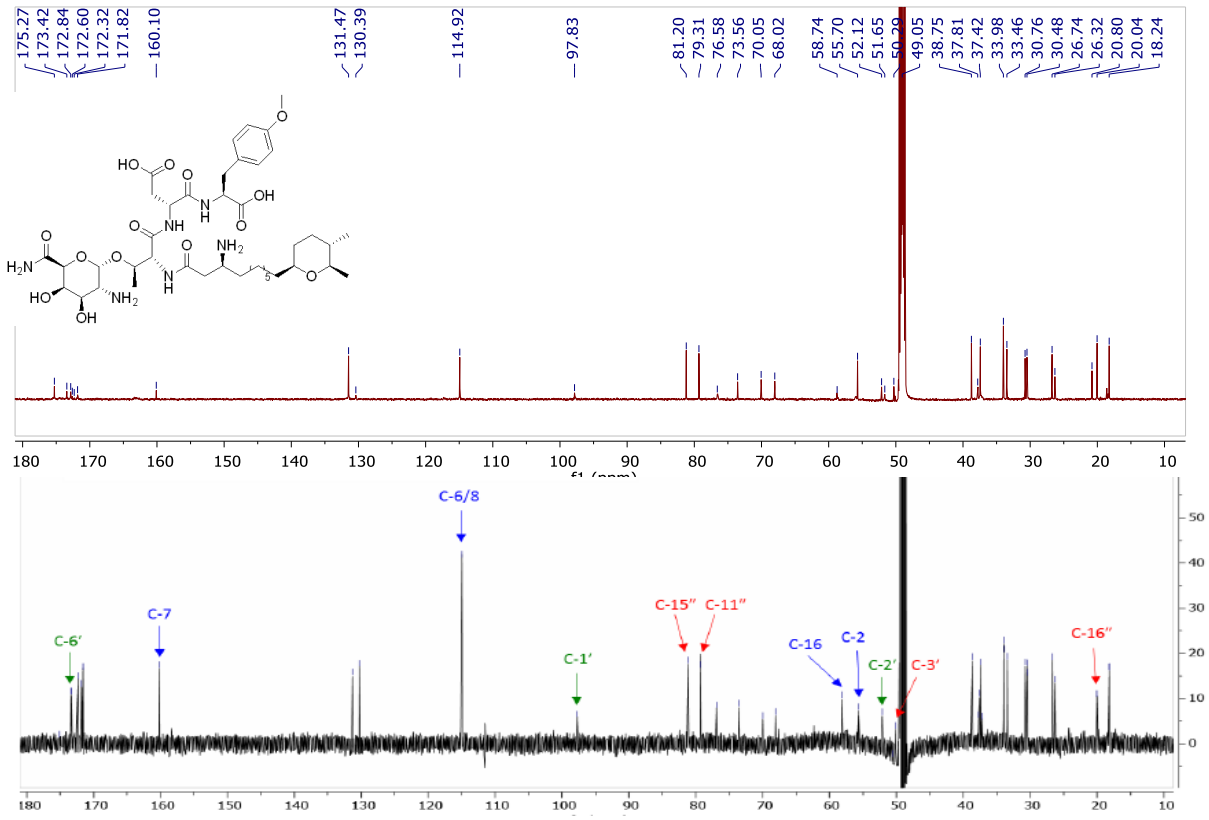
^{1}H NMR and Spectra of compound **1** in CD_3OD (140 μ L+ trace HOAc +0.01 μ L TFA)



^{13}C NMR and Spectra of compound **1** in CD_3OD (140 μ L+ trace HOAc +0.01 μ L TFA)

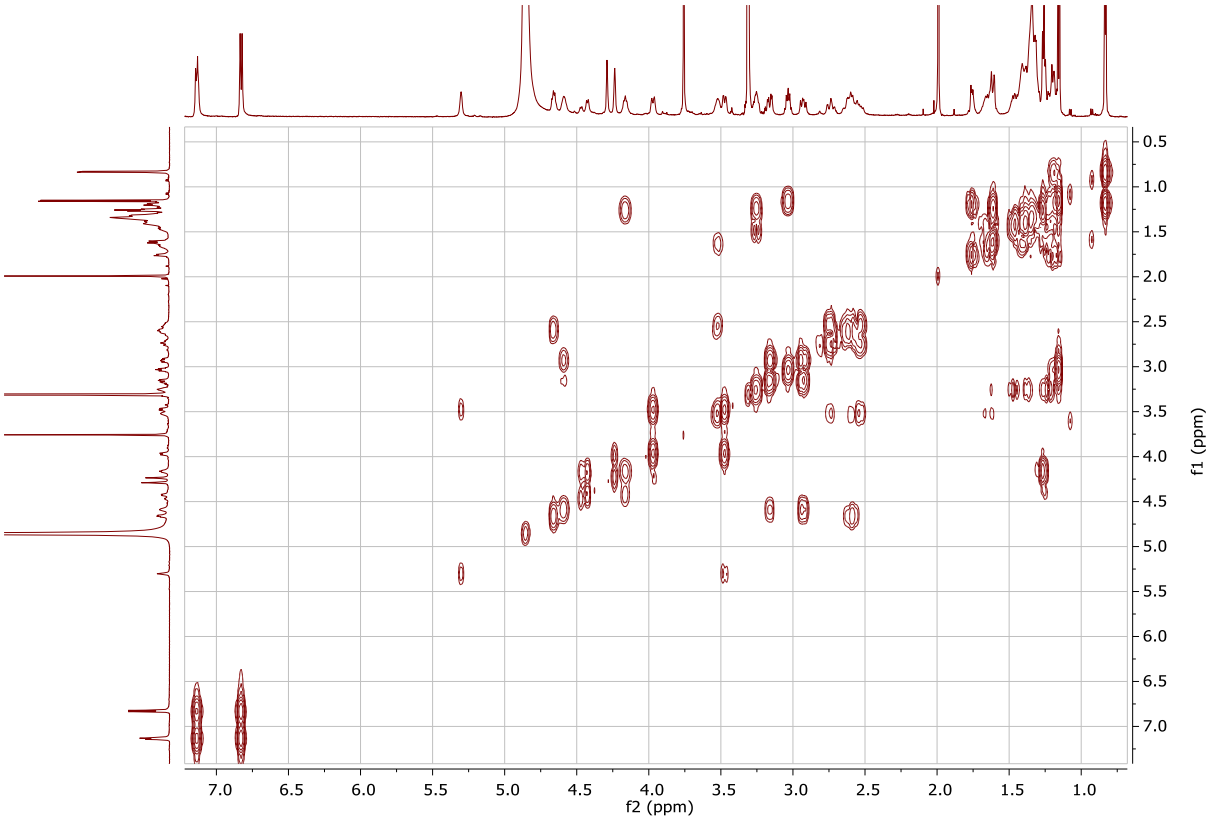
(37) the comparison of ^{1}H NMR (600 MHz) and ^{13}C NMR (150 MHz) Spectra of compound 1 and natural Characellide B in CD_3OD



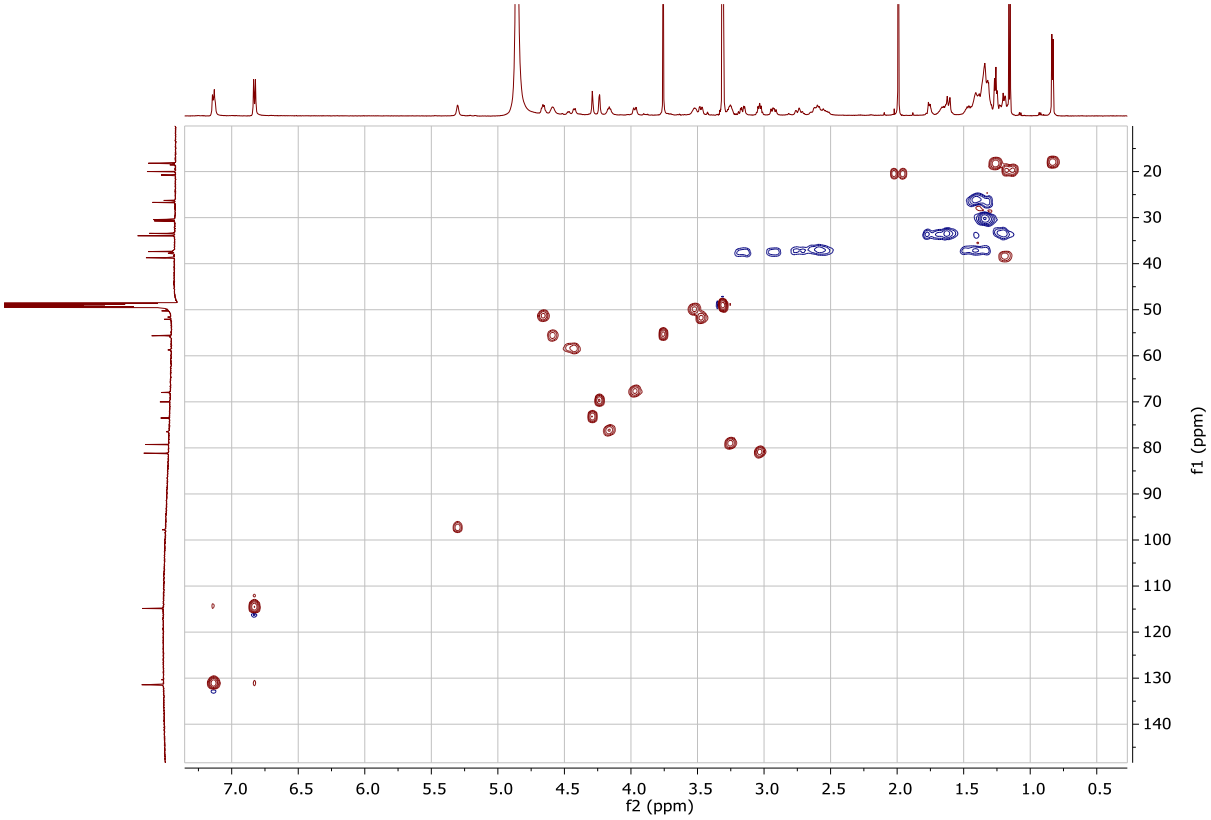


(38) H-H COSY, HSQC, HMBC NMR Spectra of compound 1 in CD_3OD

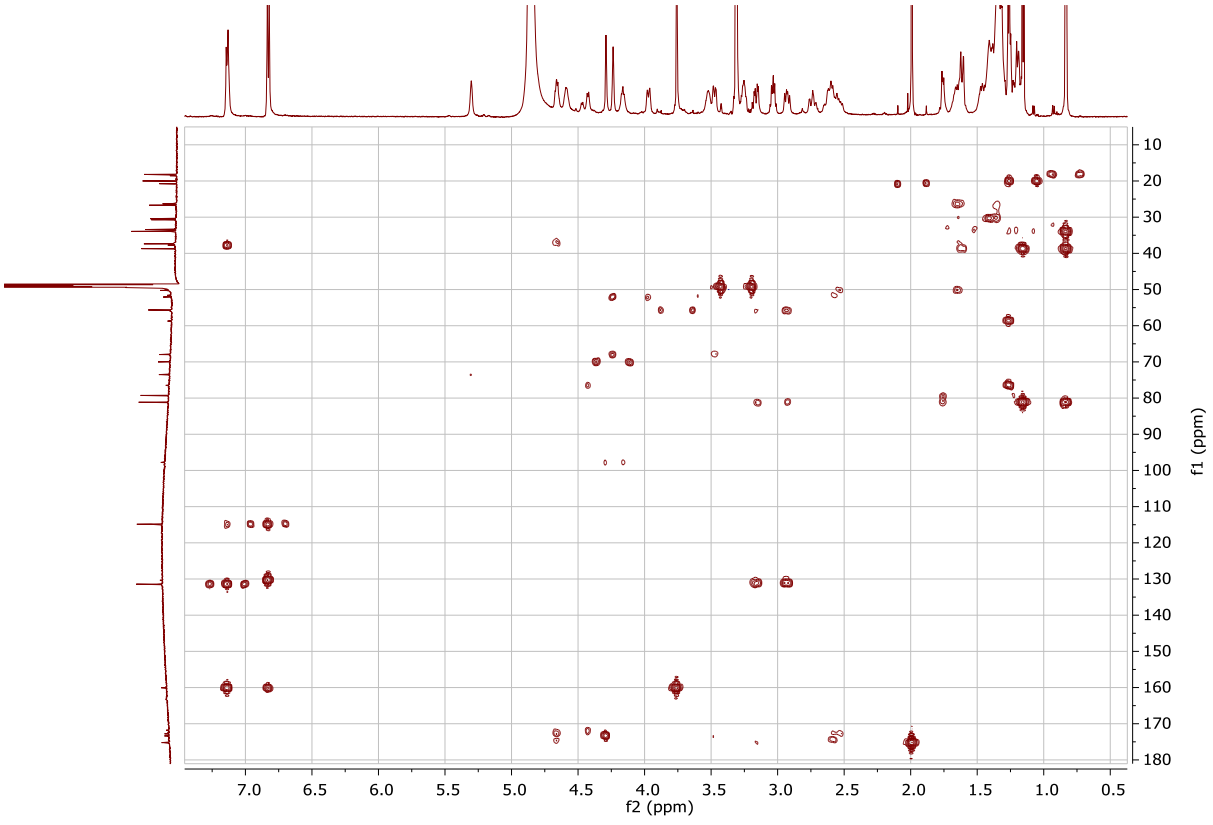
H-H COSY



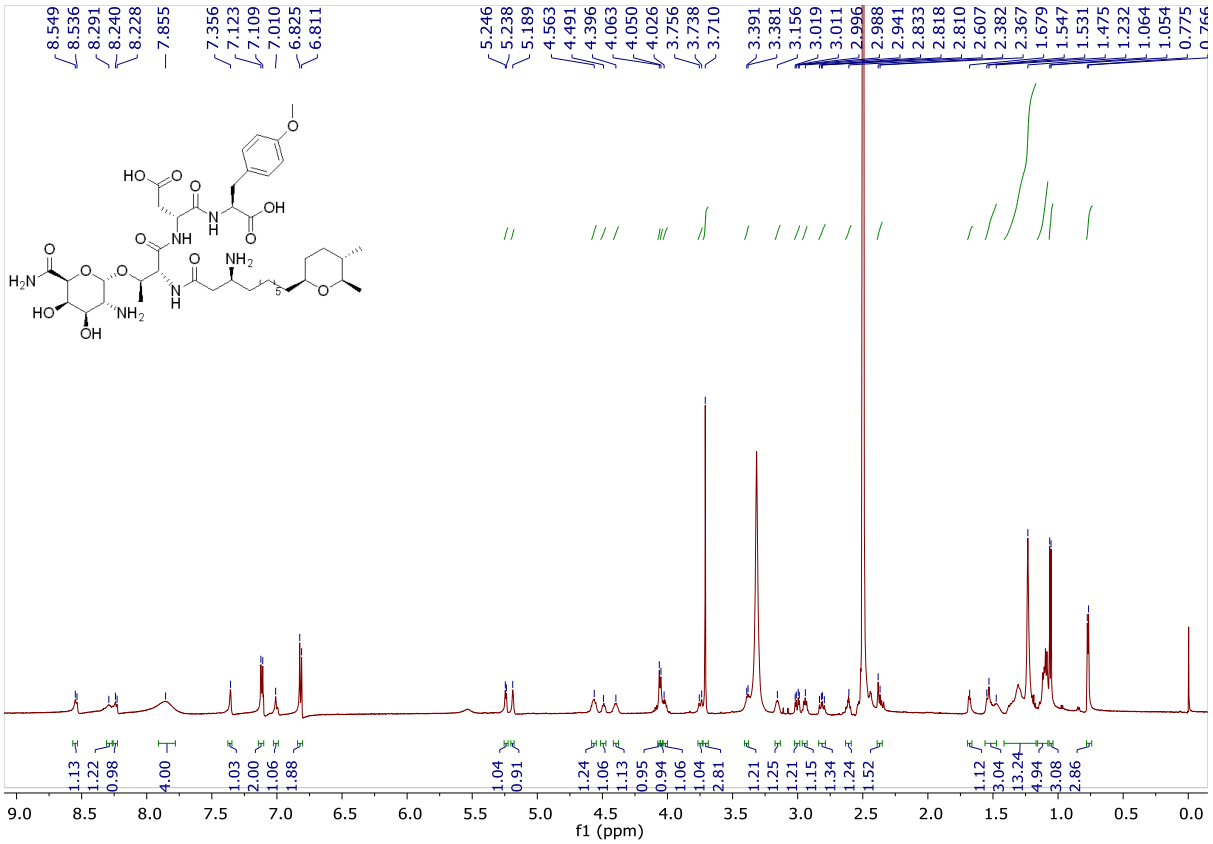
HSQC

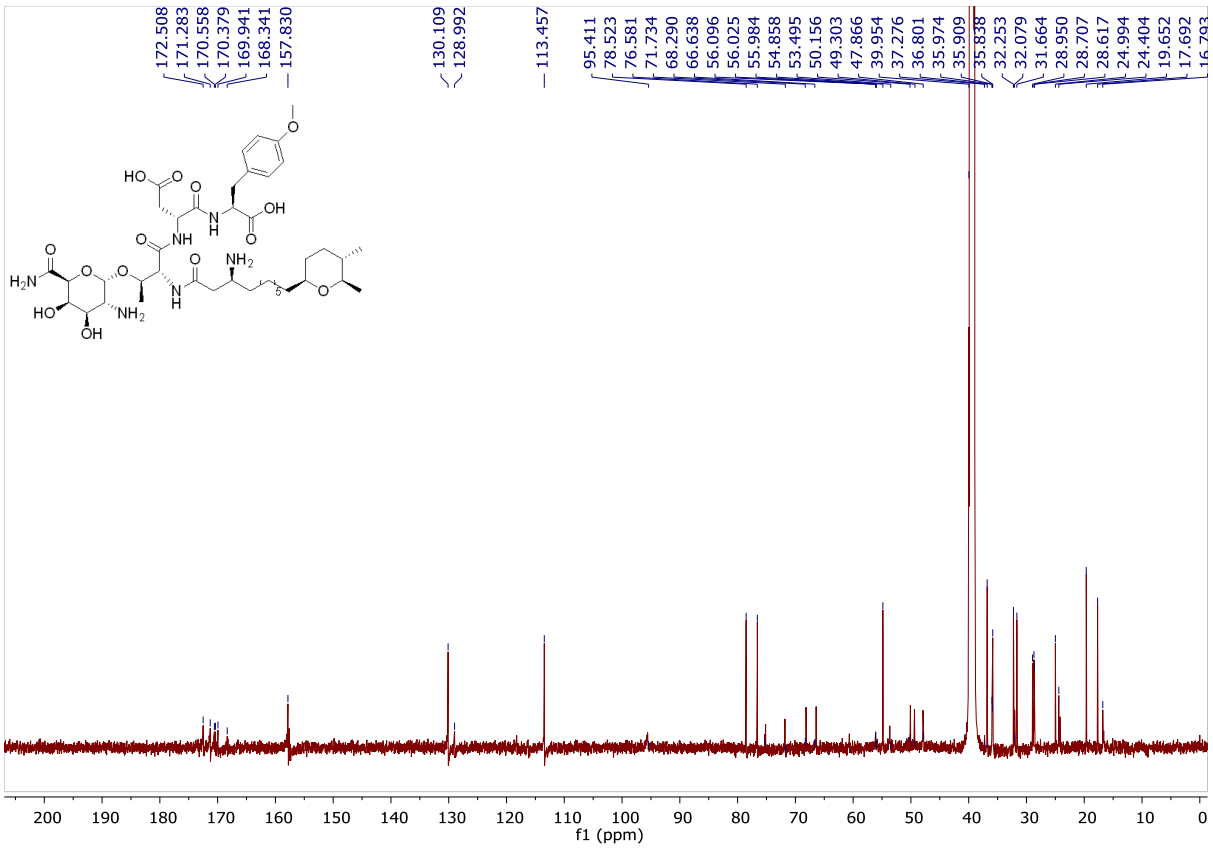


HMBC

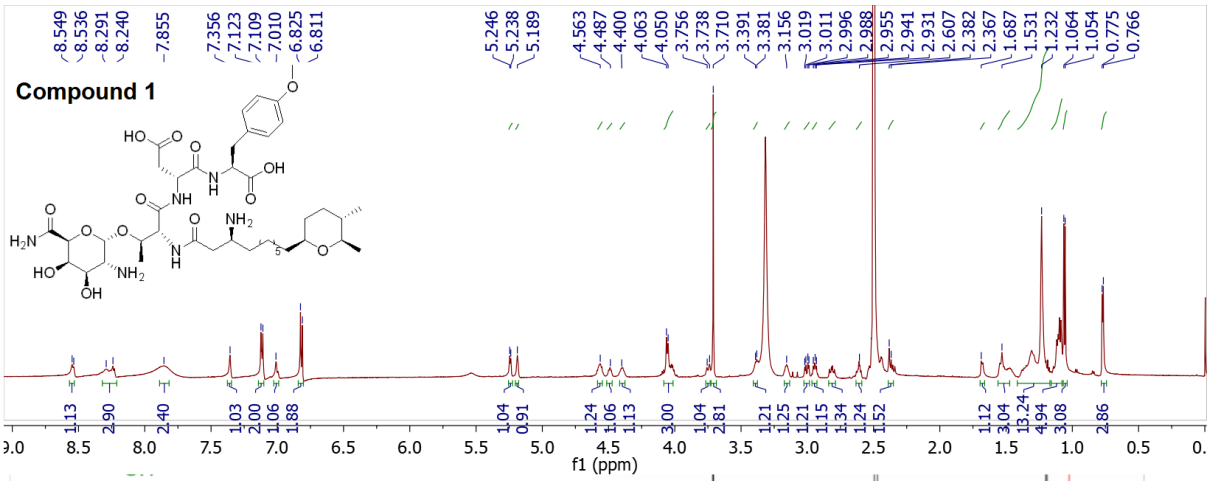


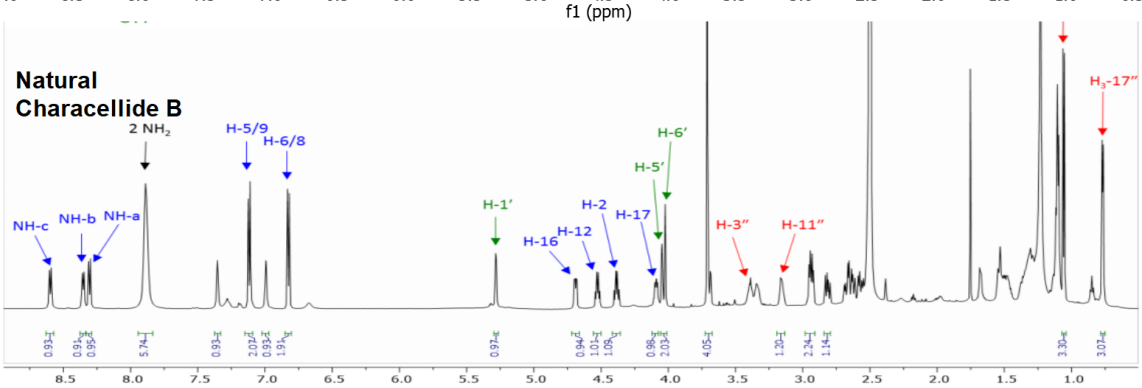
(39) ^{1}H NMR (600 MHz) and ^{13}C NMR (150 MHz) Spectra of compound 1 in DMSO-d_6

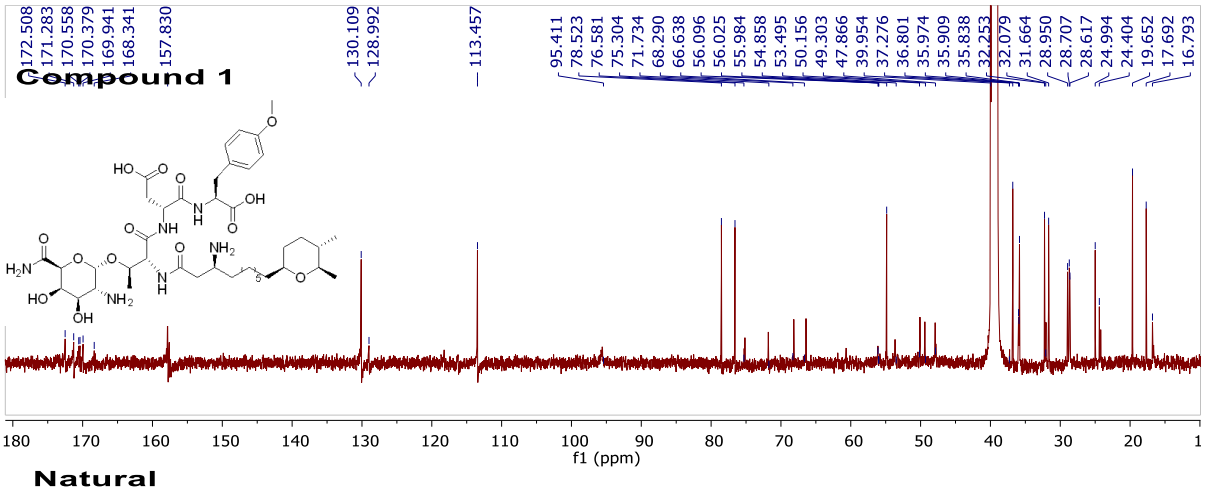


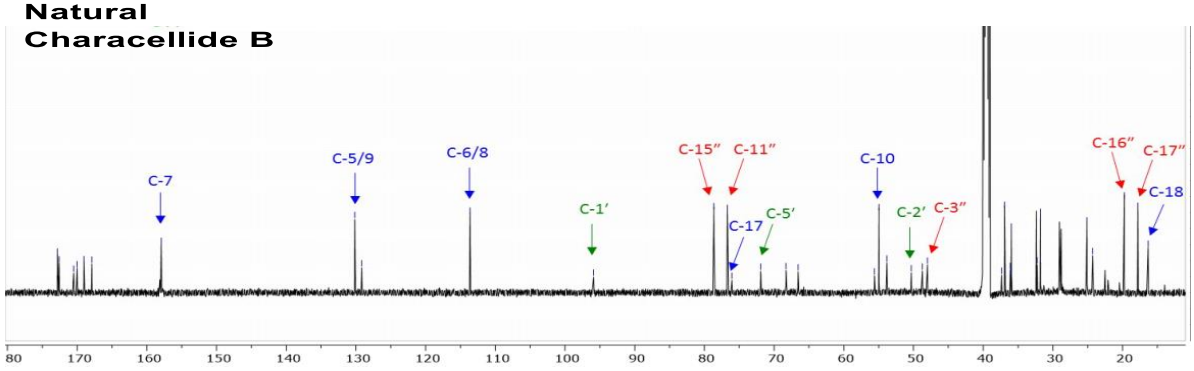


(40) the comparison of ^{1}H NMR (600 MHz) and ^{13}C NMR (150 MHz) Spectra of compound 1 and natural Characellide B in DMSO-d_6



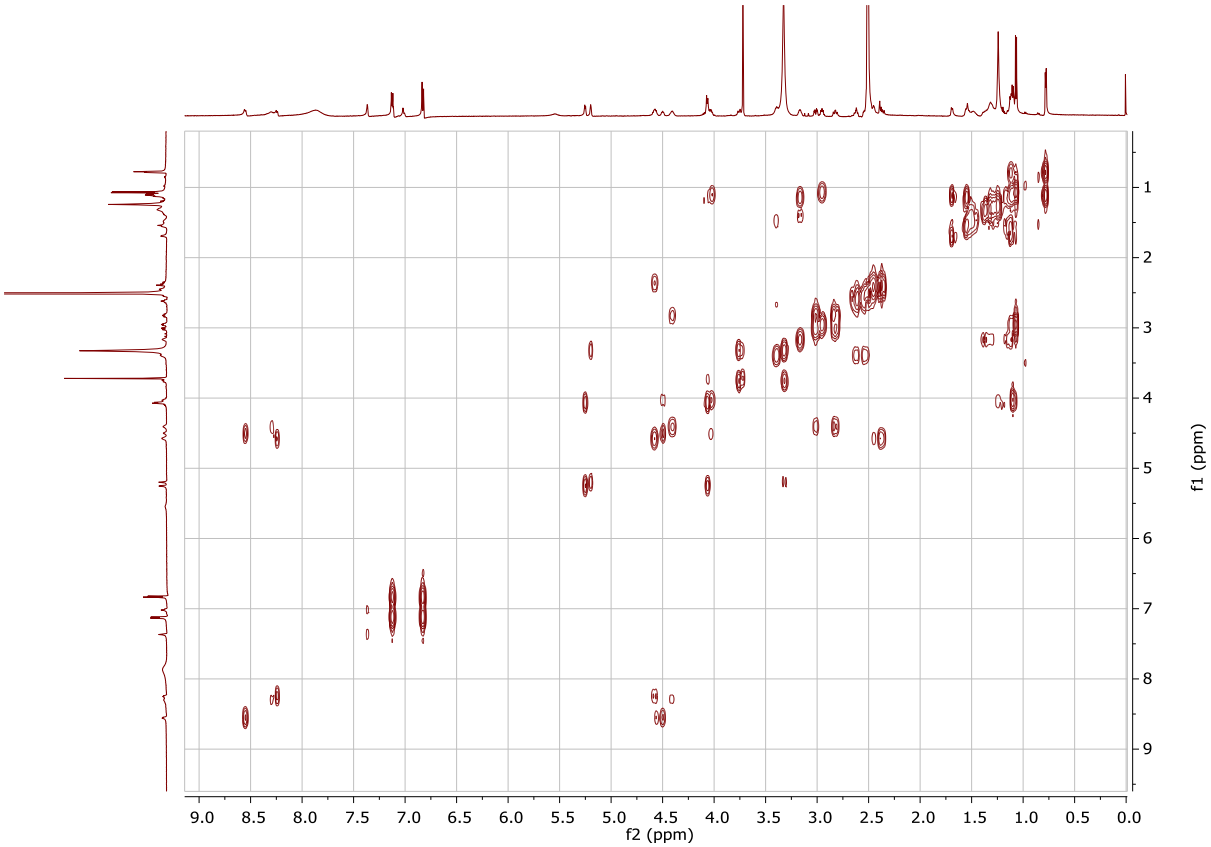




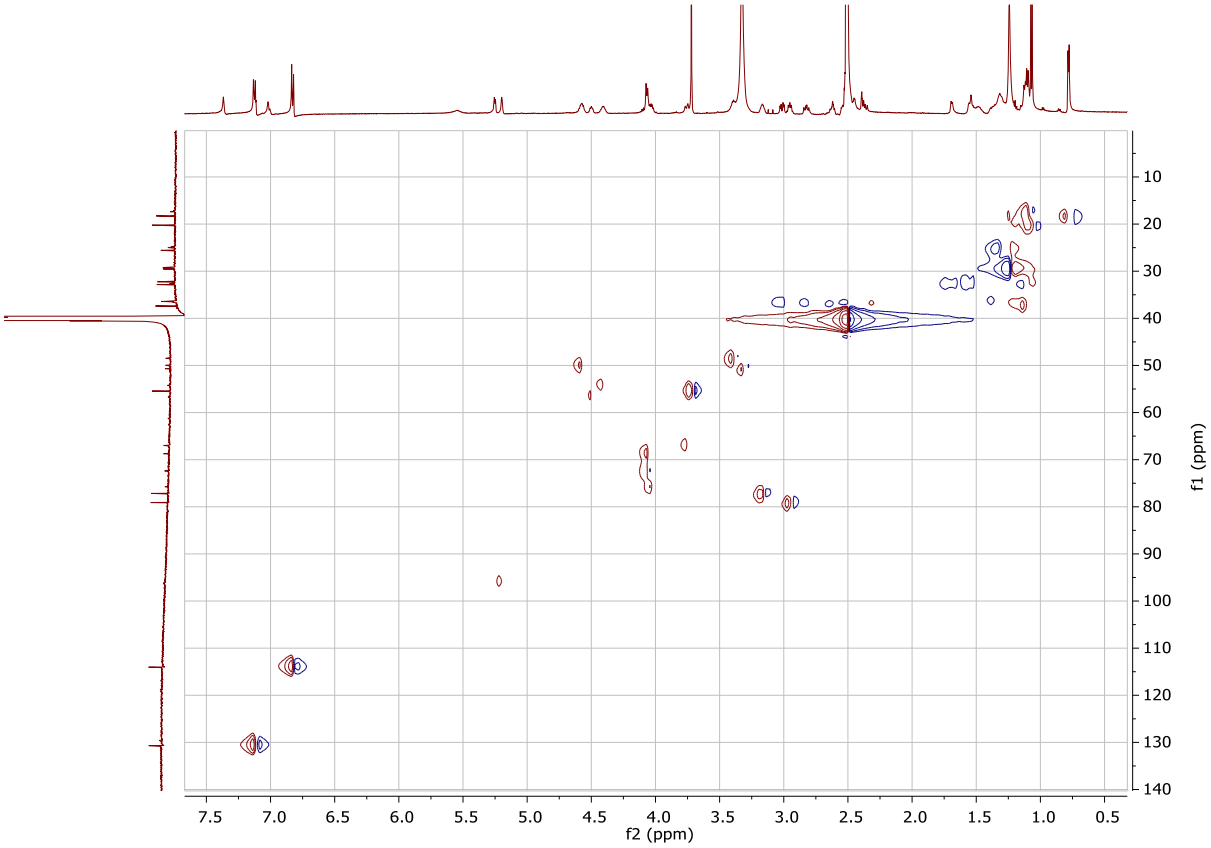


(41) H-H COSY, HSQC, HMBC Spectra of compound 1 in DMSO-d_6

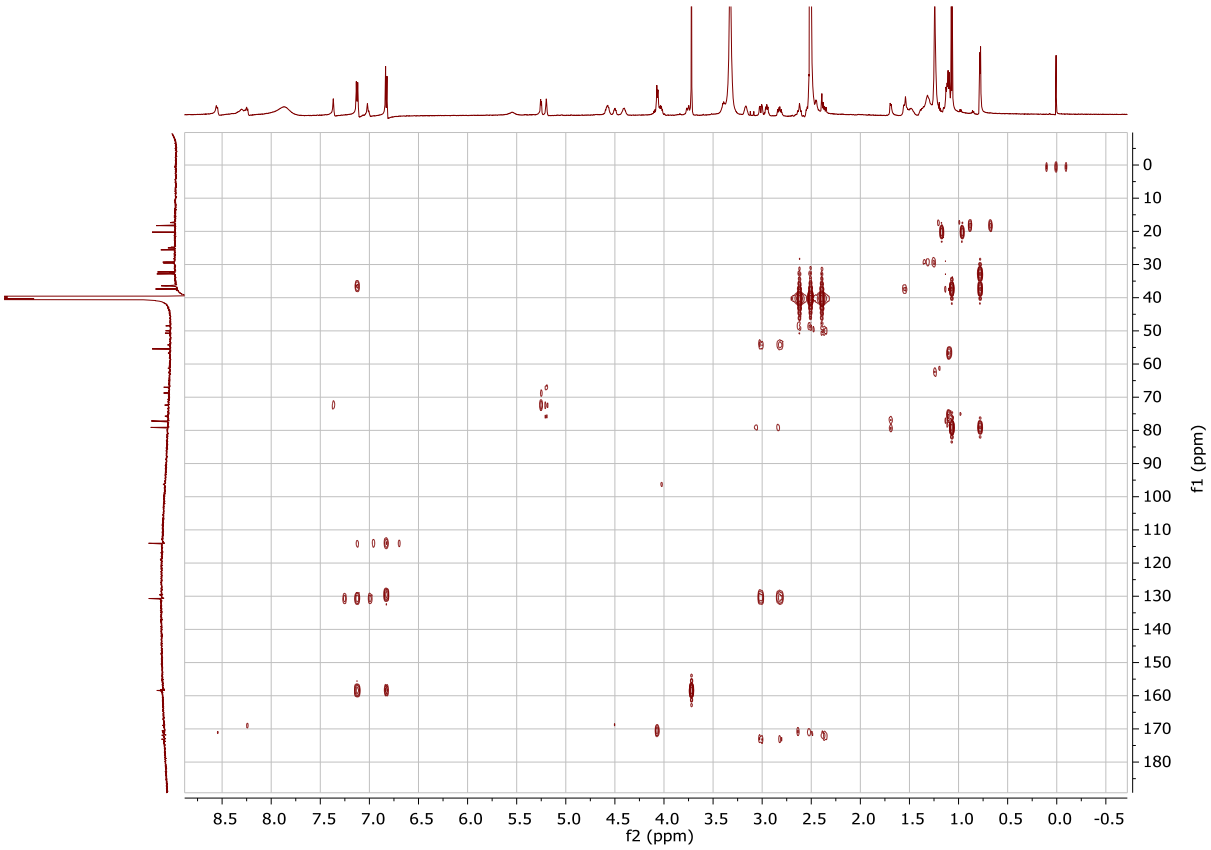
H-H COSY



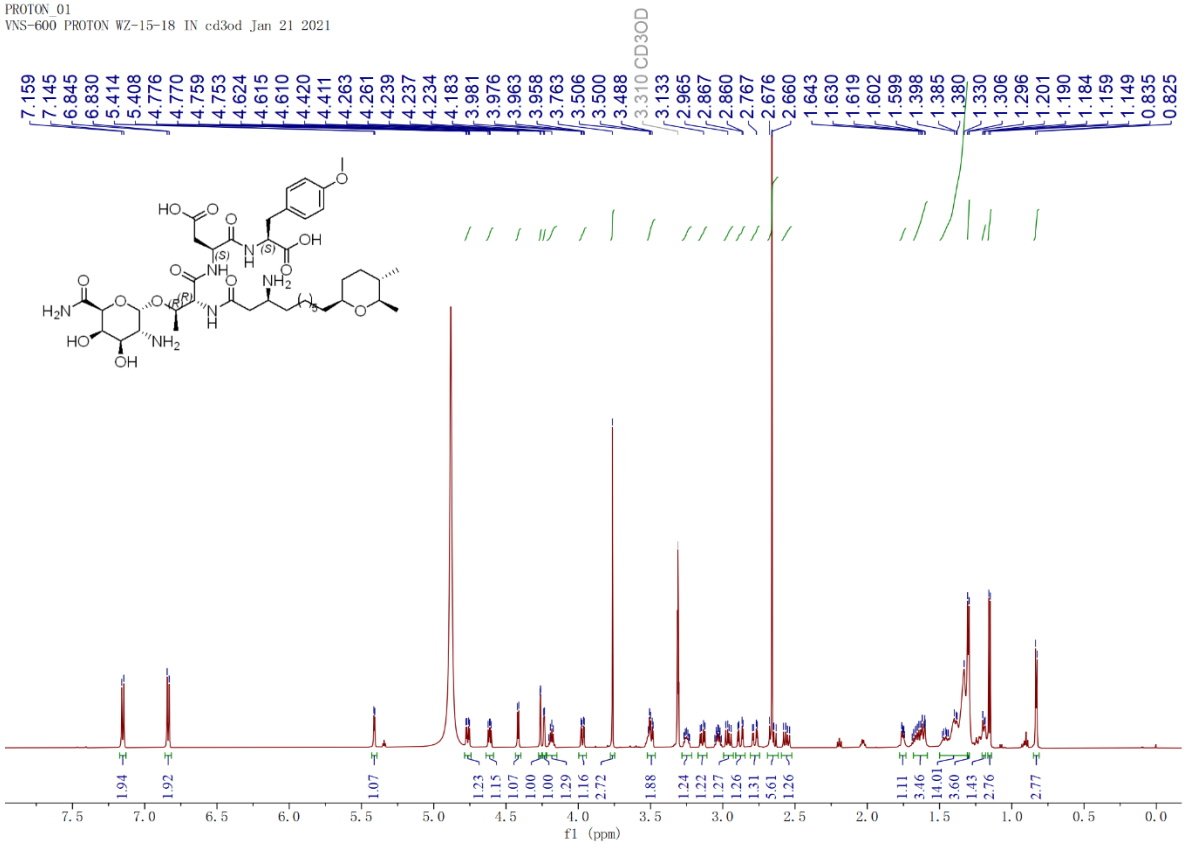
HSQC

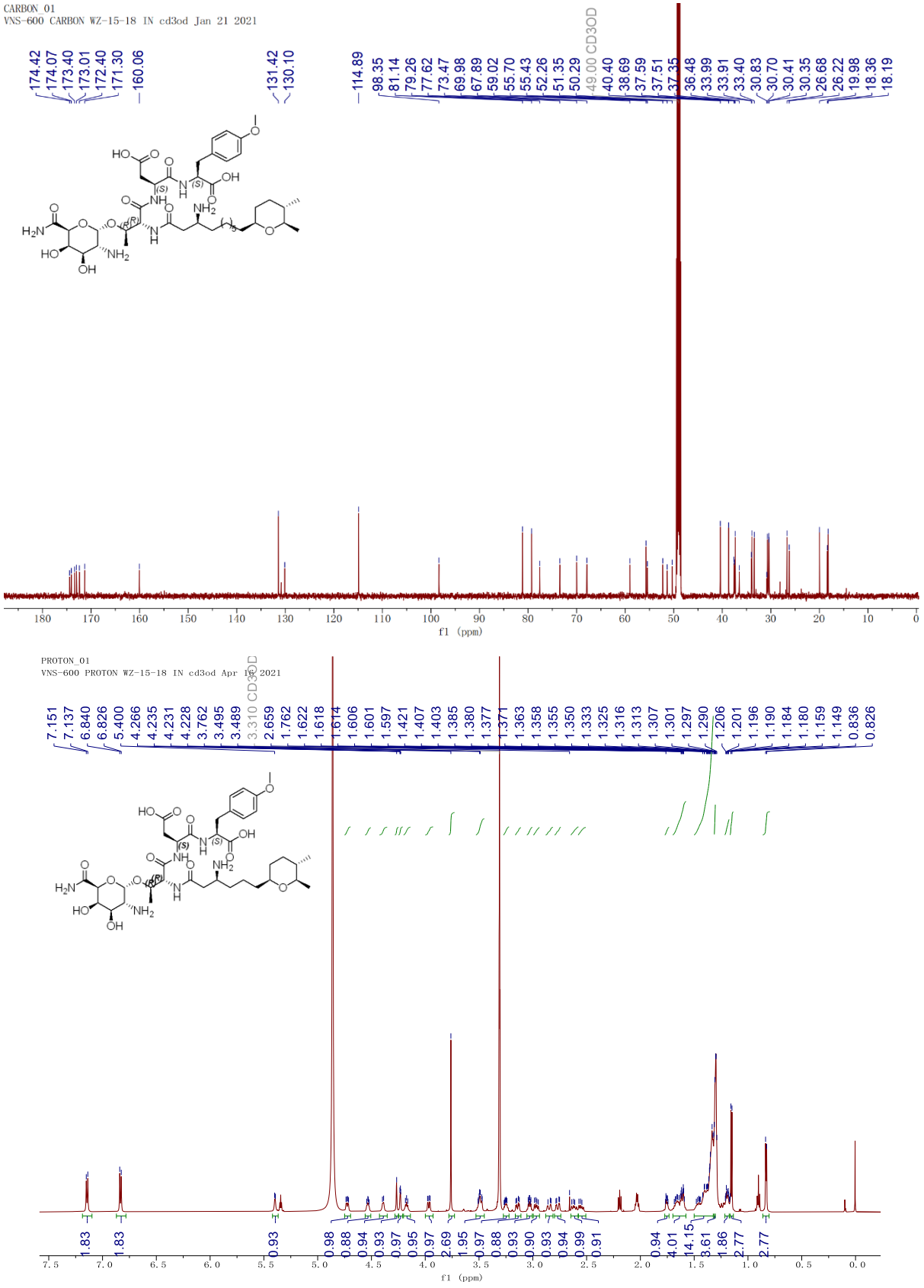


HMBC



(42) ^{1}H NMR (600 MHz) and ^{13}C NMR (150 MHz) Spectra of compound 1a in CD_3OD

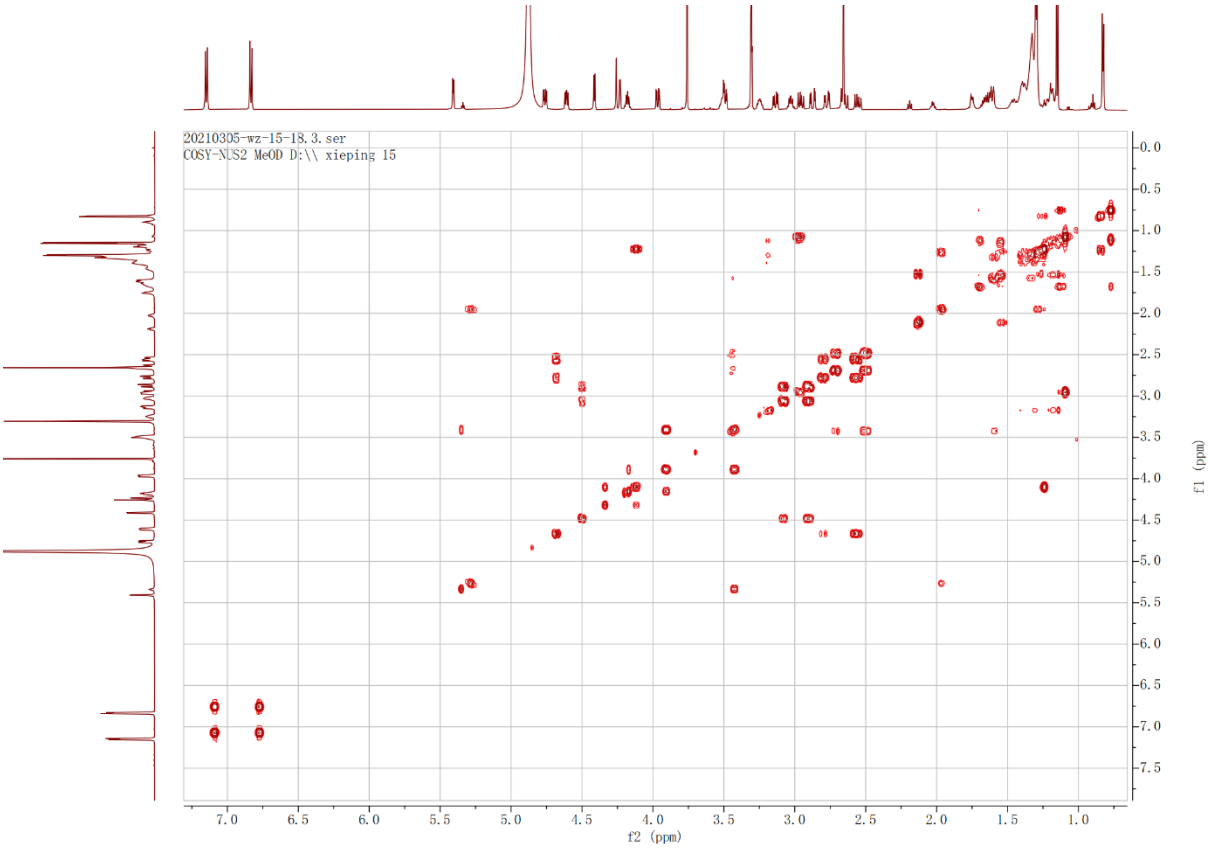




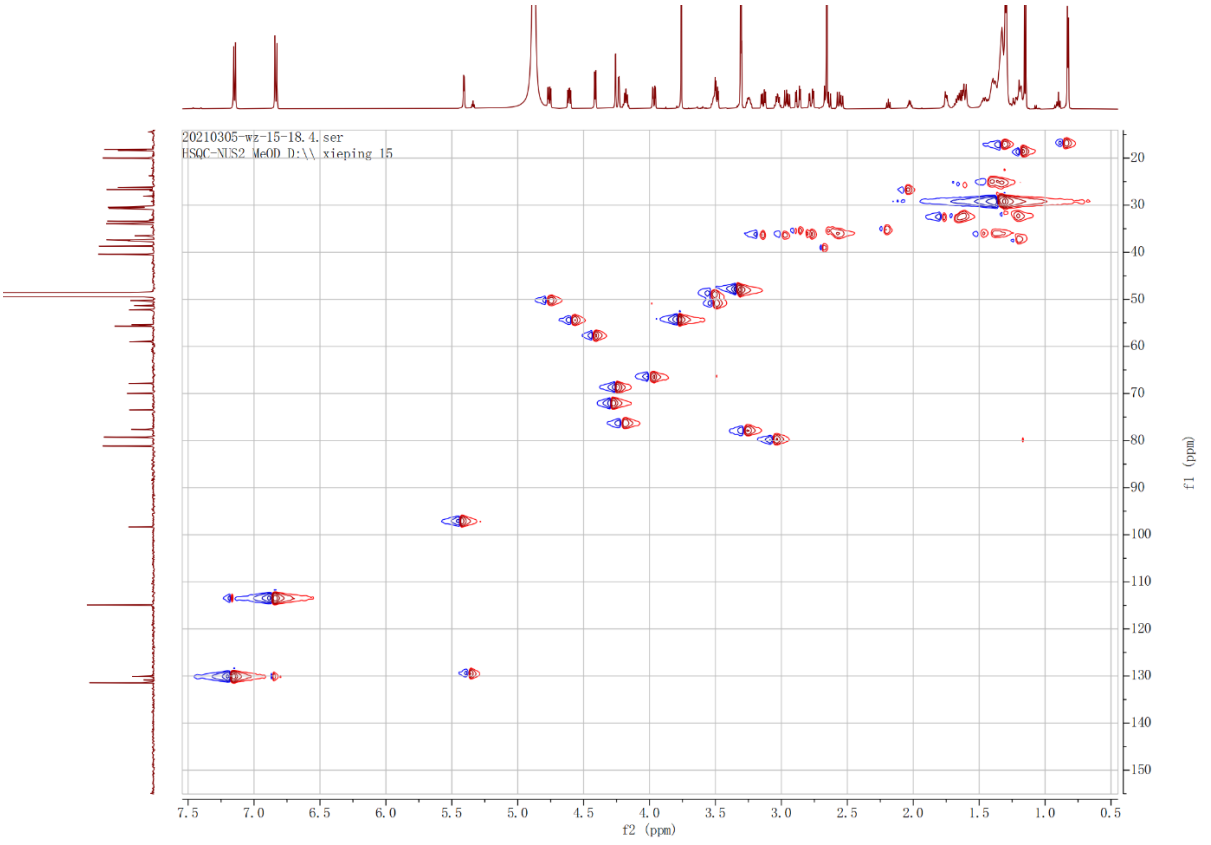
^{1}H NMR (600 MHz) Spectra of compound 1a in CD_3OD (140μL+0.01μL CF_3COOH)

(43) H-H COSY, HSQC, HMBC NMR Spectra of compound 1a in CD_3OD

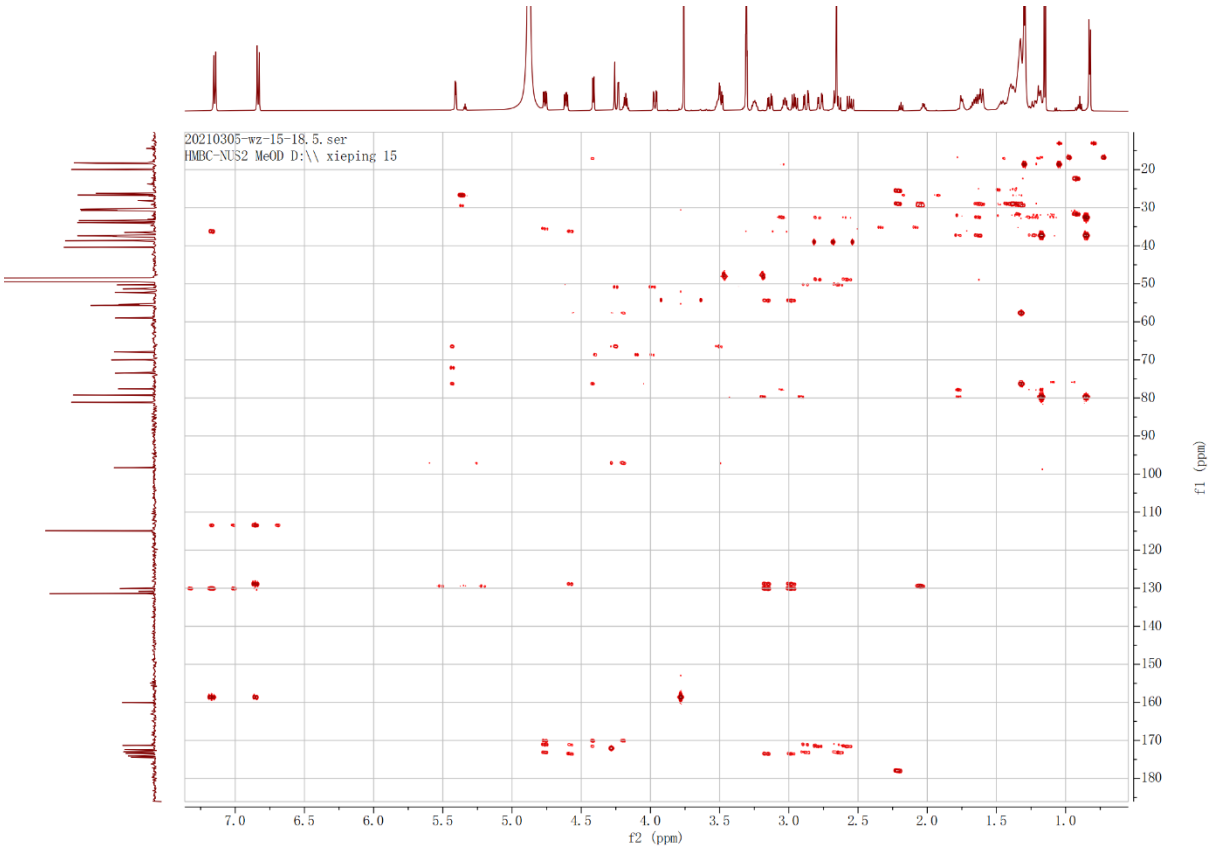
H-H COSY



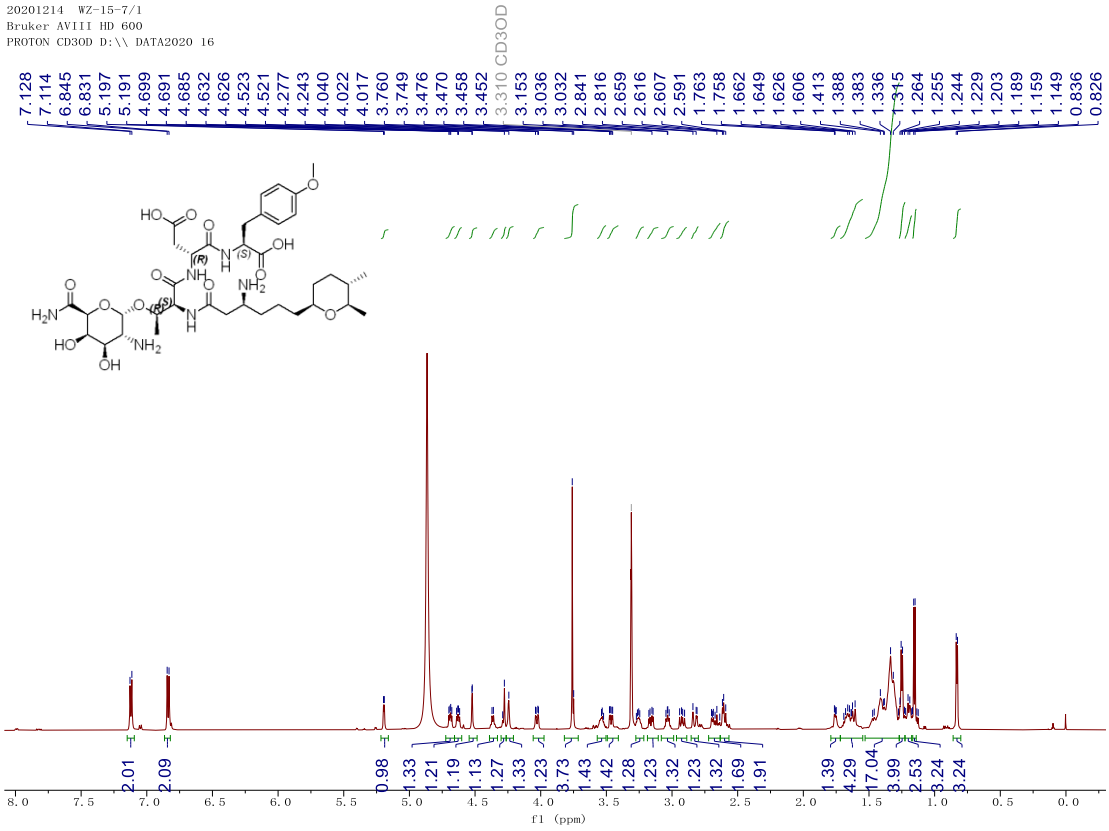
HSQC

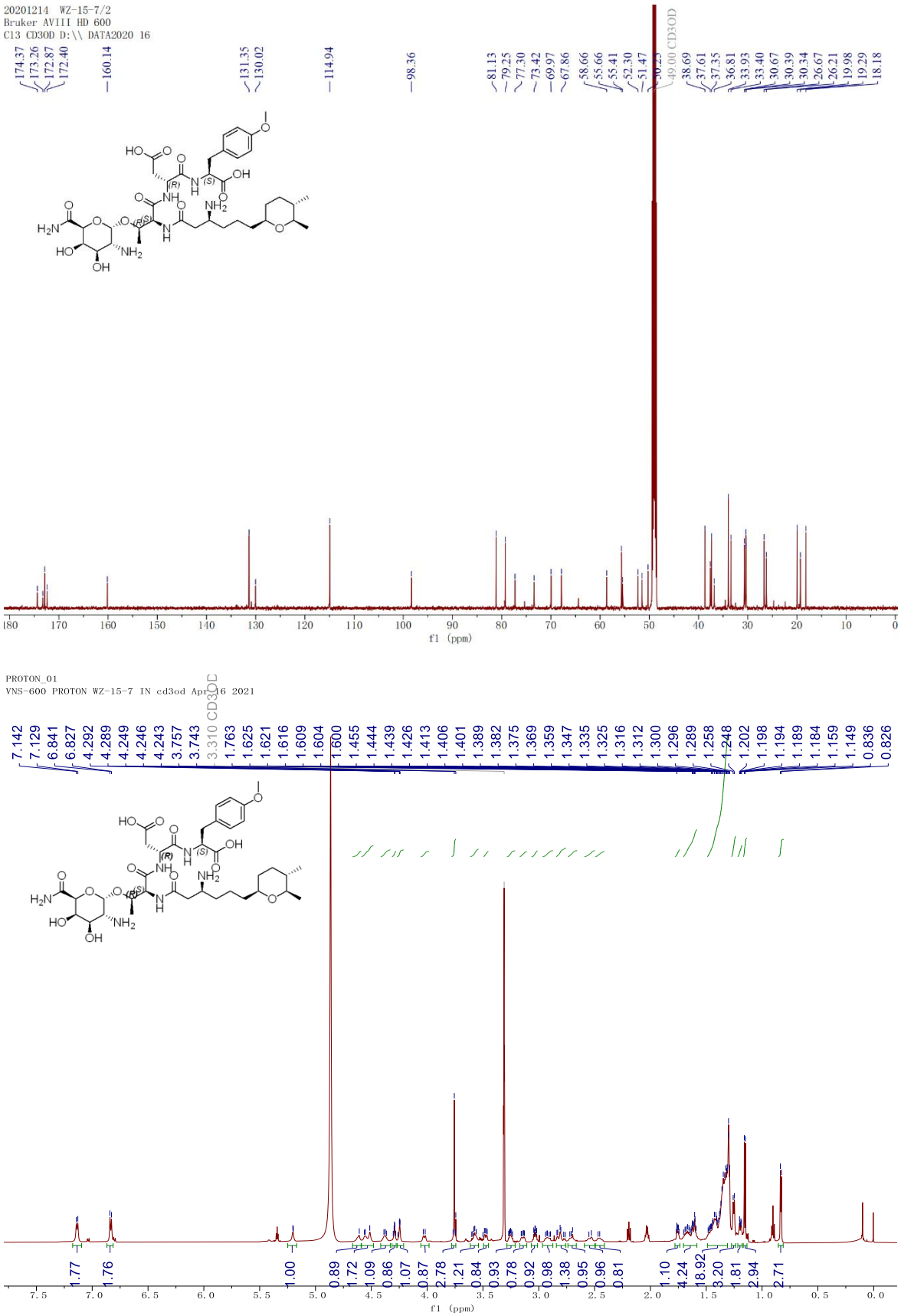


HMBC



(44) ^{1}H NMR (600 MHz) and ^{13}C NMR (150 MHz) Spectra of compound 1b in CD_3OD

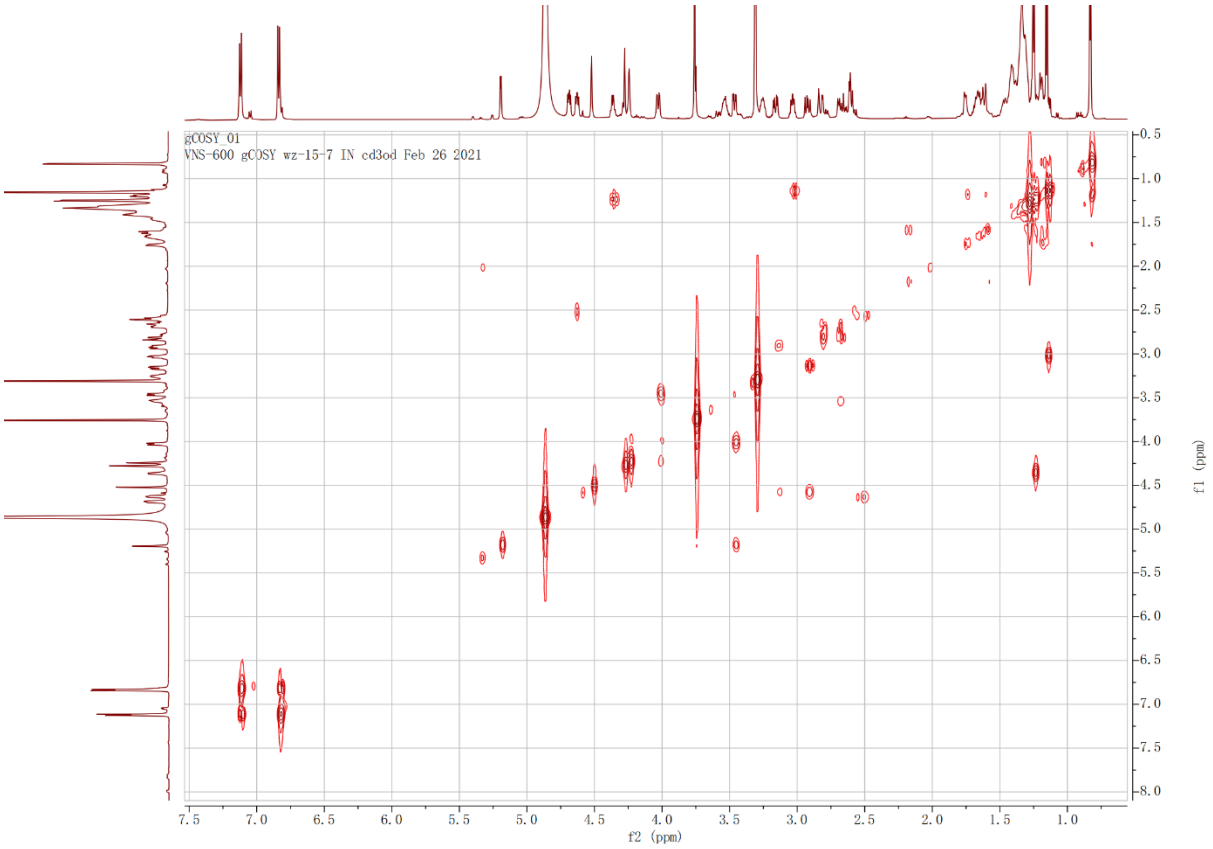




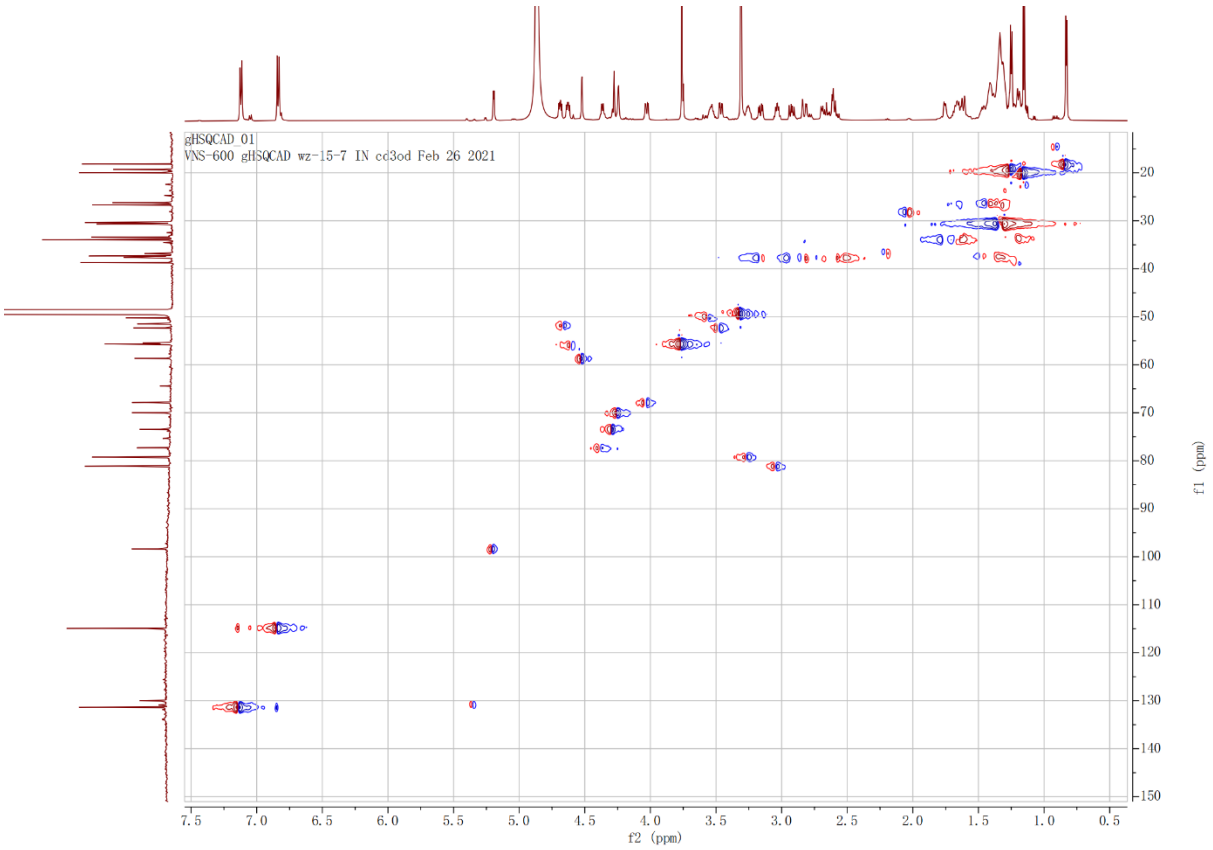
^{1}H NMR (600 MHz) Spectra of compound 1b in CD_3OD (140μL+0.01μL CF_3COOH)

(45) H-H COSY, HSQC, HMBC NMR Spectra of compound 1b in CD_3OD

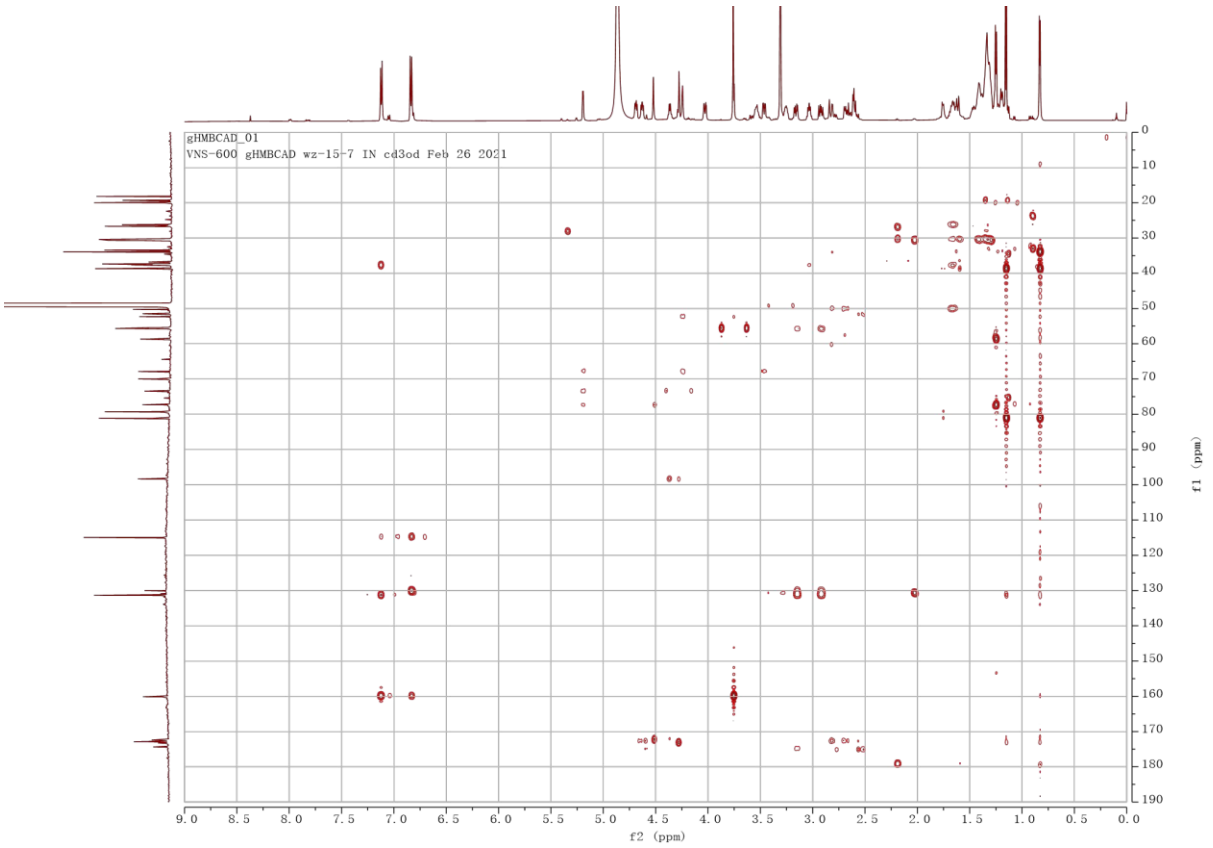
H-H COSY



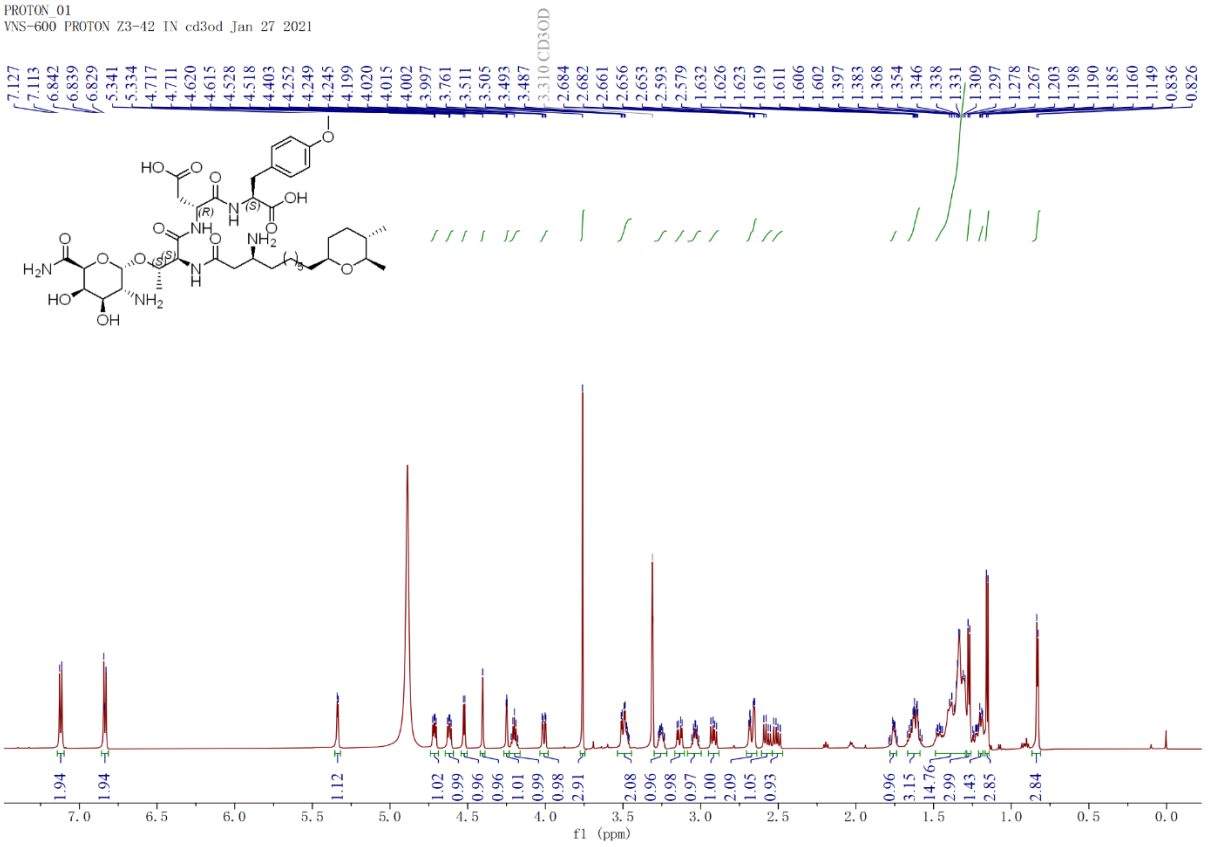
HSQC

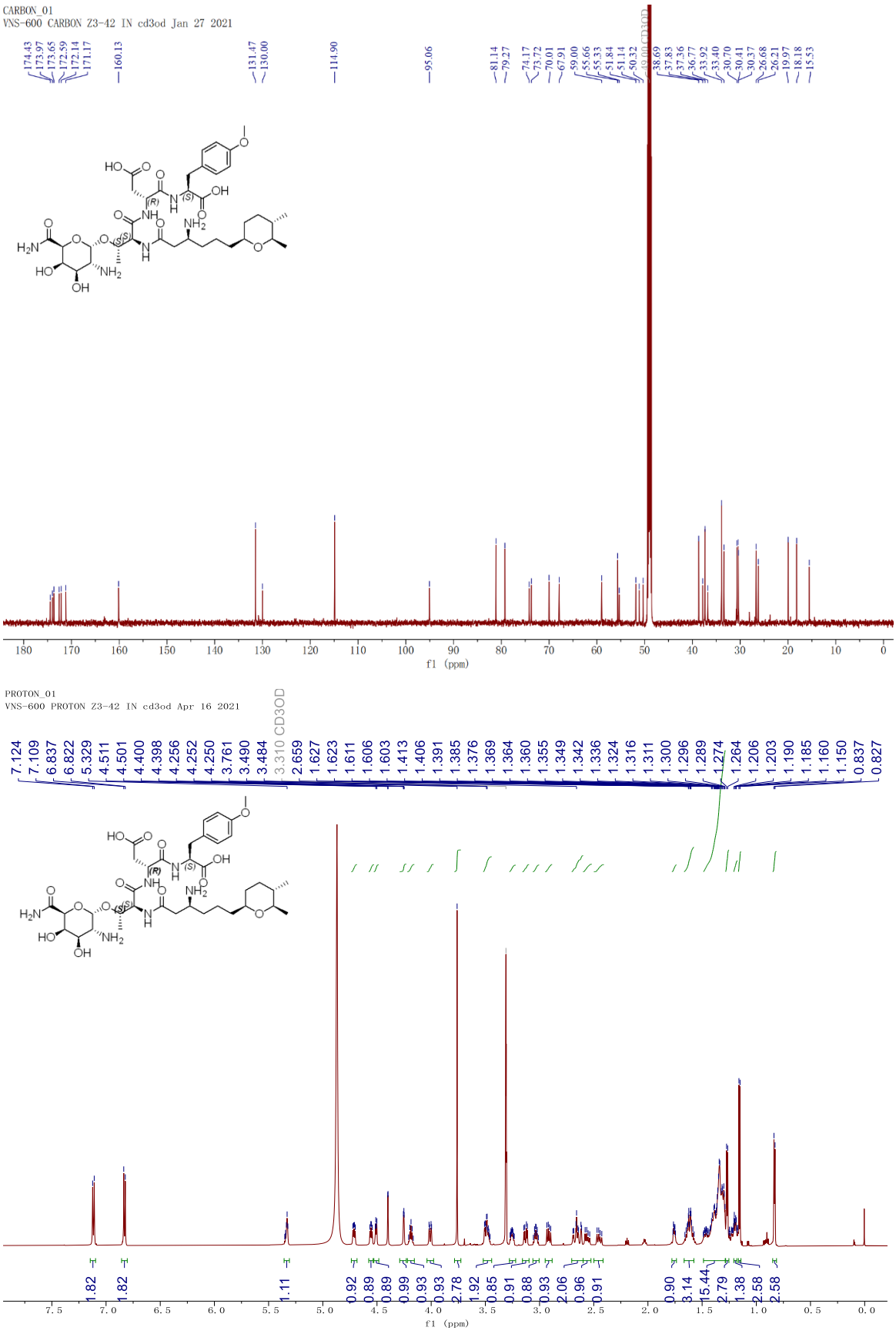


HMBC



(46) ^{1}H NMR (600 MHz) and ^{13}C NMR (150 MHz) Spectra of compound 1c in CD_3OD

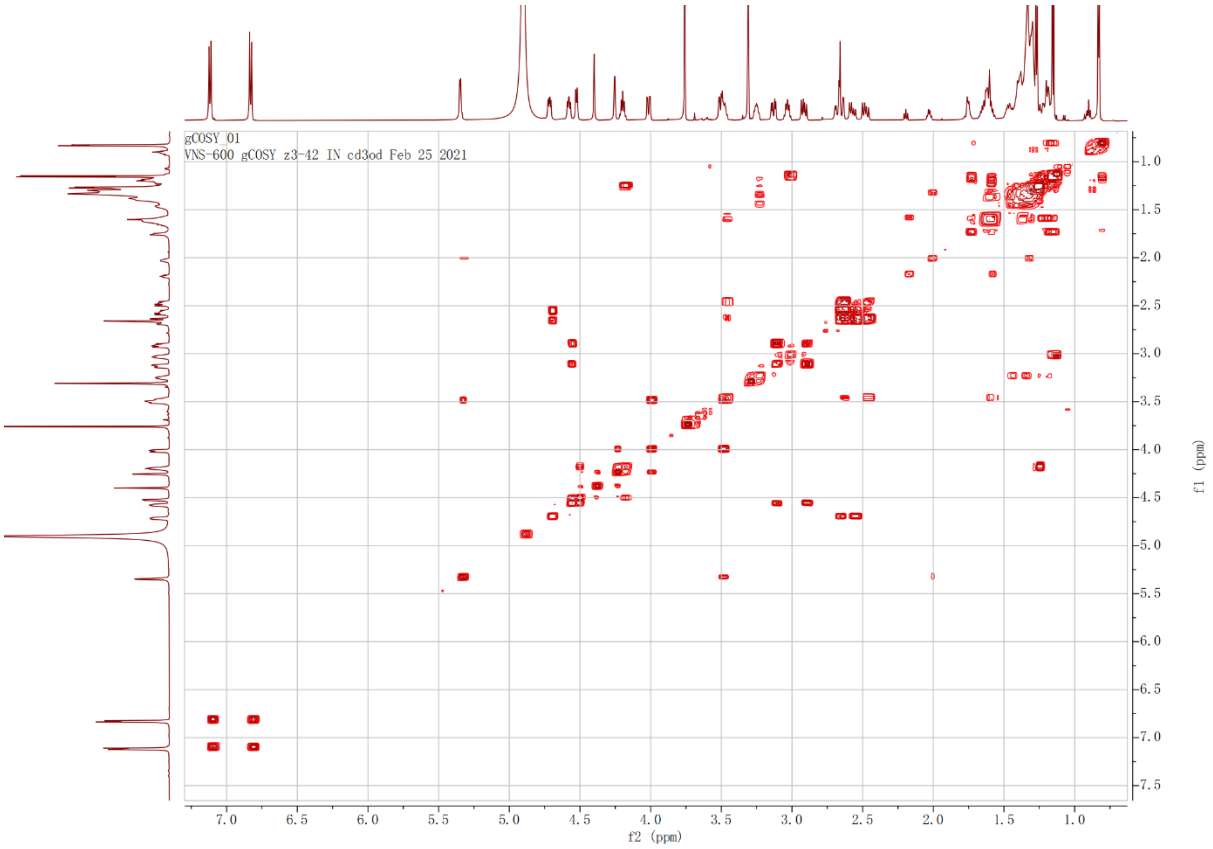




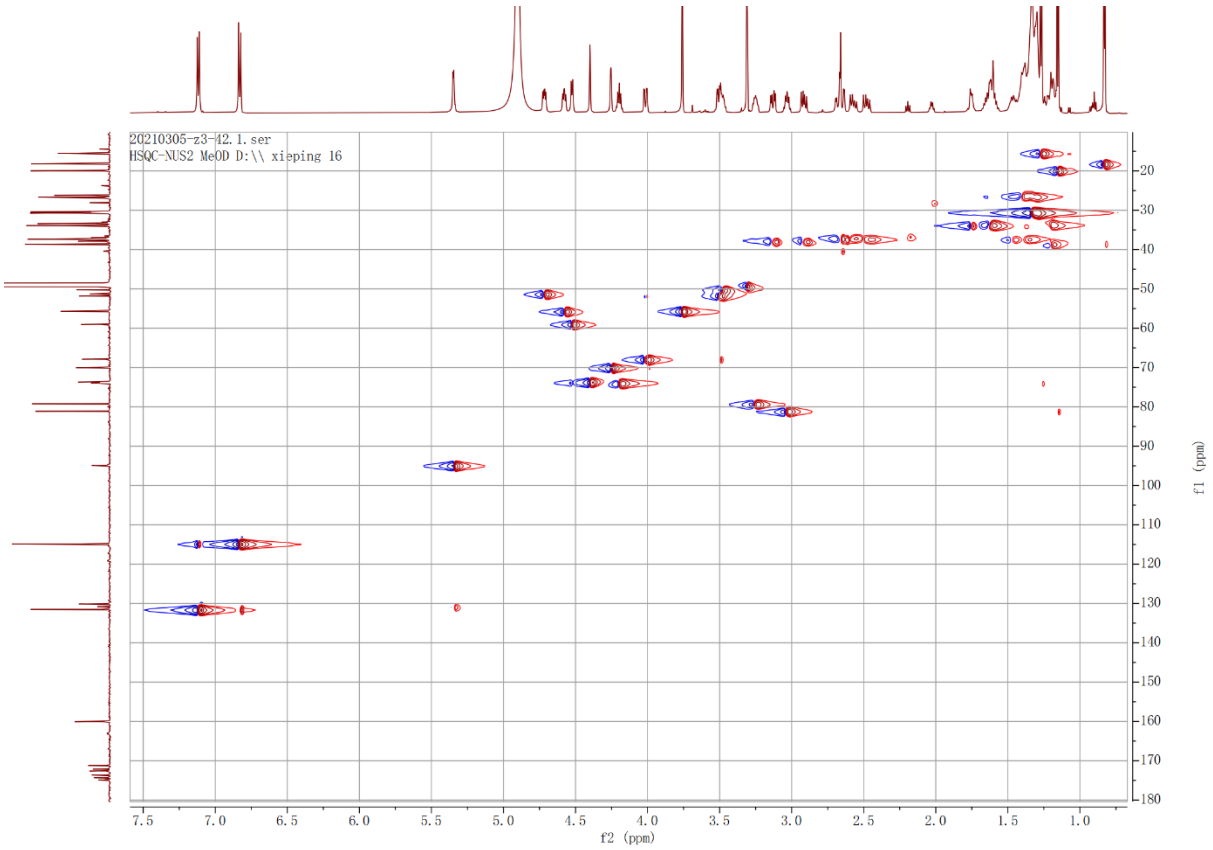
^{1}H NMR (600 MHz) Spectra of compound 1c in CD_3OD (140µL+0.01µL CF_3COOH)

(47) H-H COSY, HSQC, HMBC NMR Spectra of compound 1c in CD_3OD

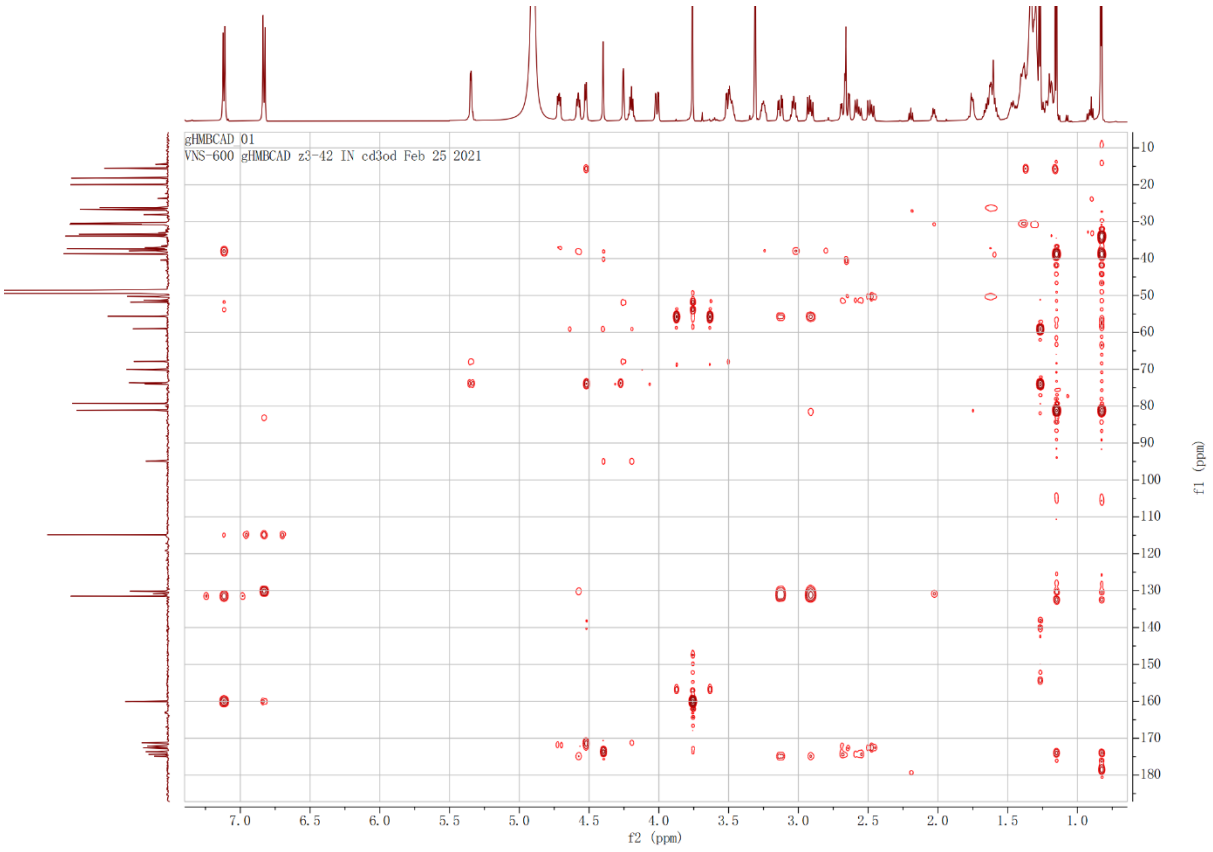
H-H COSY



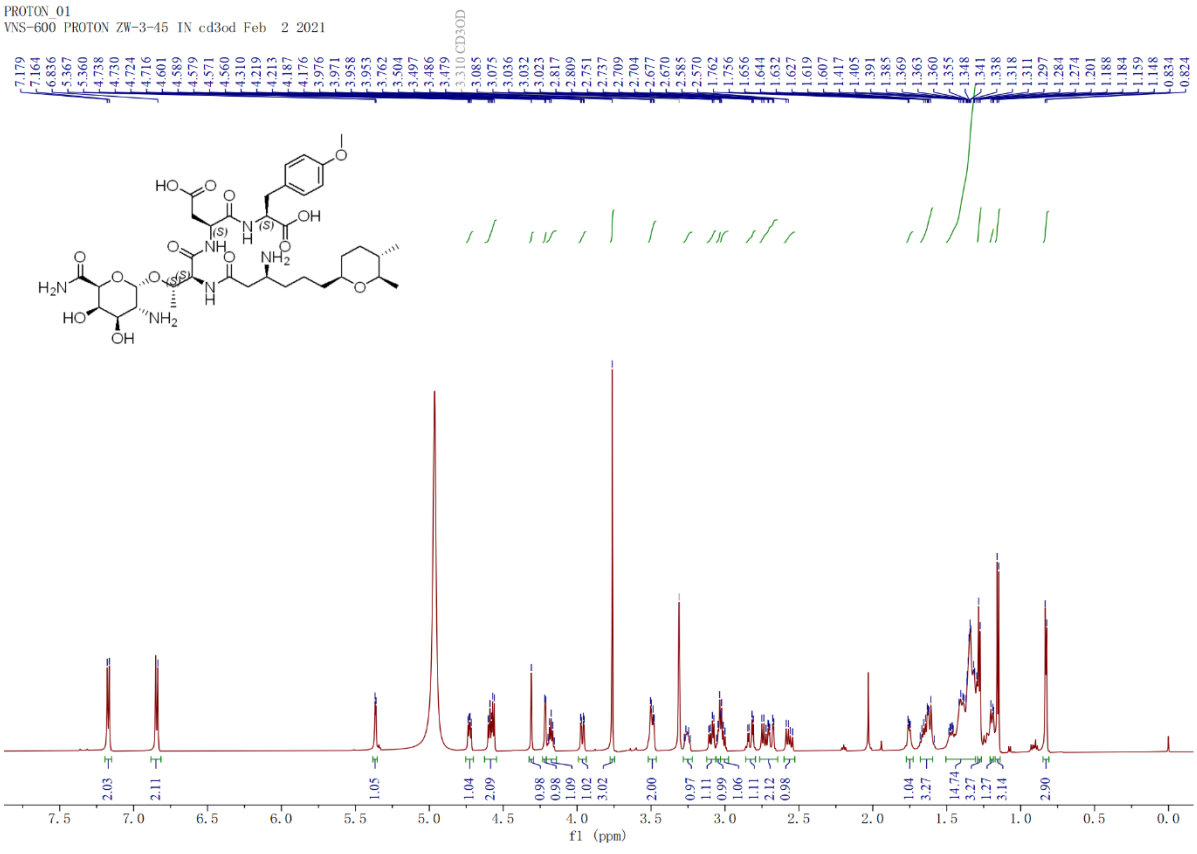
HSQC

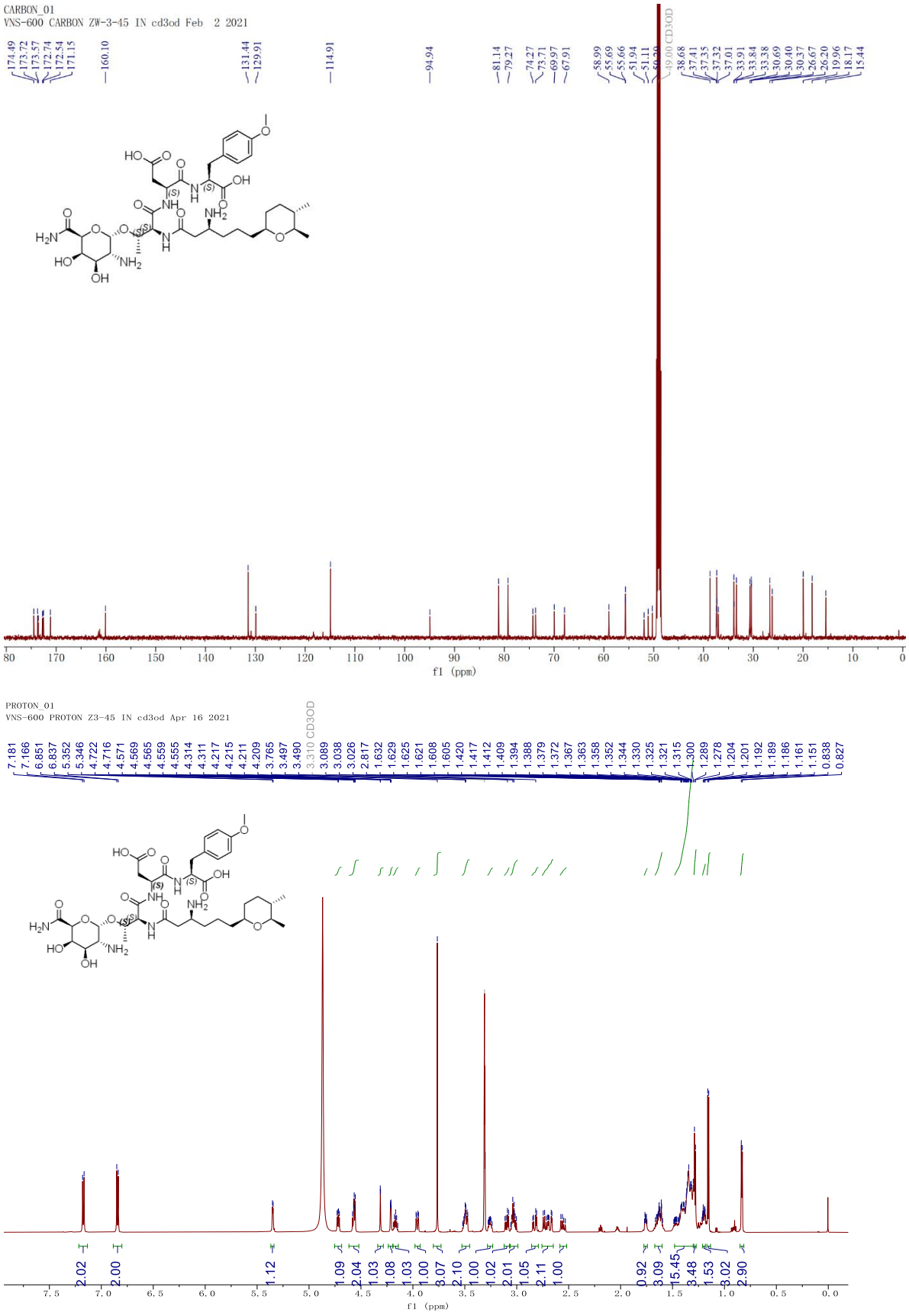


HMBC

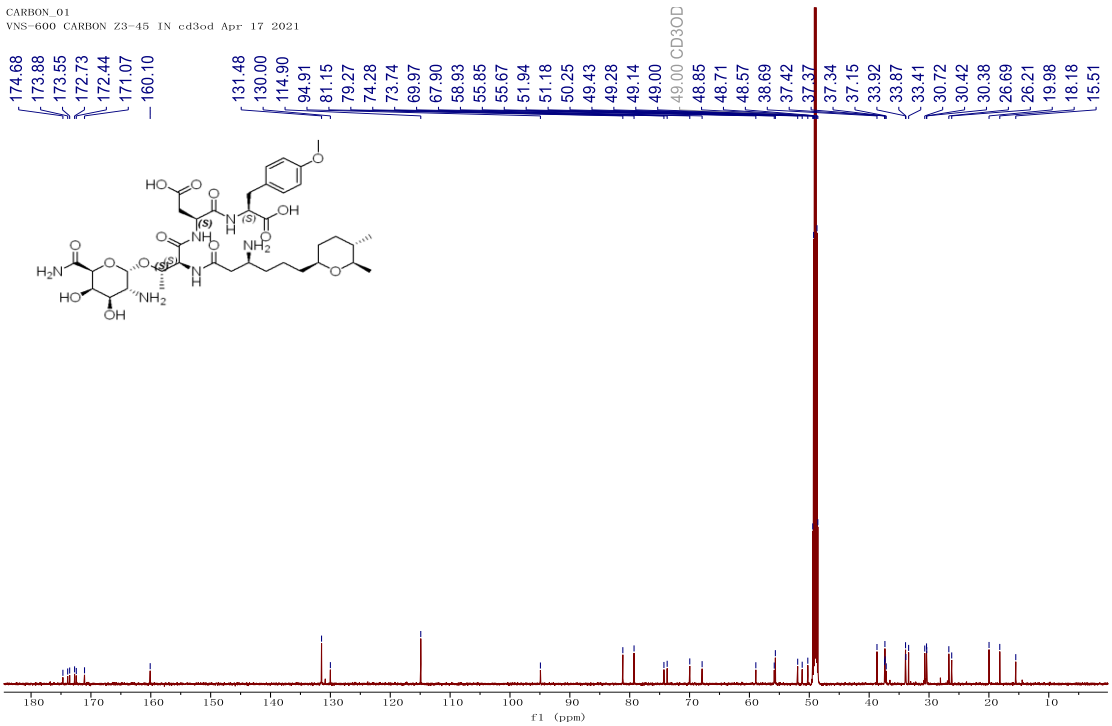


(48) ^{1}H NMR (600 MHz) and ^{13}C NMR (150 MHz) Spectra of compound 1d in CD_3OD





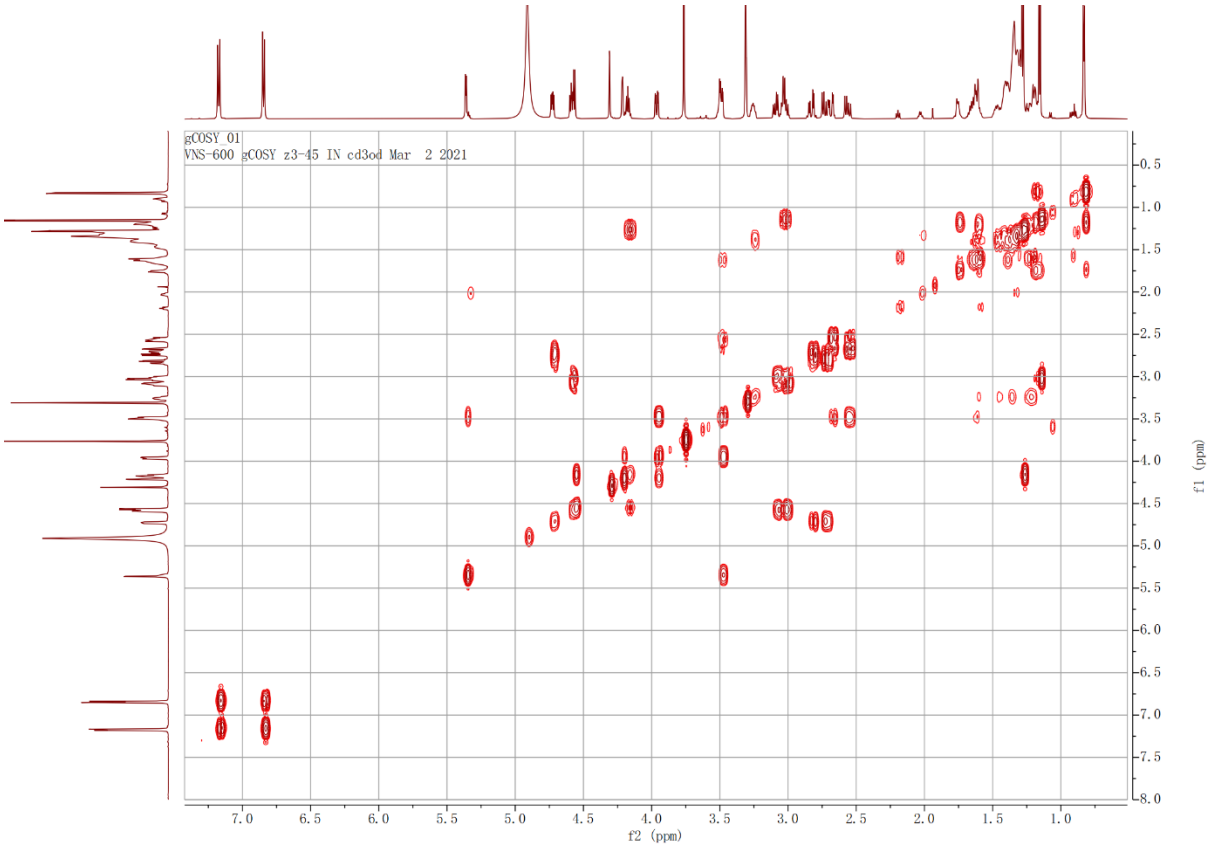
^{1}H NMR (600 MHz) Spectra of compound 1d in CD_3OD (140μL+0.01μL CF_3COOH)



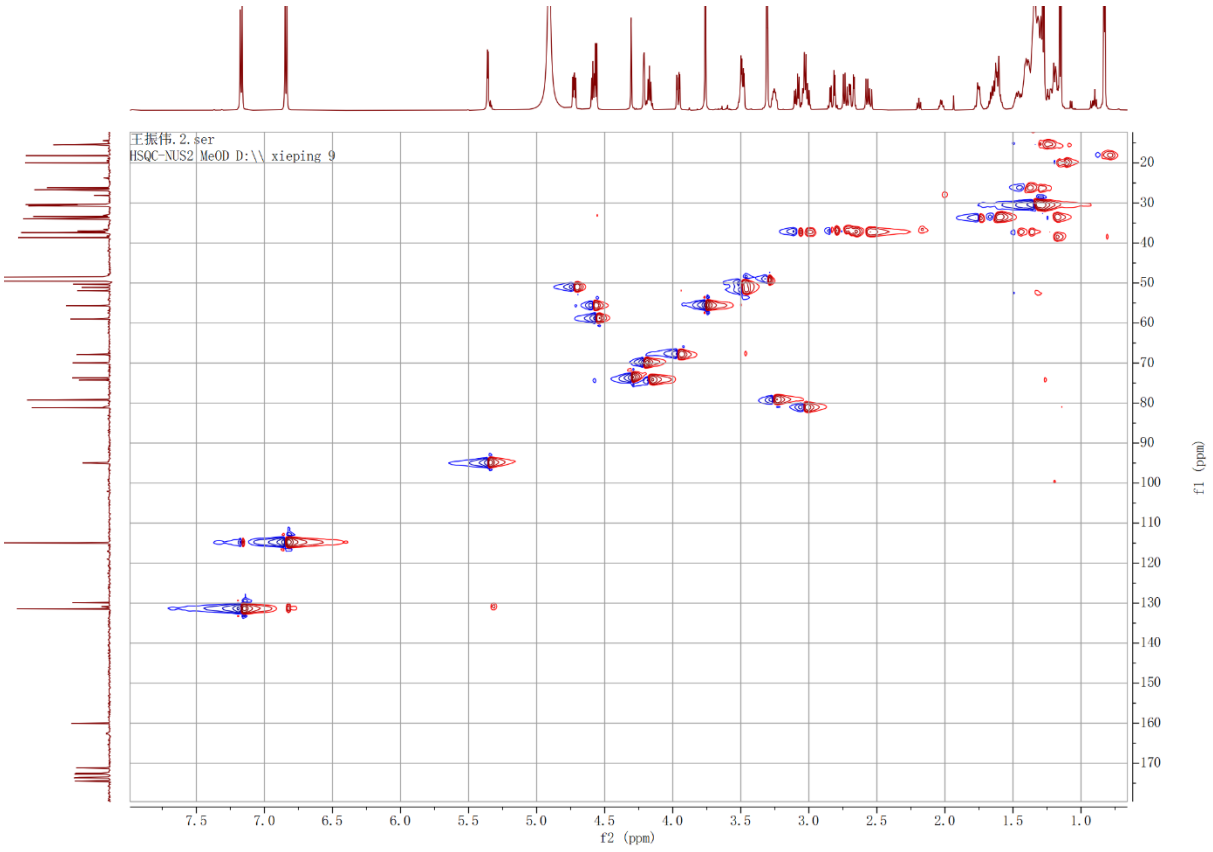
^{13}C NMR (150 MHz) Spectra of compound 1d in CD_3OD (140μL+0.01μL CF_3COOH)

(49) H-H COSY, HSQC, HMBC NMR Spectra of compound 1d in CD_3OD

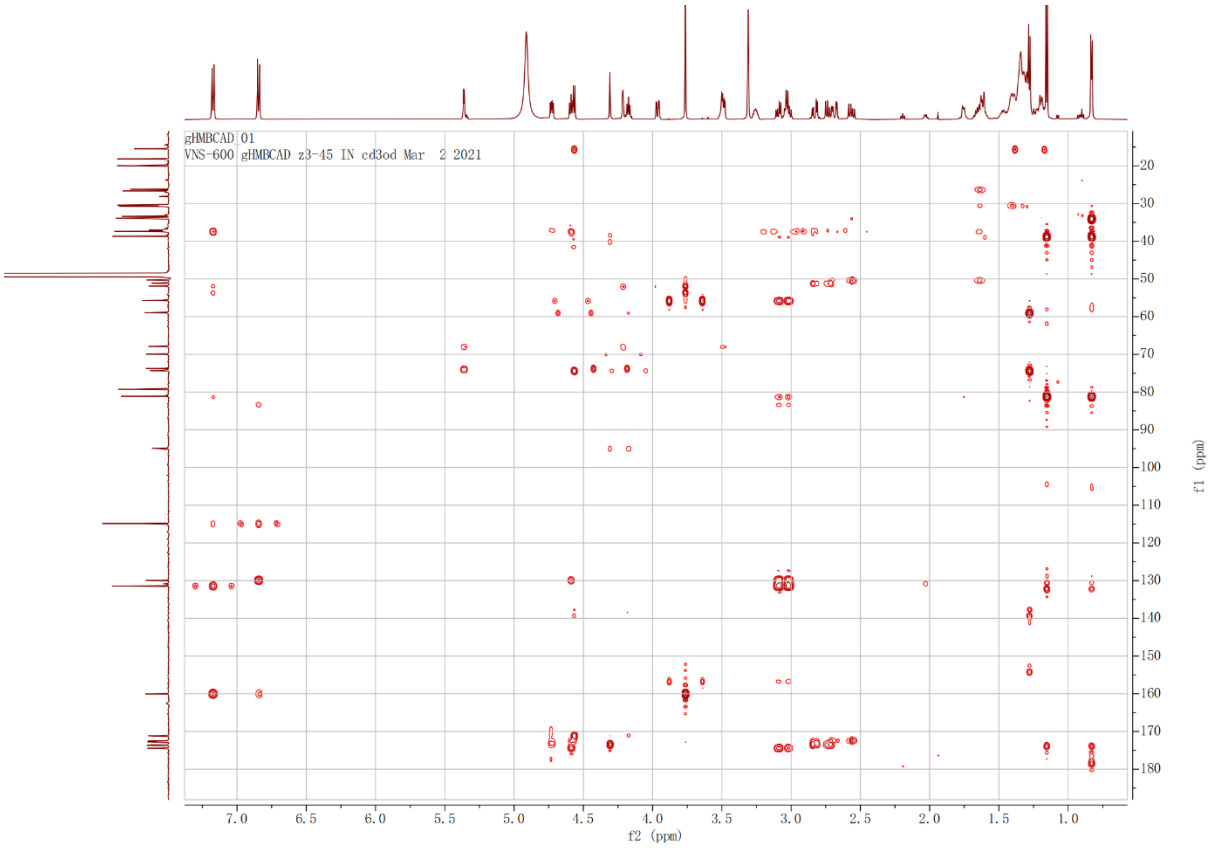
H-H COSY



HSQC

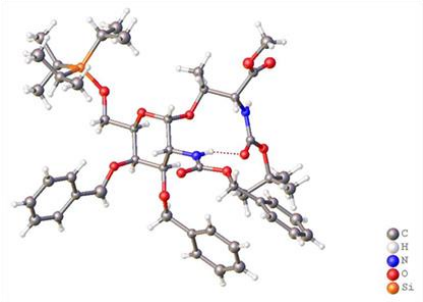

王振伟.2.ser
HSQC-NUS2 MeOD D:\\ xieping 9
f2 (ppm)
f1 (ppm)

HMBC


gHMBCAD 01
VNS-600 gHMBCAD z3-45 IN cd3od Mar 2 2021
f2 (ppm)
f1 (ppm)

5. ORTEP drawings and X-ray crystallographic data of compounds 6 and 20

ORTEP drawings and X-ray crystallographic data of compounds 6 (CCDC 1988311)

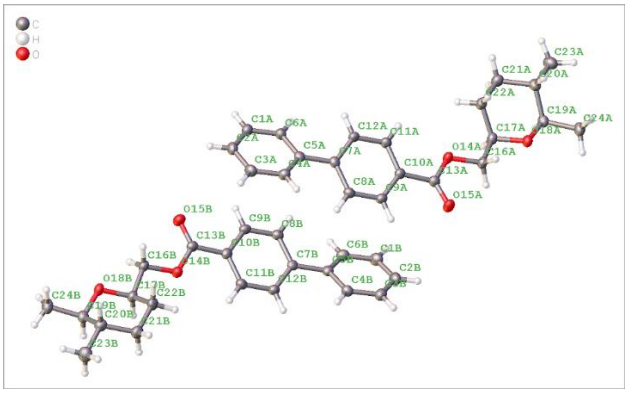


Single crystals of $C_{47}H_{67}N_2O_{11}Si$ [**compound 6**] were grown from a petroleum ether/CH_2Cl_2 solution of the compound at 25 °C. A suitable crystal was selected on a Xcalibur, Atlas, Gemini ultra diffractometer. The crystal was kept at 293(2) K during data collection. Using Olex2[2], the structure was solved with the ShelXS[3] structure solution program using Direct Methods and refined with the ShelXL[4] refinement package using Least Squares minimisation.

Identification code	exp_782
Empirical formula	$C_{47}H_{67}N_2O_{11}Si$
Formula weight	864.11
Temperature/K	293(2)
Crystal system	orthorhombic
Space group	$P2_12_12_1$
a/Å	9.51084(13)
b/Å	16.1262(2)
c/Å	34.7996(7)
α/°	90
β/°	90
γ/°	90
Volume/Å^3	5337.34(15)
Z	4
ρ_{calc}g/cm^3	1.075
μ/mm^{-1}	0.819
F(000)	1860.0
Crystal size/mm^3	0.24 × 0.19 × 0.13
Radiation	CuKα (λ = 1.54184)
2Θ range for data collection/°	7.474 to 133.638
Index ranges	$-11 \leq h \leq 10$, $-19 \leq k \leq 19$, $-41 \leq l \leq 41$
Reflections collected	43292

Independent reflections	9386 [R_{int} = 0.0387, R_{sigma} = 0.0249]
Data/restraints/parameters	9386/0/560
Goodness-of-fit on F^2	1.032
Final R indexes [I>=2σ (I)]	R_1 = 0.0421, wR_2 = 0.1106
Final R indexes [all data]	R_1 = 0.0543, wR_2 = 0.1202
Largest diff. peak/hole / e $Å^{-3}$	0.21/-0.14
Flack parameter	-0.007(13)

ORTEP drawings and X-ray crystallographic data of compounds 20 (CCDC 1988307)



Single crystals of $C_{42}H_{48}O_6$ **[compound 20]** were grown from an acetonitrile solution of the compound at 25 ºC. A suitable crystal was selected on a **XtaLAB Synergy R, HyPix** diffractometer. The crystal was kept at 100.00(10) K during data collection. Using Olex2[2], the structure was solved with the ShelXT[3] structure solution program using Intrinsic Phasing and refined with the ShelXL[4] refinement package using Least Squares minimisation.

Identification code	11_23
Empirical formula	$C_{42}H_{48}O_6$
Formula weight	648.80
Temperature/K	100.00(10)
Crystal system	monoclinic
Space group	$P2_1$
a/Å	8.54800(10)
b/Å	13.2616(2)
c/Å	15.6094(2)
α/°	90
β/°	95.0790(10)
γ/°	90
Volume/$Å^3$	1762.54(4)
Z	2
$\rho_{calc}g/cm^3$	1.223

μ/mm^{-1}	0.639
F(000)	696.0
Crystal size/mm^3	0.26 × 0.1 × 0.05
Radiation	CuKα (λ = 1.54184)
2Θ range for data collection/°	8.764 to 150.012
Index ranges	$-10 \leq h \leq 10$, $-16 \leq k \leq 14$, $-19 \leq l \leq 19$
Reflections collected	29010
Independent reflections	6692 [R_{int} = 0.0337, R_{sigma} = 0.0257]
Data/restraints/parameters	6692/1/437
Goodness-of-fit on F^2	1.034
Final R indexes [I>=2σ (I)]	R_1 = 0.0338, wR_2 = 0.0835
Final R indexes [all data]	R_1 = 0.0382, wR_2 = 0.0862
Largest diff. peak/hole / e $Å^{-3}$	0.14/-0.21
Flack parameter	0.03(5)

[2]. Dolomanov, O.V., Bourhis, L.J., Gildea, R.J, Howard, J.A.K. & Puschmann, H. (2009), J. Appl. Cryst. 42, 339-341.
[3]. Sheldrick, G.M. (2015). Acta Cryst. A71, 3-8.
[4]. Sheldrick, G.M. (2015). Acta Cryst. C71, 3-8