Supporting Information

Design, Synthesis and Immunological Evaluation of Monophosphoryl Lipid A Derivatives as Adjuvants for RBD-hFc Based SARS-CoV-2 Vaccine

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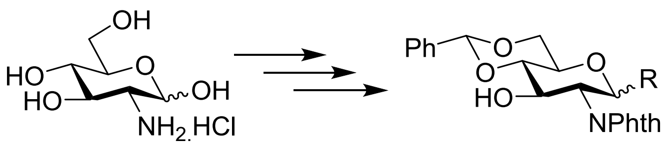
I. General Information

All materials and reagents were from commercial sources and used without further purification unless otherwise specified. Molecular sieves 4 Å were flame–dried under vacuum and cooled to rt under N_2 atmosphere immediately before use. The reactions were monitored by thin–layer chromatography (TLC) on glass–packed precoated silica gel plates and visualized by a UV detector or charring with 10% H_2SO_4 in EtOH (v/v). Purification of products was accomplished by flash column chromatography on silica gel (200-300 mesh). NMR spectra were recorded on a Bruker Avance III 400 spectrometer (^{1}H at 400 MHz, ^{13}C at 100 MHz) with chemical shifts reported in ppm using TMS as the internal standard. Signal splitting patterns are described as singlet (s), doublet (d), triplet (t), quartet (q), or multiplet (m), with coupling constants (*J*) in hertz. The high–resolution electron spray ionization mass spectra (HR–ESI–MS) were obtained using Agilent 6540 UHD Accurate Mass Quadrupole Time of Flight (Q-TOF) mass spectrometer or Waters Micromass-LCTPremier-XE mass spectrometer.

Alum adjuvant was purchased from Thermo Fisher. Fetal bovine serum (FBS) was purchased from Gibico. DSPC and cholesterol were purchased from Sigma Aldrich. HRP–linked goat anti–mouse IgG, IgG1, IgG2a, IgG2b and IgG3 antibodies were purchased from Abcam. Balb/c mice were bought from Liaoning Changsheng Biotechnology Co. LTD. (Liaoning, China). All animals were given a commercial mouse food and water ad libitum and housed in a temperature-controlled environment with a 12 hour light-dark cycle. The research was approved by the Guangzhou University of Chinese Medicine Animal Care and Use Committee. Vero E6 cells and HEK293 cells were obtained from American Type Culture Collection (ATCC). SARS -CoV-2 strain 2019n-CoV/USA_WA1/2020 was obtained from Guangdong Provincial Center for Disease Control and Prevention and the Institute of Medical Laboratory Animals of Chinese Academy of Medical Sciences. All experiments with infectious SARS-CoV-2 were performed in BSL3 facilities approved Institutional Biosafety Committee.

II. Preparation and Characterization of compounds 1–4

Compounds 11–14



11: R= βOBn; **12**: R= βOCH_3
13: R= βN_3; **14**: R= αN_3

The synthesis of **11-14** started from commercially available D-glucosamine hydrochloride using similar approaches to previous work with six steps.[1]

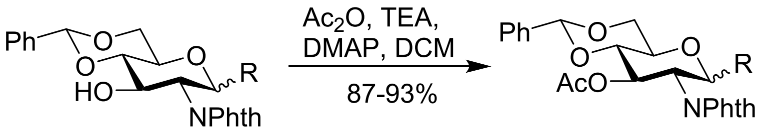
Compound 11: ^{1}H NMR (400 MHz, $CDCl_3$) δ 7.84 – 7.63 (m, 4H, Ar-H), 7.54 – 7.46 (m, 2H, Ar-H), 7.42 – 7.33 (m, 3H, Ar-H), 7.16 – 7.93 (m, 5H, Ar-H), 5.56 (s, 1H, PhCH), 5.25 (d, J = 8.5 Hz, 1H), 4.83 (d, J = 12.3 Hz, 1H, $PhCH_2$), 4.67 – 4.57 (m, 1H), 4.51 (d, J = 12.3 Hz, 1H, $PhCH_2$), 4.40 (dd, J = 10.5, 3.9 Hz, 1H), 4.28 (t, J = 10.5, 8.5 Hz, 1H), 3.85 (dd, J = 12.8, 6.7 Hz, 1H), 3.68 – 3.55 (m, 2H). ^{13}C NMR (100 MHz, $CDCl_3$) δ 167.97, 137.04, 136.86, 134.00, 131.62, 129.36, 128.39, 128.25, 127.75, 127.66, 126.35, 123.42, 101.94, 97.93, 82.15, 77.41, 77.29, 77.09, 76.77, 71.26, 68.71, 68.45, 66.13, 56.66.

Compound 12: ^{1}H NMR (400 MHz, $CDCl_3$) δ 7.82 – 7.81 (m, 2H), 7.69 – 7.67 (m, 2H), 7.49 – 7.48 (m, 2H), 7.37 - 7.34 (m, 3H), 5.55 (s, 1H), 5.16 (d, J = 9.6 Hz, 1H), 4.58 (t, J = 9.0 Hz, 1H), 4.37 (dd, J = 4.8, 10.8 Hz, 1H), 4.19 (t, J = 10.2 Hz, 1H), 3.81 (t, J = 9.6 Hz, 1H), 3,62 - 3.55 (m, 2H), 3.42 (s, 3H).

Compound 13: ^{1}H NMR (400 MHz, $CDCl_3$) δ 7.91 – 7.83 (m, 2H, Ar-H), 7.77 – 7.71 (m, 2H, Ar-H), 7.52 – 7.47 (m, 2H, Ar-H), 7.41 – 7.35 (m, 3H, Ar-H), 5.58 (s, 1H, PhCH), 5.45 (d, J = 9.4 Hz, 1H), 4.66 (dd, J = 10.4, 9.0 Hz, 1H), 4.42 (dd, J = 10.4, 4.8 Hz, 1H), 4.16 (dd, J = 10.4, 9.4 Hz, 1H), 3.83 (t, J = 10.2 Hz, 1H), 3.73 (td, J = 9.6, 4.8 Hz, 1H), 3.61 (t, J = 9.0 Hz, 1H).^{13}C NMR (100 MHz, $CDCl_3$) δ 136.75, 134.39, 131.52, 129.49, 129.30, 128.43, 126.30, 123.71, 115.36, 102.03, 86.25, 81.83, 77.36, 77.25, 77.05, 76.73, 68.36, 68.28, 55.88.

Compound 14: ^{1}H NMR (400 MHz, $CDCl_3$) δ 7.89 – 7.84 (m, 2H, Ar-H), 7.77 – 7.72 (m, 2H, Ar-H), 7.58 – 7.42 (m, 2H, Ar-H), 7.45 – 7.33 (m, 3H, Ar-H), 5.66 – 5.52 (m, 2H), 5.35 (t, J = 9.9 Hz, 1H), 4.37 (dp, J = 10.7, 3.5 Hz, 2H), 4.15 – 4.11 (m, 1H), 3.81 (dd, J = 11.6, 8.8 Hz, 1H), 3.62 (t, J = 9.4 Hz, 1H).

Compounds 15-18



11: R= βOBn; **12**: R= βOCH_3
13: R= βN_3; **14**: R= αN_3

15: R= βOBn; **16**: R= βOCH_3
17: R= βN_3; **18**: R= αN_3

To a solution of **11-14** (2.44 mmol), DMAP (0.07 mmol) and TEA (7.32 mmol) in anhydrous DCM (20.0 mL) was added Ac_2O (3.66 mmol) at 0 °C. After the complete consumption of compound **11-14** monitored by TLC, the reaction was diluted by DCM and washed with water. After removing the solvent, the residue was purified by silica gel column chromatography using PE/EA as eluent to give the desired product **15-18** (87-93% yield).

Compound 15: ^{1}H NMR (400 MHz, $CDCl_3$) δ 7.83 – 7.68 (m, 4H, Ar-H), 7.48 – 7.43 (m, 2H, Ar-H), 7.39 – 7.33 (m, 3H, Ar-H), 7.14 – 6.96 (m, 5H, Ar-H), 5.88 (dd, J = 10.2, 8.7 Hz, 1H), 5.55 (s, 1H), 5.45 (d, J = 8.4 Hz, 1H), 4.85 (d, J = 12.2 Hz, 1H), 4.53 (d, J = 12.2 Hz, 1H), 4.44 (dd, J = 10.4, 4.5 Hz, 1H), 4.34 (dd, J = 10.4, 8.4 Hz, 1H), 3.87 (t, J = 10.0 Hz, 1H), 3.81 – 3.71 (m, 2H).

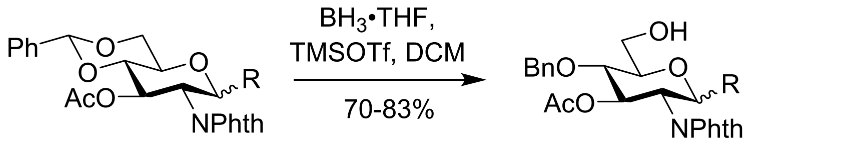
***Compound 16*:** ^{1}H NMR (400 MHz, $CDCl_3$) δ 7. 91 – 7.81 (m, 2H), 7.77 –7.70 (m, 2H), 7.51 – 7.43 (m, 2H), 7.41 – 7.29 (m, 3H), 5.88 (dd, J = 10.3, 8.7 Hz, 1H), 5.55 (s, 1H), 5.37 (d, J = 8.4 Hz, 1H), 4.43 (dd, J = 10.5, 4.3 Hz, 1H), 4.28 (dd, J = 10.3, 8.4 Hz, 1H), 3.89 – 3.71 (m, 3H), 3.45 (s, 3H), 1.89 (s, 3H). ^{13}C NMR (100 MHz, $CDCl_3$) δ 170.19, 136.92, 134.25, 129.18, 129.01, 128.27, 126.26, 123.60, 101.68, 99.65, 79.37, 77.25, 69.80, 68.72, 66.22, 57.28, 55.31, 20.60.

***Compound* 17:** ^{1}H NMR (400 MHz, $CDCl_3$) δ 7.93 – 7.84 (m, 2H), 7.80 – 7.72 (m, 2H), 7.49 – 7.44 (m, 2H), 7.41 – 7.33 (m, 3H), 5.90 (dd, J = 8.8, 10.1, 1H), 5.71 (d, J = 9.3, 1H), 5.56 (s, 1H), 4.46 (d, J = 6.0, 1H), 4.21 (dd, J = 9.4, 10.2, 1H), 3.90 – 3.78 (m, 3H), 1.90 (s, 3H). ^{13}C NMR (100 MHz, $CDCl_3$) δ 170.08, 136.69, 134.59, 134.43, 129.28, 128.30, 126.25, 123.80, 101.77, 86.09, 78.96, 69.46, 68.39, 54.73, 20.54. HRMS (ESI-TOF) *m/z*: $[M + Na]^+$ calcd for $C_{23}H_{20}N_4NaO_7$, 487.1224; found: 487.1213.

***Compound 18*:** ^{1}H NMR (400 MHz, $CDCl_3$) δ 7.92 – 7.87 (m, 2H), 7.80 – 7.74 (m, 2H), 7.49 – 7.44 (m, 2H), 7.40 – 7.34 (m, 3H), 6.61 (dd, J = 9.4, 11.2, 1H), 5.54 (d, J = 3.9, 2H), 4.61 (dd, J = 4.4, 11.2, 1H), 4.39 (dd, J = 5.0, 10.4, 1H), 4.27 (td, J = 5.0, 9.8, 1H), 3.82 (t, J = 10.2, 1H), 3.69 (t, J = 9.5, 1H), 1.93 (s, 3H).^{13}C NMR (100 MHz,

$CDCl_3$) δ 168.67, 136.80, 134.51, 129.07, 128.28, 126.14, 123.83, 101.60, 88.28, 68.50, 65.62, 64.82, 53.46, 20.80. HRMS (ESI-TOF) *m/z*: $[M + Na]^+$ calcd for $C_{23}H_{20}N_4NaO_7$, 487.1224; found: 487.1224.

Compounds 19-22



15: R= βOBn; **16**: R= βOCH_3 **19**: R= βOBn; **20**: R= βOCH_3
17: R= βN_3; **18**: R= αN_3 **21**: R= βN_3; **22**: R= αN_3

A mixture of **15-18** (0.12 mmol) and BH_3·THF (30.45 mmol) was stirred in anhydrous DCM (5.0 mL) at 0 °C for 15 min. Then, TMSOTf (0.13 mmol) was added. After the complete consumption of compound **15-18** monitored by TLC, triethylamine/MeOH (1.0 mL, 1:10, v/v) was added to quench the reaction. The solvent was removed in vacuo, and the residue was purified by silica gel column chromatography using DCM/acetone (10:1, v/v) as eluent to give **19-22** (70-83% yield).

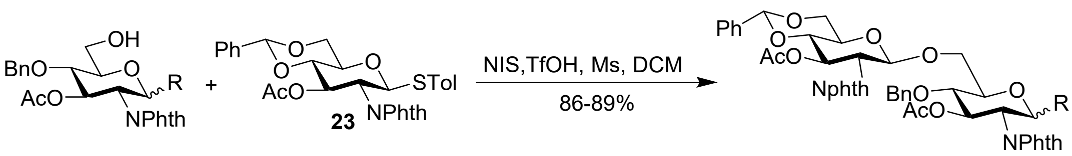
Compound 19: ^{1}H NMR (400 MHz, $CDCl_3$) δ 7.78 - 7.75 (m, 2H), 7.73 - 7.69 (m, 2H), 7.36 – 7.26 (m, 7H), 7.10 - 7.09(m, 3H), 5.79 (dd, *J* = 8.9, 10.7, 1H), 5.46 (d, *J* = 8.5, 1H), 4.80 (d, *J* = 12.2, 1H), 4.66 (d, *J* = 5.5, 2H), 4.55 (d, *J* = 12.2, 1H), 4.24 (dd, *J* = 8.4, 10.6, 1H), 3.95 (dd, *J* = 2.5, 12.1, 1H), 3.82 – 3.76 (m, 2H), 3.65 – 3.60 (m, 1H), 1.77 (s, 3H). ^{13}C NMR (100 MHz, $CDCl_3$) δ 170.05, 167.67, 137.71, 136.97, 134.05, 128.49, 128.23, 127.93, 127.79, 127.65, 123.44.

Compound 20: ^{1}H NMR (400 MHz, $CDCl_3$) δ 7.89 – 7.80 (m, 2H), 7.76 – 7.70 (dd, *J* = 2.9, 5.6, 2H), 7.36 – 7.31 (m, 2H), 7.30 - 7.27 (m, 2H), 5.81 (m, 1H), 5.79 (dd, J = 10.7, 8.9 Hz, 1H), 5.35 (d, J = 8.4 Hz, 1H), 4.73 – 4.63 (m, 2H), 4.17 (dd, J = 10.7, 8.5 Hz, 1H), 3.98 (dd, J = 12.2, 2.6 Hz, 1H), 3.86 – 3.79 (m, 2H), 3.64 (ddd, J = 9.8, 3.7, 2.6 Hz, 1H), 3.44 (s, 3H), 1.78 (s, 3H). ^{13}C NMR (100 MHz, $CDCl_3$) δ 170.04, 137.57, 134.43,128.56, 128.05, 127.85, 123.73, 85.57, 74.86, 72.81, 61.36, 54.60, 20.51.

Compound 21: ^{1}H NMR (400 MHz, $CDCl_3$) δ 7.90 - 7.83 (m, 2H), 7.77 - 7.72 (m, 2H), 7.36 - 7.26 (m, 5H), 5.83 - 5.77 (m, 1H), 5.71 (dd, *J* = 1.3, 9.4, 1H), 4.73 - 4.64 (m, 2H), 4.14 -4.08 (m, 1H), 4.01 (dd, *J* = 2.4, 12.3, 1H), 3.88 - 3.82 (m, 2H), 3.73 (ddd, *J* = 2.4, 3.6, 9.9, 1H), 1.78 (s, 3H). ^{13}C NMR (100 MHz, $CDCl_3$) δ 170.04, 137.57, 134.43,128.56, 128.05, 127.85, 123.73, 85.57, 74.86, 72.81, 61.36, 54.60, 20.51.

Compound 22: ^{1}H NMR (400 MHz, $CDCl_3$) δ 7.90 - 7.83 (m, 2H), 7.79 - 7.71 (m, 2H), 7.36 - 7.31 (m, 4H), 7.31 - 7.27 (m, 1H), 6.50 (dd, J = 9.2, 11.4, 1H), 5.52 (d, J = 4.3, 1H), 4.75 - 4.62 (m, 2H), 4.53 (dd, J = 4.3, 11.4, 1H), 4.10 (dt, J = 2.7, 10.5, 1H), 3.98 - 3.88 (m, 2H), 3.78 (t, J = 9.5, 1H), 1.80 (s, 3H). ^{13}C NMR (100 MHz, $CDCl_3$) δ 168.91, 137.47, 134.51, 131.22, 128.53, 128.26, 128.02, 123.74, 87.81, 74.57, 73.61, 68.34, 61.01, 53.47, 20.92. HRMS (ESI-TOF) *m/z*: [M + Na]$^+$ calcd for $C_{23}H_{20}N_4NaO_7$, 489.1381; found: 489.1383.

Compounds 24 – 27



19: R= βOBn; **20**: R= βOCH$_3$
21: R= βN$_3$; **22**: R= αN$_3$
24: R= βOBn; **25**: R= βOCH$_3$
26: R= βN$_3$; **27**: R= αN$_3$

A mixture of the glycosyl donor **23** (0.71 mmol), which was synthesized with a similar method to previous work,[2] and glycosyl acceptor **19-22** (0.65 mmol) in anhydrous DCM (2.0 mL) was stirred at rt under N_2 atmosphere for 4 h. Then, the reaction mixture was cooled to -30 °C, and NIS (1.94 mmol) was added. After stirring for 1 h, the temperature droped to -40 °C, and TfOH (0.16 mmol) was added. After stirring for another 15 min, the reaction mixture was filtered through a pad of Celite and the residue was washed with DCM (40.0 mL). The combined filtrate was washed with saturated aqueous $Na_2S_2O_4$ solution, followed by saturated aqueous $NaHCO_3$ solution and brine. The organic layer was concentrated in vacuo, and the residue was purified by silica gel column chromatography using PE/EA as eluent to give the desired products **24-27** (86-89% yield).

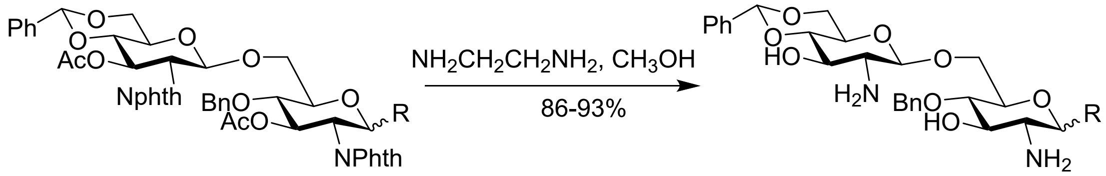
***Compound 24*:** ^{1}H NMR (400 MHz, $CDCl_3$) δ 7.78 - 7.73 (m, 3H), 7.71 - 7.67 (m, 2H), 7.63 7.57 (m, 2H), 7.50 - 7.45 m, 2H), 7.39 - 7.35 (m, 3H), 7.26 - 7.22 (m, 3H), 7.07 - 7.04 (m, 4H), 5.90 (dd, J = 9.1, 10.4, 1H), 5.67 (ddd, J = 1.9, 8.5, 10.8, 1H), 5.61 - 5.54 (m, 2H), 5.30 - 5.26 (m, 1H), 4.63 (d, J = 12.1, 1H), 4.44 (ddd, J = 3.4, 8.2, 10.8, 2H), 4.40 - 4.32 (m, 3H), 4.15 (td, J = 11.0, 2.4 Hz, 2H), 3.93 - 3.63 (m, 6H), 3.54 (t, J = 9.3, 1H), 1.90 (d, J = 0.9, 3H), 1.70 (d, J = 0.9, 3H). ^{13}C NMR (100 MHz, $CDCl_3$) δ 170.24, 169.94, 167.56, 137.42, 136.97, 136.92, 134.46, 134.23, 133.99, 131.31, 129.75, 129.17, 128.99, 128.37, 128.25, 128.14, 127.82, 127.79, 127.76, 127.63, 127.54, 127.46, 126.26, 123.56, 123.38, 101.66, 98.51, 96.87, 74.47, 74.26, 72.94, 70.80, 69.83, 68.68, 68.23, 66.28, 55.30, 55.01, 29.70, 20.61, 20.49. HRMS (ESI-TOF) *m/z*: [M + Na]$^+$ calcd for $C_{53}H_{48}N_2NaO_{15}$, 975.2947; found: 975.2927.

Compound 25**:** ^{1}H NMR (400 MHz, $CDCl_3$) δ 7.85 - 7.77 (m, 4H), 7.72 7.61 (m, 4H), 7.50 - 7.43 (m, 2H), 7.40 - 7.34 (m, 3H), 7.25 - 7.22 (m, 2H), 7.04 (dd, *J* = 2.4, 6.3, 2H), 5.91 (ddd, J = 10.4, 9.0, 1.2 Hz, 1H), 5.66 (ddd, *J* = 1.3, 8.7, 10.3, 1H), 5.61 - 5.55 (m, 2H), 5.18 (dd, *J* = 1.2, 8.4, 1H), 4.48 - 4.33 (m, 4H), 4.16 - 4.05 (m, 2H), 3.89 (t, *J* = 10.1, 1H), 3.80 (ddd, *J* = 7.0, 10.1, 20.1, 3H), 3.64 (dd, *J* = 5.0, 10.1, 1H), 3.53 (t, *J* = 9.3, 1H), 3.24 (d, *J* = 1.3, 3H), 1.90 (d, *J* = 1.3, 3H), 1.70 (d, *J* = 1.2, 3H). ^{13}C NMR (100 MHz, $CDCl_3$) δ 170.26, 170.01, 137.43, 136.92, 134.28, 134.14, 131.36, 129.19, 128.40, 128.28, 127.85, 127.45, 126.27, 123.59, 123.47, 101.67, 98.63, 98.55, 74.55, 74.28, 73.12, 69.83, 68.69, 68.23, 66.35, 56.63, 55.28, 54.92, 26.93, 20.63, 20.50. HRMS (ESI-TOF) *m/z*: [M + Na]$^+$ calcd for $C_{47}H_{44}N_2NaO_{15}$, 899.2634; found: 899.2618.

Compound 26**:** ^{1}H NMR (400 MHz, $CDCl_3$) δ 7.86 - 7.79 (m, 4H), 7.73 - 7.71 (m, 2H), 7.69 - 7.64 (m, 2H), 7.50 - 7.45 (m, 2H), 7.39 - 7.35 (dd, *J* = 2.0, 5.2, 3H), 7.25 - 7.20 (m, 3H), 7.04 - 6.99 (m, 2H), 5.89 (dd, *J* = 9.1, 10.3, 1H), 5.69 - 5.60 (m, 2H), 5.57 - 5.51 (m, 2H), 4.48 - 4.39 (m, 2H), 4.38 -4.30 (m, 2H), 4.13 (dd, *J* = 1.7, 11.3, 1H), 4.02 (dd, *J* = 9.4, 10.6, 1H), 3.93 - 3.81 (m, 3H), 3.76 (td, *J* = 4.7, 9.6, 1H), 3.69 (ddd, *J* = 1.7, 4.8, 9.9, 1H), 3.59 (dd, *J*=8.8, 10.0, 1H), 1.91 (s, 3H), 1.70 (s, 3H). ^{13}C NMR (100 MHz, $CDCl_3$) δ 170.24, 169.89, 137.25, 136.92, 134.29, 131.32, 129.19, 128.41, 128.28, 127.91, 127.43, 126.28, 123.66, 101.70, 98.65, 85.24, 79.20, 76.46, 74.71, 72.76, 69.86, 68.69, 67.91, 66.41, 55.25, 54.42, 20.63, 20.42. HRMS (ESI-TOF) *m/z*: [M + Na]$^+$ calcd for $C_{46}H_{41}N_5NaO_{14}$, 910.2542; found: 910.2533.

Compound 27**:** ^{1}H NMR (400 MHz, $CDCl_3$) δ 7.86 - 7.83 (m, 2H), 7.76 - 7.70 (m, 4H), 7.60 - 7.56 (m, 2H), 7.50 - 7.46 (m, 2H), 7.41 - 7.30 (dd, *J* = 1.9, 5.1, 4H), 7.22 - 7.16 (m, 3H), 6.96 - 6.90 (m, 2H), 6.36 (dd, *J* = 9.1, 11.4, 1H), 5.90 (t, *J* = 9.6, 1H), 5.60 (d, *J* = 8.4, 1H), 5.57 (s, 1H), 5.36 (d, *J* = 4.2, 1H), 4.46 (ddt, *J* = 4.2, 8.4, 11.5, 3H), 4.19 (t, *J* = 11.3, 2H), 4.10 (d, *J* = 10.7, 2H), 3.95 (d, *J* = 10.1, 1H), 3.90 - 3.85 (m, 2H), 3.80 (dt, *J* = 4.7, 9.5, 1H), 3.52 (t, *J* = 9.5, 1H), 1.89 (s, 3H), 1.68 (s, 3H). ^{13}C NMR (100 MHz, $CDCl_3$) δ 170.23, 169.88, 137.27, 136.94, 134.30, 131.33, 129.19, 128.42, 128.28, 127.91, 127.44, 126.28, 123.66, 101.70, 98.67, 85.25, 79.21, 76.48, 74.71, 72.77, 69.88, 68.69, 67.91, 66.42, 55.26, 54.44, 20.63, 20.42. HRMS (ESI-TOF) *m/z*: [M + Na]$^+$ calcd for $C_{46}H_{41}N_5NaO_{14}$, 910.2542; found: 910.2534.

Compounds **28-31**



24: R= βOBn; **25**: R= βOCH_3
26: R= βN_3; **27**: R= αN_3

28: R= βOBn; **29**: R= βOCH_3
30: R= βN_3; **31**: R= αN_3

To a solution of **24-27** (0.32 mmol) in anhydrous MeOH (17.0 mL) was added ethylenediamine (2.0 mL) with dropwise. Then, the reaction mixture was stirred at 80 °C for 10 h. After the complete consumption of compound **24-27** monitored by TLC, the solvent was removed in vacuo. The residue was purified by silica gel column chromatography using PE/EA with 1% triethylamine as eluent to give the desired products **28-31** (86-93% yield).

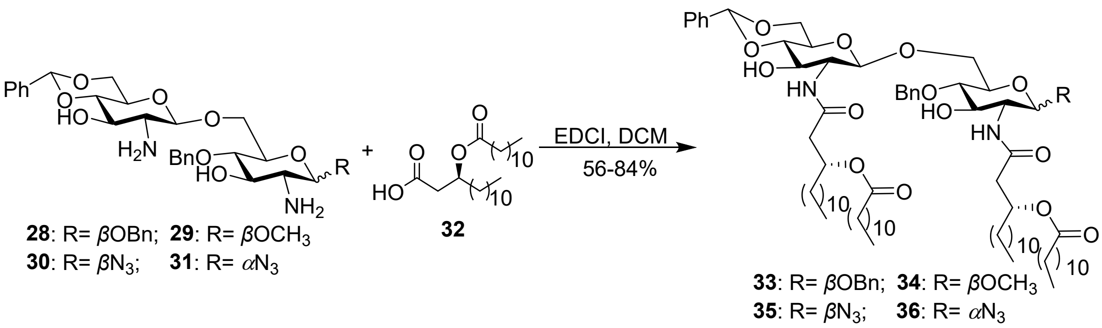
Compound 28: ^{1}H NMR (400 MHz, CD_3OD) δ 7.55 - 7.46 (m, 2H), 7.43 - 7.28 (m, 12H), 5.59 (s, 1H), 4.99 - 4.91 (m, 2H), 4.71 - 4.61 (m, 2H), 4.46 (t, J = 8.2, 2H), 4.25 (dd, J = 4.9, 10.3, 1H), 4.11 (dd, J = 2.0, 11.4, 1H), 3.82 - 3.78 (m, 2H), 3.63 - 3.46 (m, 4H), 3.45 - 3.35 (m, 2H), 2.81 (td, J = 3.6, 8.8, 9.4, 2H). ^{13}C NMR (100 MHz, CD_3OD) δ 138.47, 137.72, 137.45, 128.56, 128.06, 127.95, 127.86, 127.72, 127.68, 127.65, 127.54, 127.38, 127.34, 126.13, 103.87, 101.65, 81.37, 78.67, 78.48, 75.89, 74.70, 74.40, 72.40, 70.79, 70.42, 68.71, 68.26, 66.65, 57.66, 57.10. HRMS (ESI-TOF) *m/z*: $[M + Na]^+$ calcd for $C_{33}H_{40}N_2NaO_9$, 631.2626; found: 631.2605.

Compound 29: ^{1}H NMR (400 MHz, $CDCl_3$) δ 7.52 - 7.46 (m, 2H), 7.40 - 7.29 (m, 8H), 5.53 (s, 1H), 4.84 (d, J = 11.4, 1H), 4.71 (d, J = 11.5, 1H), 4.32 (dd, J = 5.5, 9.3, 2H), 4.17 (d, J = 10.7, 1H), 4.04 (d, J = 7.8, 1H), 3.80 - 3.69 (m, 2H), 3.62 - 3.34 (m, 10H), 2.84 (t, J = 8.5, 1H), 2.63 (t, J = 8.9, 1H). ^{13}C NMR (100 MHz, $CDCl_3$) δ 138.17, 137.08, 129.30, 128.62, 128.38, 128.05, 127.89, 126.27, 105.00, 104.90, 101.93, 81.35, 74.66, 74.62, 73.30, 69.18, 68.74, 66.50, 57.78, 57.52, 57.29. HRMS (ESI-TOF) *m/z*: $[M + Na]^+$ calcd for $C_{27}H_{36}N_2NaO_9$, 555.2313; found: 555.2308.

Compound 30: ^{1}H NMR (400 MHz, CD_3OD) δ 7.51 - 7.47 (m, 2H), 7.39 - 7.27 (m, 9H), 5.58 (s, 1H), 4.96 (d, J = 11.1, 2H), 4.65 (d, J = 11.2, 1H), 4.51 (d, J = 9.0, 1H), 4.38 (d, J = 8.0, 1H), 4.25 (dd, J = 4.8, 10.3, 1H), 4.11 (dd, J = 2.0, 11.2, 1H), 3.79 (d, J = 10.1, 1H), 3.72 (dd, J = 6.1, 11.2, 1H), 3.63 (ddd, J = 1.9, 6.3, 8.2, 1H), 3.55 - 3.35 (m, 6H), 2.73 (t, J = 8.4, 1H), 2.53 (t, J = 9.3, 1H). ^{13}C NMR (100 MHz, CD_3OD) δ 138.45, 137.74, 128.53, 127.94, 127.68, 127.63, 127.37, 126.11, 104.19, 101.64, 90.87, 81.37, 78.04, 76.77, 76.70, 74.40, 72.64, 68.81, 68.27, 66.62, 57.77, 57.05. HRMS (ESI-TOF) *m/z*: $[M + Na]^+$ calcd for $C_{26}H_{33}N_5NaO_8$, 566.2225; found: 566.2221.

Compound 31: ^{1}H NMR (400 MHz, $CDCl_3$) δ 7.53 - 7.47 (m, 2H), 7.40 - 7.32 (m 8H), 5.53 (s, 1H), 5.35 (s, 1H), 4.88 (d, *J* = 11.2, 1H), 4.72 (d, *J* = 11.4, 1H), 4.31 (s, 2H), 4.17 (d, *J* = 10.8, 1H), 3.97 (d, *J* = 9.3, 1H), 3.79 (d, *J* = 11.2, 2H), 3.55 (s, 3H), 3.42 (s, 2H), 2.88 (s, 1H), 2.77 (s, 1H). ^{13}C NMR (100 MHz, $CDCl_3$) δ 138.21, 137.06, 129.28, 128.59, 128.36, 127.99, 127.83, 126.25, 104.92, 101.91, 91.06, 81.24, 74.49, 74.30, 73.20, 72.19, 68.68, 66.56, 57.70, 55.36. HRMS (ESI-TOF) *m/z*: $[M + Na]^+$ calcd for $C_{26}H_{33}N_5NaO_8$, 566.2221; found: 566.2213.

Compounds 33-36



28: R= βOBn; **29**: R= βOCH3
30: R= βN3; **31**: R= αN3
32
33: R= βOBn; **34**: R= βOCH3
35: R= βN3; **36**: R= αN3

A mixture of the **28-31** (16 µmol), fatty acid **32** (40 µmol) and EDCI (0.16 mmol) was stirred in anhydrous DCM (4.0 mL) at rt under N_2 atmosphere. After the complete consumption of compound **28-31** monitored by TLC, the reaction mixture was diluted with DCM (30.0 mL) and washed with brine. The organic layer was dried over anhydrous Na_2SO_4, filtered and concentrated. The residue was purified by silica gel column chromatography using DCM/acetone as eluent to give **33-36** (56-84% yield).

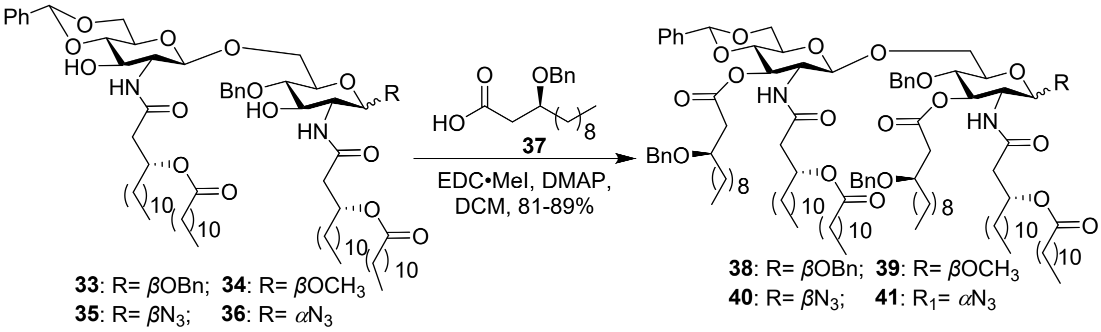
Compound 33**:** ^{1}H NMR (400 MHz, $CDCl_3$) δ 7.58 – 7.46 (m, 2H), 7.40 – 7.26 (m, 21H), 6.08 – 6.01 (m, 2H), 5.54 (s, 1H), 5.11 – 5.05 (m, 2H), 4.98 (d, *J* = 11.2 Hz, 1H), 4.88 (d, *J* = 11.8 Hz, 1H), 4.79 (d, *J* = 8.4 Hz, 1H), 4.68 – 4.52 (m, 3H), 4.33 – 4.29 (m, 1H), 4.14 (dd, *J* = 9.1, 2.8 Hz, 2H), 3.87 (t, *J* = 8.9 Hz, 1H), 3.78 – 3.72 (m, 2H), 3.60 (t, *J* = 7.0 Hz, 1H), 3.55 (t, *J* = 8.9 Hz, 2H), 3.50 – 3.36 (m, 4H), 2.70 – 1.92 (m, 12H), 1.58 (s, 12H), 1.24 (d, *J* = 4.3 Hz, 94H), 0.88 (t, *J* = 6.6 Hz, 17H). ^{13}C NMR (100 MHz, $CDCl_3$) δ 174.35, 174.13, 171.38, 138.26, 137.09, 136.99, 129.16, 128.62, 128.46, 128.25, 128.18, 128.06, 127.90, 126.38, 101.95, 100.61, 99.15, 81.46, 78.31, 77.22, 76.18, 74.61, 74.45, 71.48, 71.32, 70.98, 70.60, 68.61, 66.37, 59.14, 42.41, 34.58, 34.48, 31.92, 29.64, 29.57, 29.53, 29.36, 29.31, 29.18, 25.27, 24.99, 22.69, 14.13. HRMS (ESI-TOF) *m/z*: $[M + Na]^+$ calcd for $C_{33}H_{40}N_2NaO_9$, 1447.9833; found: 1447.9844.

Compound 34**:** ^1H NMR (400 MHz, $CDCl_3$) δ 7.52 - 7.47 (m, 2H), 7.38 - 7.30 (m, 8H), 6.12 (d, J = 22.1 Hz, 2H), 5.53 (s, 1H), 5.12 (d, J = 19.7, 2H), 4.98 (d, J = 11.1, 1H), 4.80 (d, J = 8.2, 1H), 4.65 (d, J = 11.1, 1H), 4.43 (s, 1H), 4.31 (dd, J = 4.6, 10.5, 1H), 4.19 - 4.09 (m, 2H), 3.90 (dd, J = 6.7, 12.7, 1H), 3.75 (q, J = 9.0, 9.7, 2H), 3.58 - 3.37 (m, 10H), 2.50 (d, J = 5.8, 2H), 2.31 (dq, J = 8.2, 9.1, 16.2, 6H), 1.77 - 1.37 (m, 12H), 1.30 - 1.23 (m, 65H), 0.88 (t, J = 6.6, 12H). ^{13}C NMR (100 MHz, $CDCl_3$) δ 174.30, 174.08, 171.41, 137.08, 129.15, 128.47, 128.24, 128.08, 127.92, 126.37, 101.93, 100.85, 100.63, 81.45, 78.38, 74.58, 74.49, 71.47, 71.30, 71.02, 68.61, 68.43, 66.40, 59.20, 57.92, 56.36, 42.42, 34.59, 34.53, 34.46, 31.92, 29.64, 29.53, 29.36, 29.32, 29.20, 25.28, 25.23, 25.00, 22.70, 14.12. HRMS (ESI-TOF) *m/z*: $[M + Na]^+$ calcd for $C_{79}H_{132}N_2NaO_{15}$, 1371.9520; found:1371.9237.

Compound 35**:** ^1H NMR (400 MHz,$CDCl_3$) δ 7.45 - 7.39 (m, 2H), 7.33 - 7.21 (m, 8H), 6.19 (d, J = 7.6, 1H), 6.05 (d, J = 6.3, 1H), 5.45 (s, 1H), 5.05 (dp, J = 6.3, 25.3, 2H), 4.86 (d, J = 11.3, 1H), 4.71 (t, J = 8.4, 2H), 4.57 (d, J = 11.2, 1H), 4.24 (dd, J = 4.8, 10.5, 1H), 4.09 - 3.99 (m, 2H), 3.85 (t, J = 9.3, 1H), 3.70 (d, J = 10.1, 1H), 3.64 - 3.54 (m, 2H), 3.53 - 3.34 (m, 4H), 3.28 (t, J = 8.9, 1H), 2.47 - 2.17 (m, 8H), 1.77 - 1.32 (m, 12H), 1.28 - 1.12 (m, 64H), 0.81 (t, J = 6.7, 12H). ^{13}C NMR (100 MHz, $CDCl_3$) δ 174.53, 174.47, 171.47, 171.37, 138.01, 137.09, 129.16, 128.52, 128.25, 128.08, 128.01, 126.38, 101.92, 100.91, 87.62, 81.47, 75.65, 74.63, 71.50, 71.32, 68.58, 66.37, 58.93, 56.95, 42.59, 42.21, 34.64, 34.57, 34.45, 31.93, 29.66, 29.60, 29.58, 29.54, 29.37, 29.33, 29.21, 25.31, 25.22, 25.03, 24.98, 22.70, 14.13. HRMS (ESI-TOF) *m/z*: $[M + Na]^+$ calcd for $C_{78}H_{129}N_5NaO_{14}$, 1382.9428; found:1382.9151.

Compound 36**:** ^1H NMR (400 MHz, $CDCl_3$) δ 77.52 - 7.47 (m, 2H), 7.35 - 7.29 (m, 8H), 6.03 (d, J = 6.4, 1H), 5.94 (d, J = 8.4, 1H), 5.53 (s, 1H), 5.43 (d, J = 4.2, 1H), 5.16 (dt, J = 11.8, 5.8 Hz, 1H), 5.10 - 5.01 (m, 1H), 4.90 (d, J = 11.2, 1H), 4.82 (d, J = 8.3, 1H), 4.66 (d, J = 11.2, 1H), 4.32 (dd, J = 4.6, 10.4, 1H), 4.22 (t, J = 9.2, 1H), 4.17 - 4.09 (m, 2H), 3.92 (dt, J = 2.7, 10.1, 1H), 3.84 - 3.71 (m, 3H), 3.57 - 3.41 (m, 4H), 2.50 (d, J = 6.1, 2H), 2.39 - 2.23 (m, 6H), 1.86 - 1.45 (m, 12H), 1.31 - 1.21 (d, J = 4.9, 65H), 0.91 - 0.83 (m, 12H). ^{13}C NMR (100 MHz, $CDCl_3$) δ 174.05, 170.69, 138.08, 129.16, 128.62, 128.26, 128.10, 127.97, 126.38, 101.93, 100.46, 88.16, 81.40, 74.74, 73.11, 72.00, 71.59, 71.14, 70.59, 68.59, 67.87, 66.41, 59.19, 52.97, 42.52, 42.10, 34.59, 34.56, 34.50, 34.34, 31.92, 29.64, 29.58, 29.56, 29.52, 29.36, 29.31, 29.28, 29.20, 29.18, 25.30, 25.18, 24.99, 24.97, 22.69, 14.12. HRMS (ESI-TOF) *m/z*: $[M + Na]^+$ calcd for $C_{26}H_{33}N_5NaO_8$, 1382.9428; found: 1382.9140.

Compounds 38-41



A mixture of the **33-36** (90 μmol), fatty acid **37** (200 μmol) and DMAP (18 μmol) was stirred in anhydrous DCM (4.0 mL) at rt. The reaction mixture was then cooled to 0 °C, and EDC·MeI (400 μmol) was added. After the complete consumption of compound **33-36** monitored by TLC, the reaction mixture was diluted with DCM (30.0 mL) and washed with brine. The organic layer was dried over anhydrous Na_2SO_4, filtered and concentrated. The residue was purified by silica gel column chromatography using DCM/acetone as eluent to give **38-41** (81 – 89% yield).

Compound 38**:** ^{1}H NMR (400 MHz, $CDCl_3$) δ 7.41 - 7.37 (m, 7.4, 2H), 7.34 - 7.31 (m, 4H), 7.28 - 7.26 (m, 4H), 7.25 - 7.21 (m, 8H), 7.21 - 7.18 (m, 2H), 5.83 (dd, *J* = 8.6, 13.1, 2H), 5.41 (s, 1H), 5.33 (t, *J* = 9.8, 1H), 5.19 - 5.12 (m, 1H), 5.03 (dq, *J* = 6.0, 17.3, 2H), 4.85 (d, *J* = 12.3, 1H), 4.76 (d, *J* = 8.2, 1H), 4.65 - 4.55 (m, 3H), 4.49 (dd, *J* = 8.2, 12.4, 4H), 4.44 - 4.38 (m, 1H), 4.30 (dd, *J* = 4.9, 10.5, 1H), 4.01 (dd, J = 10.5, 6.5 Hz, 2H), 3.87 - 3.77 (m, 3H), 3.76 - 3.69 (m, 2H), 3.64 (t, *J* = 9.4, 1H), 3.56 (d, *J* = 6.3, 2H), 3.44 (td, *J* = 5.0, 9.7, 1H), 2.66 (dd, *J* = 6.3, 15.0, 1H), 2.62 - 2.41 (m 4H), 2.40 - 2.18 (m, 8H), 2.15 (dd, *J* = 5.8, 14.9, 1H), 1.59 - 1.45 (m, 12H), 1.30 - 1.20 (m, 95H), 0.88 (t, *J* = 6.7, 18H). ^{13}C NMR (100 MHz, $CDCl_3$) δ 173.78, 173.53, 171.66, 171.30, 169.66, 169.53, 138.50, 138.46, 137.61, 137.50, 136.91, 129.02, 128.48, 128.44, 128.32, 128.30, 128.16, 127.88, 127.82, 127.79, 127.73, 127.71, 127.68, 127.55, 127.52, 126.14, 101.42, 101.35, 99.76, 78.82, 75.61, 75.46, 74.87, 74.28, 71.40, 71.31, 71.15, 70.99, 70.88, 70.14, 68.62, 68.01, 66.34, 55.14, 53.96, 41.76, 41.58, 39.61, 39.55, 34.54, 34.47, 34.42, 34.18, 34.14, 31.95, 29.74, 29.71, 29.68, 29.67, 29.65, 29.63, 29.60, 29.56, 29.49, 29.48, 29.41, 29.40, 29.38, 29.27, 29.23, 25.25, 25.20,

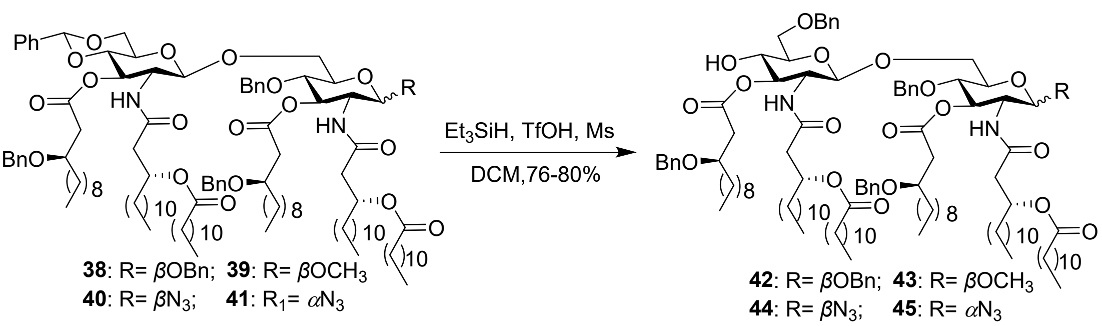
25.05, 25.00, 22.72, 14.15. HRMS (ESI-TOF) *m/z*: $[M + Na]^+$ calcd for $C_{123}H_{192}N_2NaO_{19}$, 2024.4012; found: 2024.3636.

Compound 39: ^{1}H NMR (400 MHz, $CDCl_3$) δ 7.39 (dd, *J* = 2.2, 7.6, 2H), 7.27 (d, *J* = 4.3, 8H), 7.26 - 7.22 (m, 8H), 7.21 - 7.18 (m, 2H), 5.83 (dd, *J* = 8.7, 16.7, 2H), 5.42 (s, 1H), 5.37 (s, 1H), 5.18 (t, J = 8.3 Hz, 1H), 5.04 (dt, *J* = 6.2, 19.6, 2H), 4.85 (d, *J* = 8.3, 1H), 4.57 (d, *J* = 11.3, 1H), 4.52 - 4.38 (m, 7H), 4.31 (dd, *J* = 4.9, 10.5, 1H), 4.01 (d, *J* = 10.8, 1H), 3.91 (d, *J* = 9.5, 1H), 3.85 - 3.76 (m, 4H), 3.75 - 3.70 (m, 2H), 3.65 (s, 1H), 3.56 - 3.53 (m, 2H), 3.50 (dd, *J* = 4.7, 9.8, 1H), 3.44 (s, 3H), 2.68 - 2.62 (m, 1H), 2.58 - 2.42 (m, 4H), 2.40 - 2.23 (m, 9H), 2.19 (d, *J* = 5.9, 1H), 1.62 - 1.51 (m, 12H), 1.28 - 1.22 (m, 95H), 0.88 (t, *J* = 6.7, 18H). ^{13}C NMR (100 MHz, $CDCl_3$) δ 173.81, 173.54, 171.66, 169.67, 138.47, 138.42, 129.01, 128.45, 128.31, 128.28, 128.15, 127.90, 127.83, 127.71, 127.54, 127.51, 126.11, 101.52, 101.41, 101.26, 78.81, 77.23, 75.90, 75.60, 75.44, 74.81, 74.30, 71.34, 71.28, 71.14, 71.11, 70.86, 68.60, 67.99, 66.42, 56.19, 55.24, 53.78, 41.89, 41.56, 39.56, 34.53, 34.49, 34.38, 34.16, 31.93, 29.72, 29.69, 29.66, 29.61, 29.55, 29.49, 29.46, 29.40, 29.37, 29.35, 29.25, 25.26, 25.22, 25.19, 25.04, 25.00, 22.70, 14.12. HRMS (ESI-TOF) *m/z*: $[M + Na]^+$ calcd for $C_{117}H_{188}N_2NaO_{19}$, 1948.3699; found:1948.3439.

Compound 40: ^{1}H NMR (400 MHz,$CDCl_3$) δ 7.41 - 7.36 (m, 2H), 7.29 - 7.26 (m, 9H), 7.26 - 7.22 (m, 7H), 7.21 - 7.16 (m, 2H), 5.92 (d, *J* = 9.0, 1H), 5.78 (d, *J* = 8.6, 1H), 5.43 (s, 1H), 5.33 (q, *J* = 9.5, 1H), 5.18 (t, *J* = 9.6, 1H), 5.06 (dq, *J* = 6.4, 26.2, 2H), 4.84 (d, *J* = 8.3, 1H), 4.59 (dd, *J* = 10.2, 15.6, 2H), 4.52 - 4.38 (m, 5H), 4.33 (dd, *J* = 4.9, 10.6, 1H), 4.02 (d, *J* = 11.4, 1H), 3.94 - 3.71 (m, 6H), 3.64 (dt, *J* = 7.6, 15.1, 2H), 3.57 - 3.46 (m, 3H), 2.65 (dd, *J* = 6.2, 15.1, 1H), 2.58 - 2.44 (m, 3H), 2.38 - 2.16 (m, 8H), 1.66 - 1.50 (m, 12H), 1.32 - 1.18 (m, 95H), 0.88 (t, *J* = 6.7, 18H). ^{13}C NMR (100 MHz, $CDCl_3$) δ 172.87, 172.48, 170.74, 170.33, 168.87, 168.73, 137.40, 136.35, 135.83, 128.00, 127.46, 127.30, 127.28, 127.13, 126.96, 126.86, 126.71, 126.68, 126.57, 126.51, 125.10, 100.63, 100.42, 87.26, 74.58, 74.55, 74.40, 73.69, 73.55, 70.37, 70.22, 70.09, 69.92, 67.58, 66.87, 65.41, 54.07, 52.85, 40.75, 40.47, 38.48, 33.56, 33.46, 33.36, 33.23, 33.18, 33.04, 30.91, 28.70, 28.67, 28.64, 28.60, 28.58, 28.53, 28.48, 28.42, 28.38, 28.35, 28.33, 28.23, 24.21, 24.17, 24.04, 23.98, 21.68, 13.11. HRMS (ESI-TOF) *m/z*: $[M + Na]^+$ calcd for $C_{116}H_{185}N_5NaO_{18}$, 1959.3607; found: 1959.3299.

Compound 41: ^{1}H NMR (400 MHz, $CDCl_3$) δ 7.40 - 7.37 (m, 2H), 7.34 - 7.27 (m, 7H), 7.25 (d, *J* = 3.9, 9H), 7.19 (dd, *J* = 2.8, 6.8, 2H), 5.97 (d, *J* = 8.2, 1H), 5.87 (d, *J* = 8.3, 1H), 5.48 (d, *J* = 4.1, 1H), 5.42 (s, 1H), 5.18 (dd, *J* = 9.2, 10.9, 1H), 5.11 - 5.06 (m, 1H), 4.98 (t, J = 6.1 Hz, 1H), 4.93 (d, *J* = 8.3, 1H),4.62 - 4.56 (m, 1H), 4.33 (dd, *J* = 4.8, 10.4, 1H), 4.18 (td, *J* = 4.1, 7.8, 1H), 4.03 (d, *J* = 10.7, 1H), 3.99 - 3.93 (m, 1H), 3.88 - 3.74 (m, 6H), 3.68 (dt, *J* = 4.7, 9.4, 2H), 3.54 (td, *J* = 5.0, 9.7, 1H), 2.68 - 2.43 (m, 5H), 2.36 - 2.24 (m, 8H), 2.09 (dd, *J* = 5.4, 15.1, 1H), 1.63 - 1.47 (m, 12H), 1.29 - 1.21(m, 95H), 0.88 (t, *J* = 6.8, 18H). ^{13}C NMR (100 MHz, $CDCl_3$) δ 173.74, 173.10, 172.59, 171.14, 169.98, 169.81, 138.41, 138.39, 137.51, 136.87, 129.01, 128.52, 128.33, 128.29, 128.15, 127.98, 127.70, 127.59, 127.53, 126.13, 101.43, 101.04, 88.01, 75.67, 75.30, 75.21, 74.83, 72.69, 72.23, 71.24, 71.20, 71.14, 70.84, 70.62, 68.56, 67.45, 66.42, 55.54, 52.19, 41.55, 41.50, 39.61, 39.42, 34.46, 34.37, 34.32, 34.18, 31.93, 29.73, 29.71, 29.68, 29.65, 29.61, 29.57, 29.53, 29.47, 29.40, 29.36, 29.24, 29.22, 25.28, 25.22, 25.18, 25.04, 25.00, 22.69, 14.12. HRMS (ESI-TOF) *m/z*: [M + Na]$^+$ calcd for $C_{116}H_{185}N_5NaO_{18}$, 1959.3607; found: 1959.3299.

Compounds **42-45**



A mixture of **38-41** (90.1 μmol) and 4 Å molecular sieves was stirred in anhydrous DCM (10.0 mL) at rt for 15 min. Then, Et_3SiH (326.4 μmol) and TfOH (271.8 μmol) were added at –78 °C. After the complete consumption of compound **38-41** monitored by TLC, triethylamine/MeOH (1.0 mL, 1:10, v/v) was added to quench the reaction. The solvent was removed in vacuo, and the residue was purified by silica gel column chromatography using DCM/acetone as eluent to give **42-45** (76-80% yield).

Compound 42: ^{1}H NMR (400 MHz, $CDCl_3$) δ 7.34 - 7.26 (m, 18H), 7.25 - 7.16 (m, 7H), 5.70 (d, J = 9.8, 2H), 5.12 (t, J = 8.6, 1H), 5.02 (dd, J = 13.6, 7.8 Hz, 3H), 4.83 (d, J = 12.1, 1H), 4.67 (d, J = 8.0, 1H), 4.63 - 4.41 (m, 10H),4.02 (d, J = 9.1 Hz, 2H), 3.82 (dq, J = 6.0, 23.3, 3H), 3.70 (d, J = 4.1, 3H), 3.63 (t, J = 9.1, 1H), 3.56 (d, J = 7.6, 2H), 3.48 (q, J = 4.5, 1H), 2.74- 2.39 (m, 5H), 2.37 - 2.20 (m, 9H), 1.60 - 1.45 (m, 12H), 1.32 - 1.20 (m, 95H), 0.88 (t, J = 6.6, 18H). ^{13}C NMR (100 MHz, $CDCl_3$) δ 173.61, 173.50, 172.23, 171.65, 169.55, 169.47, 138.49, 138.10, 137.83, 137.62, 137.47, 128.44, 128.42, 128.38, 128.27, 127.90, 127.85, 127.80, 127.74, 127.72, 127.67, 127.66, 127.49, 100.91, 99.76, 75.92, 75.41, 74.97, 74.85, 74.26, 74.21, 73.63, 71.26, 71.16, 70.97, 70.90, 70.56, 70.19, 70.10, 67.79, 54.09, 54.02, 41.71, 41.61, 39.65, 39.55, 34.50, 34.45, 34.18, 34.10, 31.93, 29.72, 29.69, 29.66, 29.63, 29.59, 29.55, 29.47, 29.39, 29.36, 29.24, 29.21, 25.23, 25.20, 25.18, 25.02, 24.98, 22.70, 14.12. HRMS (ESI-TOF) m/z: $[M + Na]^+$ calcd for $C_{123}H_{194}N_2NaO_{19}$, 2026.4168; found: 2026.3898.

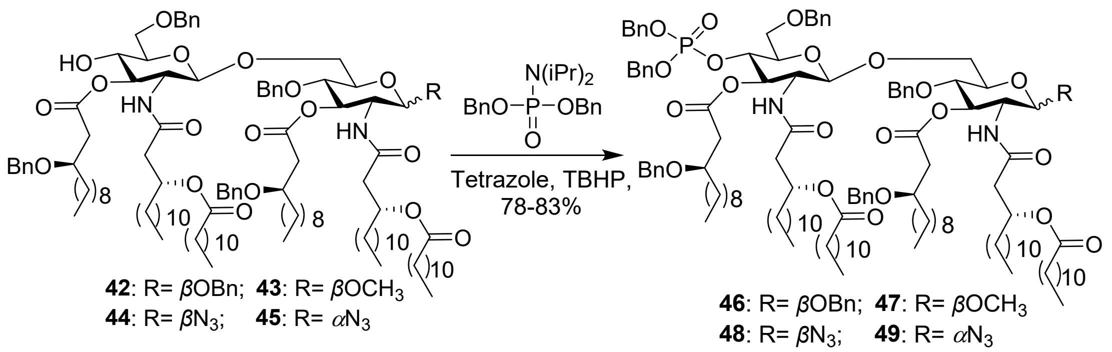
Compound 43: ^{1}H NMR (400 MHz, $CDCl_3$) δ 7.35 - 7.26 (m, 14H), 7.24 - 7.17 (m, 6H), 5.78 (dd, J = 8.7, 17.7, 2H), 5.16 (d, J = 9.0, 1H), 5.10 - 4.99 (m, 3H), 4.72 (d, J = 8.2, 1H), 4.59 - 4.45 (m, 8H), 4.42 - 4.38 (m, 1H), 4.02 (d, J = 11.0, 1H), 3.95 - 3.77 (m, 4H), 3.71 (d, J = 4.6, 3H), 3.64 (t, J = 9.1, 1H), 3.53 (dd, J = 5.7, 10.8, 3H), 3.41 (s, 3H), 2.63 (dd, J = 7.4, 14.8, 1H), 2.57 - 2.50 (m, 2H), 2.44 (d, J = 5.1 Hz, 1H), 2.35 (dd, J = 6.7, 14.7, 2H), 2.28 (t, J = 7.6, 5H), 2.19 (dd, J = 6.5, 15.4, 1H), 1.68 - 1.48 (m, 12H), 1.29 - 1.21 (m, 95H), 0.88 (t, J = 6.7, 18H). ^{13}C NMR (100 MHz, $CDCl_3$) δ 173.63, 173.50, 172.24, 171.67, 169.61, 169.54, 138.49, 138.09, 137.83, 137.61, 128.45, 128.40, 128.39, 128.27, 127.90, 127.87, 127.82, 127.75, 127.71, 127.68, 127.49, 101.55, 100.83, 75.96, 75.41, 74.92, 74.81, 74.30, 73.64, 71.24, 71.15, 71.10, 70.90, 70.49, 70.14, 67.69, 56.18, 54.10, 53.81, 41.87, 41.60, 39.65, 39.53, 34.50, 34.18, 34.14, 34.11, 34.06, 31.93, 29.72, 29.69, 29.66, 29.62, 29.59, 29.55, 29.49, 29.46, 29.39, 29.37, 29.35, 29.24, 25.25, 25.20, 25.03, 25.00, 22.70, 14.13. HRMS (ESI-TOF) m/z: $[M + Na]^+$ calcd for $C_{117}H_{190}N_2O_{19}$, 1950.3855; found: 1950.3600.

Compound 44: ^{1}H NMR (400 MHz, $CDCl_3$) δ 7.34 - 7.27 (m 15H), 7.23 - 7.21 (m, 3H), 7.19 - 7.16 (m, 2H), 5.85 (d, *J* = 9.0, 1H), 5.74 (d, *J* = 8.5, 1H), 5.15 (d, *J* = 9.6, 1H), 5.10 - 5.00 (m, 3H), 4.72 (d, *J* = 8.2, 1H), 4.62 - 4.42 (m, 11H), 4.02 (d, *J* = 11.4, 1H), 3.92 - 3.76 (m, 5H), 3.72 (d, *J* = 4.7, 3H), 3.63 (d, *J* = 9.4, 2H), 3.57 - 3.51 (m, 2H), 2.64 (dd, *J* = 7.3, 14.7, 1H), 2.52 (dt, *J* = 5.5, 15.7, 2H), 2.45 (d, *J* = 5.1 Hz, 1H), 2.40 - 2.11 (m, 10H), 1.63 - 1.50 (m, 12H), 1.28 - 1.22 (m, 95H), 0.88 (t, *J* = 6.7, 18H). ^{13}C NMR (100 MHz, $CDCl_3$) δ 173.78, 172.28, 171.77, 169.86, 169.68, 138.42, 138.10, 137.88, 137.41, 128.47, 128.41, 128.34, 127.94, 127.76, 127.71, 127.60, 101.16, 88.34, 75.63, 75.40, 74.77, 74.56, 74.34, 73.67, 71.23, 71.15, 71.00, 70.93, 70.44, 70.17, 67.66, 54.07, 53.87, 41.75, 41.56, 39.65, 39.47, 34.57, 34.49, 34.21, 34.09, 31.95, 29.73, 29.68, 29.62, 29.52, 29.40, 29.27, 25.23, 25.07, 25.02, 22.72, 14.16, 14.14.

HRMS (ESI-TOF) m/z: [M + Na]$^+$ calcd for $C_{116}H_{187}N_5NaO_{18}$, 1961.3763; found: 1961.3488.

Compound 45: ^{1}H NMR (400 MHz, $CDCl_3$) δ 7.35 - 7.26 (m, 14H), 7.25 - 7.17 (m, 6H), 5.94 (d, J = 8.1, 1H), 5.75 (d, J = 8.2, 1H), 5.46 (d, J = 4.1, 1H), 5.20 - 5.05 (m, 3H), 5.00 (q, J = 5.9, 1H), 4.77 (d, J = 8.1, 1H), 4.60 - 4.41 (m, 8H), 4.22 - 4.12 (m, 1H), 4.03 (d, J = 10.8, 1H), 3.95 (dd, J = 3.8, 10.0, 1H), 3.89 - 3.63 (m, 8H), 3.55 (dt, J = 4.6, 9.3, 1H), 2.64 (dd, J = 7.2, 14.7, 1H), 2.54 (ddd, J = 3.4, 6.1, 15.9, 2H), 2.42 (dd, J = 5.2, 15.8, 1H), 2.36 - 2.22 (m, 7H), 2.13 (dd, J=5.3, 14.8, 1H), 1.66 - 1.46 (m, 12H), 1.31 - 1.19 (m, 95H), 0.88 (td, J = 1.4, 6.8, 18H). ^{13}C NMR (100 MHz, $CDCl_3$) δ 173.58, 173.11, 172.58, 172.17, 169.92, 169.67, 138.40, 138.06, 137.79, 137.61, 128.47, 128.44, 128.40, 128.29, 127.92, 127.89, 127.77, 127.74, 127.71, 127.68, 127.52, 100.65, 87.99, 75.95, 75.30, 75.18, 74.77, 74.33, 73.63, 72.73, 72.41, 71.22, 71.15, 70.85, 70.73, 70.63, 70.21, 66.97, 54.29, 41.61, 41.47, 39.58, 34.45, 34.35, 34.19, 34.12, 34.03, 31.93, 29.73, 29.71, 29.68, 29.65, 29.62, 29.60, 29.58, 29.53, 29.47, 29.41, 29.39, 29.36, 29.23, 25.22, 25.17, 25.04, 25.00, 22.70, 14.13. HRMS (ESI-TOF) *m/z*: [M + Na]$^+$ calcd for $C_{116}H_{187}N_5NaO_{18}$, 1961.3763; found: 1961.3372.

Compounds 46-49



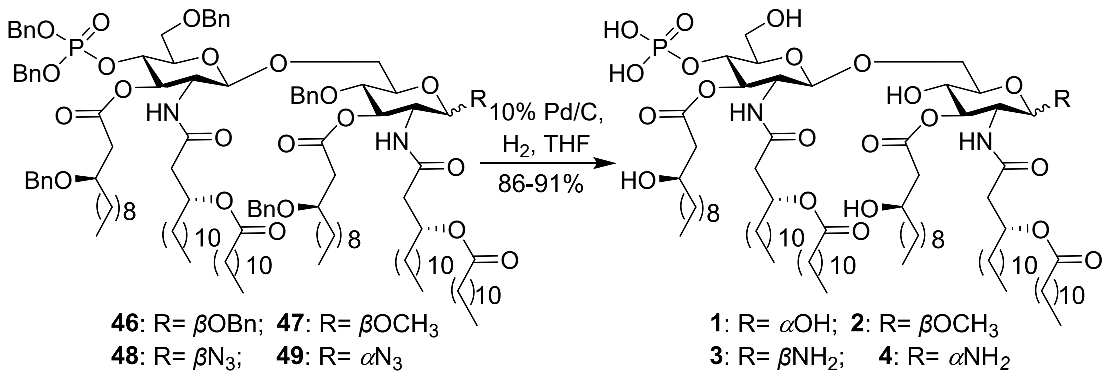
To a solution of **42-45** (40.2 μmol) in anhydrous DCM (1.0 mL) and acetonitrile (2.0 mL) at rt under N_2 atmosphere was added dibenzyl diisopropylphosphoramidite (913.0 μmol) and 1,2,4-triazole (0.45 M, 1.3 mL, 913.0 μmol). After the complete consumption of compound **42-45** monitored by TLC, the mixture was cooled to 0 °C, and TBHP (1540.0 μmol) was added with dropwise. Then, the reaction performed at rt for 1 h. The mixture was filtered through a pad of Celite and the filtrate was concentrated in vacuo. The crude product was purified by silica gel column chromatography using DCM/MeOH as eluent to give **46-49** (78-83% yield).

Compound 46: ^{1}H NMR (400 MHz, $CDCl_3$) δ 7.38 - 7.27 (m, 23H), 7.25 - 7.14 (m, 12H), 5.73 (d, *J* = 8.7, 1H), 5.60 (s, 1H), 5.47 (d, *J* = 9.4 Hz, 1H), 5.04 (ddd, *J* = 11.8, 21.2, 27.0, 5H), 4.88 (d, *J* = 7.6, 4H), 4.63 - 4.37 (m, 11H), 4.01 (d, *J* = 10.4, 2H), 3.76 (tt, *J* = 5.8, 12.1, 4H), 3.68 - 3.34 (m, 6H), 2.57 - 2.40 (m, 4H), 2.37 - 2.14 (m, 8H), 2.04 - 1.94 (m, 2H), 1.66 - 1.46 (m, 12H), 1.28 - 1.17 (m, 95H), 0.88 (t, *J* = 6.7, 18H). ^{13}C NMR (100 MHz, $CDCl_3$) δ 169.78, 138.49, 138.20, 137.52, 135.59, 128.53, 128.50, 128.47, 128.42, 128.31, 128.27, 128.01, 127.93, 127.85, 127.71, 127.66, 127.63, 127.58, 127.48, 99.88, 75.65, 75.39, 74.84, 74.35, 73.33, 71.26, 70.97, 70.93, 70.47, 70.23, 69.59, 68.60, 68.07, 55.87, 54.06, 41.71, 41.14, 39.54, 38.67, 34.48, 34.45, 34.19, 34.09, 34.01, 31.93, 29.75, 29.72, 29.70, 29.67, 29.63, 29.60, 29.54, 29.47, 29.43, 29.40, 29.38, 29.36, 29.28, 29.20, 25.39, 25.23, 25.18, 25.14, 25.01, 24.98, 22.70, 14.13. ^{31}P NMR (162 MHz, $CDCl_3$) δ –2.14. HRMS (ESI-TOF) m/z: $[M + Na]^+$ calcd for $C_{137}H_{207}N_2NaO_{22}P$, 2286.4770; found: 2286.4549.
Compound 47: ^{1}H NMR (400 MHz,$CDCl_3$) *δ* 7.37 - 7.27 (m, 26H), 7.25 - 7.17 (m, 14H), 5.82 (d, *J* = 9.3, 1H), 5.63 (d, *J* = 7.7, 1H), 5.48 (t, *J* = 9.6, 1H), 5.17 - 4.95 (m, 9H), 4.88 (dd, *J* = 3.0, 7.5, 4H), 4.53 - 4.37 (m, 10H), 4.02 - 3.92 (m, 2H), 3.84 - 3.70 (m, 5H), 3.65 (d, *J* = 8.6, 2H), 3.53 (d, *J* = 6.2, 2H), 3.42 (s, 5H), 2.51 (dt, *J* = 7.1, 11.2, 3H), 2.45 - 2.41 (m, 2H), 2.28 (dt, *J* = 4.1, 8.6, 8H), 2.00 (dd, *J* = 5.5, 15.3, 2H), 1.62 - 1.52 (m, 12H), 1.29 - 1.22 (m, 95H), 0.88 (t, *J* = 6.7, 18H). ^{13}C NMR (100 MHz, $CDCl_3$) *δ* 169.62, 138.49, 135.61, 128.53, 128.50, 128.43, 128.32, 128.27, 128.01, 127.94, 127.87, 127.71, 127.58, 127.49, 101.62, 99.77, 75.65, 75.39, 75.03, 74.75, 74.37, 74.14, 73.34, 72.23, 71.23, 71.13, 70.91, 70.46, 69.60, 69.54, 68.58, 67.98, 56.31, 55.92, 53.84, 41.86, 41.09, 39.52, 38.66, 34.48, 34.19, 34.12, 33.98, 31.93, 29.75, 29.72, 29.70, 29.66, 29.64, 29.62, 29.54, 29.46, 29.43, 29.39, 29.37, 29.28, 29.24, 25.38, 25.26, 25.17, 25.02, 25.00, 22.70, 14.13. ^{31}P NMR (162 MHz, $CDCl_3$) *δ* -2.19. HRMS (ESI-TOF) *m/z*: $[M + Na]^+$ calcd for $C_{131}H_{203}N_2NaO_{22}P$, 2210.4457; found: 2210.4262.
Compound 48: ^{1}H NMR (400 MHz, $CDCl_3$) δ 7.32 - 7.26 (m, 23H), 7.22 (dt, *J* = 3.2, 8.5, 10H), 7.16 (dd, *J* = 3.0, 6.8, 2H), 5.88 (d, *J* = 9.1, 1H), 5.58 (d, *J* = 7.8, 1H), 5.44 (dd, *J* = 8.8, 10.5, 1H), 5.15 - 4.97 (m, 6H), 4.91 - 4.83 (m, 5H), 4.61 - 4.37 (m, 14H), 3.99 (d, J = 11.6, 1H), 3.91 (dd, J = 3.4, 10.1, 1H), 3.85 - 3.50 (m, 12H), 3.39 (dt, *J* = 8.0, 10.5, 1H), 2.52 (dt, *J* = 6.4, 15.4, 3H), 2.45 - 2.38 (m, 3H), 2.35 - 2.18 (m, 10H), 2.04 (d, J = 5.0 Hz, 2H), 1.61- 1.52 (m, 12H), 1.27 - 1.22 (m, 95H), 0.89 - 0.86 (m, 18H). ^{13}C NMR (100 MHz, $CDCl_3$) δ 173.85, 169.85, 135.53, 128.70, 128.54, 128.51, 128.47, 128.42, 128.34, 128.30, 128.26, 128.02, 127.95, 127.91, 127.85, 127.72,

127.67, 127.62, 127.58, 127.55, 127.51, 127.42, 99.99, 75.62, 75.36, 74.57, 74.10, 73.33, 71.20, 70.93, 69.58, 69.49, 67.84, 53.74, 41.69, 40.99, 39.46, 38.62, 34.54, 34.46, 34.28, 34.16, 34.07, 33.96, 31.93, 29.73, 29.70, 29.66, 29.61, 29.54, 29.37, 29.28, 29.24, 25.38, 25.23, 25.17, 25.13, 25.03, 24.99, 22.70, 22.56, 22.39, 14.13. ^{31}P NMR (162 MHz, $CDCl_3$) δ -2.18. HRMS (ESI-TOF) m/z: $[M + Na]^+$ calcd for $C_{130}H_{200}N_5NaO_{21}P$, 1961.3763; found: 2221.4044.

Compound 49: ^{1}H NMR (400 MHz, $CDCl_3$) δ 7.35 - 7.27 (m, 20H), 7.24 - 7.18 (m, 10H), 5.97 (d, *J* = 8.3, 1H), 5.64 (d, *J* = 7.4, 1H), 5.54 (t, *J* = 9.7, 1H), 5.46 (d, *J* = 4.2, 1H), 5.20 - 4.96 (m, 6H), 4.88 (t, *J* = 5.6, 4H), 4.59 - 4.40 (m, 10H), 4.19 (td, *J* = 4.0, 7.7, 8.2, 1H), 4.04 (d, *J* = 11.1, 1H), 3.95 (t, *J* = 5.9 Hz, 1H), 3.87 - 3.61 (m, 9H), 3.35 - 3.28 (m, 1H), 2.56 - 2.20 (m, 14H), 1.58 (dd, *J* = 7.1, 14.0, 12H), 1.28 - 1.21 (m, 95H), 0.88 (t, *J* = 6.7, 18H). ^{13}C NMR (100 MHz, $CDCl_3$) δ 173.13, 169.94, 138.47, 138.14, 135.54, 128.54, 128.50, 128.46, 128.41, 128.30, 128.12, 128.01, 127.95, 127.86, 127.78, 127.74, 127.70, 127.57, 127.53, 127.50, 99.56, 75.27, 75.10, 74.83, 74.23, 73.29, 72.72, 71.22, 70.95, 70.85, 70.18, 69.59, 68.62, 52.16, 41.49, 41.01, 39.56, 38.53, 34.45, 34.40, 34.19, 33.91, 31.93, 29.77, 29.73, 29.70, 29.66, 29.62, 29.53, 29.44, 29.40, 29.37, 29.21, 25.46, 25.18, 25.11, 25.03, 24.99, 22.70, 14.13. ^{31}P NMR (162 MHz, $CDCl_3$) δ -2.22. HRMS (ESI-TOF) m/z: $[M + Na]^+$ calcd for $C_{130}H_{200}N_5NaO_{21}P$, 2221.4366; found: 2221.3975.

Compounds 1 – 4



A mixture of **46-49** (2.0 μmol), Pd/C (5.0 mg) in THF was stirred under an atmosphere of H_2 at rt for 24h. After the complete consumption of compound **46-49** monitored by TLC, the resulting mixture was filtered through a pad of Celite and the filtrate was concentrated in vacuum to give **1-4** (86-91% yield).

Compound 1: ^{1}H NMR (400 MHz, $CDCl_3/CD_3OD$) δ 5.37 - 5.33 (m, 2H), 5.21 - 4.99 (m, 4H), 4.07 - 4.05 (m ,2H), 3.87 - 3.84 (m ,2H), 3.71 - 3.66(m, 4H), 2.47 - 2.29 (m, 14H), 1.65 - 1.54 (m, 12H), 1.32 - 1.22 (m, 94H), 0.89 (t, J = 6.6 Hz, 18H).

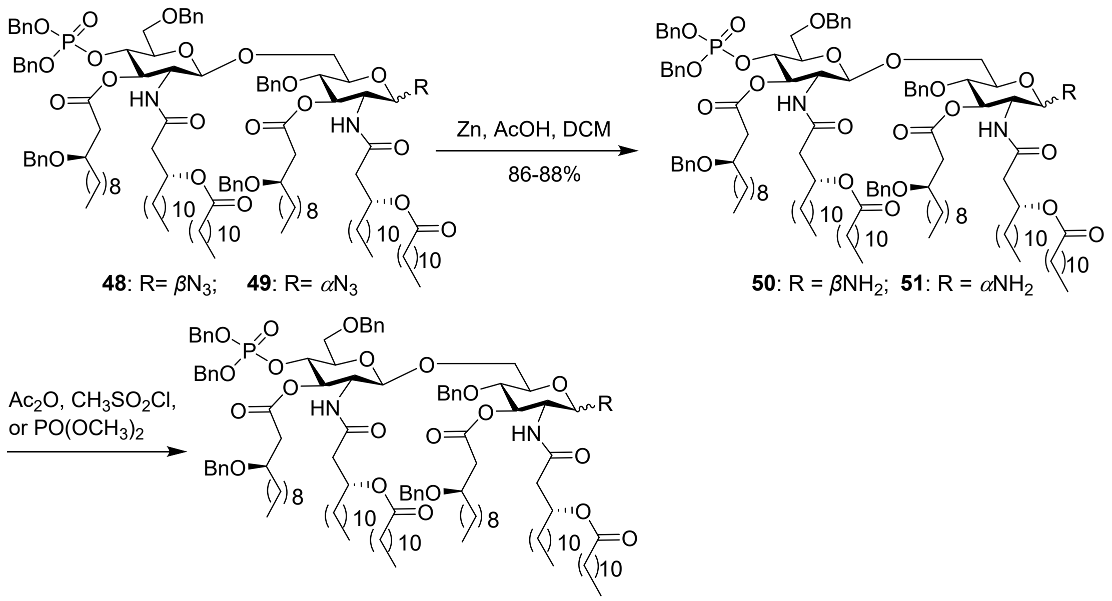
Compound 2: ^{1}H NMR (400 MHz, $CDCl_3/CD_3OD$) δ 5.45 - 4.62 (m, 6H), 4.10 - 3.61 (m, 11H), 2.55 – 2.12 (m, 14H), 1.62 - 1.43 (m, 12H), 1.22 - 1.17 (m, 94H), 0.82 - 0.78 (m, 18H).

Compound 3: ^{1}H NMR (400 MHz, $CDCl_3/CD_3OD$) δ 4.08 - 3.94 (m 18H), 2.50 - 2.25 (m, 14H), 1.65 - 1.61 (m 12H), 1.29 - 1.27 (m, 94H), 0.90 - 0.88 (m, 18H).

Compound 4: ^{1}H NMR (400 MHz, $CDCl_3/CD_3OD$) δ 5.11 - 4.97 (m, 12 H), 4.31 - 3.58 (m, 6H), 2.47 - 2.17 (m, 14H), 1.65 - 1.60 (m, 12H), 1.19 - 1.18 (m 94H), 0.78 - 0.77 (m, 18H).

III. Preparation and Characterization of compounds 5-8

Compounds 52-55



48: R= βN_3; **49**: R= αN_3 **50**: R = βNH_2; **51**: R = αNH_2

52: R = βNHAc; **53**: R = $\beta NHSO_2CH_3$;
54: R = $\beta NHPO(OCH_3)_2$; **55**: R = $\alpha NHPO(OCH_3)_2$

A suspension of **48-49** (0.07 mmol), active zinc (3.5 mmol), and acetic acid (50 uL) in DCM (6 mL) was stirred at rt for 1 h. Upon completion, the resulting solution was filtrated and washed with DCM. The filtrate was neutralized with saturated $NaHCO_3$ solution, washed with brine, dried over anhydrous Na_2SO_4, and concentrated in vacuo. The products were used for the next step without further purification.

A solution of **50-51** (2 mmol) and pyridine (0.2 mmol) in anhydrous DCM (4 mL) was added acylation reagent with dropwise. After the complete consumption of compound **50-51** monitored by TLC, the resulting mixture was diluted with DCM, washed with brine, dried over anhydrous Na_2SO_4 and evaporated in vacuo. The product was purified by flash column chromatography to give **52-55**.

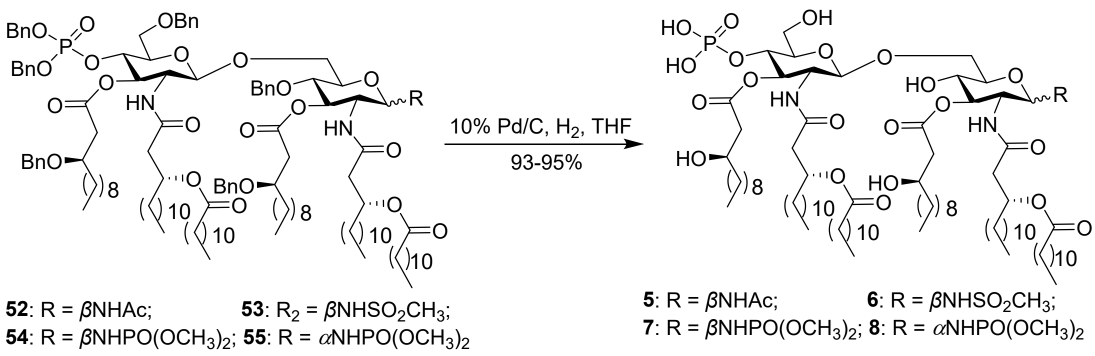
Compound 52**:** ^{1}H NMR (400 MHz, $CDCl_3$) *δ* 7.54 - 7.47 (m, 2H), 7.317.27 (m, 12H), 7.26 - 7.18 (m, 16H), 7.15 (dd, *J* = 2.5, 7.1, 2H), 6.61 (d, *J* = 7.8, 1H), 5.37 - 5.30 (m, 1H), 5.30 - 5.24 (m, 1H), 5.15 - 5.07 (m, 4H), 4.98 (dd, *J* = 6.7, 9.7, 1H), 4.90 - 4.76 (m, 6H), 4.54 (dt, *J* = 3.9, 10.8, 3H), 4.45 (dd, *J* = 4.2, 11.0, 6H), 4.33 (dd, *J* = 6.0, 10.4, 2H), 4.11 - 3.90 (m, 4H), 3.86 - 3.72 (m, 5H), 3.68 - 3.52 (m, 4H), 3.31 (dd, *J* = 6.8, 11.8, 1H), 2.60 - 2.46 (m, 5H), 2.38 (dd, *J* = 6.0, 16.3, 2H), 2.34 - 2.17 (m, 9H), 2.03 - 1.98 (m, 4H), 1.58 - 1.45 (m, 12H), 1.29 - 1.22 (m, 95H), 0.90 - 0.86 (m, 18H). ^{13}C NMR (100 MHz, $CDCl_3$) *δ* 172.95, 172.39, 138.87, 138.22, 136.97, 135.62, 128.49, 128.32, 128.29, 128.13, 128.08, 128.05, 127.95, 127.89, 127.72, 127.69, 127.62, 127.51, 127.24, 101.41, 80.51, 75.45, 75.35, 75.20, 74.73, 74.32, 73.41, 73.14, 72.04, 71.27, 70.94, 70.55, 69.65, 69.60, 69.51, 69.46, 69.10, 67.27, 53.80, 53.13, 41.70, 40.83, 39.59, 39.24, 34.68, 34.45, 34.31, 34.08, 33.98, 31.94, 29.76, 29.72, 29.70, 29.66, 29.61, 29.57, 29.48, 29.41, 29.38, 29.24, 29.19, 25.31, 25.20, 25.15, 25.10, 25.07, 23.37, 22.70, 14.13. ^{31}P NMR (162 MHz, $CDCl_3$) *δ* -1.81. HRMS (ESI-TOF) *m/z*: $[M + Na]^+$ calcd for $C_{130}H_{200}N_5NaO_{21}P$, 2237.4566; found: 2237.4156.

Compound 53**:** ^{1}H NMR (400 MHz, $CDCl_3$) *δ* 7.31 - 7.28 (q, *J* = 2.5, 13H), 7.25 - 7.14 (m, 17H), 6.48 (d, *J* = 7.7, 1H), 6.36 (d, *J* = 8.0, 1H), 6.24 (d, *J* = 9.0, 1H), 5.26 (dd, *J* = 8.8, 10.5, 1H), 5.17 - 4.96 (m, 5H), 4.94 (d, *J* = 8.4, 1H), 4.88 - 4.82 (m, 5H), 4.74 (dd, *J* = 7.7, 9.4, 1H), 4.56 - 4.33 (m, 12H), 3.95 (t, *J* = 10.0, 2H), 3.82 - 3.70 (m, 6H), 3.64 (t, *J* = 6.9, 3H), 3.44 (t, *J* = 9.3, 1H), 2.99 (s, 3H), 2.57 - 2.42 (m, 5H), 2.29 (qd, *J* = 3.7, 9.4, 11.5, 8H), 2.11 (d, *J* = 6.7, 1H), 1.62 - 1.49 (m, 12H), 1.27 - 1.23 (m, 95H), 0.88 (d, *J* = 1.4, 18H). ^{13}C NMR (100 MHz, $CDCl_3$) *δ* 138.24, 135.55, 128.54, 128.51, 128.39, 128.35, 128.32, 128.27, 128.13, 128.05, 127.99, 127.90, 127.83, 127.72, 127.66, 127.62, 127.57, 127.46, 83.91, 75.56, 75.28, 74.19, 73.28, 72.68, 71.23, 70.81, 70.43, 69.64, 69.59, 69.52, 69.46, 68.83, 54.46, 42.85, 41.18, 39.49, 38.86, 34.61, 34.36, 34.21, 34.06, 31.93, 29.71, 29.67, 29.61, 29.56, 29.53, 29.44, 29.38, 29.26, 29.20, 25.28, 25.22, 25.19, 25.11, 25.07, 24.99, 22.70, 14.13. ^{31}P NMR (162 MHz, $CDCl_3$) δ -2.09. HRMS (ESI-TOF) *m/z*: $[M + Na]^+$ calcd for $C_{131}H_{204}N_3NaO_{23}PS$, 2273.4236; found: 2273.3806.

Compound 54**:** ^{1}H NMR (400 MHz, $CDCl_3$) *δ* 8.12 - 8.02 (m, 1H), 7.30 - 7.26 (m, 18H), 7.24 - 7.12 (m, 12H), 6.61 (d, *J* = 8.3, 1H), 5.22 (t, *J* = 9.6, 1H), 5.10 (dt, *J* = 8.2, 16.1, 3H), 4.95 (dd, *J* = 3.4, 8.7, 1H), 4.84 (t, *J* = 10.2, 4H), 4.58 - 4.41 (m, 8H), 4.33 (t, *J* = 9.7, 2H), 4.12 - 4.06 (m, 1H), 3.99 - 3.78 (m, 5H), 3.68 (m, 11H), 3.28 (t, *J* = 9.0, 1H), 2.59 - 2.47 (m, 4H), 2.40 - 2.34 (m, 2H), 2.27 (q, *J* = 6.2, 7.4, 6H), 2.10 - 1.97 (m, 2H), 1.63 - 1.49 (m, 12H), 1.29 - 1.18 (m, 95H), 0.88 (t, *J* = 6.5, 18H). ^{13}C NMR (100 MHz, $CDCl_3$) δ 173.70, 171.17, 138.89, 138.20, 136.99, 135.63, 128.50, 128.45, 128.29, 128.10, 128.04, 127.98, 127.92, 127.88, 127.74, 127.69, 127.59, 127.50, 127.21, 101.36, 84.14, 75.80, 75.57, 75.35, 74.58, 74.37, 73.44, 73.13, 72.17, 71.34, 70.93, 70.30, 69.63, 69.57, 69.48, 69.09, 66.70, 53.82, 52.92, 41.05, 40.89, 39.62, 39.39, 34.69, 34.52, 34.39, 34.18, 34.14, 33.87, 31.94, 29.74, 29.71, 29.66, 29.61, 29.57, 29.47, 29.41, 29.38, 29.24, 25.30, 25.19, 25.14, 25.04, 22.70, 14.13. ^{31}P NMR (162 MHz, $CDCl_3$) δ 8.08, -1.84. HRMS (ESI-TOF) *m/z*: $[M + H]^+$ calcd for $C_{132}H_{208}N_3O_{24}P_2$, 2281.4618; found: 2281.4264.

Compound 55**:** ^{1}H NMR (400 MHz, $CDCl_3$) δ 7.35 - 7.35-7.26 (m, 18H), 7.24 - 7.16 (m, 12H), 6.82 (d, *J* = 9.0, 1H), 6.38 (d, *J* = 8.6, 1H), 5.36 - 5.29 (m, 1H), 5.19 (t, *J* = 7.5, 1H), 5.09 (q, *J* = 5.5, 6.5, 3H), 4.97 (d, *J* = 8.4, 1H), 4.92 - 4.79(m, 5H), 4.68 (d, *J* = 10.3, 1H), 4.49 (dt, *J* = 9.8, 30.9, 8H), 4.33 (d, *J* = 11.5, 1H), 4.25 - 4.18 (m, 1H), 4.12- 4.05 (m, 1H), 3.90 - 3.70 (m, 15H), 3.30 (t, *J* = 6.8, 1H), 2.59 - 2.39 (m, 14H), 1.61 - 1.45 (m, 12H), 1.29 - 1.18 (m, 95H), 0.88 (t, *J* = 6.7, 19H).^{13}C NMR (100 MHz, $CDCl_3$) δ 174.24, 173.35, 171.68，171.15,,169.74，138.35, 138.24, 137.18, 135.68, 128.49, 128.44, 128.31, 128.26, 128.19, 128.09, 127.99, 127.92, 127.73, 127.68, 127.65, 127.57, 127.43, 127.34, 100.67, 77.22, 75.59, 75.54, 74.30, 73.28, 72.97, 71.76, 71.37, 70.83, 69.57, 69.46, 68.69, 67.14, 54.47, 53.78, 41.53, 41.20, 39.63, 39.14, 34.65, 34.45, 34.36, 34.11, 33.90, 31.94, 29.73, 29.70, 29.66, 29.62, 29.57, 29.46, 29.38, 29.28, 29.24, 25.25, 25.20, 25.08, 25.03, 24.96, 22.70, 14.13. ^{31}P NMR (162 MHz, $CDCl_3$) δ 9.00, -2.02. HRMS (ESI-TOF) m/z: $[M + H]^+$ calcd for $C_{132}H_{208}N_3O_{24}P_2$, 2281.4618; found: 2281.4196.

Compounds 5 – 8



A mixture of **52-55** (2.0 μmol), Pd/C (5.0 mg) in THF was stirred under an atmosphere of H_2 at rt for 24h. After the complete consumption of compound **52-55** monitored by TLC, the resulting mixture was filtered through a pad of Celite and the filtrate was concentrated in vacuum to give **5-8** (93-95% yield).

Compound 5**:** ^{1}H NMR (400 MHz, $CDCl_3/CD_3OD$) δ 5.06 (m 7H), 3.97 - 3.38 (m , 11H), 2.62 - 1.74 (m, 14H), 1.61 - 1.43 (m, 13H), 1.30 - 1.13 (m 95H), 0.87 – 0.69 (m, 1H).

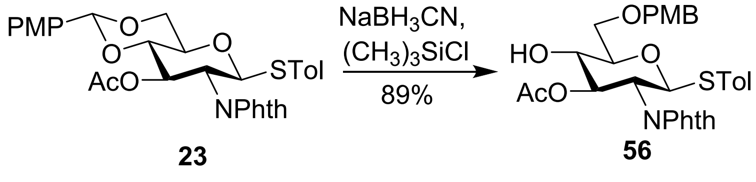
Compound 6**:** ^{1}H NMR (400 MHz, $CDCl_3/CD_3OD$) δ 5.35 - 4.82 (m, 7H), 4.32- 3.38 (m, 7H), 3.11 - 2.86 (m, 3H), 1.77 - 1.60 (m, 12H), 1.20 - 1.18 (m, 94H), 0.80 - 0.79 (m, 18H).

Compound 7**:** ^{1}H NMR (400 MHz, $CDCl_3/CD_3OD$) δ 5.17 - 4.71 (m, 4H), 4.17 - 3.28 (m, 16H), 2.52 - 2.13 (m, 12H), 1.18 - 1.17 (m, 95H), 1.18 (m, 95H), 0.78 - 0.77 (m, 18H).

Compound 8**:** ^{1}H NMR (400 MHz, $CDCl_3/CD_3OD$) δ 5.58 - 5.50 (m, 2H), 5.24 – 4.98 (m, 4H), 3.86 – 3.56 (m, 14H), 1.91 – 1.78 (m, 14H), 1.62 – 1.47 (m, 12H), 1.18 (s, 95H), 0.88 - 0.74 (m, 18H).

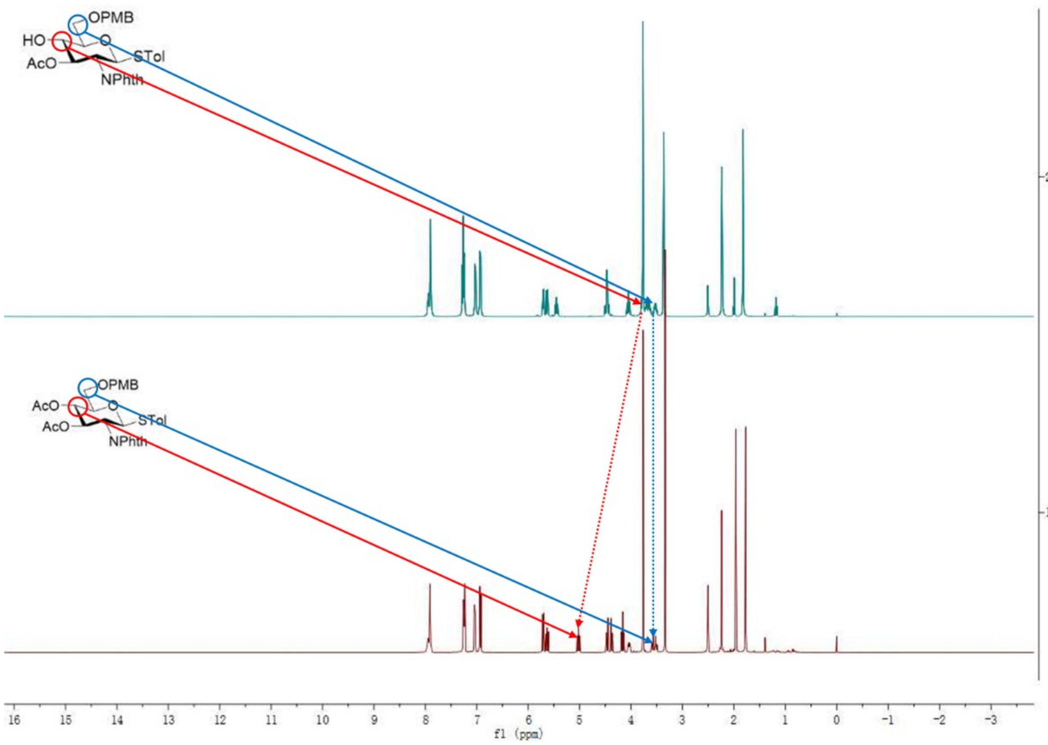
IV. Preparation and Characterization of compounds 9-10

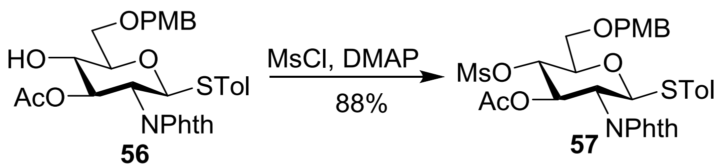
Compound 9



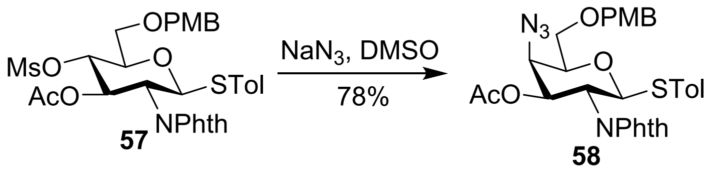
To a solution of **23** (3.6 mmol) in anhydrous DCM (5.0 mL) at 0 °C was added $NaBH_3CN$ (5.2 mmol) and CH_3SiCl (1.8 mmol). After accomplishment, the reaction was quenched by triethylamine/MeOH (1.1 mL, 1:10, v/v). After removing the solvent, the residue was purified by silica gel column chromatography using PE/EA as eluent to give the desired product **56** (89% yield). ^1H NMR (400 MHz, $CDCl_3$) δ 7.91 – 7.83(m, 2H), 7.77 – 7.71 (m, 2H), 7.52 – 7.47 (m, 2H), 7.41 – 7.35 (m, 3H), 5.58 (s, 1H), 5.45 (d, *J* = 9.4 Hz, 1H), 4.66 (dd, *J* = 10.4, 9.0 Hz, 1H), 4.42 (dd, *J* = 10.3, 4.8 Hz, 1H), 4.16 (dd, *J* = 10.4, 9.4 Hz, 1H), 3.83 (t, *J* = 10.2 Hz, 1H), 3.73 (td, *J* = 9.6, 4.8 Hz, 1H), 3.61 (t, *J* = 9.1 Hz, 1H). ^{13}C NMR (100 MHz, $CDCl_3$) *δ* 136.75, 134.39, 131.52, 129.39 (d, *J* = 18.6 Hz), 128.43, 126.30, 123.71, 102.03, 86.25, 81.83, 77.25, 68.32, 55.88. HRMS (ESI-TOF) *m/z*: $[M + Na]^+$ calcd for $C_{31}H_{31}NNaO_8S$, 600.1663; found: 600.1654.

To confirm the exposed hydroxyl group was at the C-4 position, acetylation of **56** was performed. The signal of the hydrogen atom at C-4 position in the ^1H NMR spectrum shifted from δ 3.77 ppm to δ 5.02 ppm after acetylation. However, the signal of hydrogen atoms at C-6 position in the ^1H NMR spectrum showed no significant change. These results indicated that the exposed hydroxyl group was at the C-4 position.

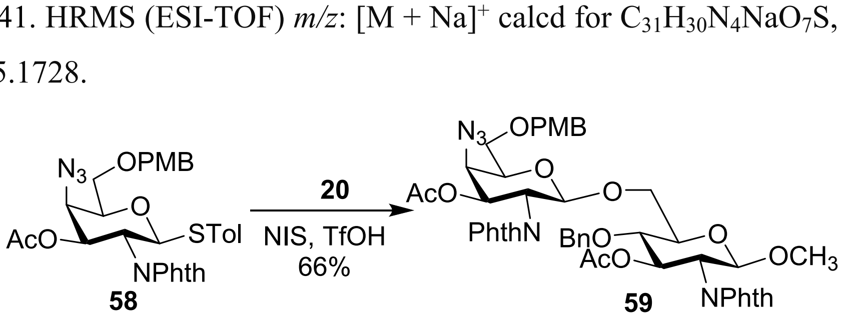




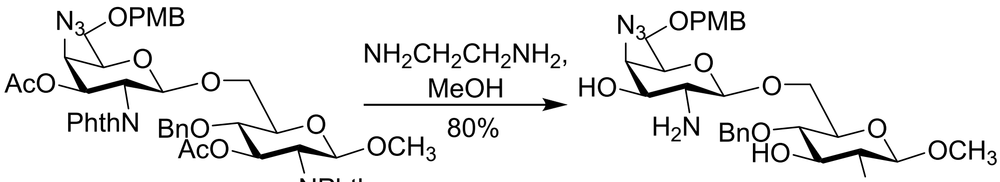
To a solution of **56** (2 mmol) in anhydrous DCM (5.0 mL) was added MsCl (3 mmol) and DMAP (0.2 mmol). After the complete consumption of compound **56** monitored by TLC, the solvent was removed by vacuo. The residue was purified by silica gel column chromatography using PE/EA as eluent to give the desired product **57** (88% yield). ^{1}H NMR (400 MHz, $CDCl_3$) δ 7.90 – 7.83 (m, 1H), 7.78 – 7.71 (m, 1H), 7.36 – 7.27 (m, 2H), 7.05 – 6.96 (m, 1H), 6.95 – 6.82 (m, 1H), 4.59 – 4.46 (m, 1H), 4.30 (td, *J* = 10.3, 1.4 Hz, 1H), 3.82 (t, *J* = 2.3 Hz, 3H), 2.92 (t, *J* = 2.2 Hz, 1H), 2.30 (s, 1H), 1.91 (d, *J* = 1.4 Hz, 2H).



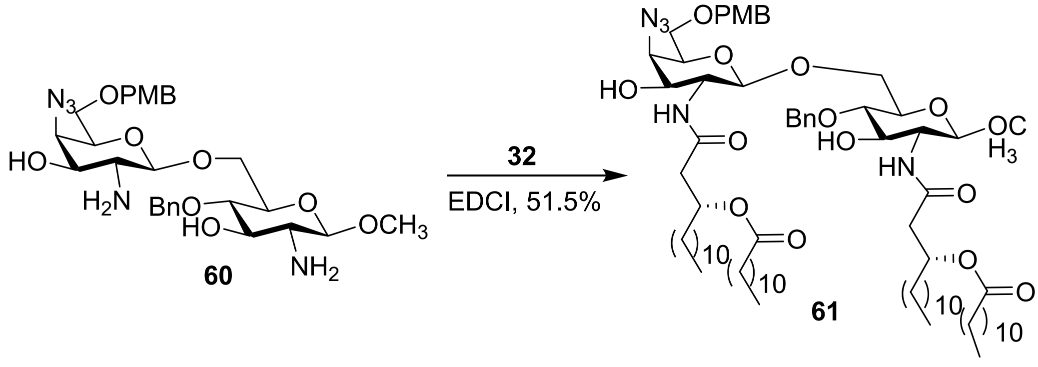
To a solution of **57** (0.8 mmol) in anhydrous DMSO (15 mL) was added NaN_3 (1.77 mmol). After the complete consumption of compound **57** monitored by TLC, the mixture was diluted with DCM and washed with saturated aqueous $NaHCO_3$ solution. The organic phase was concentrated in vacuo, and the residue was purified by flash chromatography to give the desired product **58** in 78% yield. ^{1}H NMR (400 MHz, $CDCl_3$) δ 7.91 – 7.81 (m, 2H), 7.80 – 7.70 (m, 2H), 7.25 – 7.26 (m, 2H), 7.25 – 7.23 (m, 2H), 7.09 – 6.98 (m, 2H), 6.96 – 6.82 (m, 2H), 5.81 (dd, *J* = 10.7, 3.8 Hz, 1H), 5.58 (d, *J* = 10.5 Hz, 1H), 4.61 (t, *J* = 10.6 Hz, 1H), 4.54 – 4.40 (m, 2H), 4.23 (dd, *J* = 3.8, 1.3 Hz, 1H), 3.94 (dd, *J* = 7.3, 5.8, 1.4 Hz, 1H), 3.81 (s, 3H), 3.72 – 3.58 (m, 2H), 2.29 (s, 3H), 1.94 (s, 3H). ^{13}C NMR (100 MHz, $CDCl_3$) *δ* 169.83, 168.07, 167.12, 159.40, 138.30, 134.35, 134.29, 133.11, 131.61, 131.29, 129.72, 129.68, 129.55, 127.95, 123.74, 123.57, 113.89, 84.16, 77.24, 75.73, 73.24, 70.97, 67.88, 60.32, 55.31, 50.47, 21.16, 20.41. HRMS (ESI-TOF) *m/z*: $[M + Na]^+$ calcd for $C_{31}H_{30}N_4NaO_7S$, 625.1727; found: 625.1728.



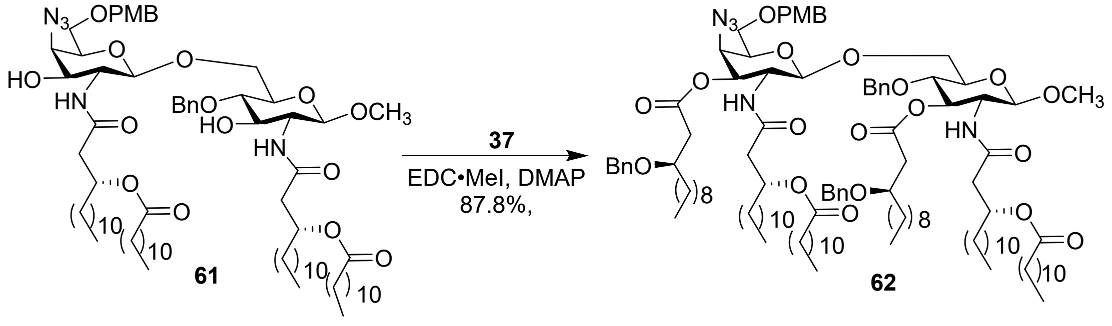
A mixture of the glycosyl donor **58** (0.25 mmol), acceptor **19-22** (0.17 mmol) and 4 Å molecular sieves (1.0 g) in anhydrous DCM (2.0 mL) was stirred at rt for 4 h. Then, the reaction mixture was cooled to -35 °C, and NIS (0.5 mmol) was added. After stirring for 1 h, TfOH (0.04 mmol) was added. After stirring for another 15 min, the reaction mixture was filtered through a pad of Celite and the residue was washed with DCM (40.0 mL). The combined filtrate was washed with saturated aqueous $Na_2S_2O_4$ solution, followed by saturated aqueous $NaHCO_3$ solution and brine. The organic layer was concentrated in vacuo, and the residue was purified by silica gel column chromatography using PE/EA as eluent to give the desired products **59** in 66% yield. ^{1}H NMR (400 MHz, $CDCl_3$) δ 7.85 - 7.76 (m, 4H), 7.73- 7.64 (m, 4H), 7.31 - 7.26 (m, 2H), 7.25 - 7.18 (m, 3H), 7.13 - 7.06 (m, 2H), 6.90 (dd, *J* = 2.0, 8.6, 2H), 5.82 (dd, *J*=1.9, 3.8, 1H), 5.64 (dd, *J*=1.9, 8.6, 1H), 5.36 (dd, *J* = 1.9, 8.4, 1H), 5.13 (dd, *J*=1.9, 8.5, 1H), 4.61 (td, *J* = 4.2, 8.6, 1H), 4.55 - 4.47 (m, 2H), 4.45 - 4.37 (m, 2H), 4.27 - 4.22 (m, 1H), 4.10 - 4.01 (m, 2H), 3.93 (t, *J* = 6.9, 1H), 3.81 (d, *J* = 1.9, 3H), 3.69 (ddd, *J* = 1.9, 6.3, 14.6, 3H), 3.61 (t, *J* = 5.0, 1H), 3.50 - 3.45 (m, 1H), 3.16 (d, *J* = 1.8, 3H), 1.97 (d, *J* = 1.9, 3H), 1.70 (d, *J* = 1.9, 3H). ^{13}C NMR (100 MHz, $CDCl_3$) δ 169.97, 169.91, 168.27, 167.80, 167.28, 159.43, 137.53, 134.29, 134.21, 131.49, 131.37, 129.70, 129.59, 128.38, 127.80, 127.54, 123.56, 123.44, 113.92, 98.46, 98.31, 74.43, 73.24, 73.16, 71.84, 70.18, 67.76, 67.60, 60.15, 56.46, 55.31, 54.92, 51.50, 20.49, 20.43. HRMS (ESI-TOF) *m/z*: $[M + Na]^+$ calcd for $C_{48}H_{47}N_5NaO_{15}$, 956.2941; found: 956.2953.



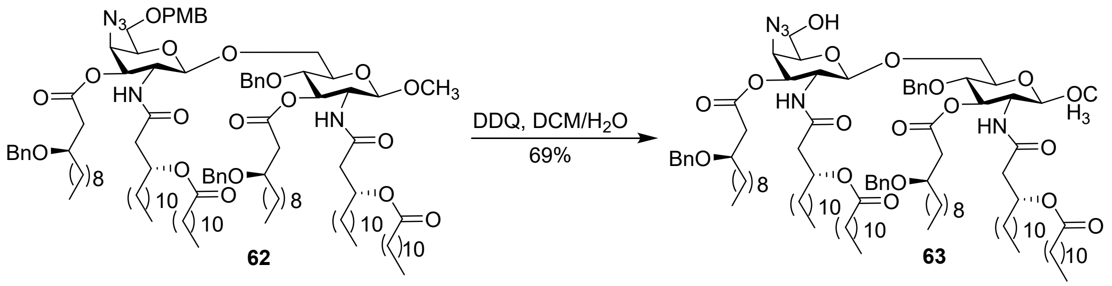
To a solution of **59** (0.11 mmol) in anhydrous MeOH (6 mL) was added ethylenediamine (0.8 mL) with dropwise. Then, the reaction mixture was stirred at 80 °C for 18 h. After the complete consumption of compound **59** monitored by TLC, the solvent was removed in vacuo. The residue was purified by silica gel column chromatography using PE/EA with 1% triethylamine as eluent to give the desired product **60** in 80% yield. ^{1}H NMR (400 MHz, $CDCl_3$) δ 7.35 -7.26 (m, 6H), 7.25 - 7.23 (m, 1H), 6.92 - .84 (m, 2H), 4.83 (d, *J* = 11.3, 1H), 4.66 (d, *J* = 11.4, 1H), 4.47 (s, 2H), 4.17 - 4.06 (m, 3H), 3.89 (d, *J* = 3.2, 1H), 3.79 (s, 3H), 3.67 - 3.56 (m, 5H), 3.49 (s, 5H), 3.33 (t, *J* = 8.8, 1H), 2.88 (t, *J* = 9.0, 1H). ^{13}C NMR (100 MHz, $CDCl_3$) δ 159.41, 138.14, 129.70, 129.58, 128.56, 127.96, 113.90, 104.46, 104.26, 78.75, 74.57, 74.49, 73.25, 72.21, 68.43, 68.17, 61.79, 57.46, 57.28, 55.30, 54.38. HRMS (ESI-TOF) *m/z*: $[M + Na]^+$ calcd for $C_{28}H_{39}N_5NaO_9$, 612.2640, found: 612.2633.



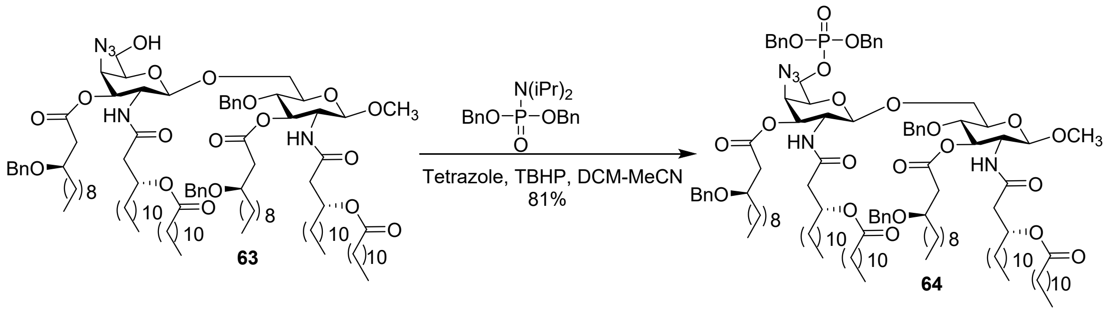
The lipid installation for amino groups in compound **60** was similar to the synthesis of compounds **33-36**, giving **61** in 51.5% yield. ^{1}H NMR (400 MHz, $CDCl_3$) δ 7.36 - 7.28 (m, 5H), 7.26 - 7.22 (m, 2H), 6.94 - 6.82 (m, 2H), 6.14 (d, *J* = 23.5, 2H), 5.17 - 5.05 (m, 2H), 4.93 (d, *J* = 11.1, 1H), 4.64 (d, *J* = 11.2, 1H), 4.54 - 4.36 (m, 4H), 4.11 (d, *J* = 10.9, 1H), 4.00 (d, *J* = 9.8, 1H), 3.93 (d, *J* = 2.8, 1H), 3.89 - 3.85 (m, 1H), 3.80 (s, 3H), 3.70 - 3.50 (m, 7H), 3.46 (s, 3H), 3.35 (t, *J* = 8.6, 1H), 2.50 (d, *J* = 5.9, 2H), 2.45 - 2.26 (m, 6H), 1.60 (q, *J* = 7.5, 6H), 1.33 - 1.22 (m, 65H), 0.88 (t, *J* = 6.6, 12H). ^{13}C NMR (100 MHz, $CDCl_3$) δ 174.25, 174.10, 172.54, 171.72, 159.40, 138.16, 129.70, 129.53, 128.45, 128.13, 127.89, 113.90, 100.75, 100.67, 78.44, 74.48, 74.40, 73.26, 72.32, 71.44, 71.31, 68.28, 61.84, 57.55, 56.15, 55.93, 55.29, 42.42, 42.16, 34.56, 34.52, 34.43, 31.92, 29.64, 29.53, 29.36, 29.32, 29.20, 25.28, 25.25, 24.99, 22.69, 14.12. HRMS (ESI-TOF) *m/z*: $[M + Na]^+$ calcd for $C_{80}H_{135}N_5NNaO_{15}$, 1428.9847; found: 1428.9577.



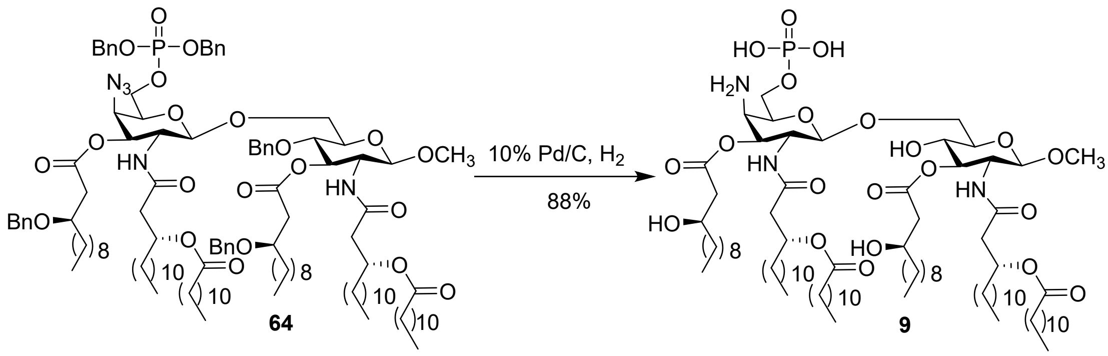
The lipid installation for hydroxy groups in compound **61** was similar to the synthesis of compounds **37-40**, giving **62** in 87.8% yield. ^{1}H NMR (400 MHz, $CDCl_3$) δ 7.33 - 7.26 (m, 8H), 7.25 - 7.16 (m, 11H), 6.89 - 6.86 (m, 2H), 5.80 (d, *J* = 9.1, 1H), 5.62 (d, *J* = 8.0, 1H), 5.42 (dd, *J* = 3.8, 10.9, 1H), 5.15 (d, *J* = 8.2 Hz, 1H), 5.04 (dt, *J* = 6.2, 17.6, 2H), 4.89 (d, *J* = 8.3, 1H), 4.58 - 4.43 (m, 11H), 4.00 - 3.78 (m, 10H), 3.76 - 3.65 (m, 4H), 3.59 - 3.48 (m, 5H), 3.45 - 3.35 (m, 4H), 2.64 - 2.52 (m, 3H), 2.45 - 2.21 (m, 10H), 2.19 - 2.13 (m, 1H), 1.56 (td, *J* = 6.2, 14.0, 14.5, 12H), 1.25 (d, *J* = 5.0, 95H), 0.88 (t, *J* = 6.7, 18H). ^{13}C NMR (100 MHz, $CDCl_3$) δ 173.60, 173.50, 171.67, 170.78, 138.48, 137.56, 129.68, 129.53, 128.39, 128.28, 127.87, 127.72, 127.67, 127.50, 113.89, 101.58, 100.15, 75.98, 75.90, 75.40, 74.77, 74.29, 73.13, 71.71, 71.44, 71.26, 71.10, 70.83, 67.64, 67.32, 60.29, 56.31, 55.27, 53.84, 52.31, 41.88, 41.52, 39.55, 39.21, 34.49, 34.19, 31.93, 29.72, 29.69, 29.66, 29.61, 29.55, 29.50, 29.46, 29.37, 29.25, 25.29, 25.25, 25.19, 25.00, 22.70, 14.13. HRMS (ESI-TOF) m/z: $[M + Na]^+$ calcd for $C_{118}H_{191}N_5NaO_{19}$, 2005.4026; found: 2005.3628.



To a solution of **62** (69 μmol) in DCM (1.9 mL) and water (0.1 mL) was added DDQ (13 μmol). Then, the reaction mixture was stirred at rt until the complete consumption of compound **62** monitored by TLC. The reaction mixture was diluted by DCM, and neutralized with saturated $NaHCO_3$ solution. After washing with brine, the organic phase was concentrated in vacuo. The residue was purified by silica gel column chromatography using PE/EA with 1% triethylamine as eluent to give the desired product **63** in 69% yield. ^{1}H NMR (400 MHz, $CDCl_3$) δ 7.37 - 7.18 (m, 5H), 7.30 - 7.26 (m, 5H), 7.26 - 7.18 (m, 5H), 5.82 (d, *J* = 9.1, 1H), 5.66 (d, *J* = 7.8, 1H), 5.45 (d, *J* = 10.7 Hz, 1H), 5.17 (t, *J* = 9.4, 1H), 5.09 - 4.97 (m, 2H), 4.87 (d, *J* = 8.2, 1H), 4.64 - 4.37 (m, 7H), 3.95 - 3.72 (m, 8H), 3.59 (td, *J* = 6.7, 19.0, 20.5, 4H), 3.43 (s, 3H), 2.67 - 2.52 (m, 3H), 2.48 - 2.13 (m, 11H), 1.56 (m, 12H), 1.25 (q, *J* = 4.7, 7.0, 95H), 0.88 (t, *J* = 6.7, 18H). ^{13}C NMR (100 MHz, $CDCl_3$) δ 173.59, 173.53, 171.66, 170.87, 138.50, 137.64, 128.43, 128.39, 128.30, 127.93, 127.86, 127.79, 127.74, 127.70, 127.53, 101.65, 100.90, 76.10, 74.95, 74.73, 74.35, 73.71, 71.61, 71.48, 71.27, 71.10, 70.93, 62.14, 59.99, 56.57, 54.00, 52.53, 41.89, 41.67, 39.55, 39.22, 34.50, 34.25, 34.17, 34.14, 31.93, 29.72, 29.69, 29.66, 29.61, 29.55, 29.49, 29.45, 29.38, 29.25, 25.26, 25.19, 25.04, 25.01, 22.70, 14.12. HRMS (ESI-TOF) m/z: $[M + Na]^+$ calcd for $C_{110}H_{183}N_5NaO_{18}$, 1885.3450; found: 1885.3141.



The phosphorylation of **63** was similar to the synthesis of **46-49** using phosphoramidite approach in a two-step one-pot manner, delivering **64** in 81% yield. ^{1}H NMR (400 MHz, $CDCl_3$) δ 7.39 - 7.29 (m, 14H), 7.26 - 7.15 (m, 11H), 6.09 (d, J = 8.9, 1H), 5.60 (s, 1H), 5.39 (s, 1H), 5.19 (t, J = 9.4, 1H), 5.05 (dt, J = 11.3, 20.6, 6H), 4.82 (s, 1H), 4.58 - 4.38 (m, 7H), 4.01 - 3.81 (m, 6H), 3.62 (s, 3H), 3.52 (s, 1H), 3.41 (s, 4H), 3.29 (s, 1H), 2.63 - 2.51 (m, 3H), 2.49 - 2.33 (m, 3H), 2.27 (t, J = 7.6, 6H), 2.19 - 2.03 (m, 2H), 1.63 - 1.53 (m, 12H), 1.32 - 1.19 (q, J = 6.8, 95H), 0.88 (t, J = 6.7, 18H). ^{31}P NMR (162 MHz, $CDCl_3$) δ -1.22. HRMS (ESI-TOF) *m/z*: $[M + Na]^+$ calcd for $C_{124}H_{196}N_5NaO_{21}P$, 2145.4053; found: 2145.4051.



The hydrogenolysis of **64** to remove all benzyl groups and reduce the azide group to amino was similar to the synthesis of **1-4**, giving compound **9** in 88% yield. ^{1}H NMR (400 MHz, $CDCl_3/CD_3OD$) δ 3.89 - 3.46 (m, 17H), 2.47 - 2.17 (m, 14H), 1.57 - 1.52 (m, 12H), 1.22 - 1.17 (m, 94H), 0.80 - 0.78 (m, 19H).

The synthesis of compound **10** was similar to the literature.[3] ^{1}H NMR (400 MHz, $CDCl_3/CD_3OD$) δ 5.21 - 4.77 (m, 2H), 4.17 - 3.86 (m ,8H), 3.79 - 3.49 (m, 3H), 3.43 - 3.32 (m, 4H), 2.47 - 2.41 (m, 14H), 1.56 - 1.44 (m, 12H), 1.20 - 1.16 (m, 94H), 0.81 - 0.78 (m, 18H).

V. RBD-hFc Protein expression and purification

The gene of SARS-CoV-2 RBD fused with the genes of hFc in its N-terminal were inserted into the plasmid of PcDNA3.1.[4] The recombinant expression plasmids were transfected with the Expi293 Expression System (Thermo Fisher Scientific) according to the manufacturer's protocol. The supernatants were harvested on the fifth-day post-transfection. The recombinant protein was purified by using MabSelect SuRe LX Fast Flow and analyzed by SDS-PAGE. Briefly, 10% Tris-glycine SDS-PAGE was used to separate the proteins, and then the proteins in the gel were stained using Coomassie Brilliant Blue to visualize the protein lines.

VI. Immunological studies of compounds 1-10 adjuvanted RBD-Fc Protein.

1. Preparation of RBD-hFc/compounds 1-10 or Al

Compounds **1-10** were first prepared as liposomes using our previously reported protocol.[5] Briefly, a mixture of DSPC, cholesterol and compounds **1-10** in a molar ratio of 65:50:10 was dissolved in the mixture of DCM, MeOH and H_2O (5:5:1, v/v). The solvents were removed under reduced pressure through rotary evaporation, a thin lipid film was formed on the vial wall. The film was hydrated with HEPES buffer (pH = 7.5) and shaken on a vortex mixer. Finally, the mixture was sonicated at rt for 15 min to give the liposomal formulation. Then, RBD-hFc protein was dissolved in PBS buffer and thoroughly mixed with liposomes of compounds **1-10** or alum adjuvant in the light of the manufacturer's instructions.

2. Mouse immunization

Each group of five female BALB/c mice (6–7 week-old) was immunized *via* intramuscular injection with RBD-hFc/**1-10** or Al (5 μg of RBD-hFc protein, 20 μg of **1-10** or 100 μg of Al in 0.1 mL PBS) on days 0 and 14 with the same protocols. Each mouse was bled from eye socket on days 14, 28 and 42. Antisera were prepared and stored at -80 °C before immunological analysis.

3. ELISA protocol and results

3.1 ELISA protocol

96-Wells plates were pre-coated by 100 μL RBD-His protein dissolved in 0.1 M carbonate buffer (pH = 9.6) overnight at 4°C, followed by blocking with 2% skim milk 1 h at 37°C. After washing with PBST buffer (0.1% Tween-20 in PBS) three times, blocking buffer (PBS containing 1% BSA) was added and the plates were incubated at rt for 1 h.After washing again, serial half-log diluted (from 1:300 to 1:656100) pooled antisera were added (3 wells were set in each group) and followed incubation at 37 °C for 1.5 h. The plates were washed with PBST three times, and then 1:1000 diluted HRP-linked goat anti-mouse IgG or 1:2000 diluted IgG1, IgG2a, IgG2b and IgG3 antibodies solution was individually added. The plates were incubated at rt for 1 h, followed by shaking and washing with PBS. Then, 100 μL of colorimetric substrate TMB was added. After incubating in the darkness for 15 min, the chromogenic reaction was quenched by 0.5 M H_2SO_4 solution (100 μL). The optical density (OD) value was measured at 450 and 570 nm wavelength. The OD values were plotted against the antiserum dilution numbers after deduction of background (570 nm), affording the best fit line utilized to calculate the antibody titer, which was defined as the dilution number when the OD value is 0.2.

3.2 ELISA results of antibody titers

Table S1. The antibody titers of IgG in days 14, 28 and 42 antisera induced by RBD-hFc/**1-10** and Al.

	Day 14			Day 28			Day 42		
	Mean	SD	N	Mean	SD	N	Mean	SD	N
RBD-hFc/**1**	3537.003	767.822	3	41415.500	672.780	3	50214.467	829.549	3
RBD-hFc/**2**	226.230	153.409	3	23587.600	1187.632	3	30763.000	643.368	3
RBD-hFc/**3**	450.221	226.307	3	35299.500	1733.183	3	40220.967	1466.131	3
RBD-hFc/**4**	6954.893	811.489	3	33586.533	531.338	3	34750.400	1654.368	3
RBD-hFc/**5**	4960.000	2538.905	3	37525.867	2816.355	3	39708.200	1806.577	3
RBD-hFc/**6**	3437.043	566.041	3	32579.667	2646.271	3	38680.500	1250.107	3
RBD-hFc/**7**	986.240	21.898	3	35135.167	532.239	3	37754.100	1071.420	3
RBD-hFc/**8**	1892.466	841.898	3	22890.200	1218.571	3	32300.200	3311.012	3
RBD-hFc/**9**	1695.807	395.025	3	26851.533	105.282	3	35567.633	3607.858	3
RBD-hFc/**10**	2692.713	312.080	3	30387.933	1167.996	3	32602.500	2065.537	3
RBD-hFc/**Al**	5615.097	1448.249	3	38851.967	2508.405	3	43872.267	927.594	3

Table S2. The antibody titers of IgG isotypes in day 28 antisera induced by RBD-hFc/**1-10** and Al.

	IgG1			IgG2a			IgG2b			IgG3		
	Mean	SD	N	Mean	SD	N	Mean	SD	N	Mean	SD	N
RBD-hFc/**1**	54757.17	5046.25	3	3472.00	615.51	3	10206.67	3087.71	3	4824.99	3833.52	3
RBD-hFc/**2**	29010.02	1841.37	3	3727.67	2213.86	3	15674.76	3384.72	3	3165.74	2656.85	3
RBD-hFc/**3**	30924.65	1777.40	3	6767.18	697.61	3	14392.02	717.76	3	1789.45	2178.88	3
RBD-hFc/**4**	36991.93	2540.71	3	6509.55	429.68	3	7881.68	1758.20	3	183.40	246.40	3
RBD-hFc/**5**	48811.13	3352.72	3	3657.08	1164.28	3	12257.73	2387.64	3	1887.41	1776.70	3
RBD-hFc/**6**	31948.64	2354.48	3	5706.79	1166.54	3	6114.10	1632.44	3	2394.81	919.95	3
RBD-hFc/**7**	42636.96	1611.70	3	5330.71	1321.35	3	10081.31	1143.51	3	5133.79	2195.03	3
RBD-hFc/**8**	33790.72	752.53	3	4867.18	390.10	3	3883.31	224.85	3	5745.13	1102.97	3
RBD-hFc/**9**	37750.41	9799.56	3	6139.61	290.73	3	3833.64	265.01	3	482.07	233.23	3
RBD-hFc/**10**	24086.73	1262.49	3	3712.89	1103.34	3	15692.17	6290.84	3	5117.33	730.17	3
RBD-hFc/**Al**	47096.41	2468.45	3	3597.53	836.49	3	3431.93	2821.042	3	662.08	884.81	3

4. FACS analyses

For recombinant proteins fusing Fc domain, 293T cells were transfected with a human ACE2 vector (10 μg pCAG-hACE2/T75). The cells were washed with PBS for three times at 48 h post-transfection. A suspension of 5.0 × 10^5 cells in EP tube was successively added 50 μL of 1:10 dilution of day 28 anti-serums and 1:50 dilution of RBD-His protein. After incubation at 0 ºC for 30 min, the cells were washed with PBS. Then, 50 μL 1:100 diluted anti-6X His tag antibody-FITC was added and incubated at 0 ºC in darkness for 30 min. The resulting cells were collected and washed with FACS buffer for another 3 times. Percent positive cells and MFI of stained cells were recorded using a FACS flow cytometer. Data were processed and analyzed with FlowJo software.

Table S3. Mean FITC-A of antisera collected mice immunized with RBD-hFc/**1-10** and RBD-hFc/Al

	Mean FITC-A	Cells
Negative control	3776.000	10000
Positive control	241256.000	10000
RBD-hFc/**1**	25693.000	10000
RBD-hFc/**2**	58568.333	10000
RBD-hFc/**3**	30108.333	10000
RBD-hFc/**4**	52091.000	10000

RBD-hFc/**5**	43850.667	10000
RBD-hFc/**6**	48938.333	10000
RBD-hFc/**7**	23469.667	10000
RBD-hFc/**8**	48634.000	10000
RBD-hFc/**9**	59931.667	10000
RBD-hFc/**10**	36485.000	10000
RBD-hFc/Al	42556.667	10000

5. Neutralization assay

Vero E6 cells were plated at 2×10^4 cells each well in 96-well tissue culture plates and grown at 37°C overnight. Mice sera were per-heated at 56 °C for 30 min. Serial 4-fold dilutions (1:4 - 1:1024) of mice sera were separately mixed with 100TCID$_{50}$ (50% tissue culture infective dose) of live SARS-CoV-2 virus and incubated at 37°C for 2 h. Each sera sample was tested for twice. For each assay, cells infected with 100 TCID$_{50}$ SARS-CoV-2 and 0.1 TCID$_{50}$ SARS-CoV-2 were respectively applied as positive and negative controls. Cytopathic effect (CPE) in wells were observed daily and recorded after 72 h of the culture. The neutralizing titers of mice sera that completely suppressed 50% CPE of the wells were calculated by Reed-Muench method.

Table S4. Neutralizing antibody titters of each group

	Neutralizing antibody titers	
	Day28	Day42
Control	2	2
RBD-hFc/**1**	32	32
RBD-hFc/**2**	4	16
RBD-hFc/**3**	32	32
RBD-hFc/**4**	16	16
RBD-hFc/**5**	16	32
RBD-hFc/**6**	8	8
RBD-hFc/**7**	16	32
RBD-hFc/**8**	8	16
RBD-hFc/**9**	32	32
RBD-hFc/**10**	8	8
RBD-hFc/Al	16	32

VII. Immunological studies of 1 combined with Al

The preparation of RBD-hFc/**1**, RBD-hFc/**2**, RBD-hFc/**1**/Al and the protocols of mouse immunization, ELISA assay, FACS analysis and neutralization assay in this study were similar to above experiments. In order to test the effect in more detail, we extended the period of observation to 100 days in this study, and each mouse was bled on days 14, 28, 42, 70 and 100 post-first immunization.

1. ELISA results

Table S5. The antibody titers of IgG in days 14, 28, 42, 70 and 100 antisera induced by RBD-hFc/**1**, RBD-hFc/Al and RBD-hFc/**1**/Al.

	RBD-hFc/**1**			RBD-hFc/Al			RBD-hFc/**1**/Al		
	Mean	SD	N	Mean	SD	N	Mean	SD	N
Day 14	4202.963	1011.788	3	14101.633	778.240	3	20589.400	1307.338	3
Day 28	57386.627	3663.078	3	53823.673	2749.799	3	94537.750	5031.524	3
Day 42	55115.930	1443.783	3	61776.823	1907.838	3	82477.633	2410.912	3
Day 70	50670.080	2003.918	3	63799.773	243.514	3	86306.073	4665.653	3
Day 100	57861.913	1585.231	3	70625.960	1338.355	3	103464.267	2637.598	3

Table S6. The antibody titers of IgG isotypes in day 28 antisera induced by RBD-hFc/**1**, RBD-hFc/Al and RBD-hFc/**1**/Al.

	RBD-hFc/**1**			RBD-hFc/Al			RBD-hFc/**1**/Al		
	Mean	SD	N	Mean	SD	N	Mean	SD	N
IgG1	75409.997	1983.040	3	67729.173	7067.518	3	106706.067	5532.533	3
IgG2a	743.396	579.670	3	605.948	304.927	3	34909.733	1502.769	3
IgG2b	8934.891	4522.230	3	8740.198	1368.598	3	31535.613	10082.001	3
IgG3	5520.773	1728.974	3	5346.062	3608.080	3	6504.777	3098.686	3

2. Analysis of IFN-γ and IL-4 levels provoked by RBD-hFc/1, RBD-hFc/Al and RBD-hFc/1/Al

Table S7. IFN-γ and IL-4 in day 28 anti-sera collected from mice immunized with RBD-hFc/**1**, RBD-hFc/Al and RBD-hFc/**1**/Al

	IFN-γ	IL-4

	Mean	SD	N	Mean	SD	N
RBD-hFc/**1**	17.410	8.524	3	17.703	10.283	3
RBD-hFc/Al	32.533	8.869	3	987.200	24.228	3
RBD-hFc/**1**/Al	43.473	3.181	3	1884.460	33.273	3

3. FACS analyses

Table S8. Mean FITC-A of antisera collected mice immunized with RBD-hFc/**1**, RBD-hFc/Al and RBD-hFc/**1**/Al

	Mean FITC-A	Cells
Negative control	2076.000	10000
Positive control	35301.667	10000
RBD-hFc/**1**	30443.667	10000
RBD-hFc/Al	35301.667	10000
RBD-hFc/**1**/Al	64441.667	10000

4. Neutralization assay

Table S9. Neutralizing antibody titters of RBD-hFc/**1**, RBD-hFc/**Al** and RBD-hFc/**1**/Al

Neutralizing antibody titers	RBD-hFc/**1**	RBD-hFc/Al	RBD-hFc/**1**/Al
Day 28	128	128	1024
Day 42	64	32	512
Day 70	64	256	1024
Day 100	270	128	1024

References

1 G. Wasonga, Y. Tatara, I. Kakizaki and X. Huang, *J. Carbohydr. Chem.*, 2013, **32**, 392–409.

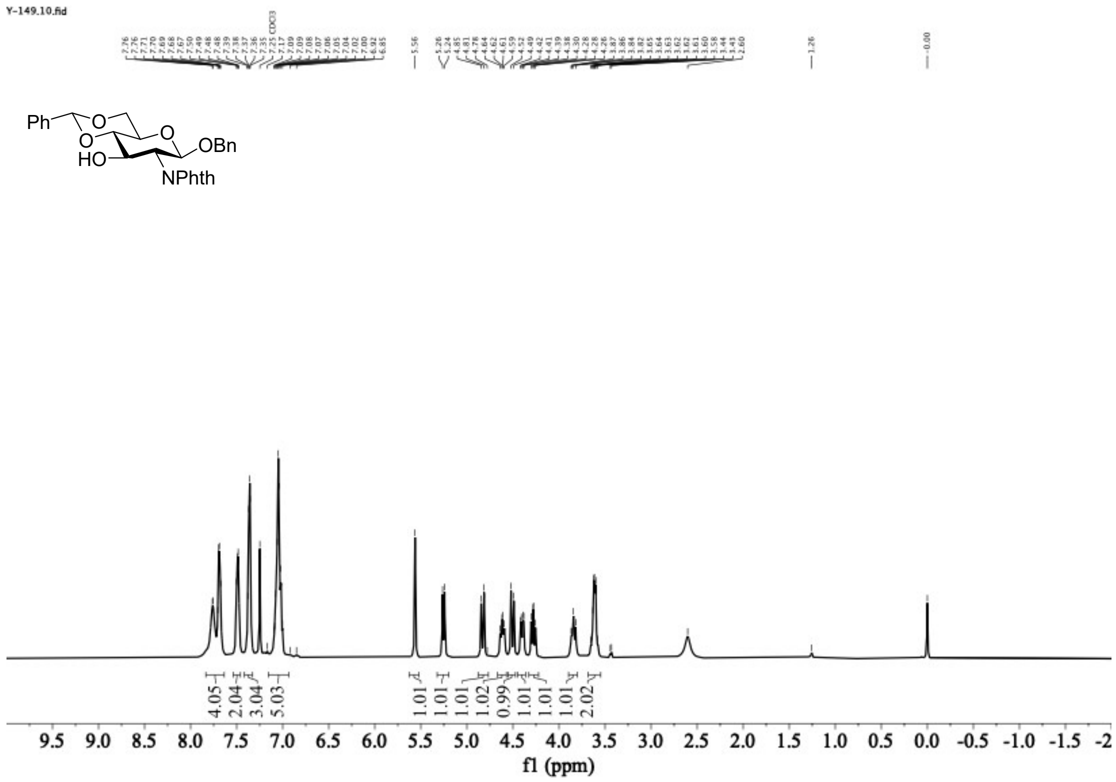
2 Q. Wang, J. Xue and Z. Guo, *Chem. Commun.*, 2009, 5536–5537.

3 L. Wang, S. Feng, S. Wang, H. Li, Z. Guo and G. Gu, *J. Org. Chem.*, 2017, **82**, 12085–12096.

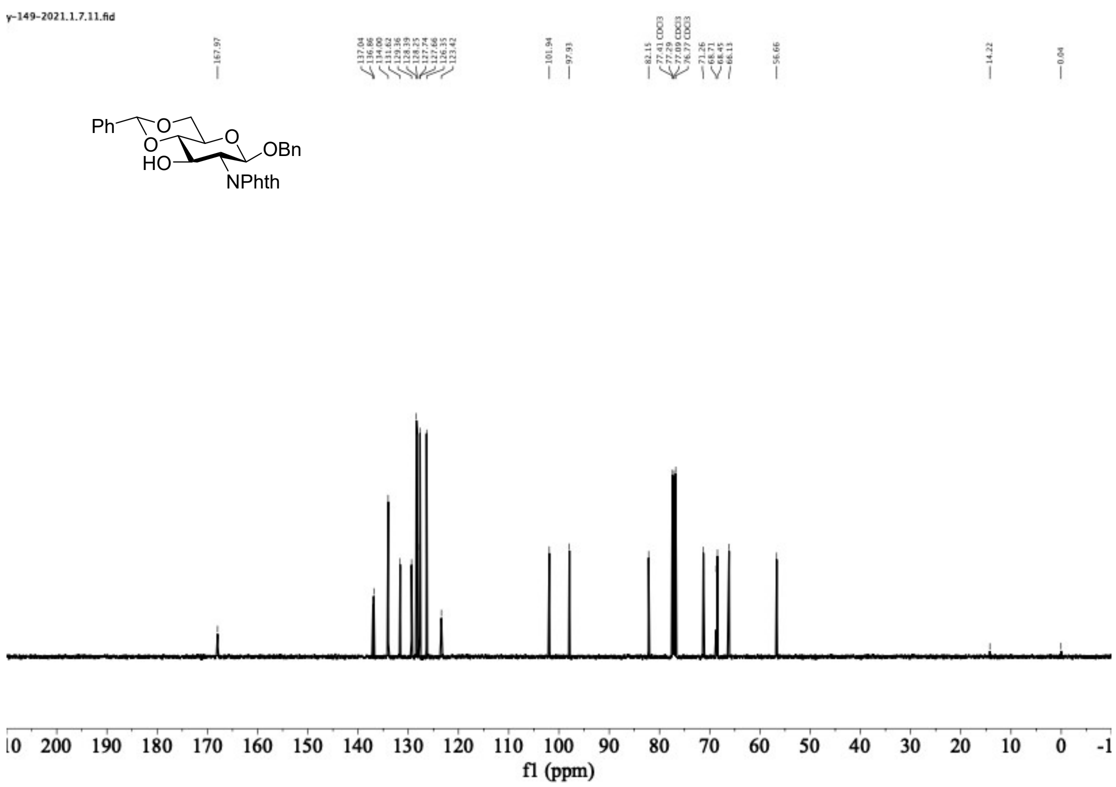
4 X. Qi, B. Ke, Q. Feng, D. Yang, Q. Lian, Z. Li, L. Lu, C. Ke, Z. Liu and G. Liao, *Chem. Commun.*, 2020, **56**, 8683–8686.

5 X. Luo, Q. Lian, W. Li, L. Chen, R. Zhang, D. Yang, L. Gao, X. Qi, Z. Liu and G. Liao, *Chem. Sci.*, 2021, **12**, 15998–16013.

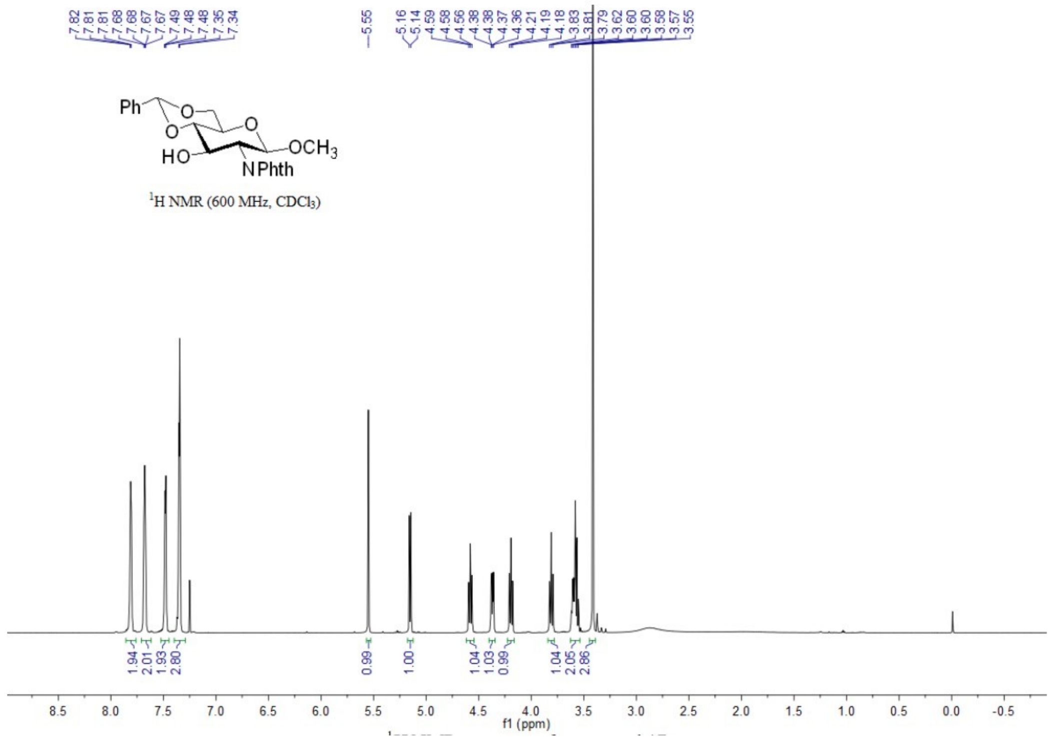
NMR and HRMS spectrum of compounds



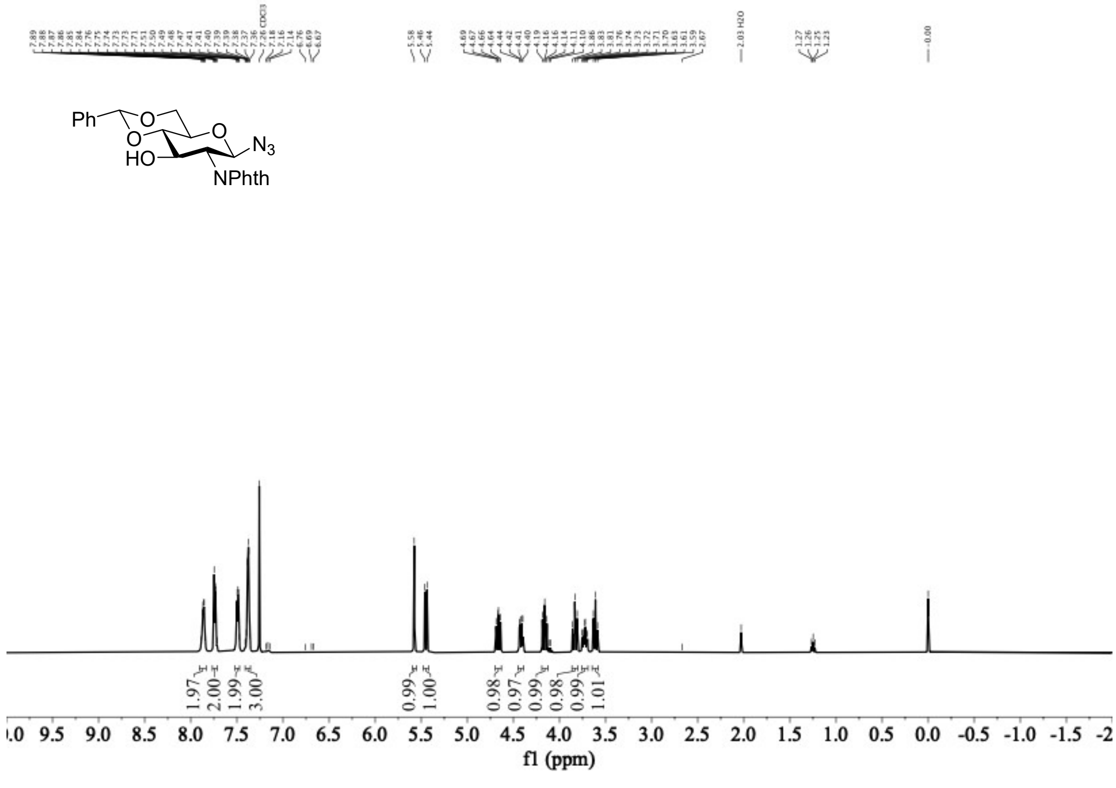
^1H NMR spectrum of compound **11** ($CDCl_3$, 400 MHz)



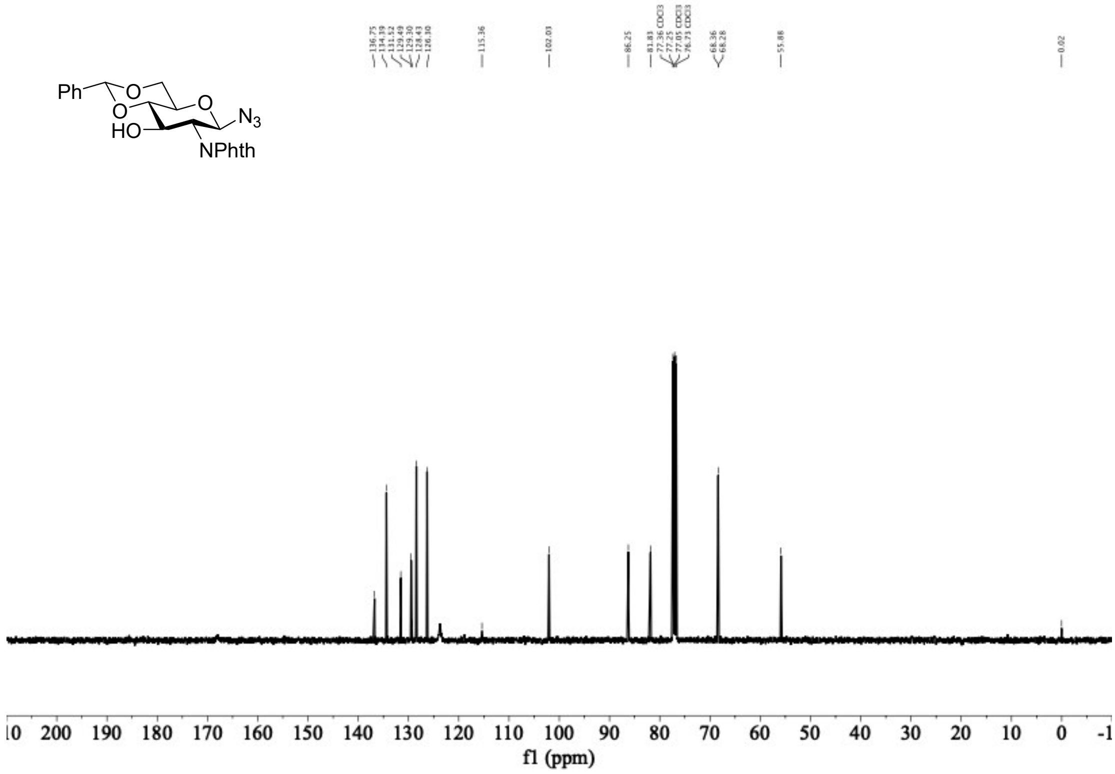
^{13}C NMR spectrum of compound **11** ($CDCl_3$, 100 MHz)



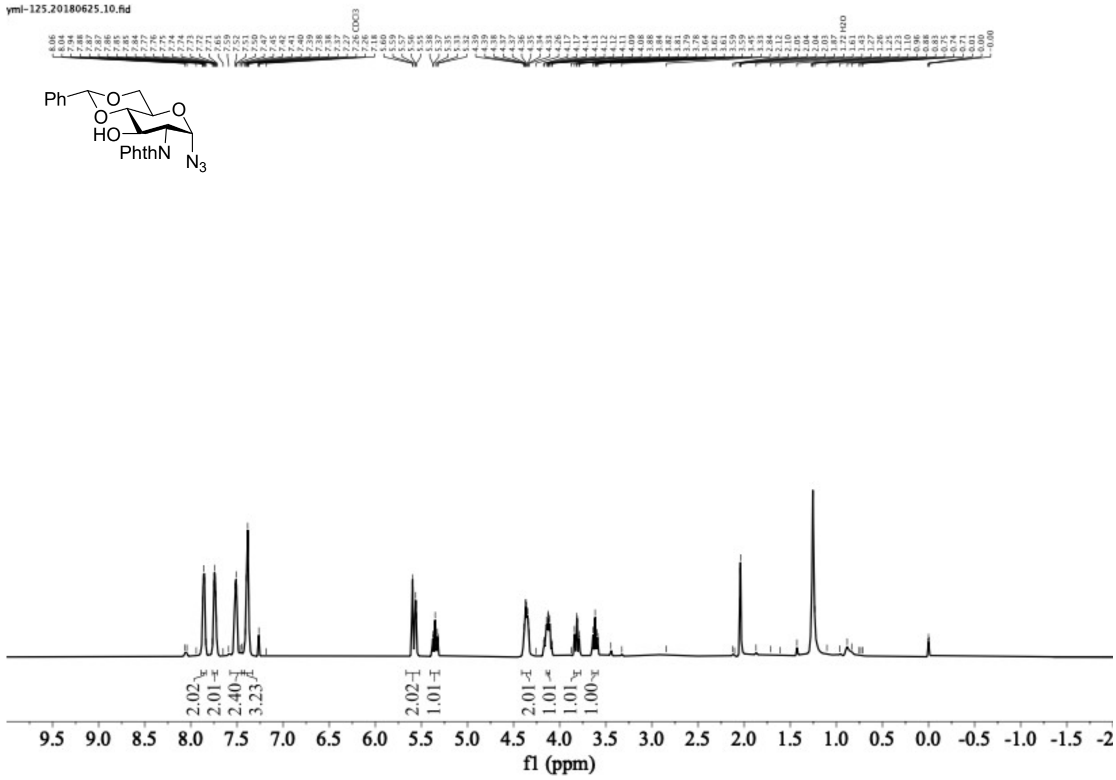
^{1}H NMR Spectrum of compound **12** ($CDCl_3$, 400 MHz)



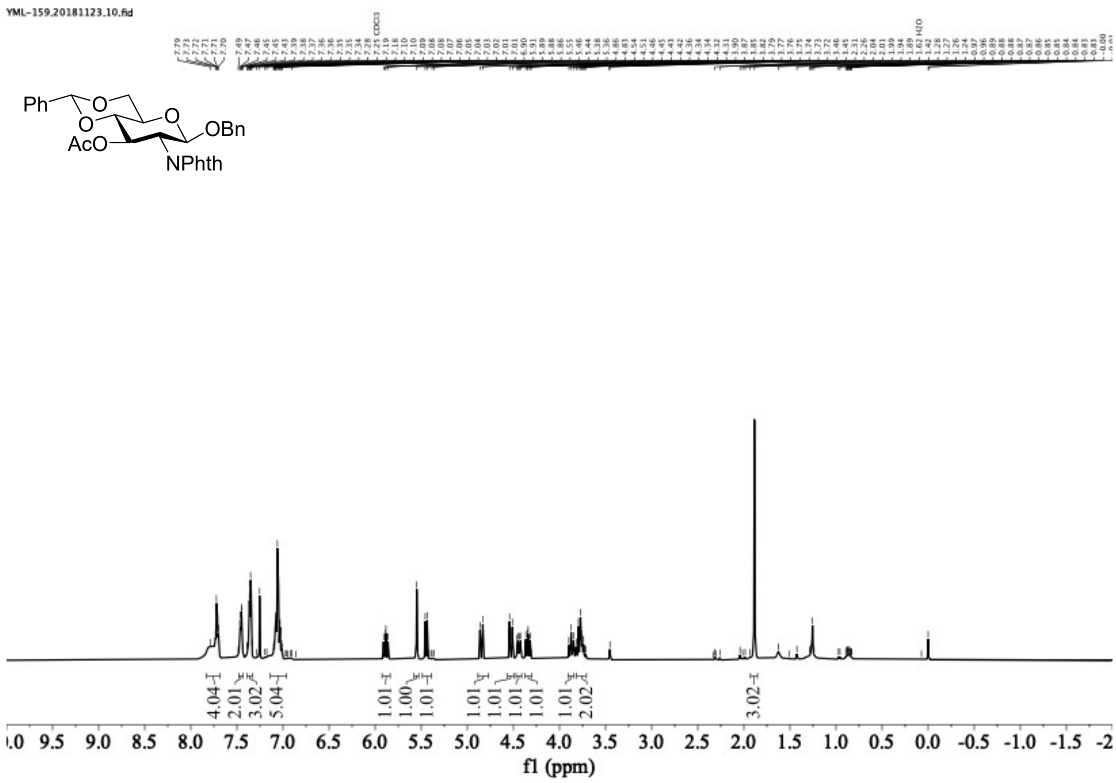
^{1}H NMR spectrum of compound **13** ($CDCl_3$, 400 MHz)



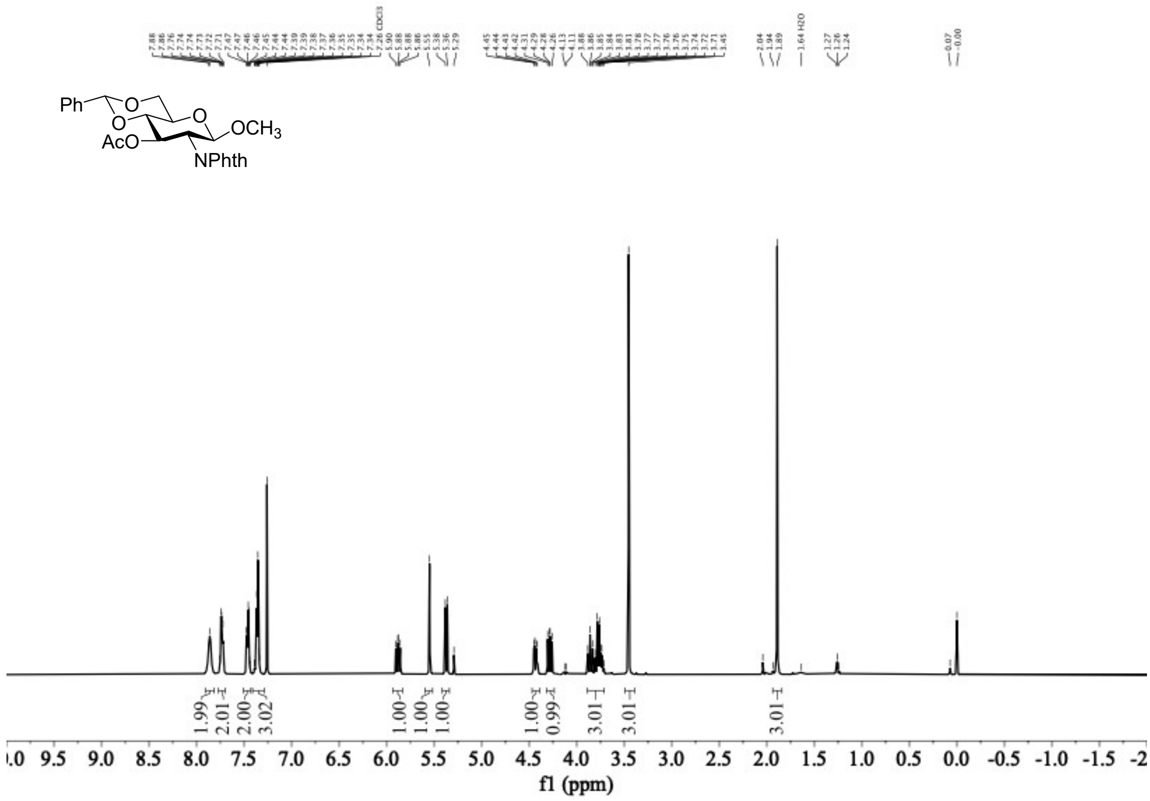
$^{13}C\{^{1}H\}$ NMR spectrum of compound **13** ($CDCl_3$, 100 MHz)



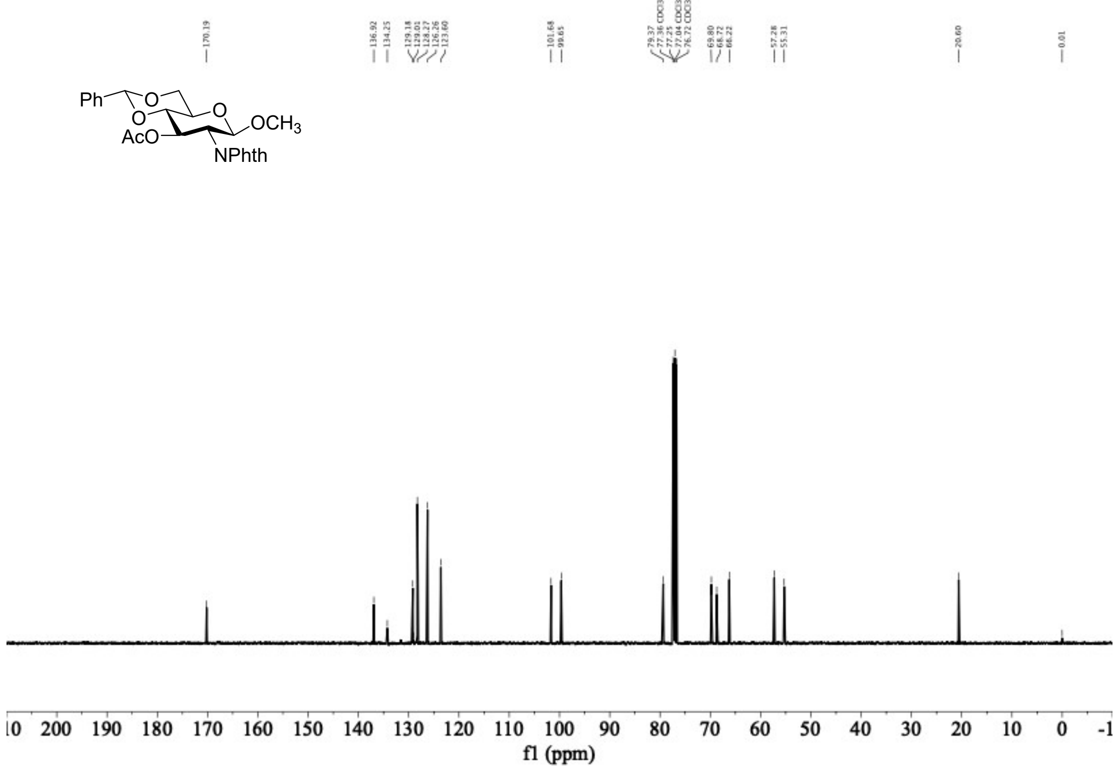
^{1}H NMR spectrum of compound **14** ($CDCl_3$, 400 MHz)



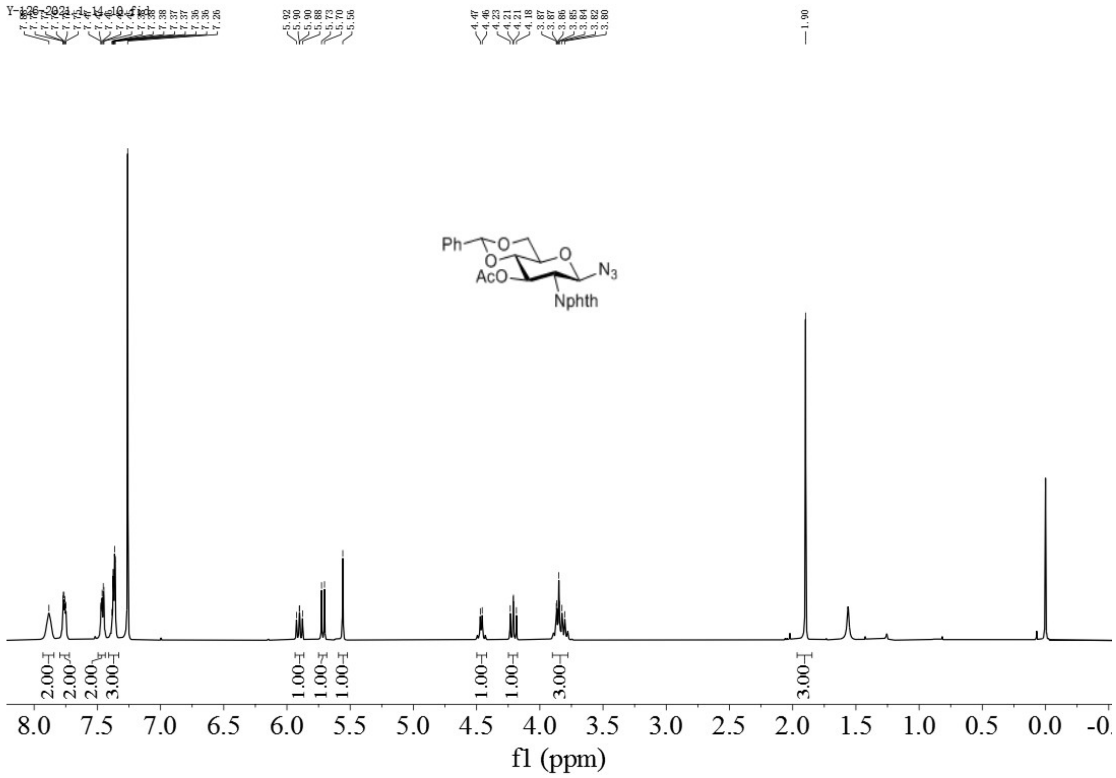
[1]H NMR spectrum of compound **15** ($CDCl_3$, 400 MHz)



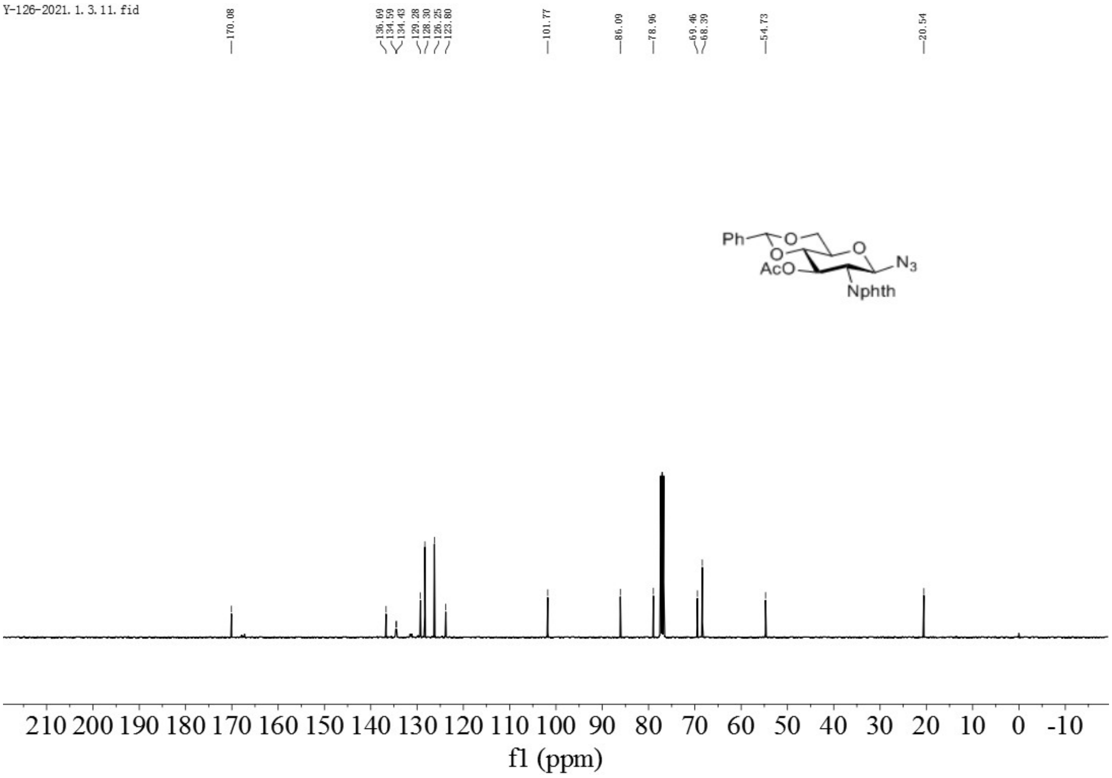
[1]H NMR spectrum of compound **16** ($CDCl_3$, 400 MHz)



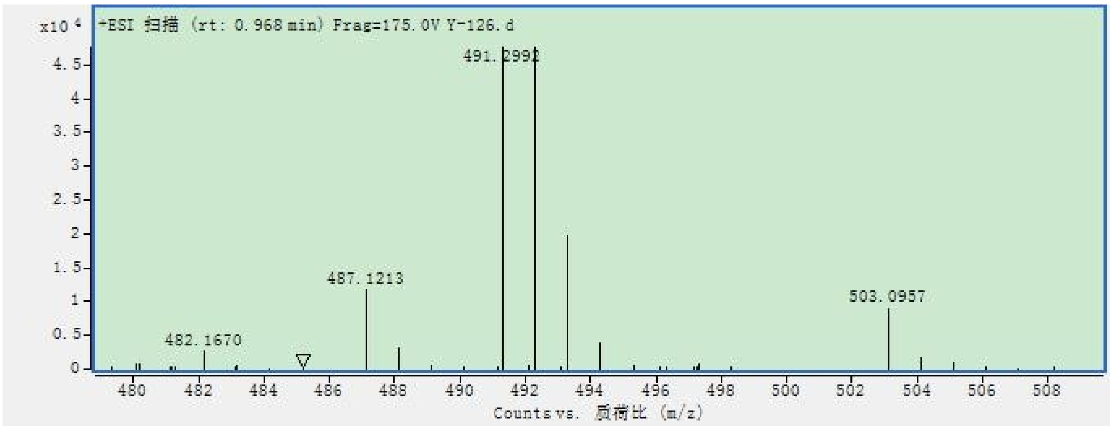
$^{13}C\{^{1}H\}$ NMR spectrum of compound **16** ($CDCl_3$, 100 MHz)



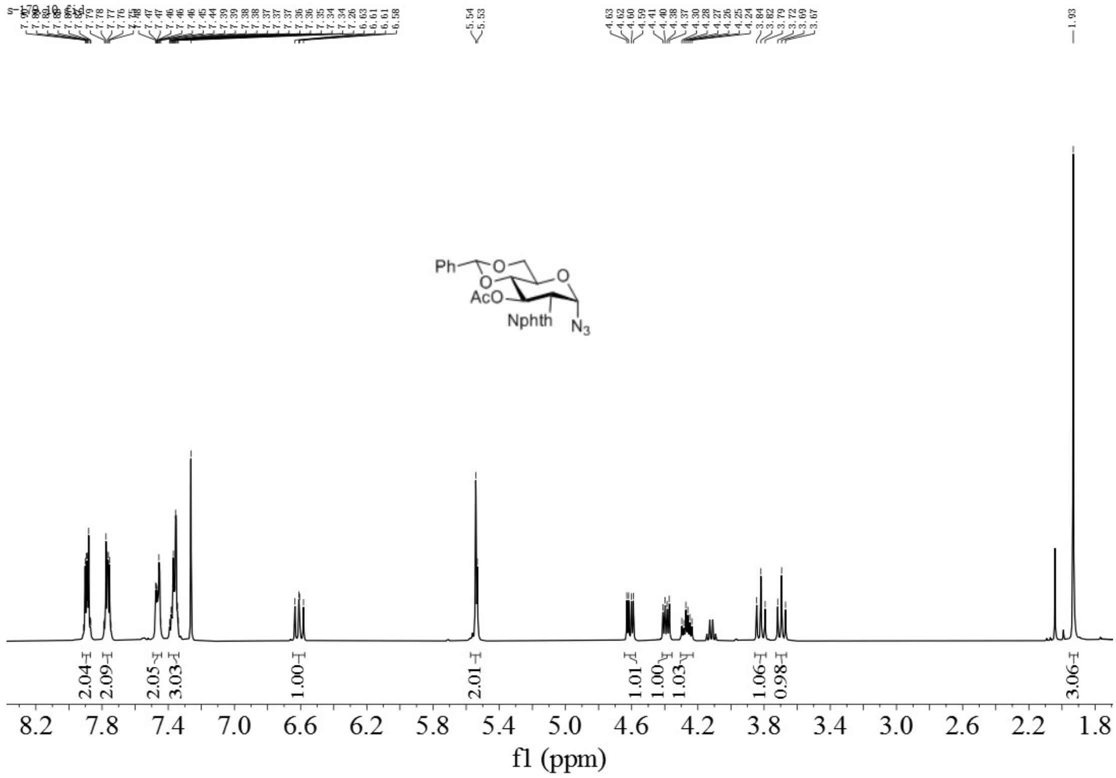
^{1}H NMR spectrum of compound **17** ($CDCl_3$, 400 MHz)



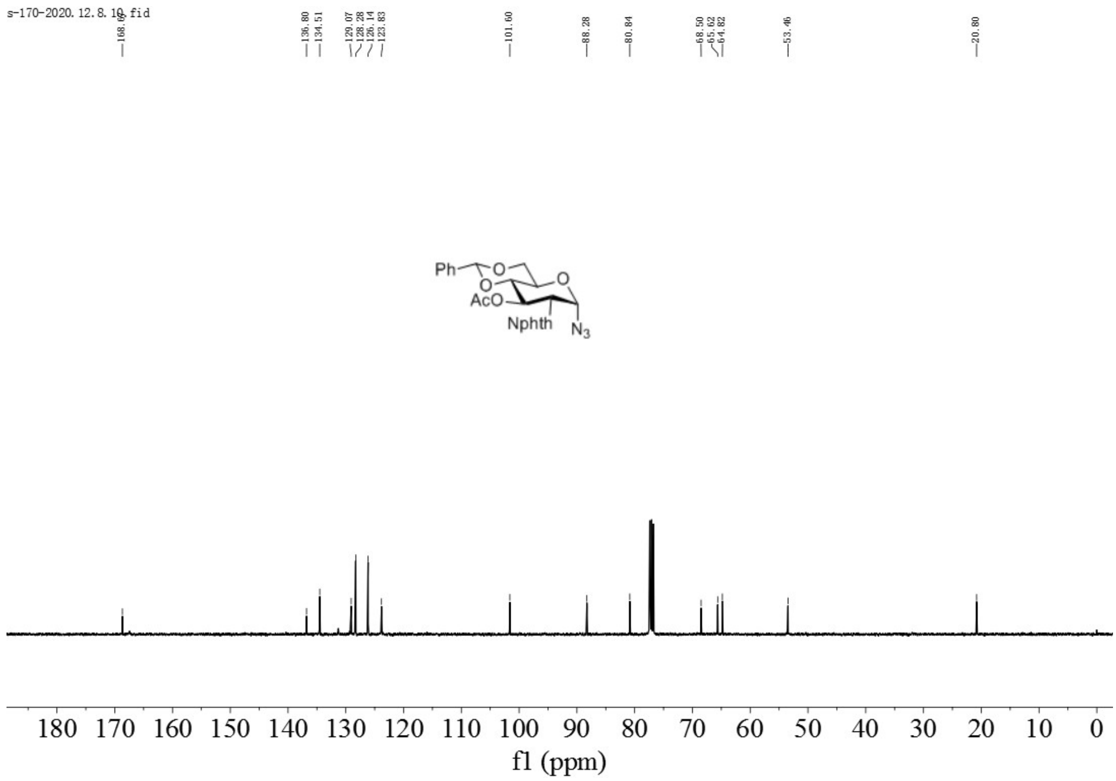
$^{13}C\{^{1}H\}$ NMR spectrum of compound **17** ($CDCl_3$, 100 MHz)



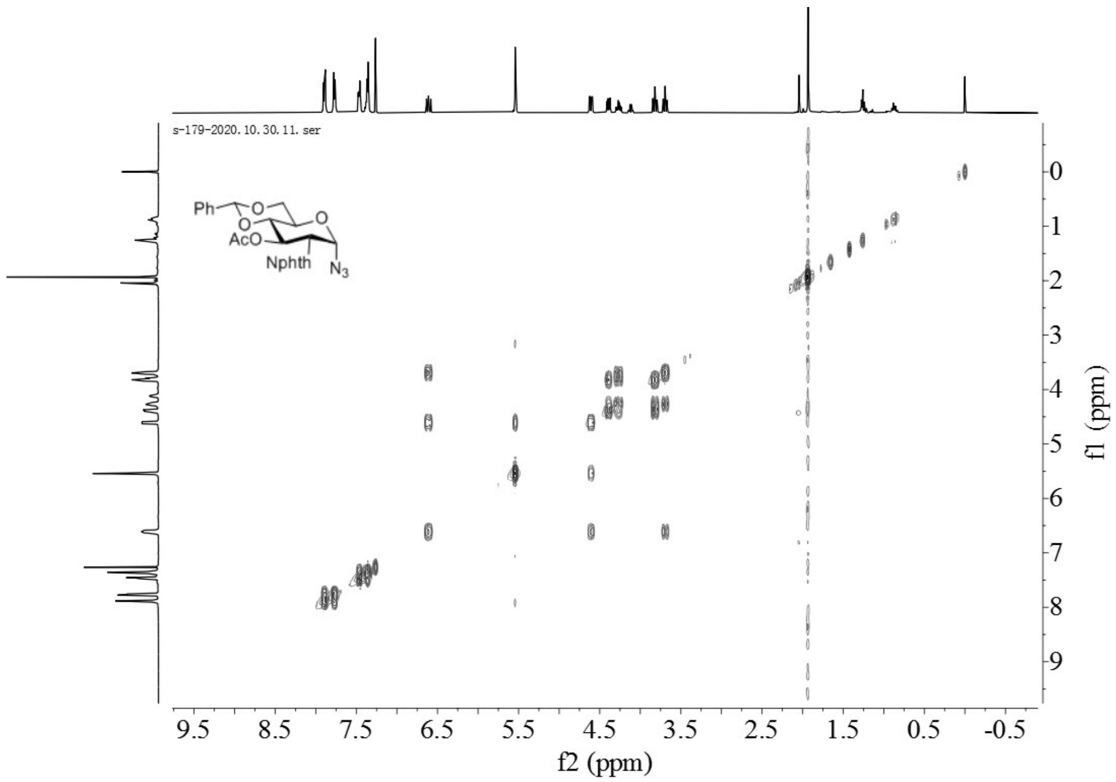
HRMS spectrum of compound **17**



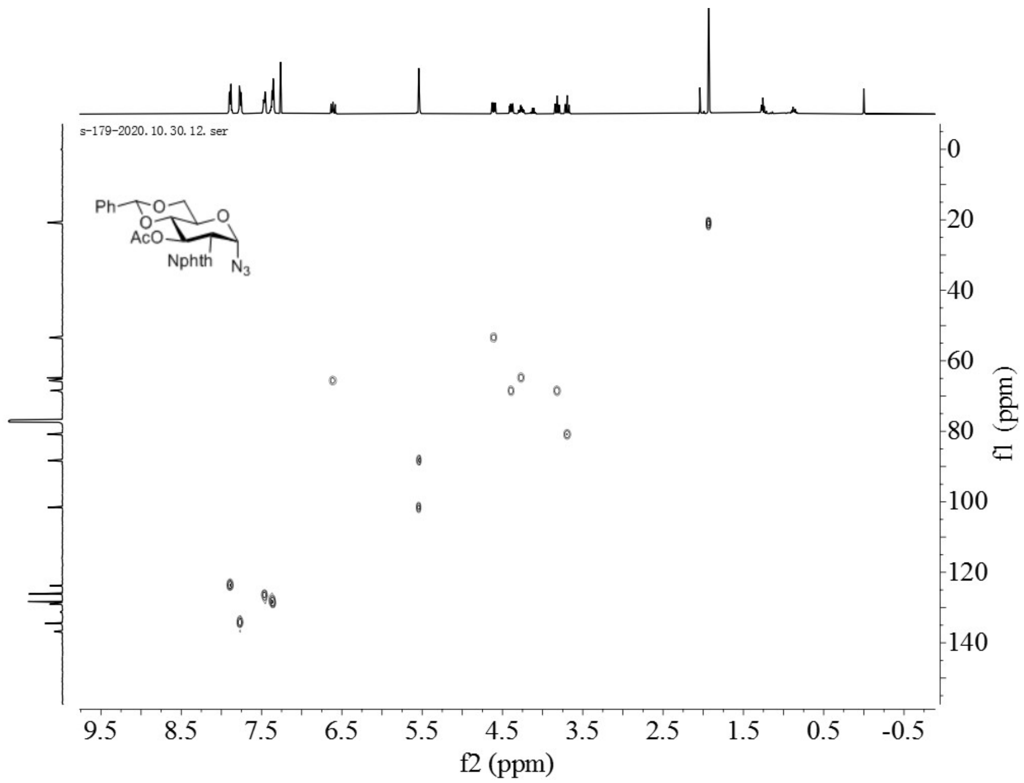
^{1}H NMR spectrum of compound **18** ($CDCl_3$, 400 MHz)



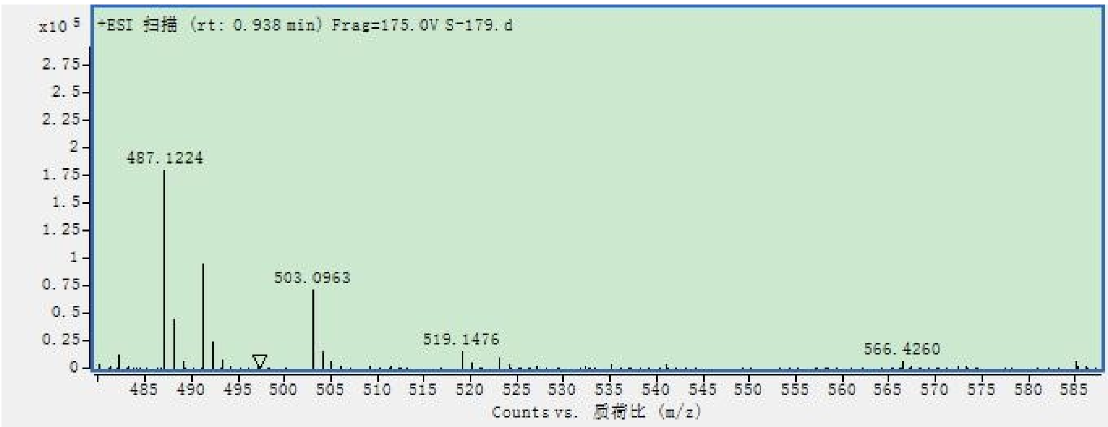
$^{13}C\{^{1}H\}$ NMR spectrum of compound **18** ($CDCl_3$, 100 MHz)



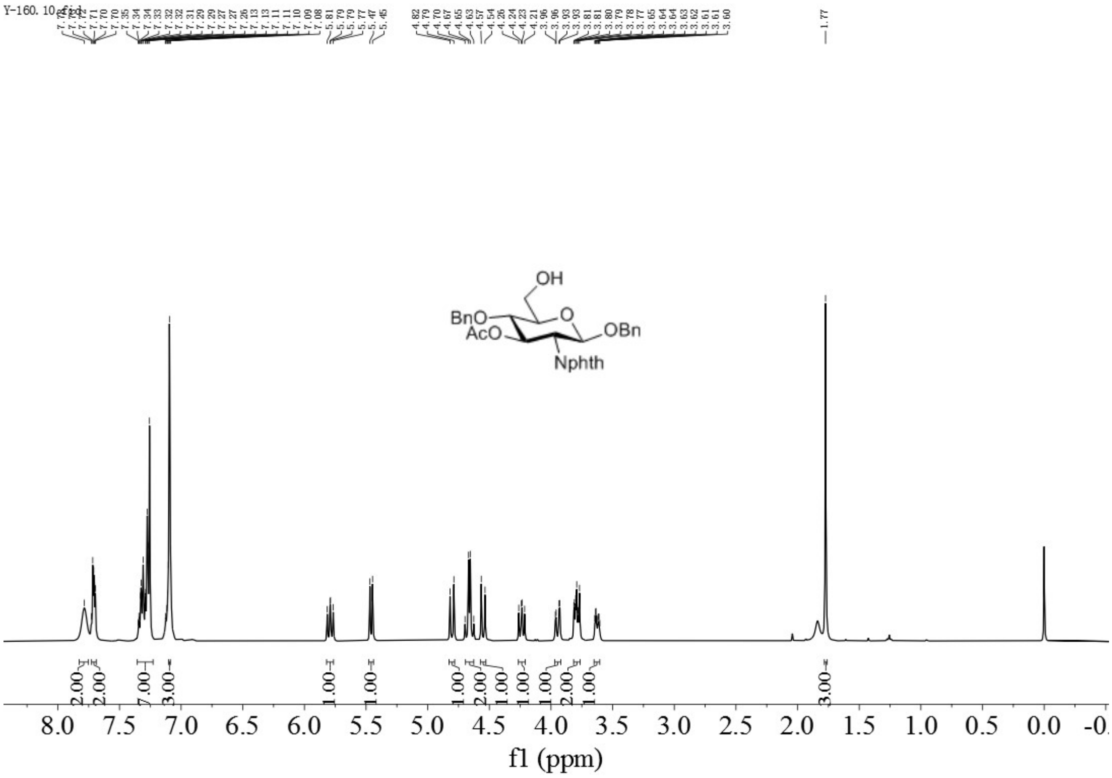
^{1}H – ^{1}H COSY spectrum of compound **18** ($CDCl_3$, 400 MHz)



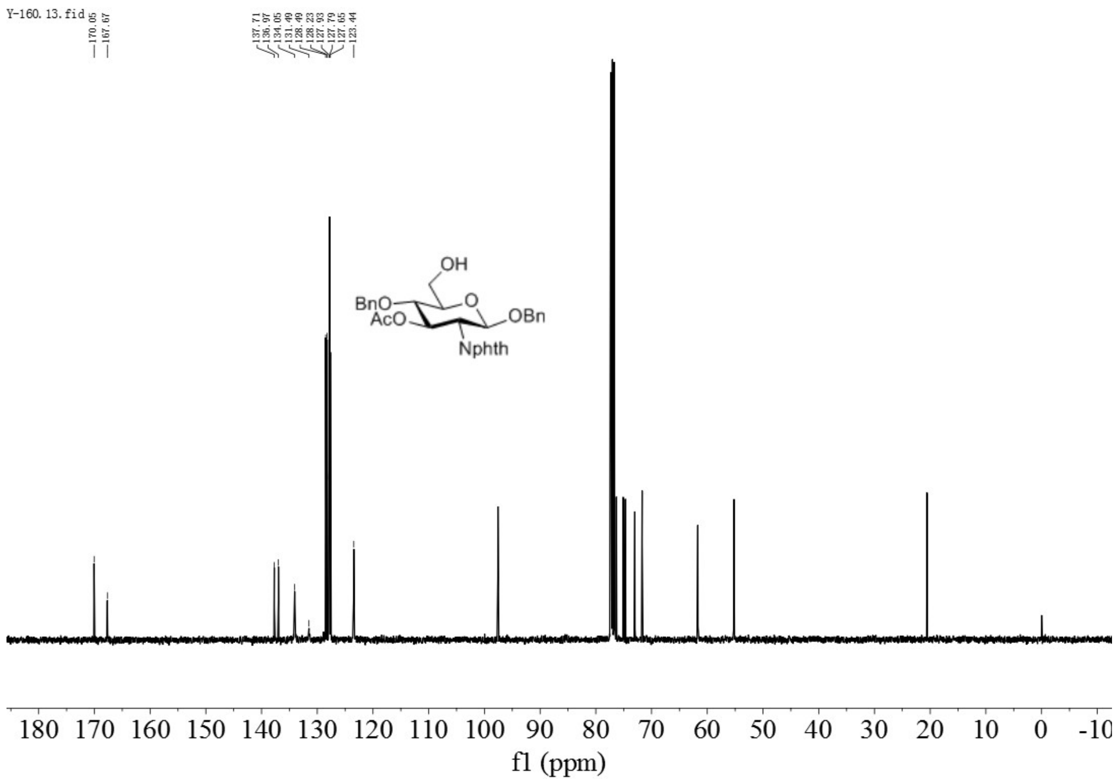
^{1}H – ^{13}C HMQC spectrum of compound **18** ($CDCl_3$, 400/100 MHz)



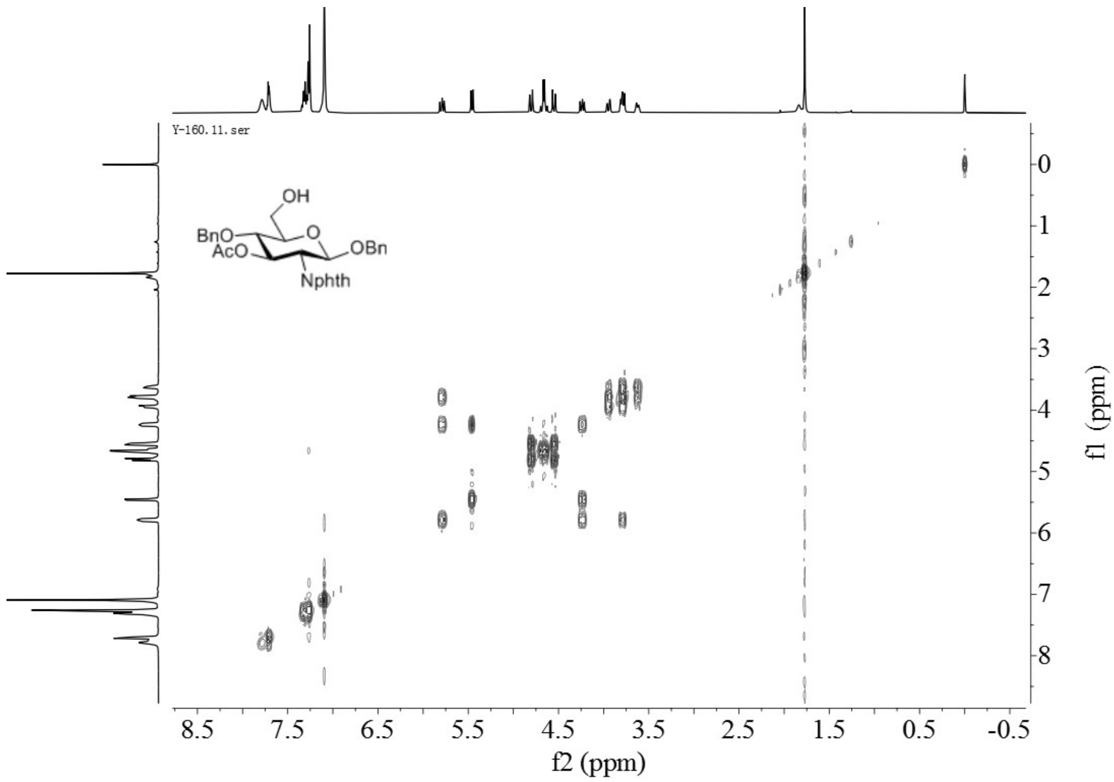
HRMS spectrum of compound **18**



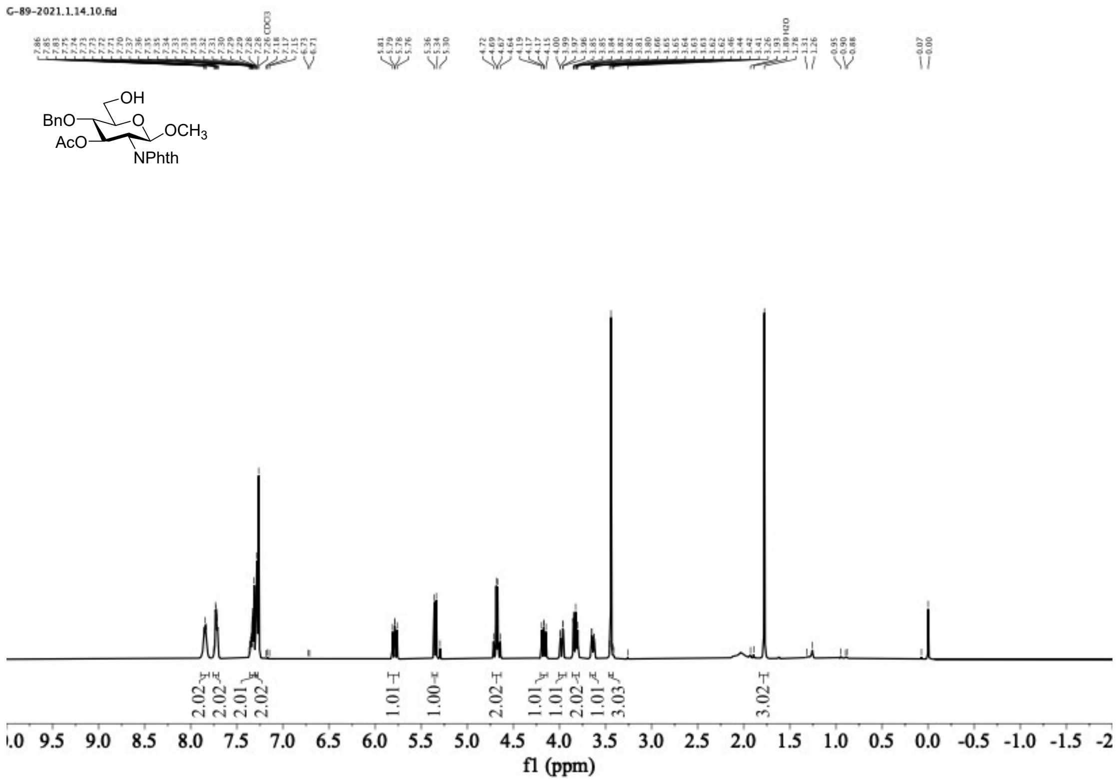
^{1}H NMR spectrum of compound **19** ($CDCl_3$, 400 MHz)



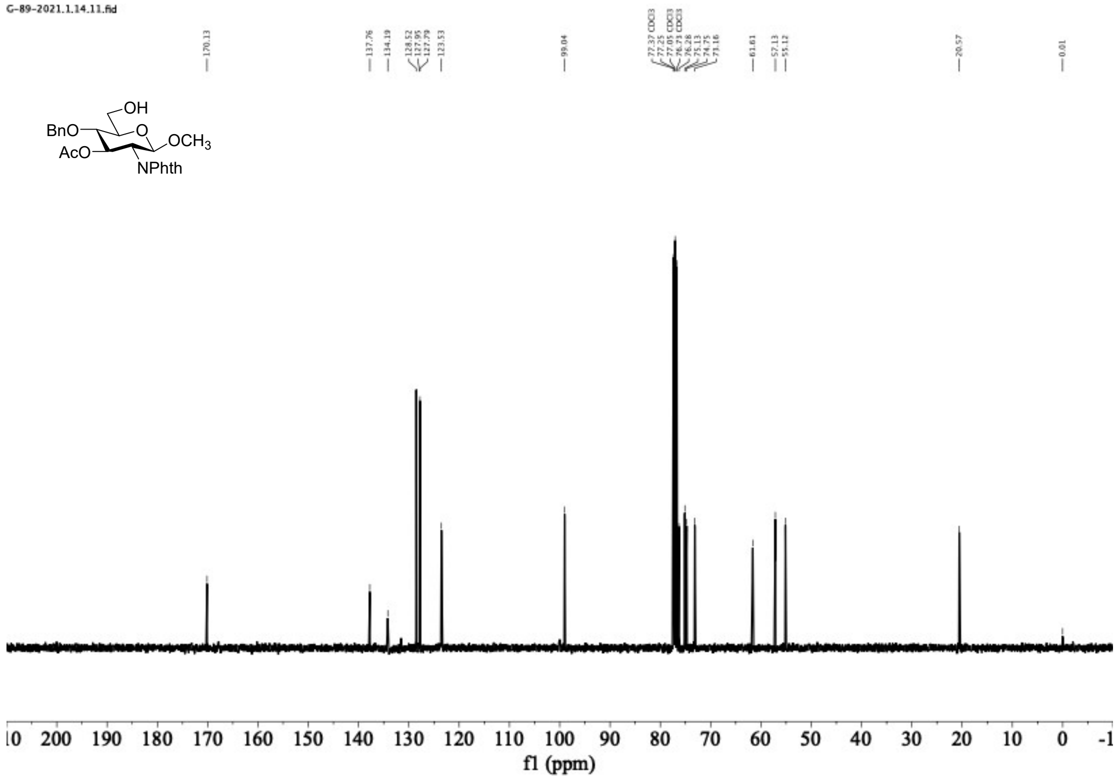
$^{13}C\{^{1}H\}$ NMR spectrum of compound **19** ($CDCl_3$, 100 MHz)



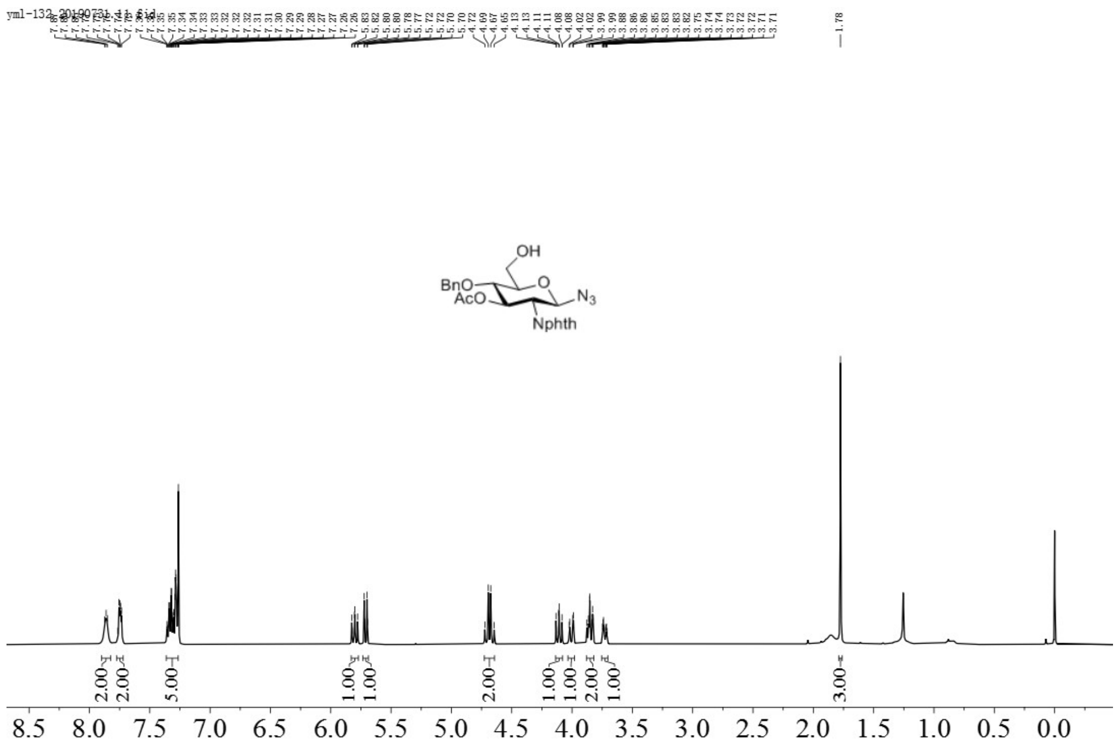
^1H – ^1H COSY spectrum of compound **19** ($CDCl_3$, 400 MHz)



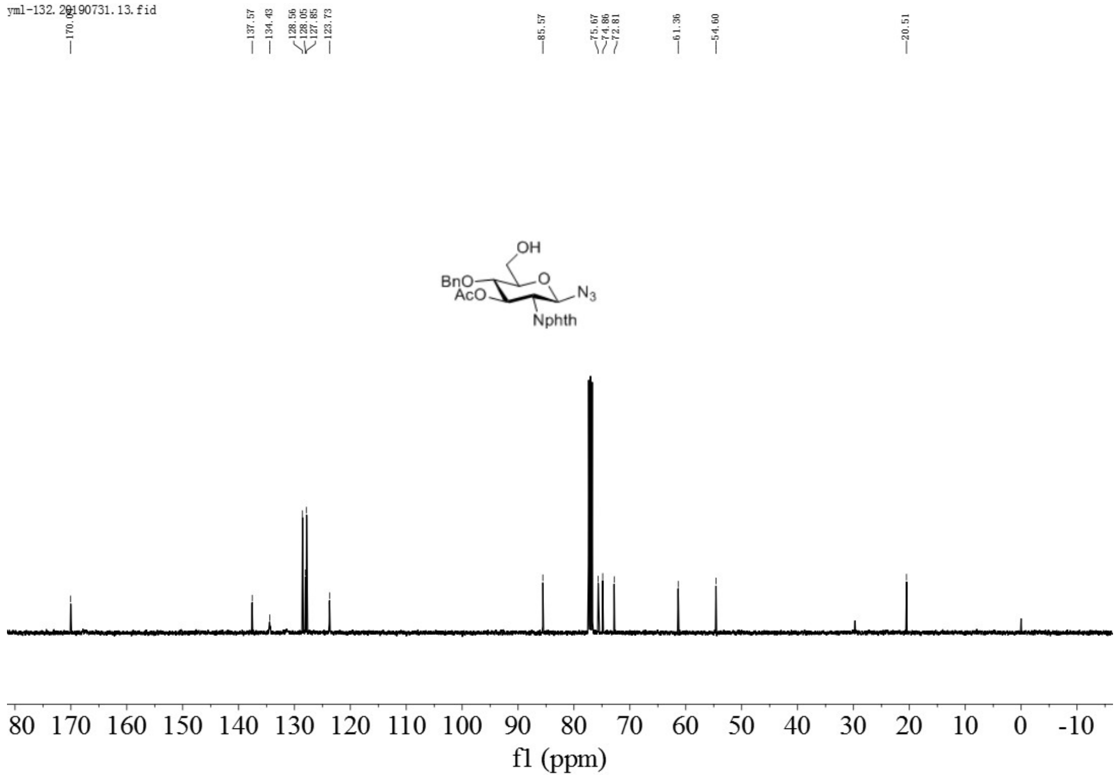
^1H NMR spectrum of compound **20** ($CDCl_3$, 400 MHz)



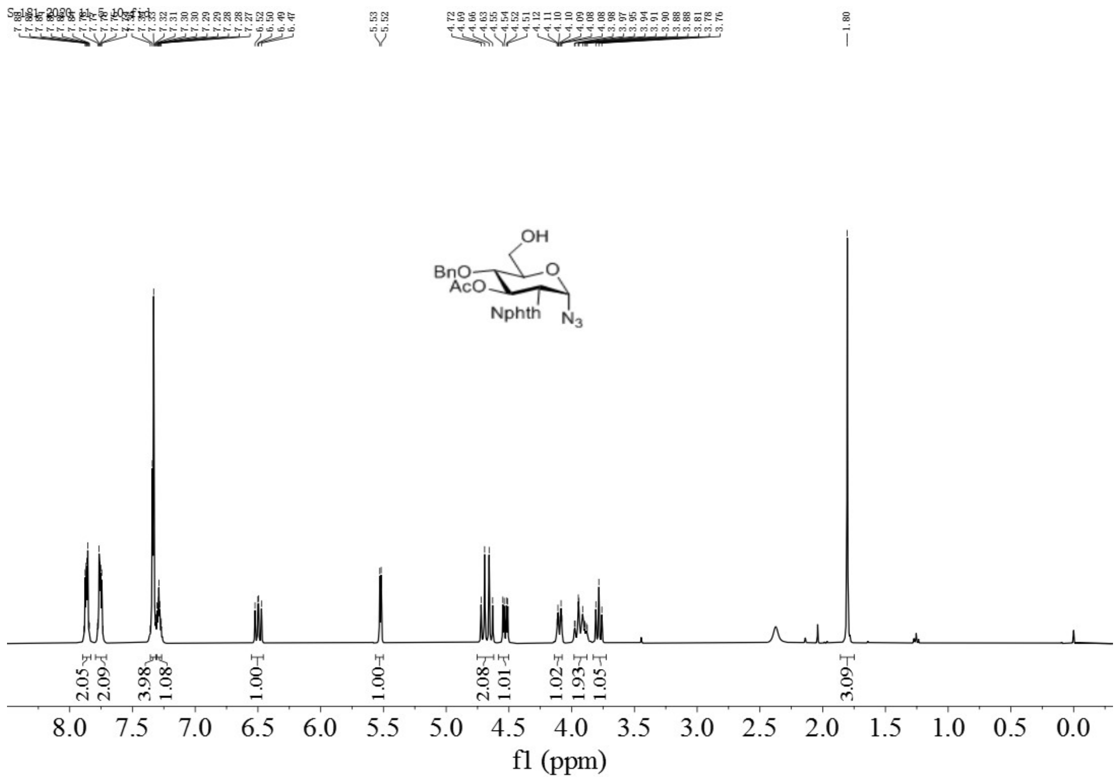
$^{13}C\{^{1}H\}$ NMR spectrum of compound **20** ($CDCl_3$, 100 MHz)



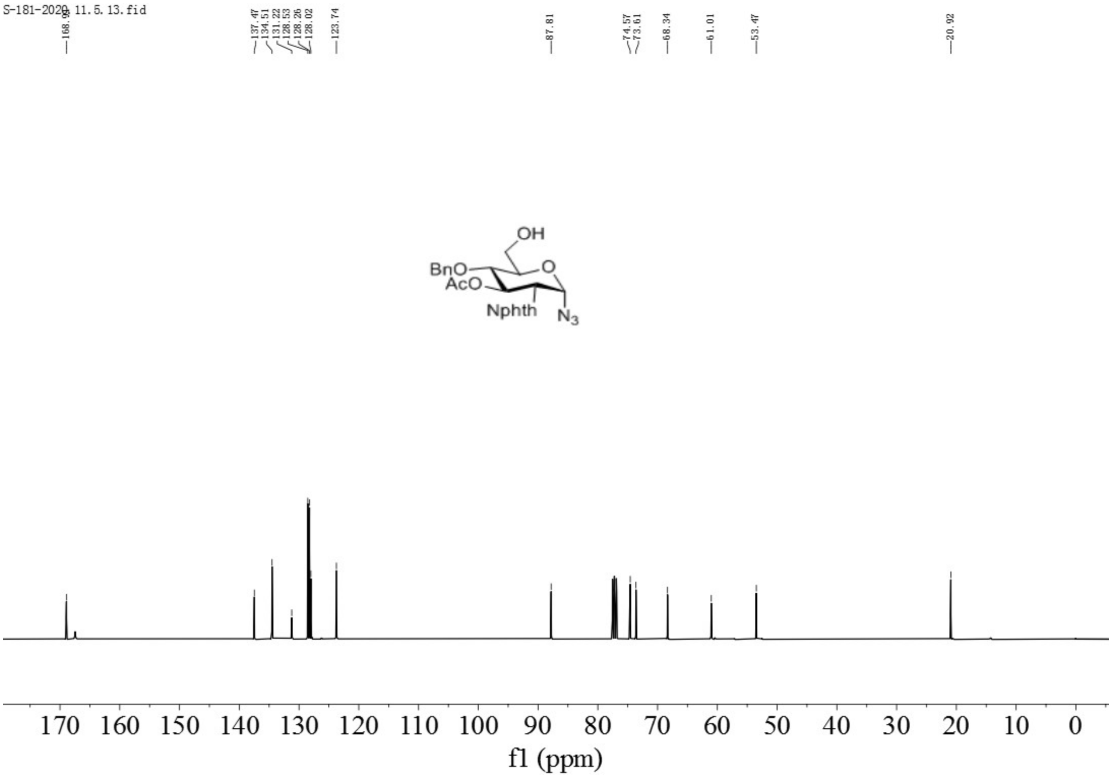
^{1}H NMR spectrum of compound **21** ($CDCl_3$, 400 MHz)



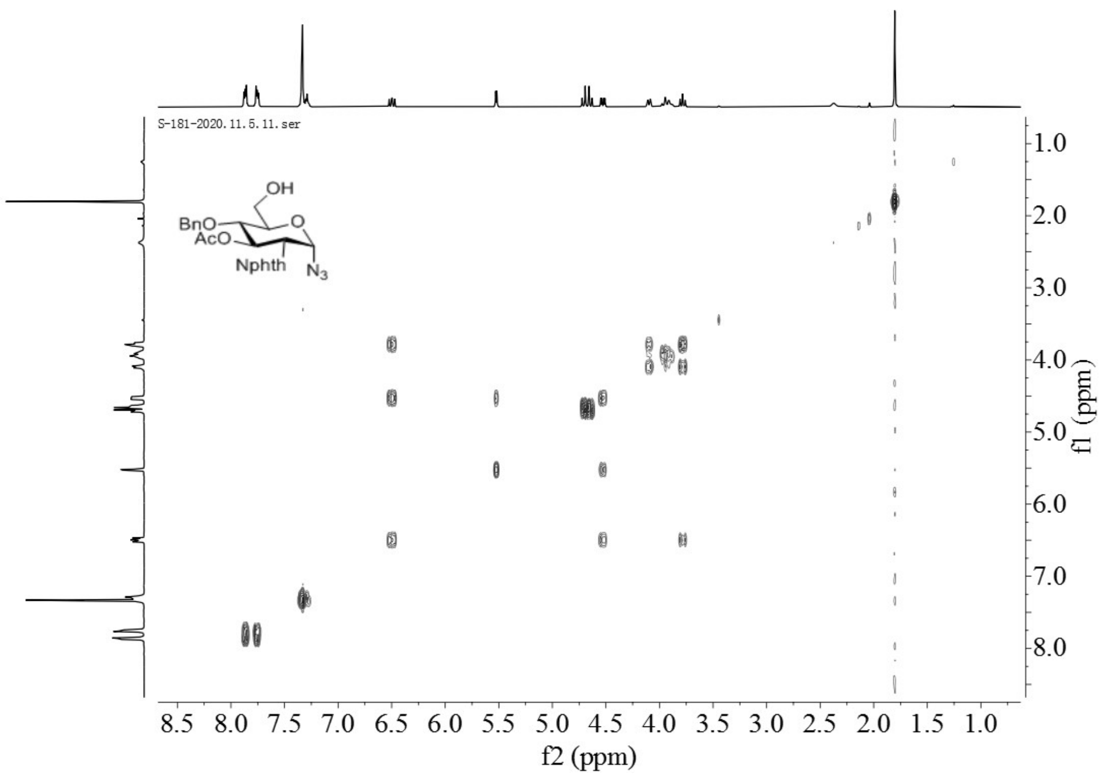
$^{13}C\{^{1}H\}$ NMR spectrum of compound **21** ($CDCl_3$, 100 MHz)



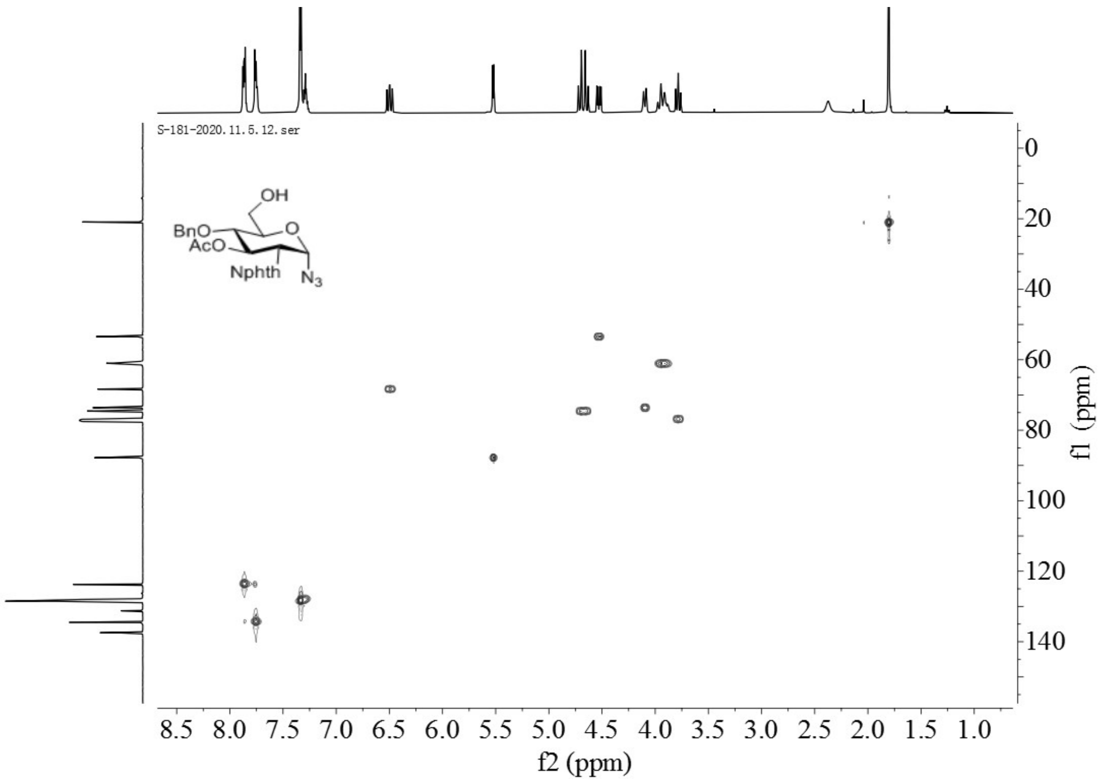
^{1}H NMR spectrum of compound **22** ($CDCl_3$, 400 MHz)



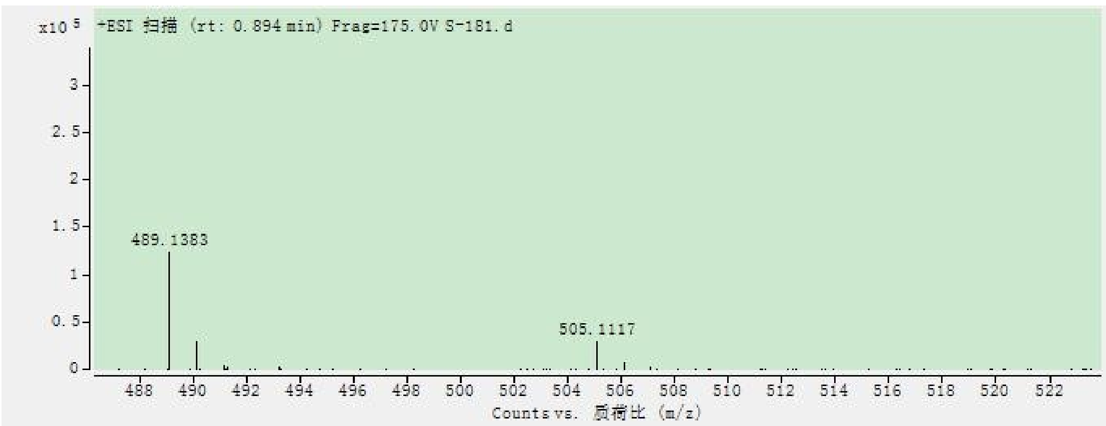
$^{13}C\{^{1}H\}$ NMR spectrum of compound **22** ($CDCl_3$, 100 MHz)



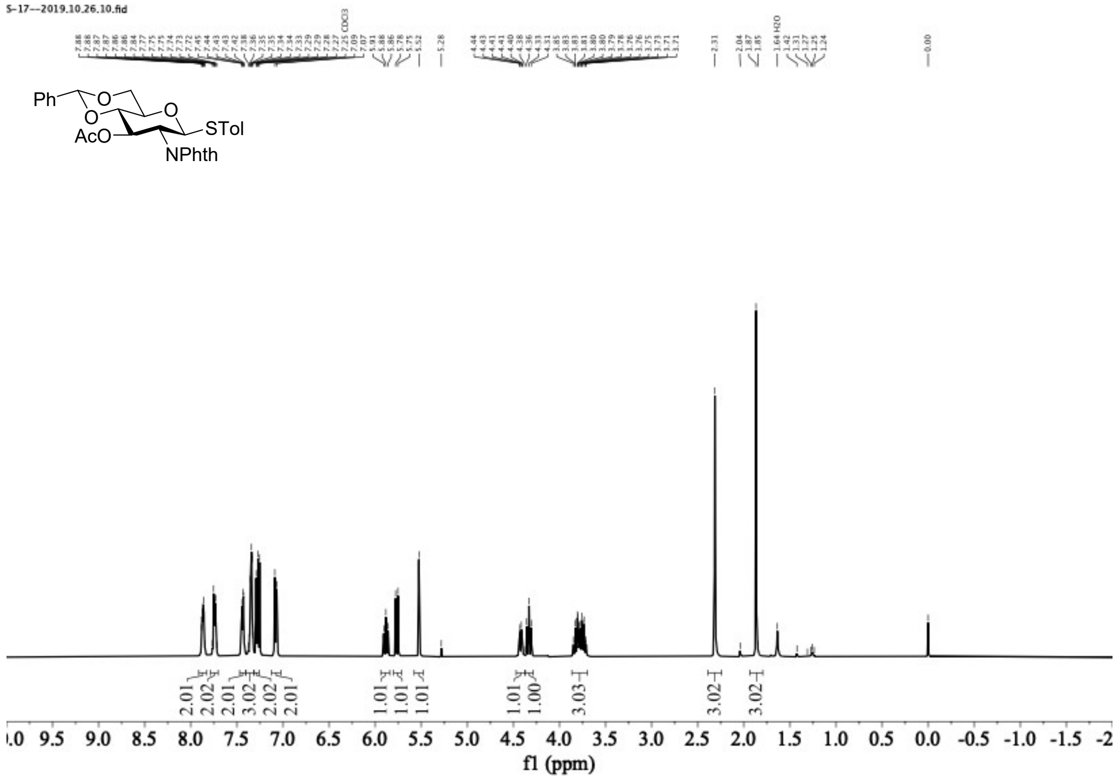
^{1}H – ^{1}H COSY spectrum of compound **22** ($CDCl_3$, 400 MHz)



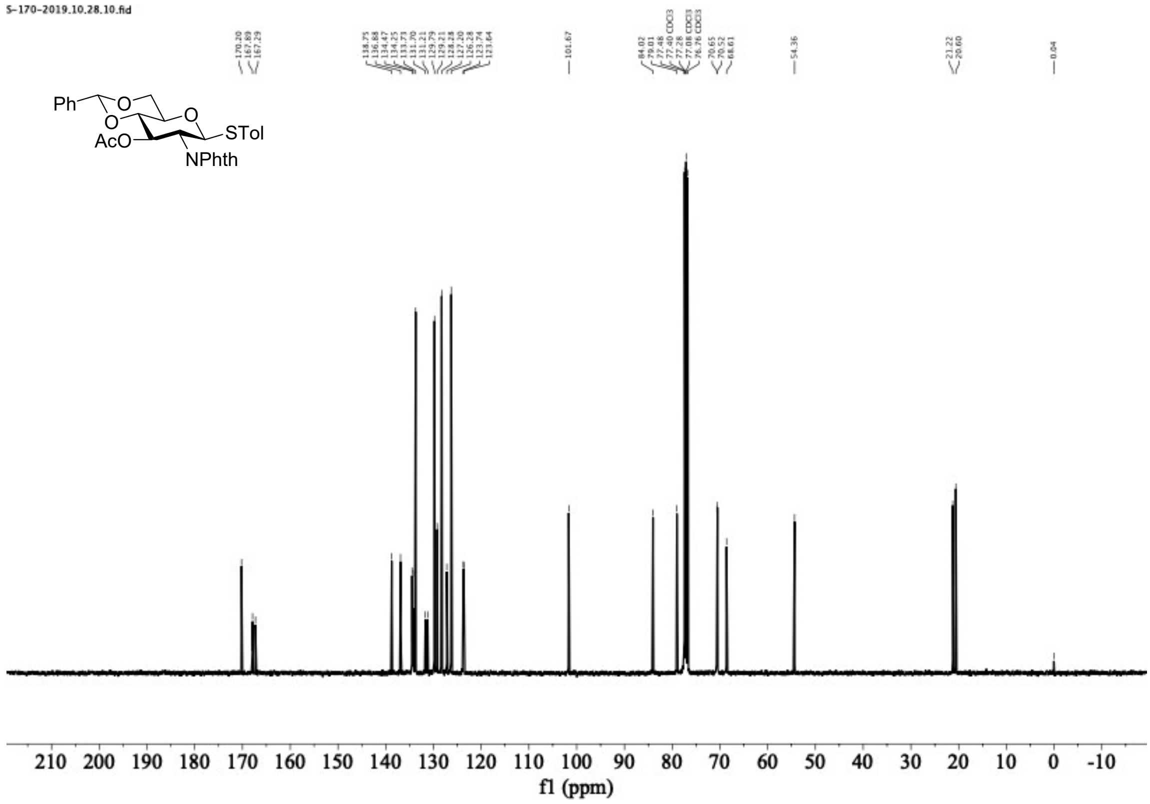
^{1}H – ^{13}C HMQC spectrum of compound **22** ($CDCl_3$, 400/100 MHz)



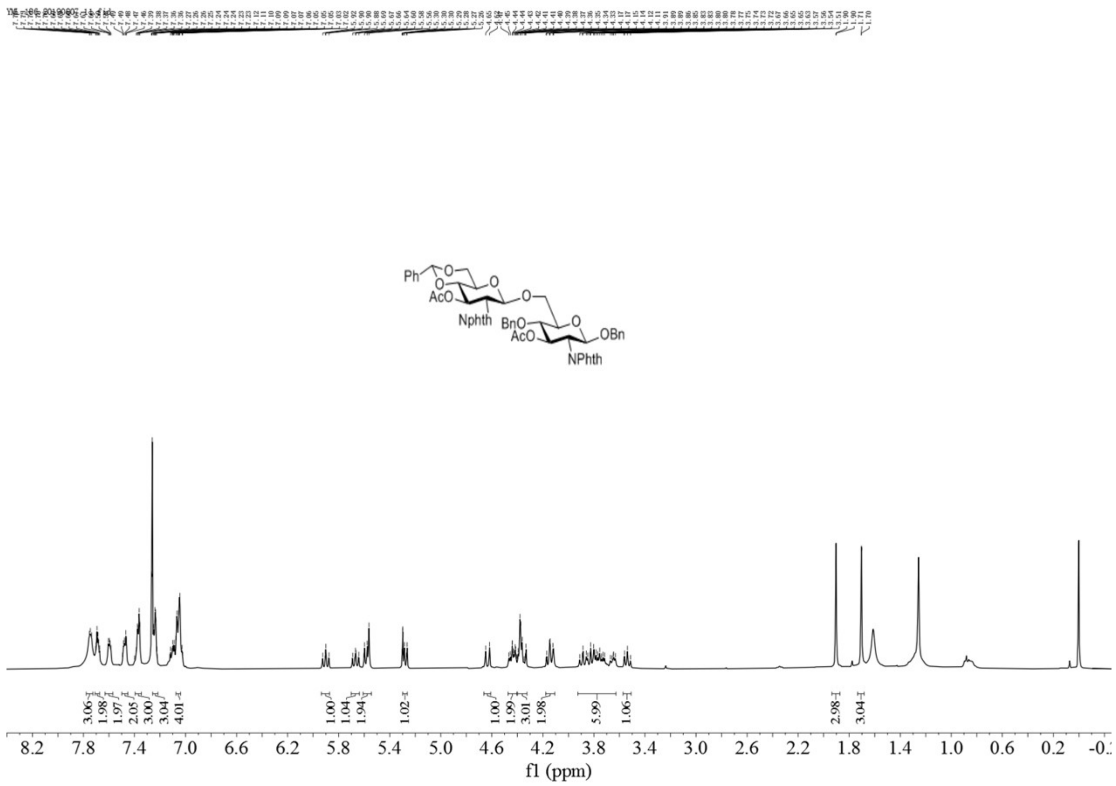
HRMS spectrum of compound **22**



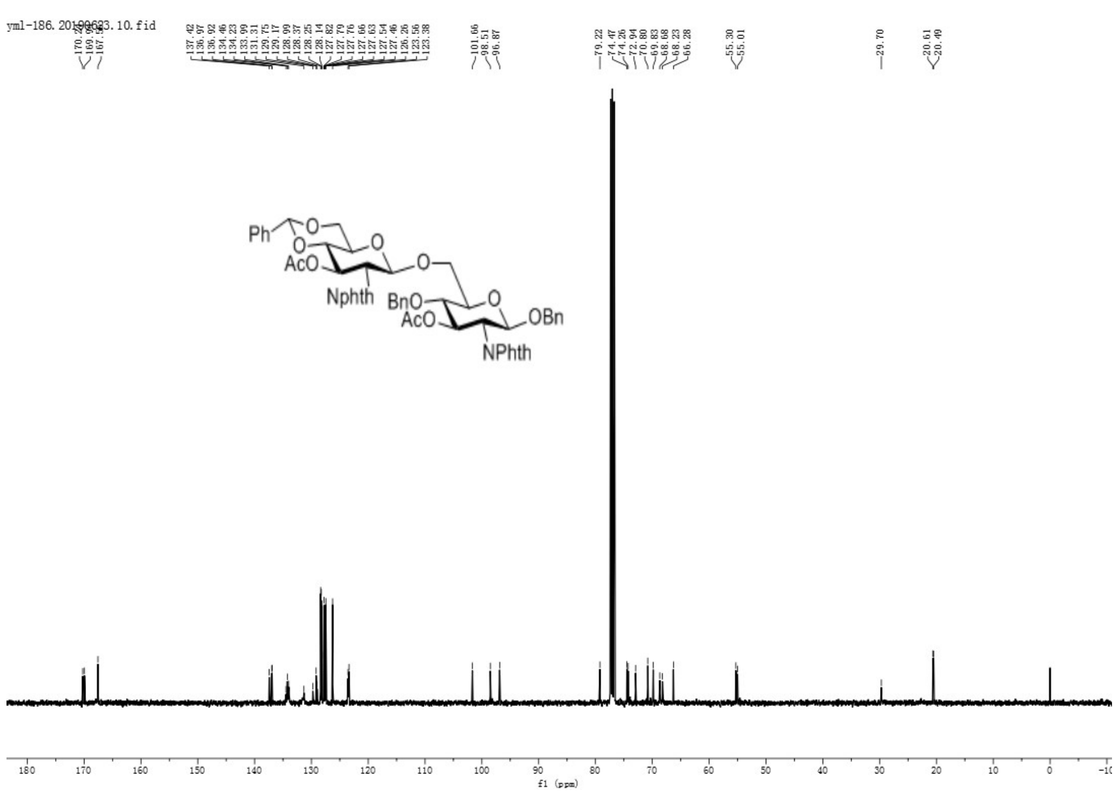
^{1}H NMR spectrum of compound **23** ($CDCl_3$, 400 MHz)



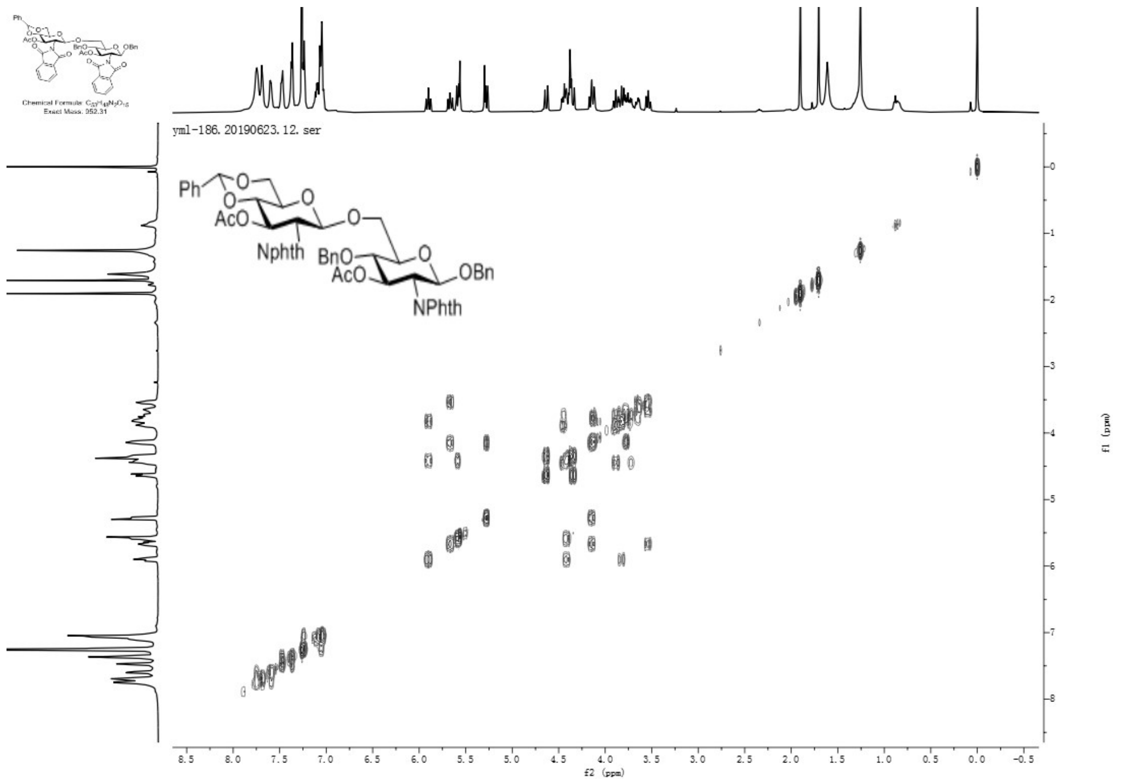
$^{13}C\{^{1}H\}$ NMR spectrum of compound **23** ($CDCl_3$, 100 MHz)



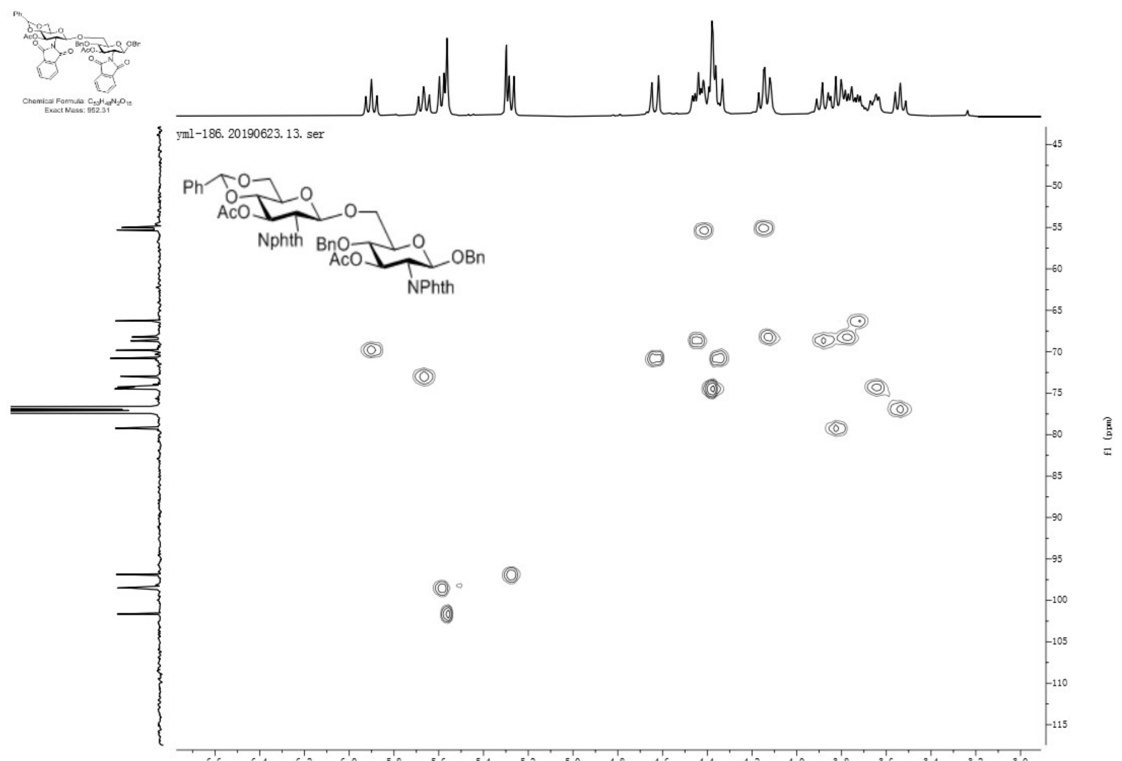
^{1}H NMR spectrum of compound 2**4** ($CDCl_3$, 400 MHz)



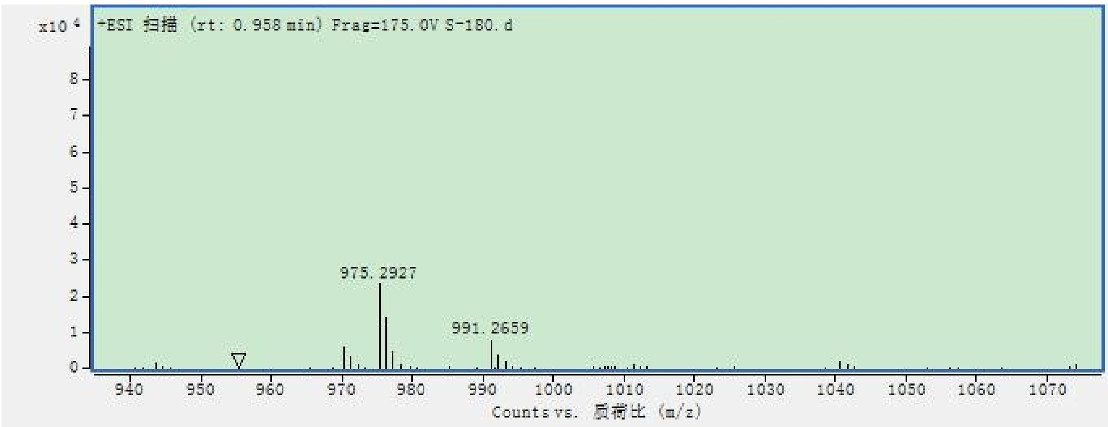
$^{13}C\{^{1}H\}$ NMR spectrum of compound **24** ($CDCl_3$, 100 MHz)



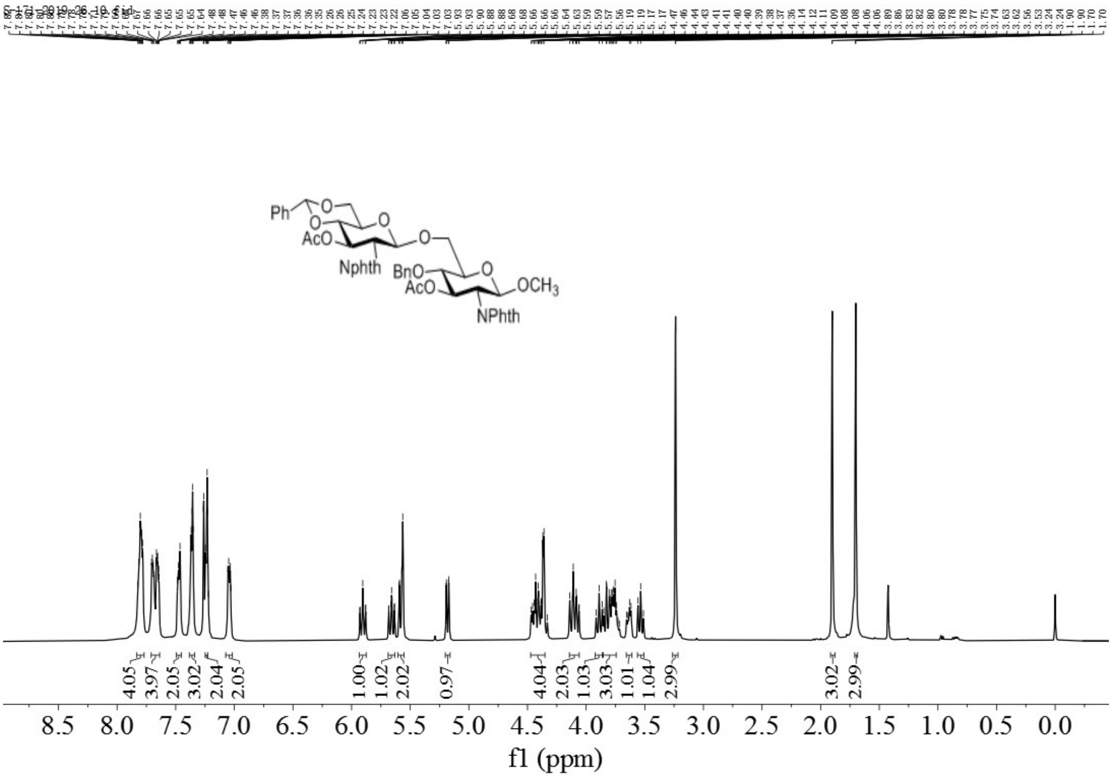
^{1}H-^{1}H COSY spectrum of compound **24** ($CDCl_3$, 400 MHz)



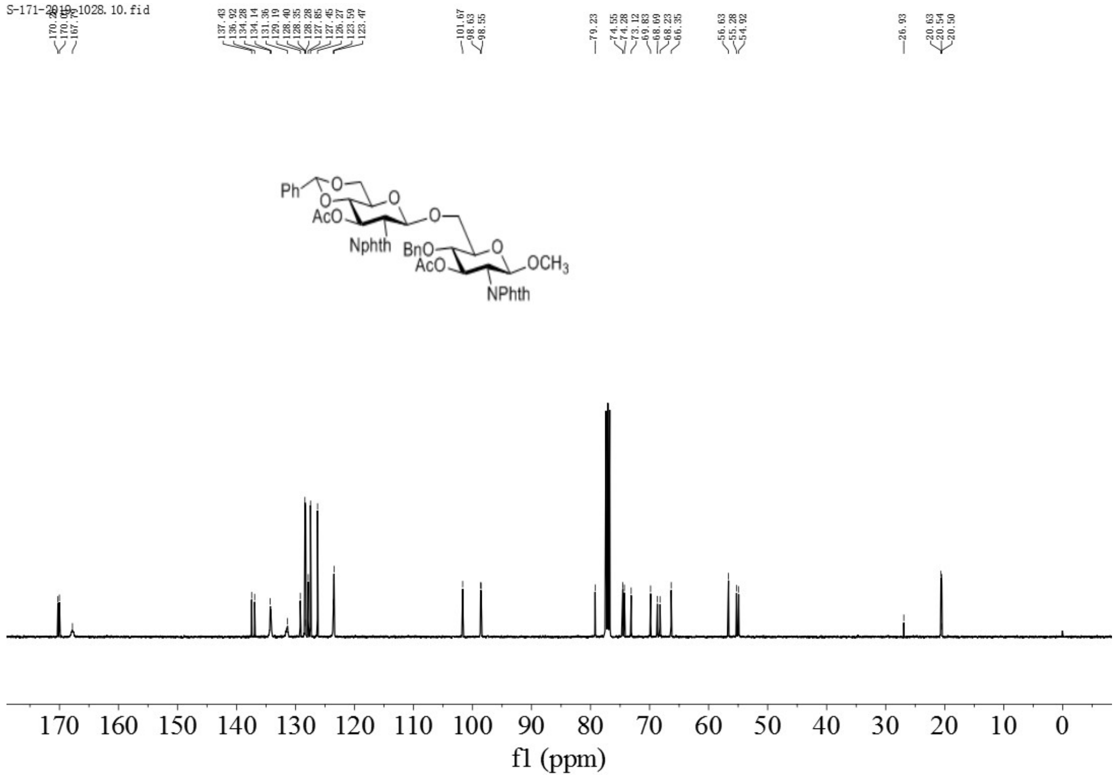
^{1}H-^{13}C HMQC spectrum of compound **24** ($CDCl_3$, 400/100 MHz)



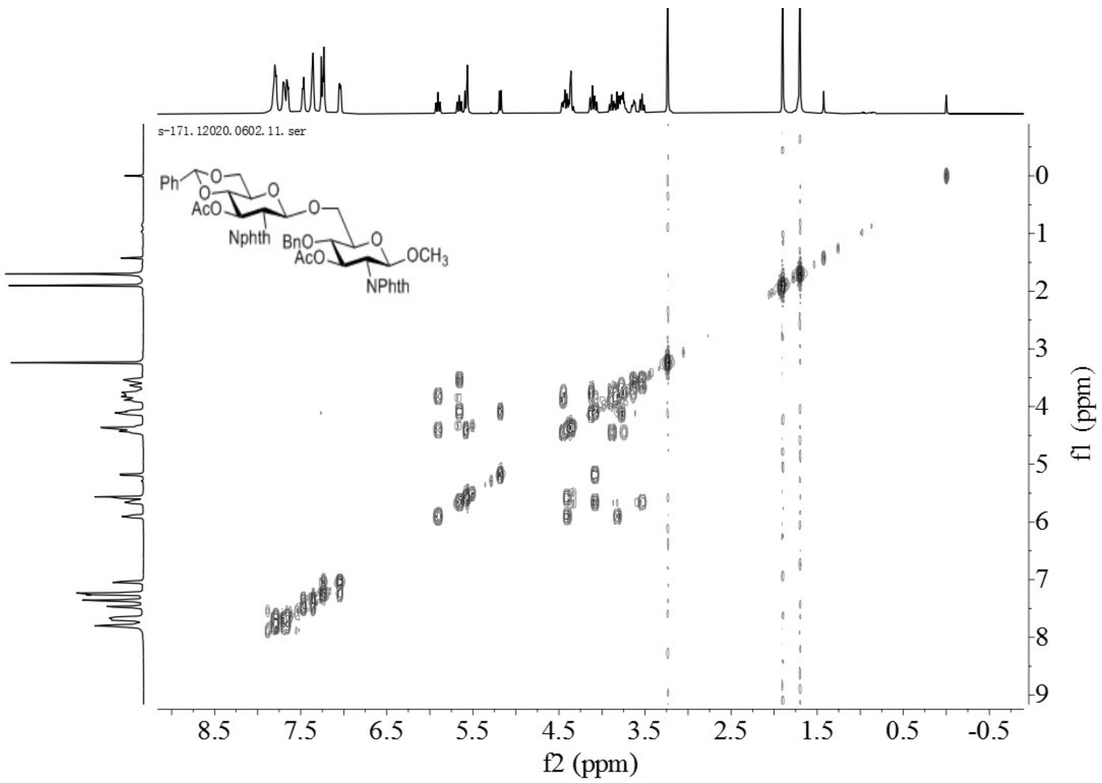
HRMS spectrum of compound **24**



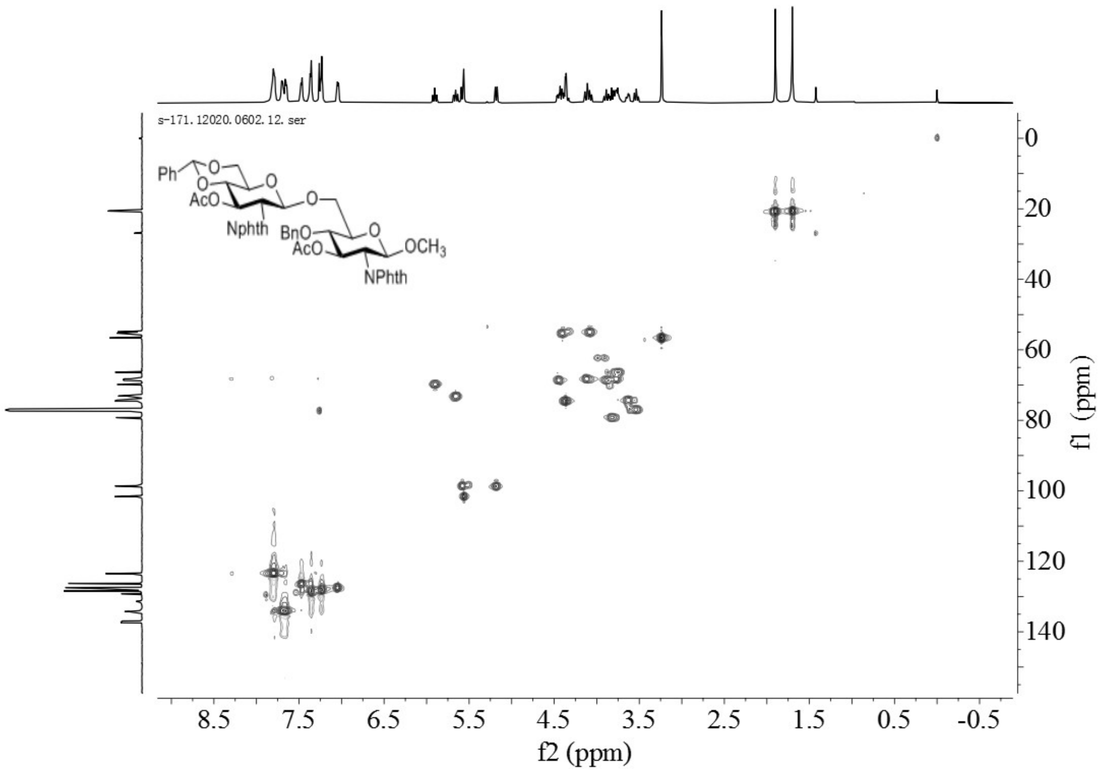
^{1}H NMR spectrum of compound **25** ($CDCl_3$, 400 MHz)



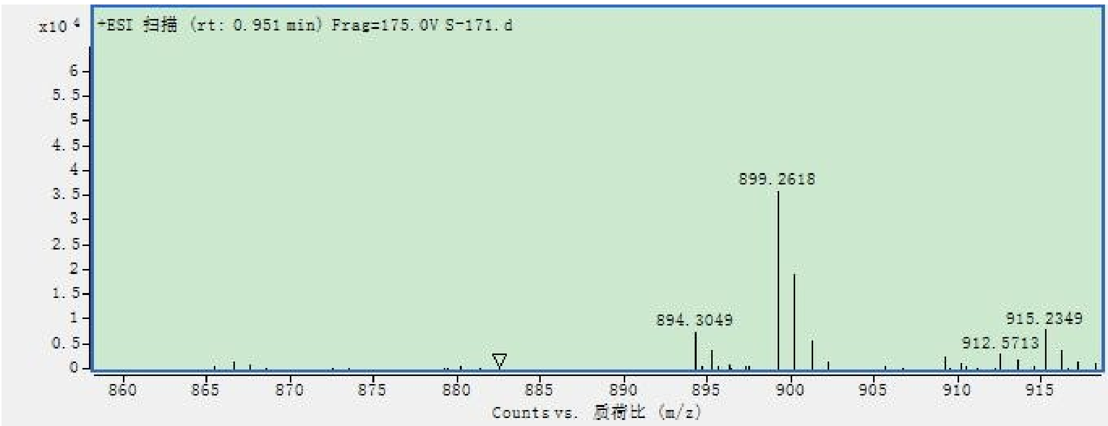
$^{13}C\{^{1}H\}$ NMR spectrum of compound **25** ($CDCl_3$, 100 MHz)



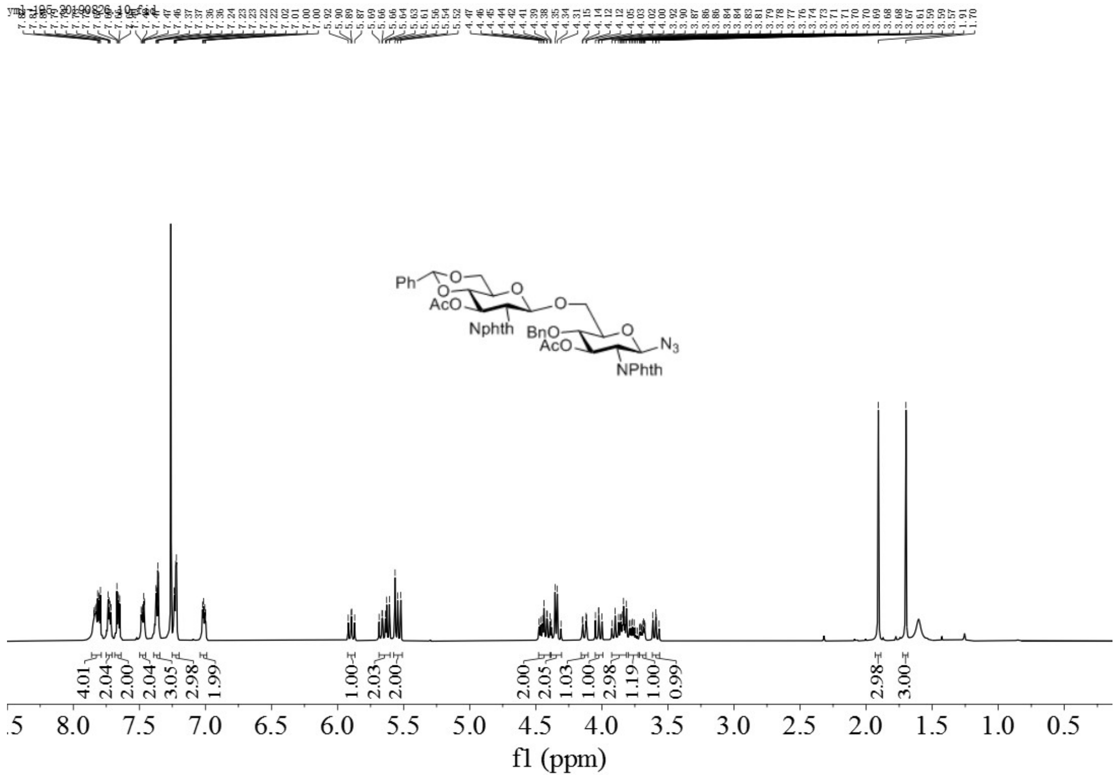
^{1}H-^{1}H COSY spectrum of compound **25** ($CDCl_3$, 400 MHz)



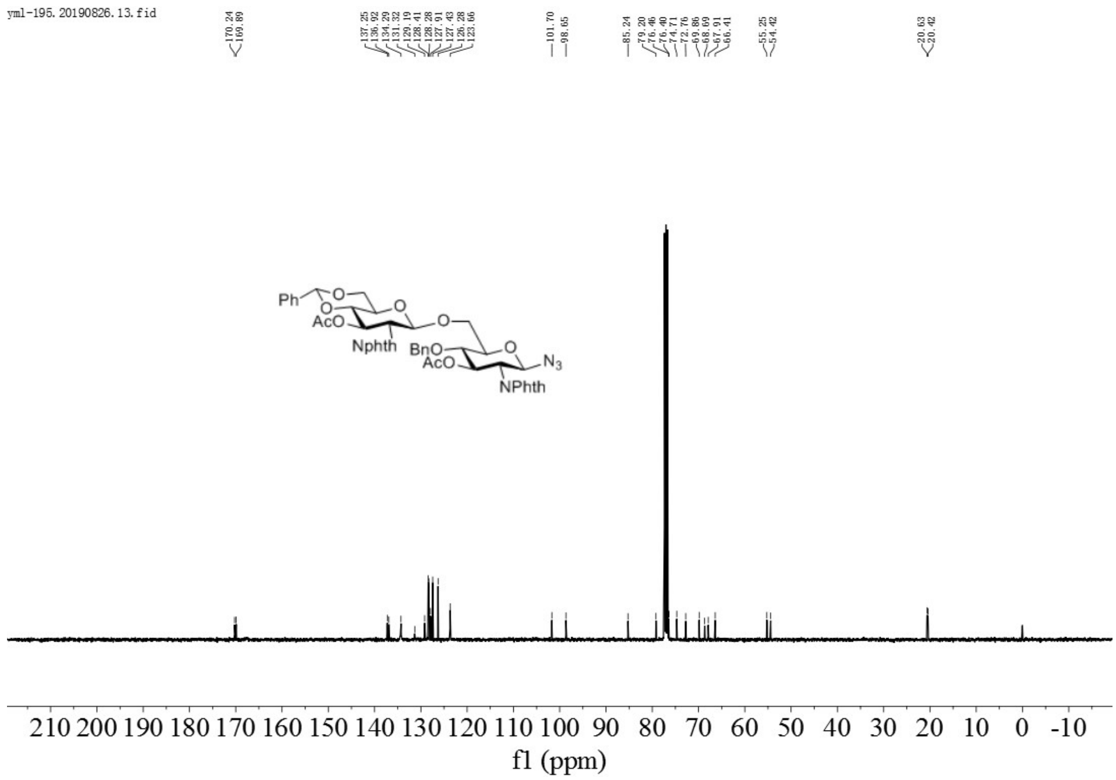
^{1}H-^{13}C HMQC spectrum of compound **25** (CDCl$_3$, 400/100 MHz)



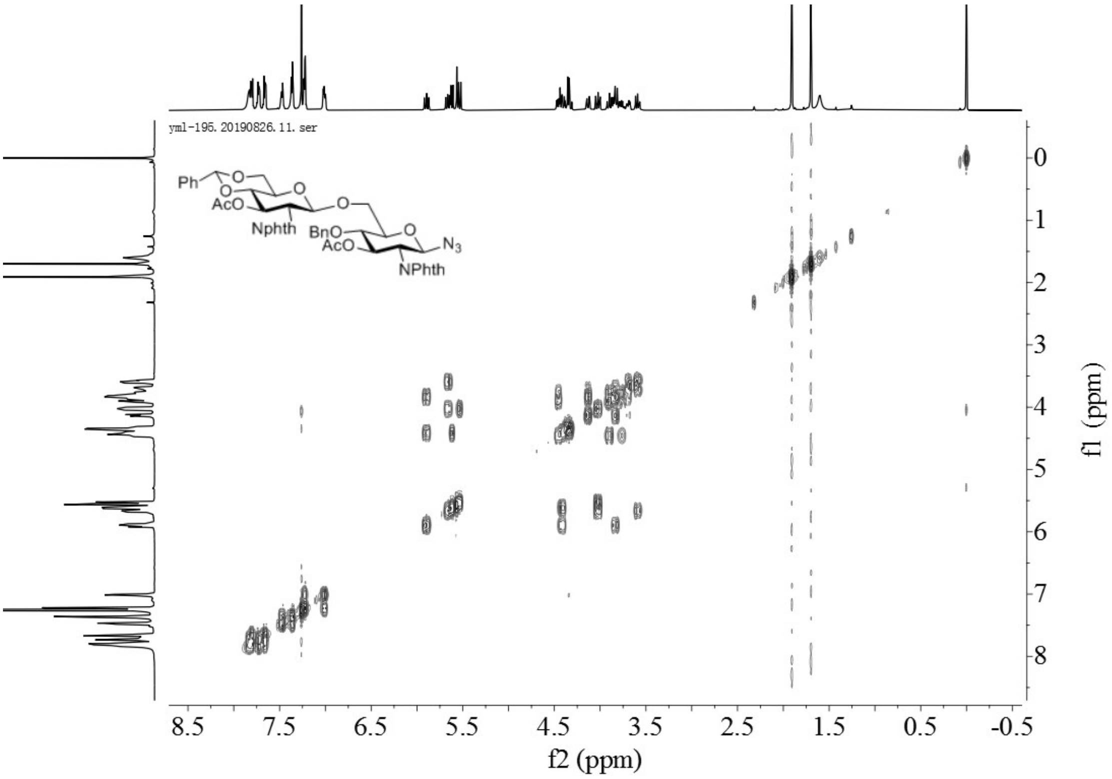
HRMS spectrum of compound **25**



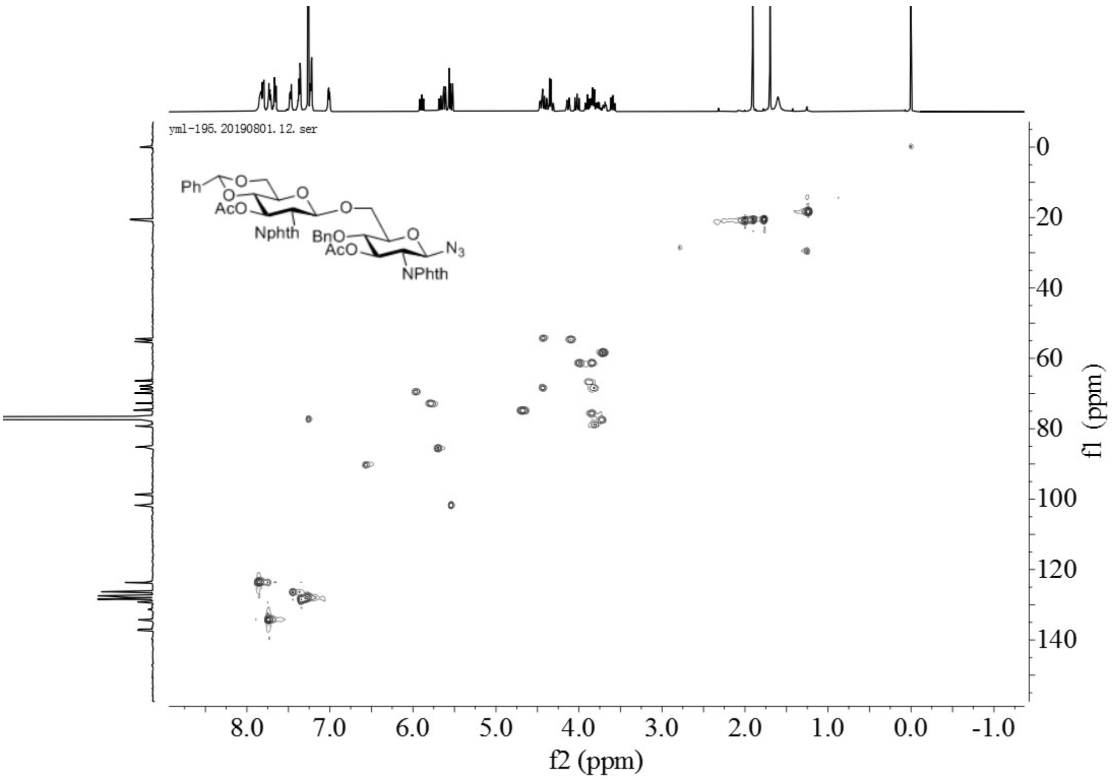
^{1}H NMR spectrum of compound **26** ($CDCl_3$, 400 MHz)



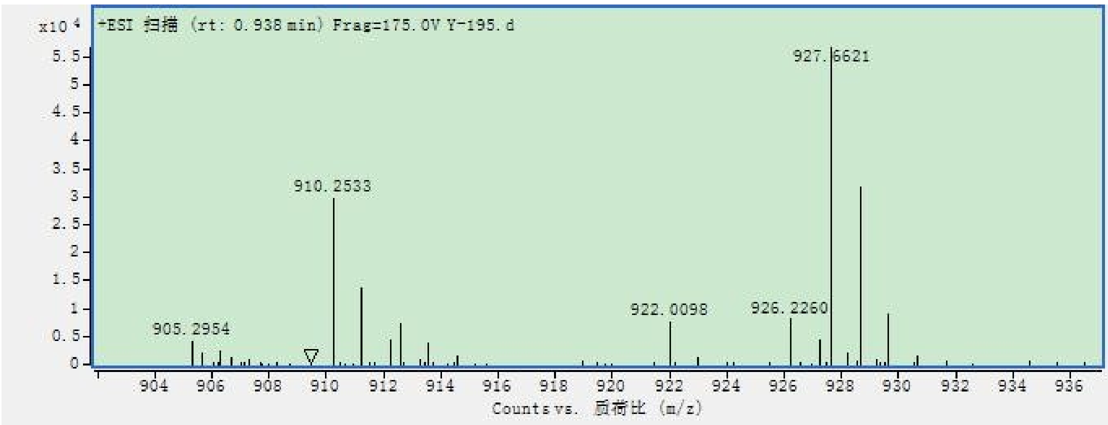
$^{13}C\{^{1}H\}$ NMR spectrum of compound **26** ($CDCl_3$, 100 MHz)



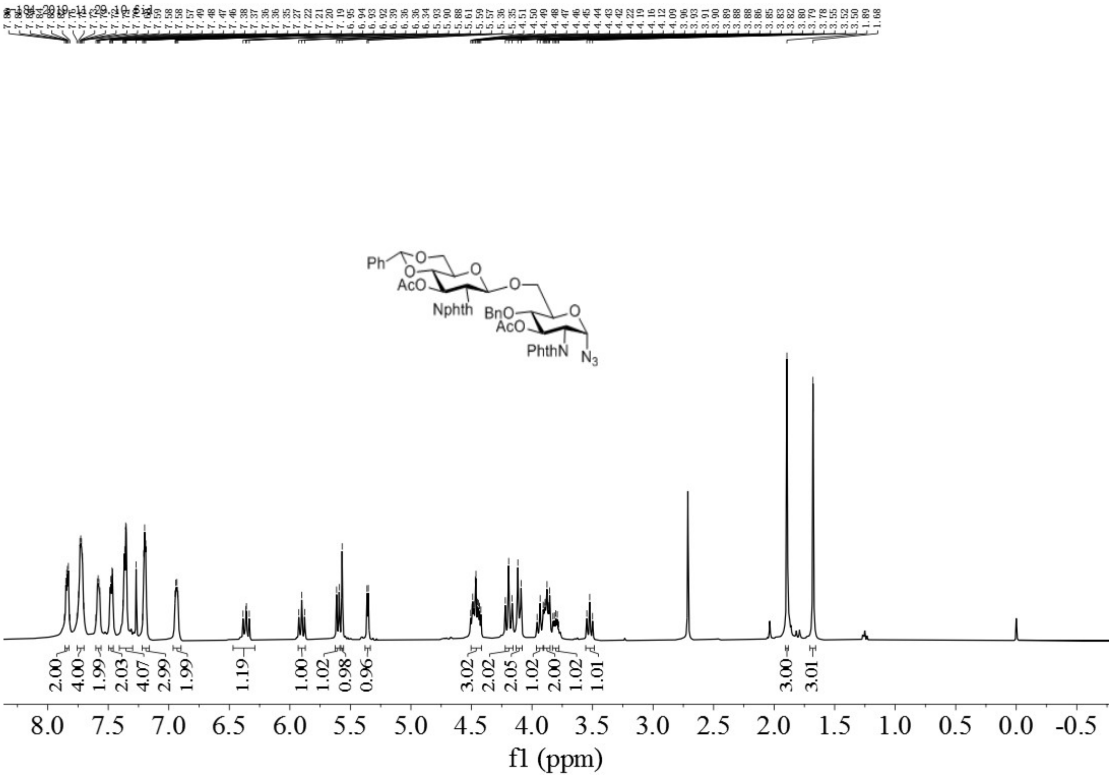
^{1}H – ^{1}H COSY spectrum of compound **26** ($CDCl_3$, 400 MHz)



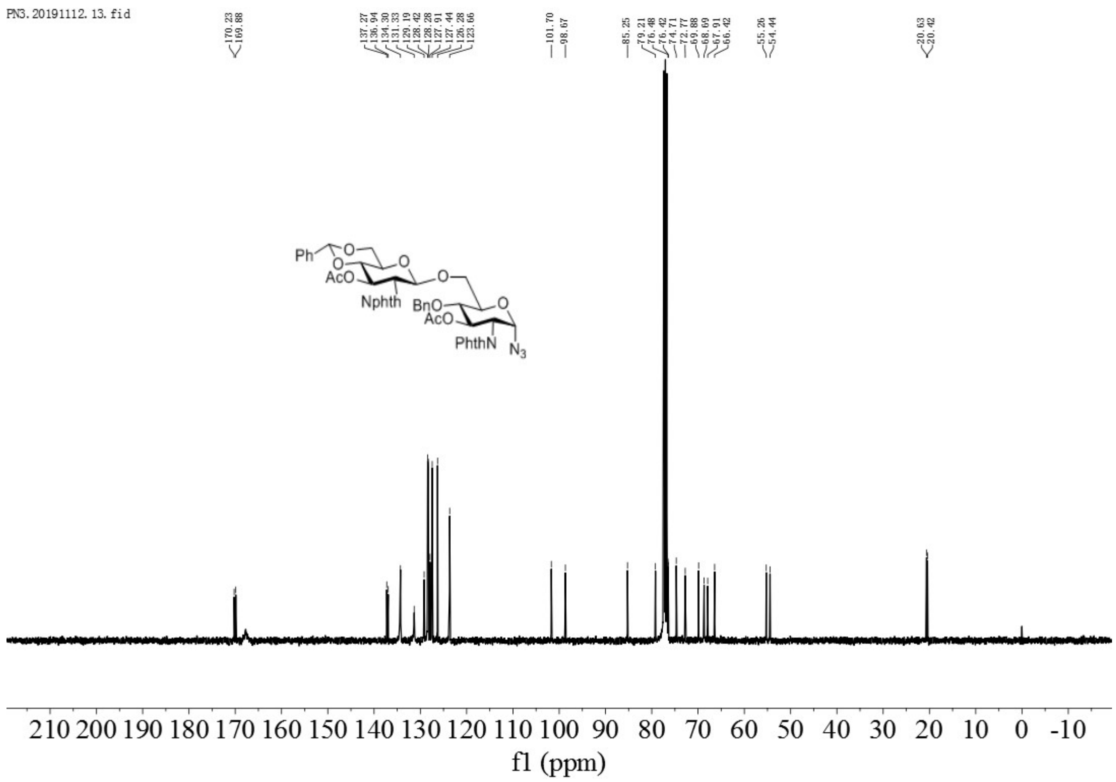
^{1}H – ^{13}C HMQC spectrum of compound **26** ($CDCl_3$, 400/100 MHz)



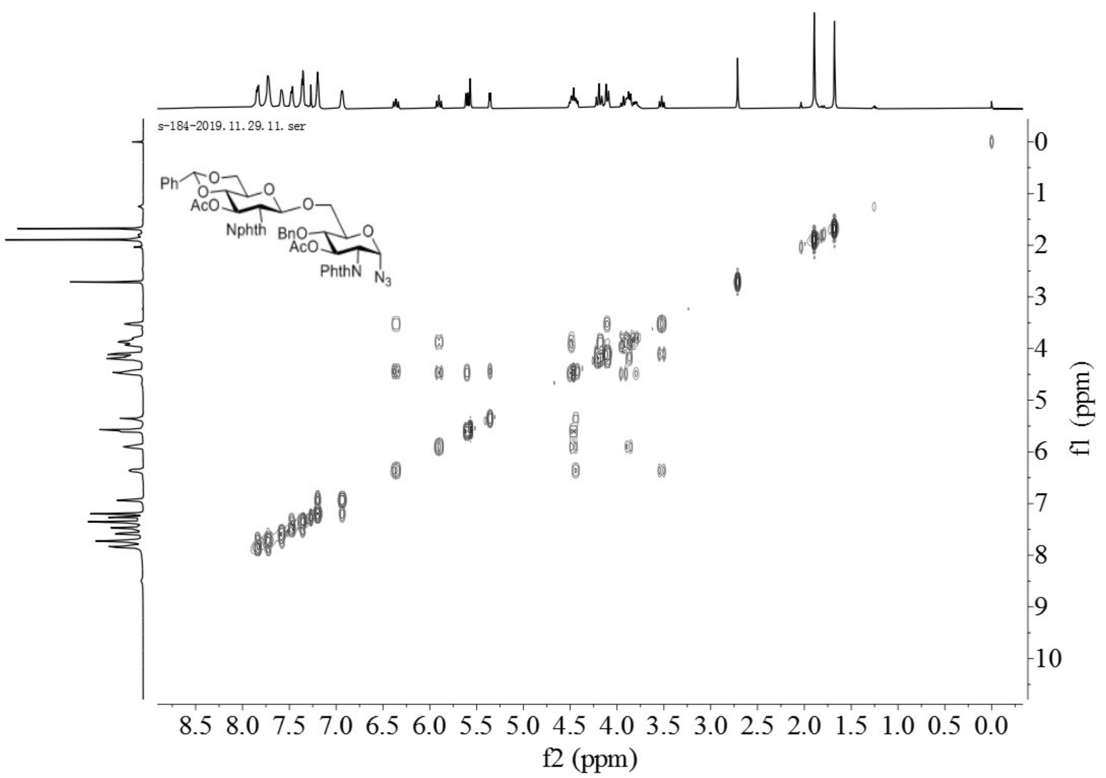
HRMS spectrum of compound **26**



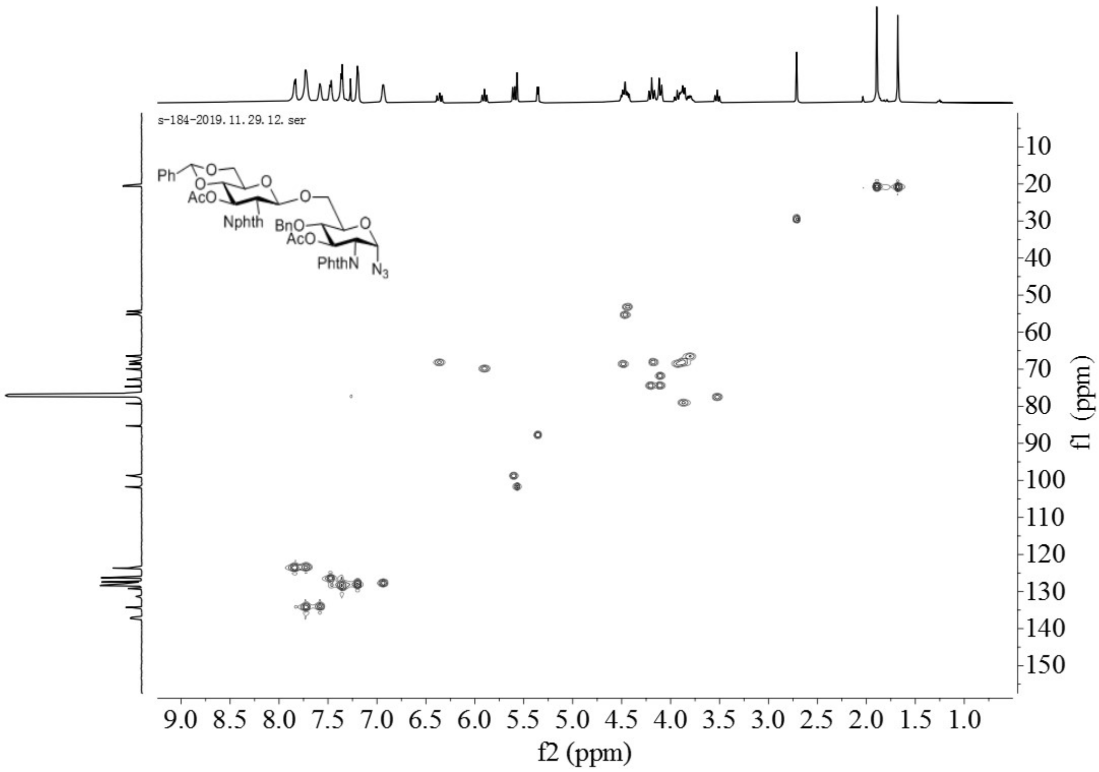
[1]H NMR spectrum of compound **27** ($CDCl_3$, 400 MHz)



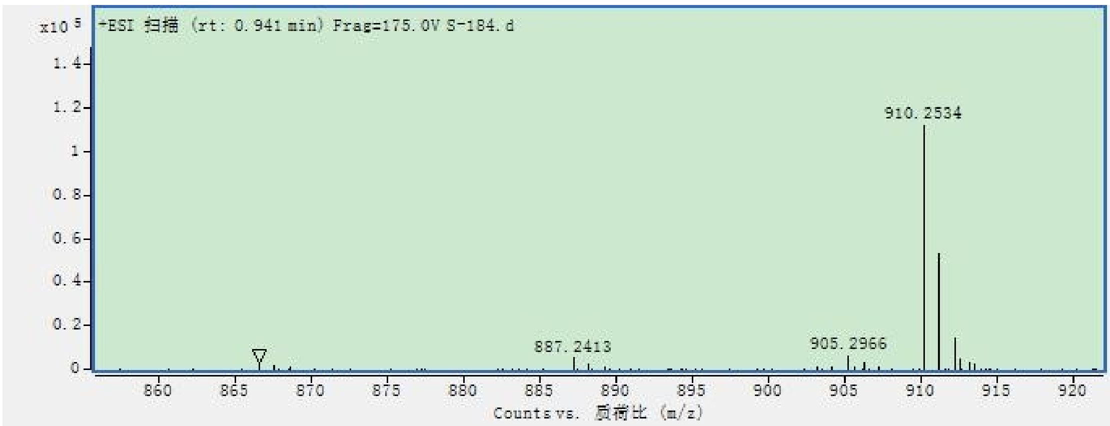
$^{13}C\{^{1}H\}$ NMR spectrum of compound **27** ($CDCl_3$, 100 MHz)



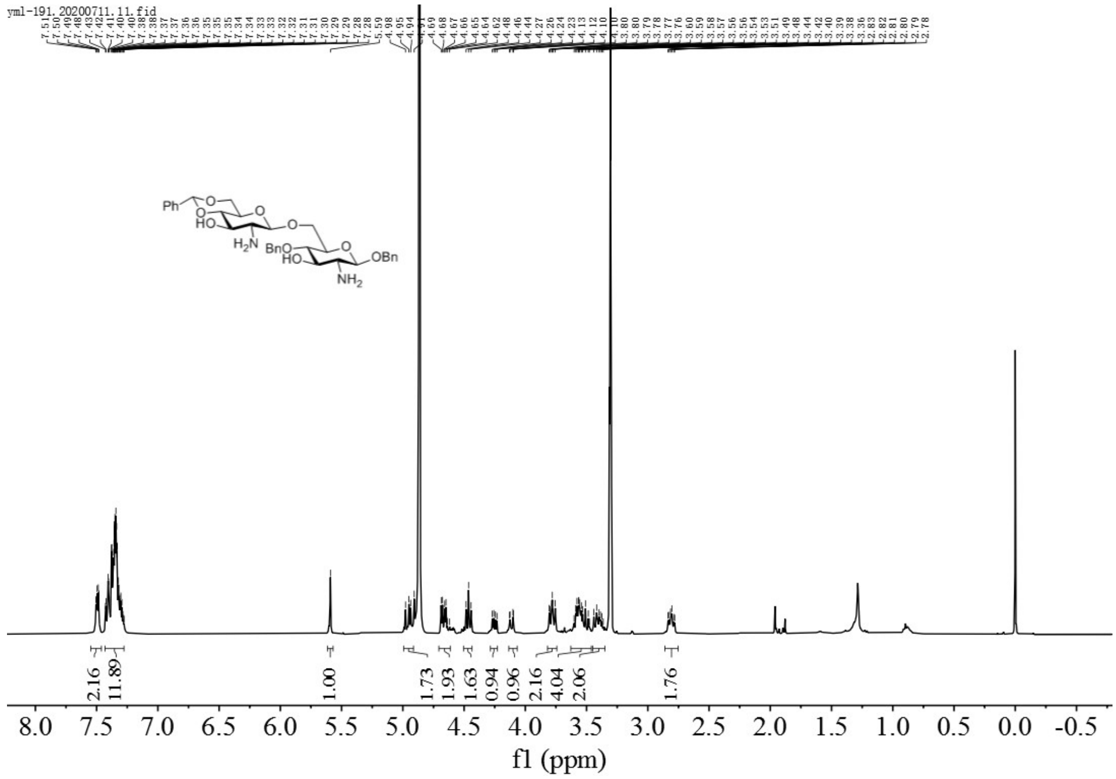
^{1}H-^{1}H COSY spectrum of compound **27** ($CDCl_3$, 400 MHz)



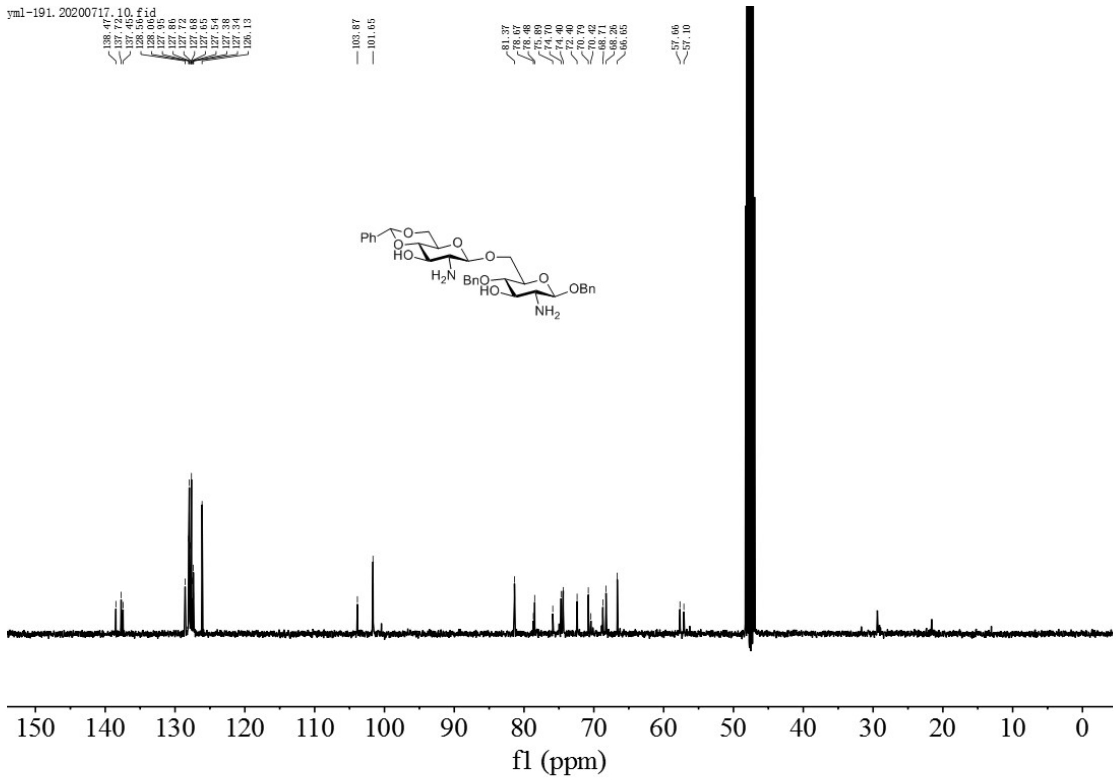
^{1}H-^{13}C HMQC spectrum of compound **27** ($CDCl_3$, 400/100 MHz)



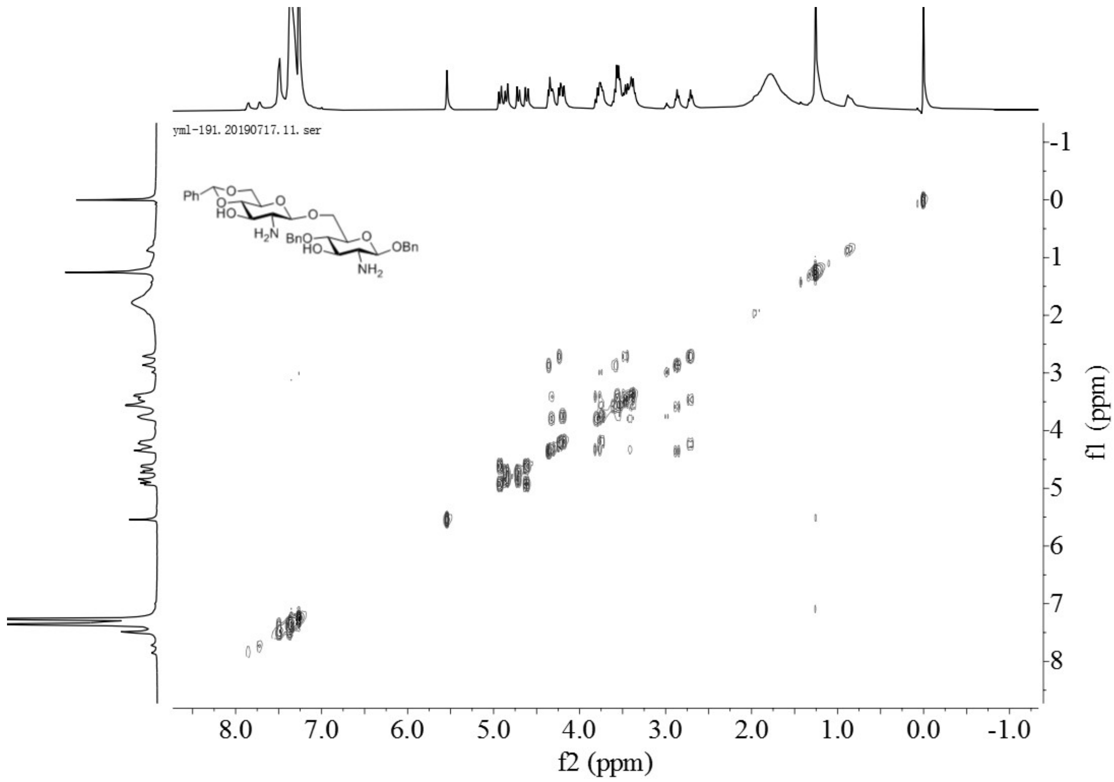
HRMS spectrum of compound **27**



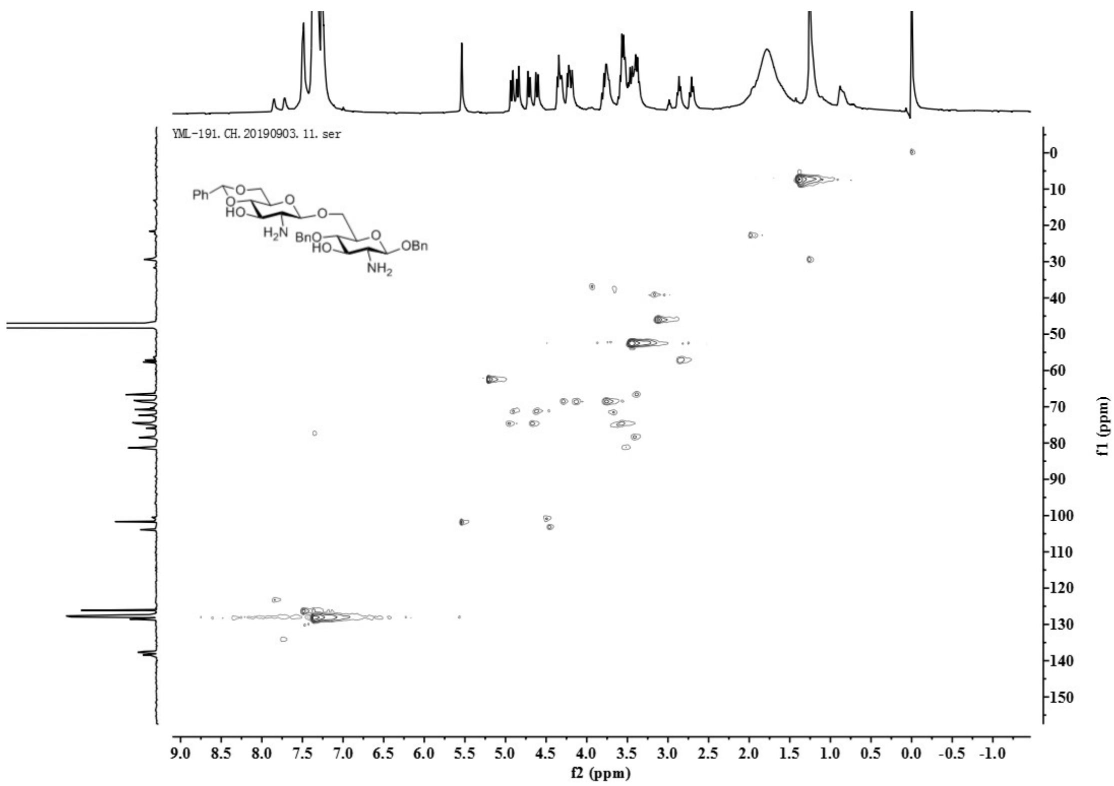
[1]H NMR spectrum of compound **28** (CD_3OD, 400 MHz)



[13]C{[1]H} NMR spectrum of compound **28** (CD_3OD_3, 100 MHz)

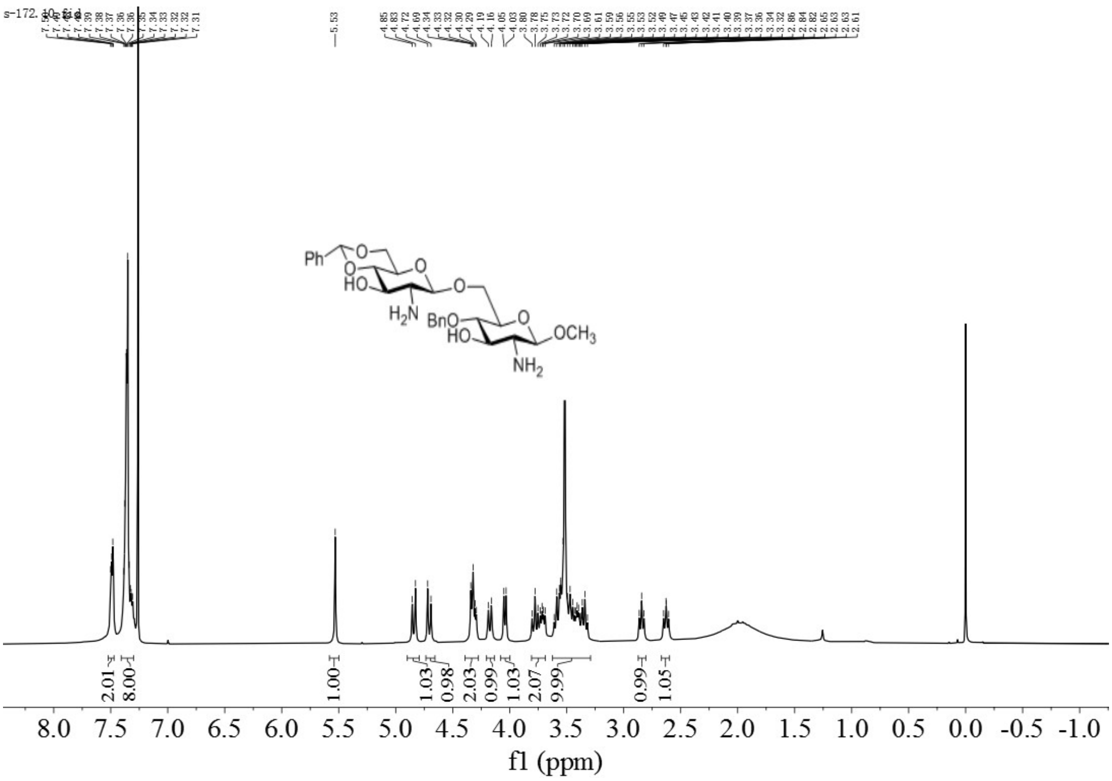


^{1}H-^{1}H COSY spectrum of compound **28** ($CDCl_3$, 400 MHz)

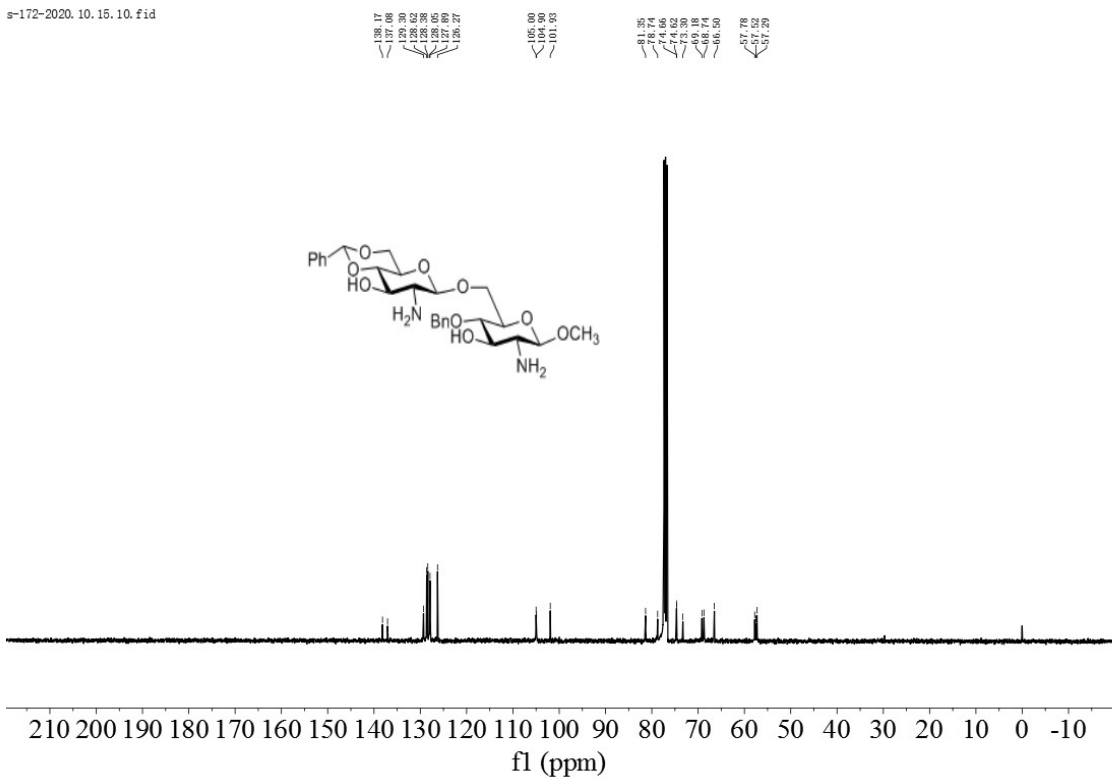


^{1}H-^{13}C HMQC spectrum of compound **28** ($CDCl_3$, 400/100 MHz)

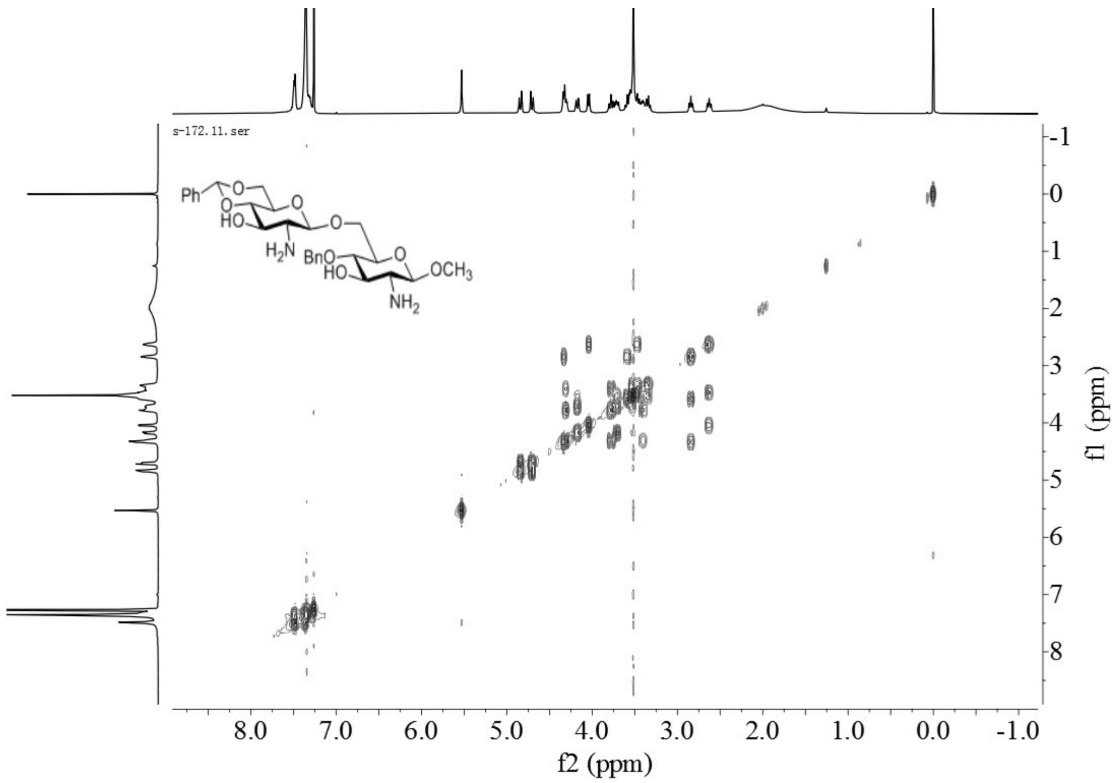
HRMS spectrum of compound **28**



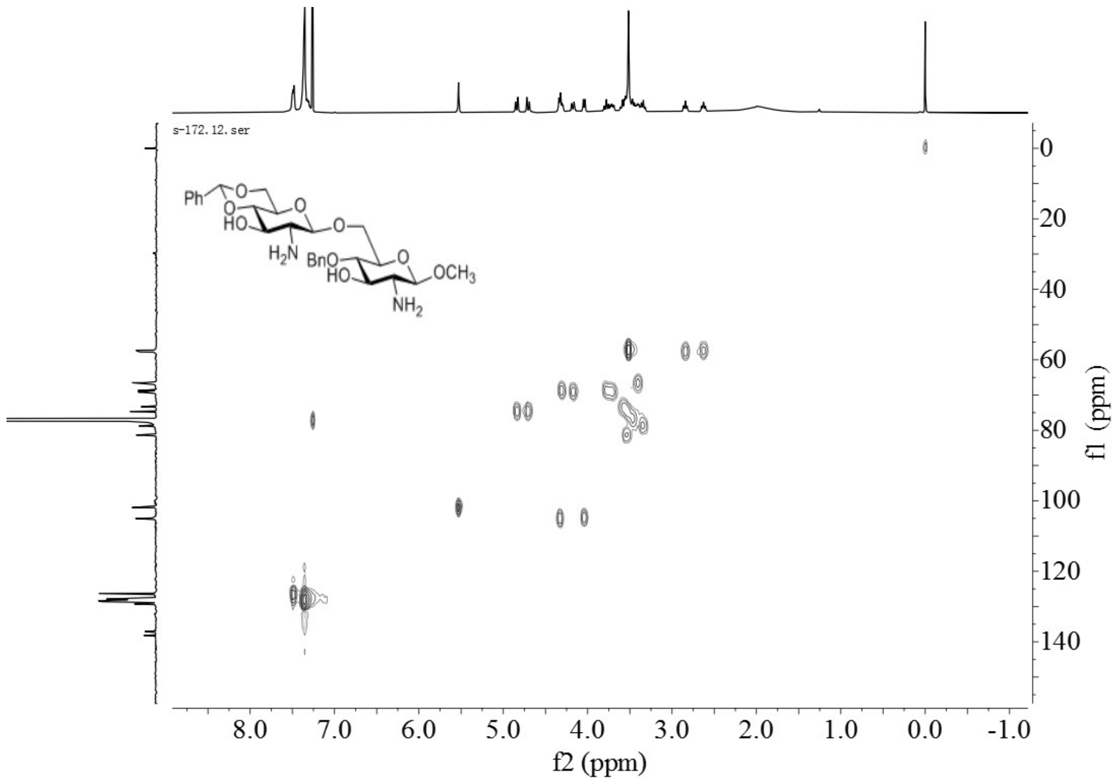
^{1}H NMR spectrum of compound **29** ($CDCl_3$, 400 MHz)



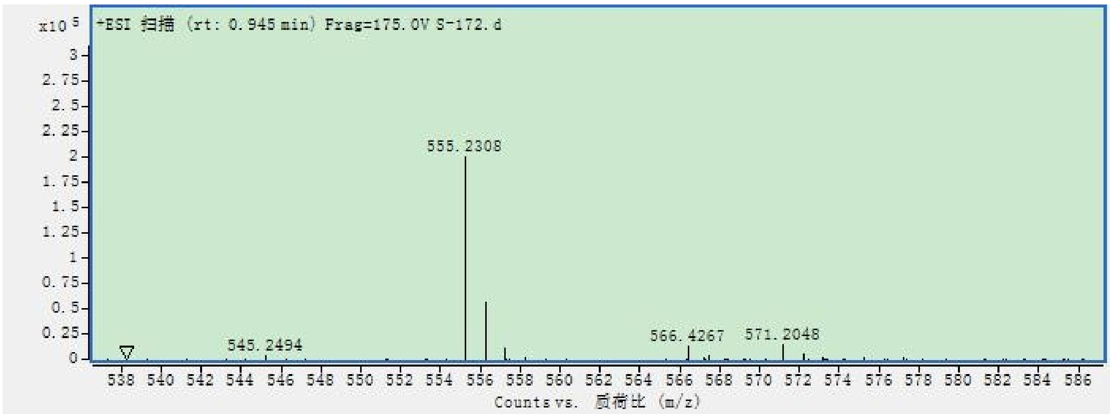
$^{13}C\{^1H\}$ NMR spectrum of compound **29** ($CDCl_3$, 100 MHz)



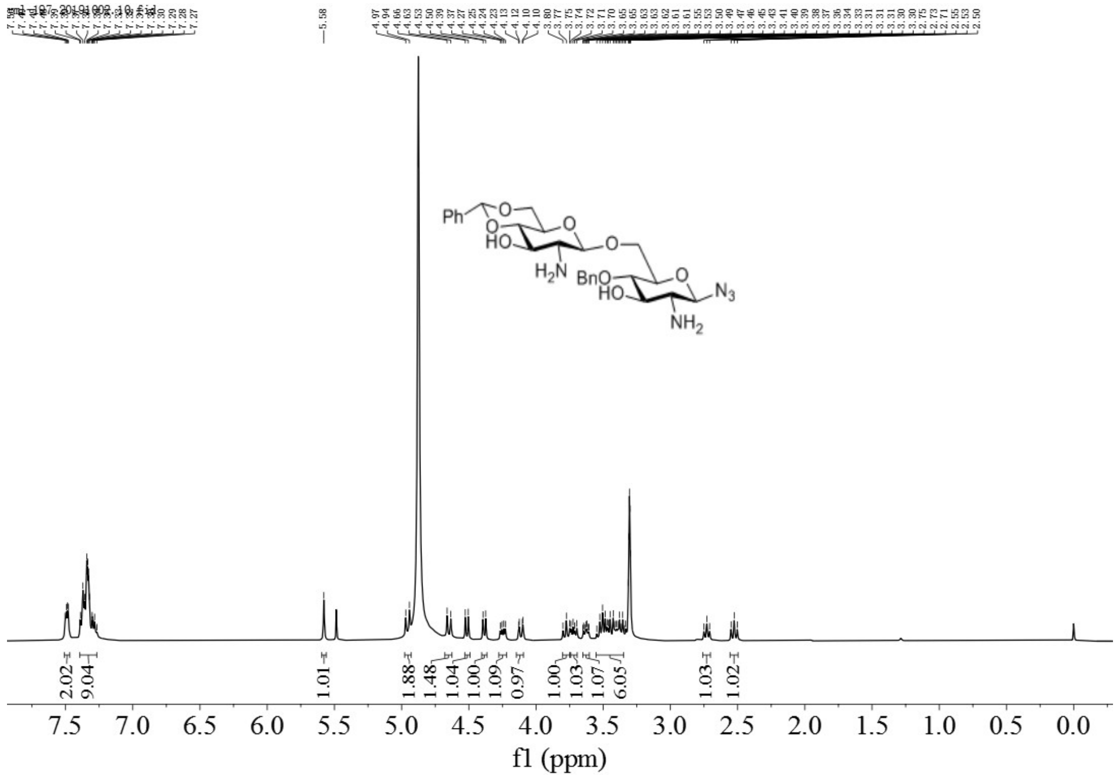
^1H-^1H COSY spectrum of compound **29** ($CDCl_3$, 400 MHz)



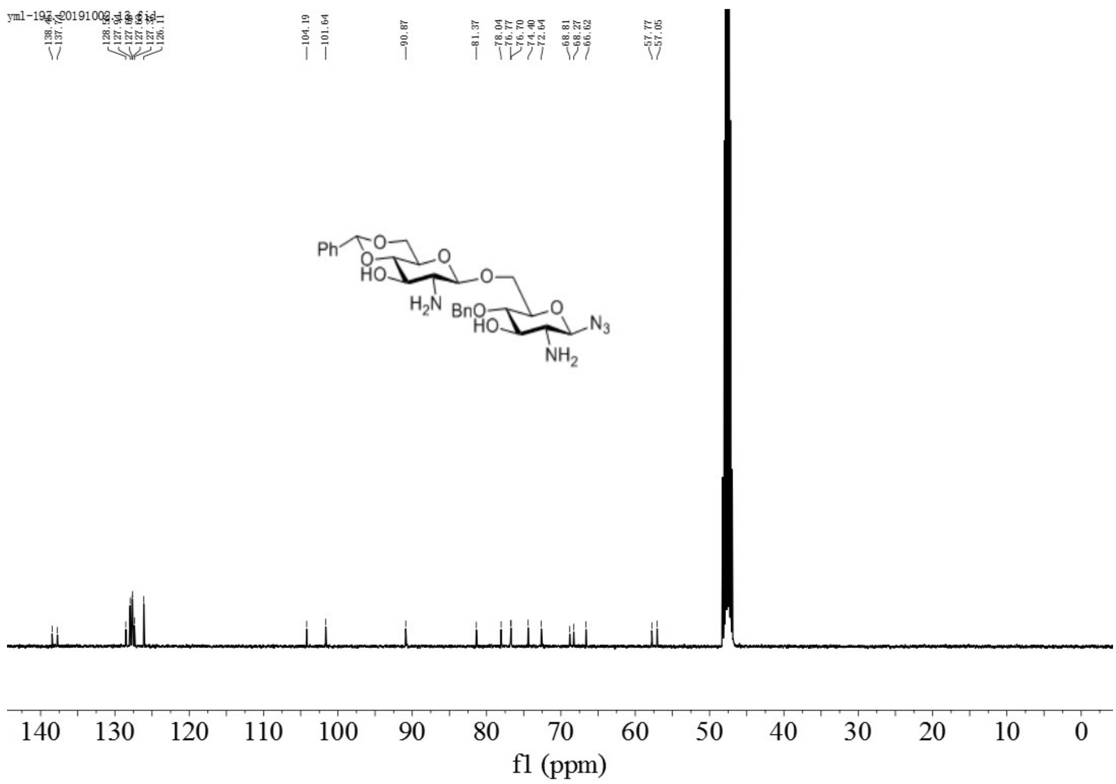
^{1}H-^{13}C HMQC spectrum of compound **29** ($CDCl_3$, 400/100 MHz)



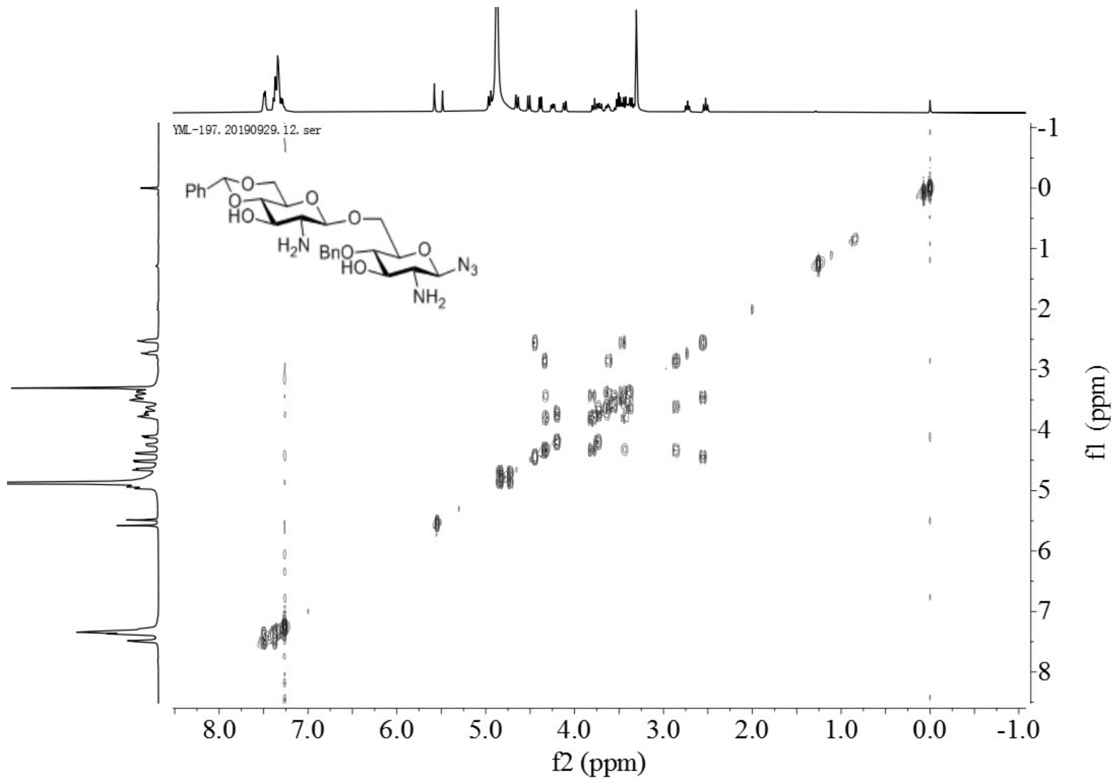
HRMS spectrum of compound **29**



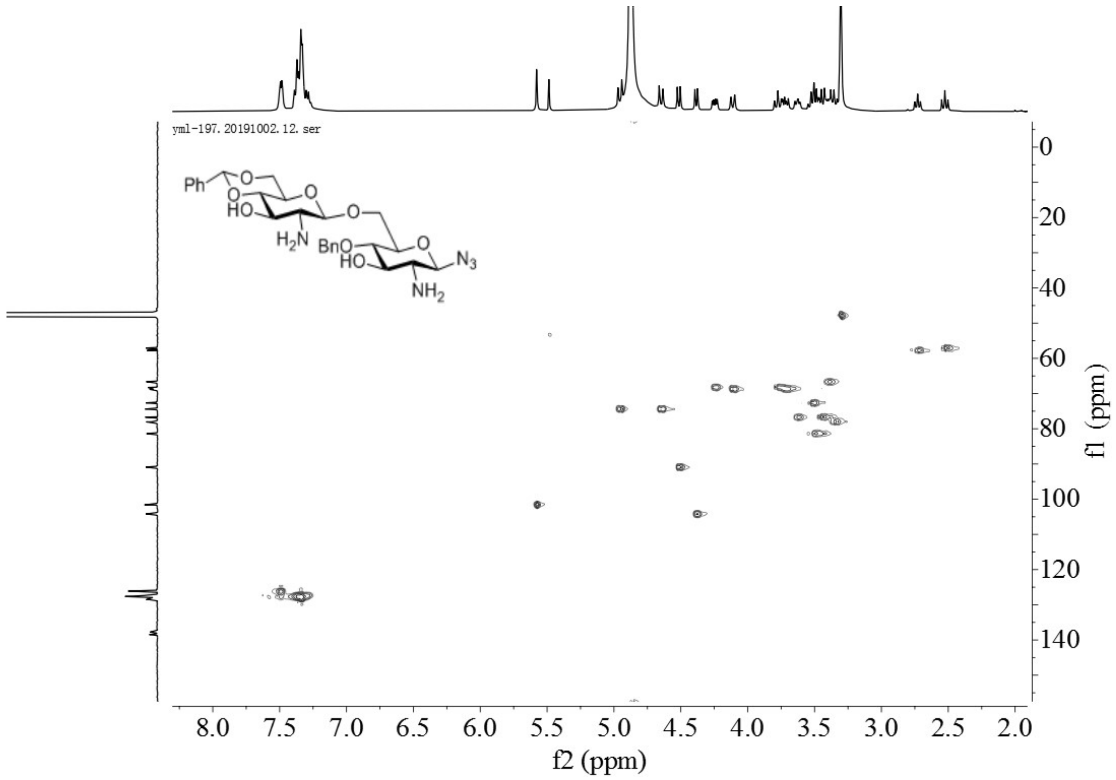
^{1}H NMR spectrum of compound **30** (CD_3OD_3, 400 MHz)



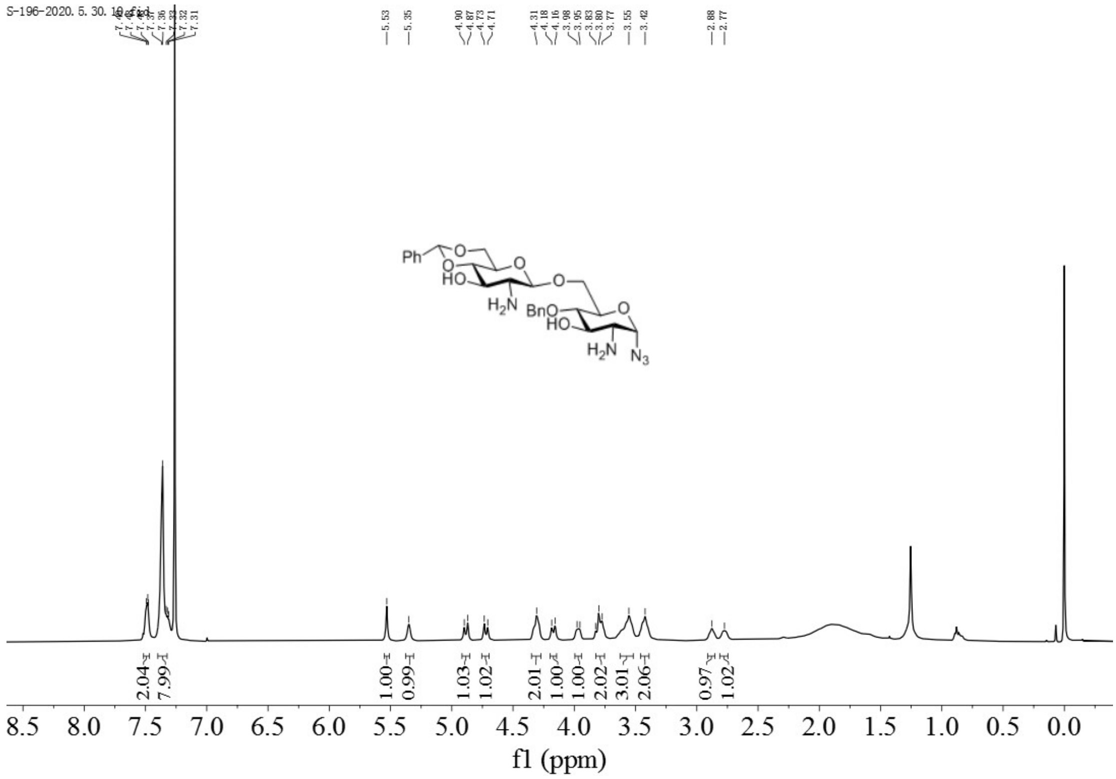
$^{13}C\{^{1}H\}$ NMR spectrum of compound **30** (CD_3OD_3, 100 MHz)



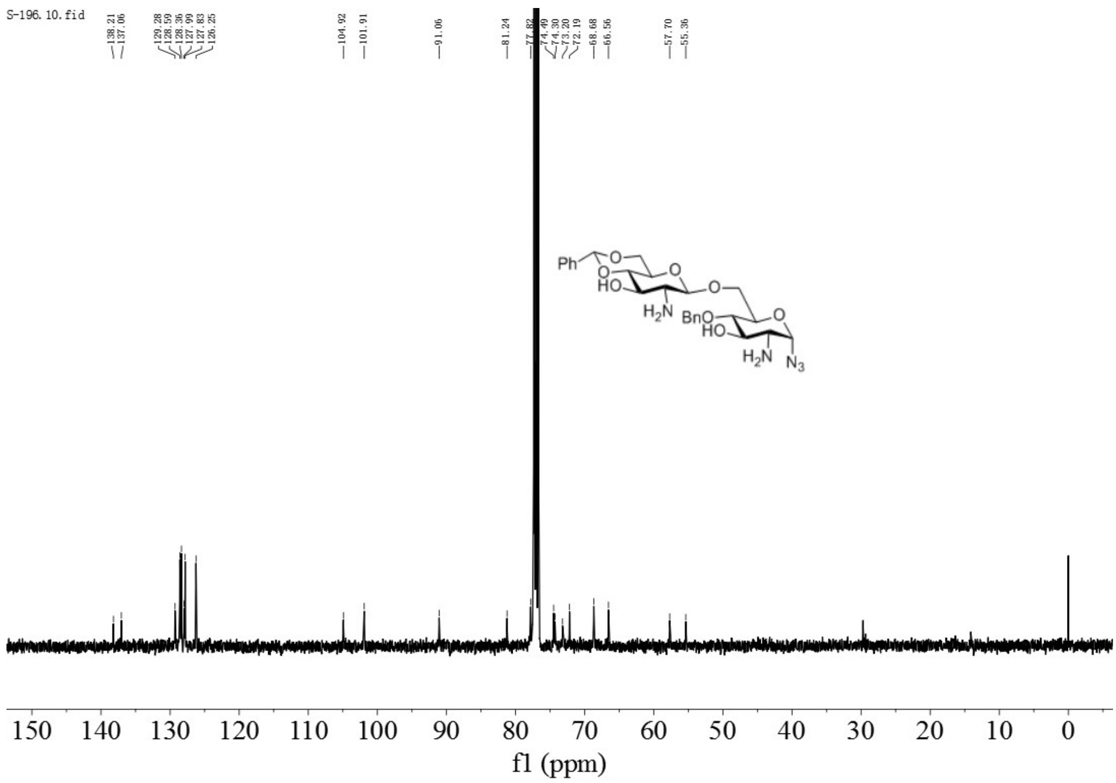
^1H – ^1H COSY spectrum of compound **30** ($CDCl_3$, 400 MHz)



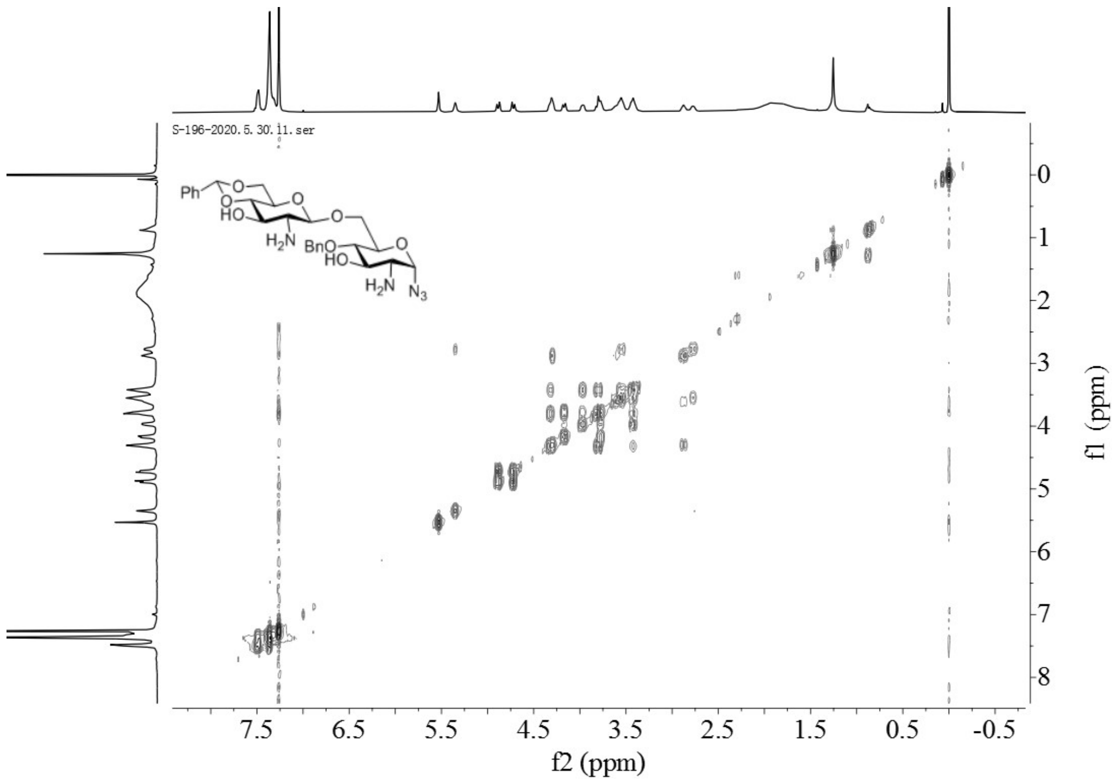
^1H – ^{13}C HMQC spectrum of compound **30** ($CDCl_3$, 400/100 MHz)



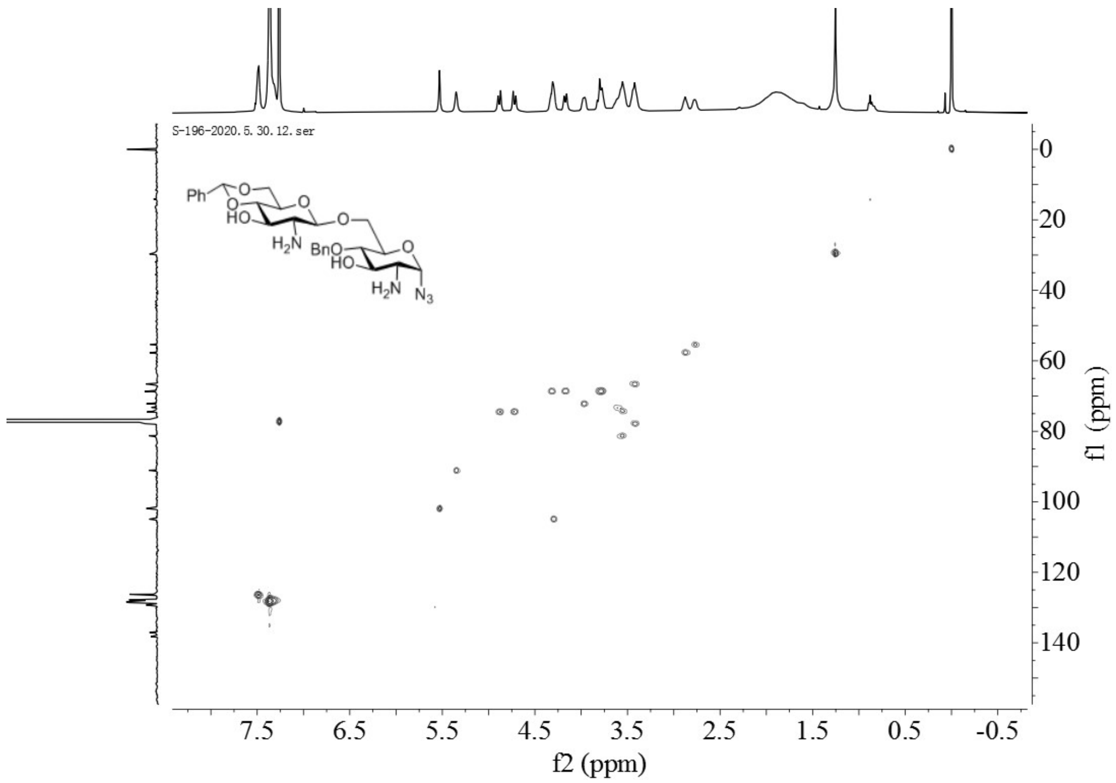
^{1}H NMR spectrum of compound **31** ($CDCl_3$, 400 MHz)



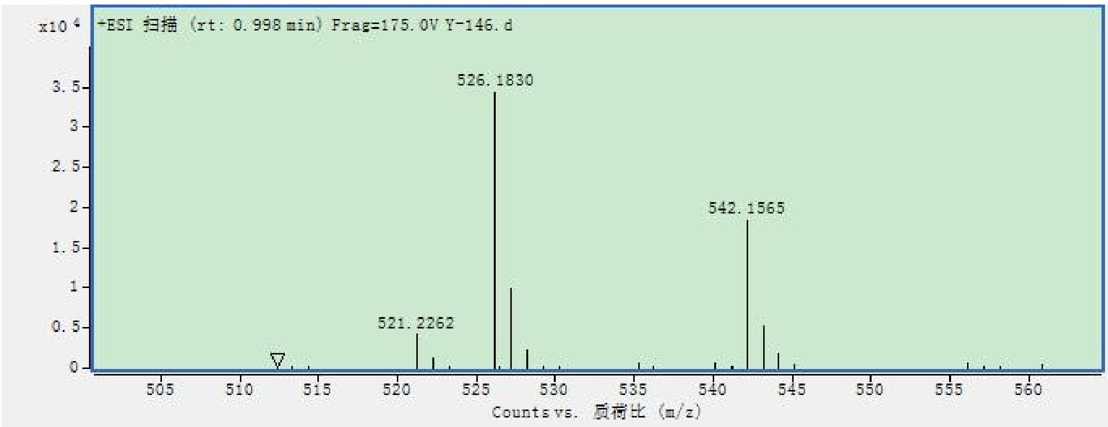
$^{13}C\{^{1}H\}$ NMR spectrum of compound **31** ($CDCl_3$, 100 MHz)



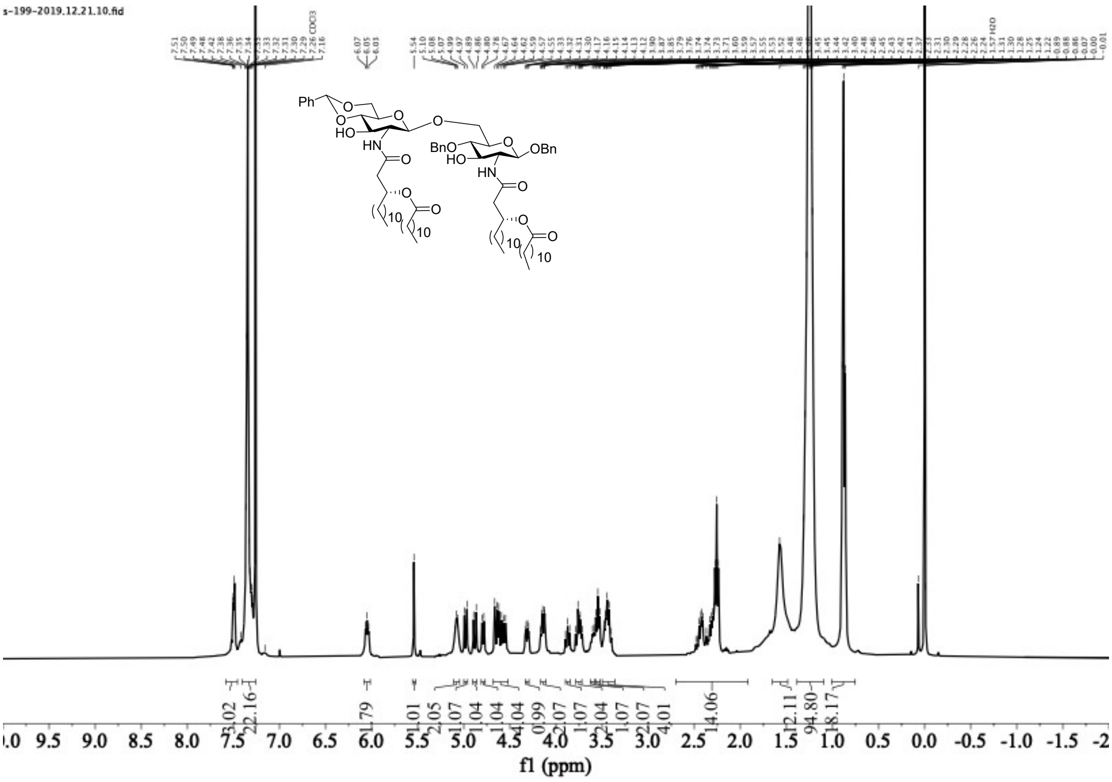
^1H-^1H COSY spectrum of compound **31** ($CDCl_3$, 400 MHz)



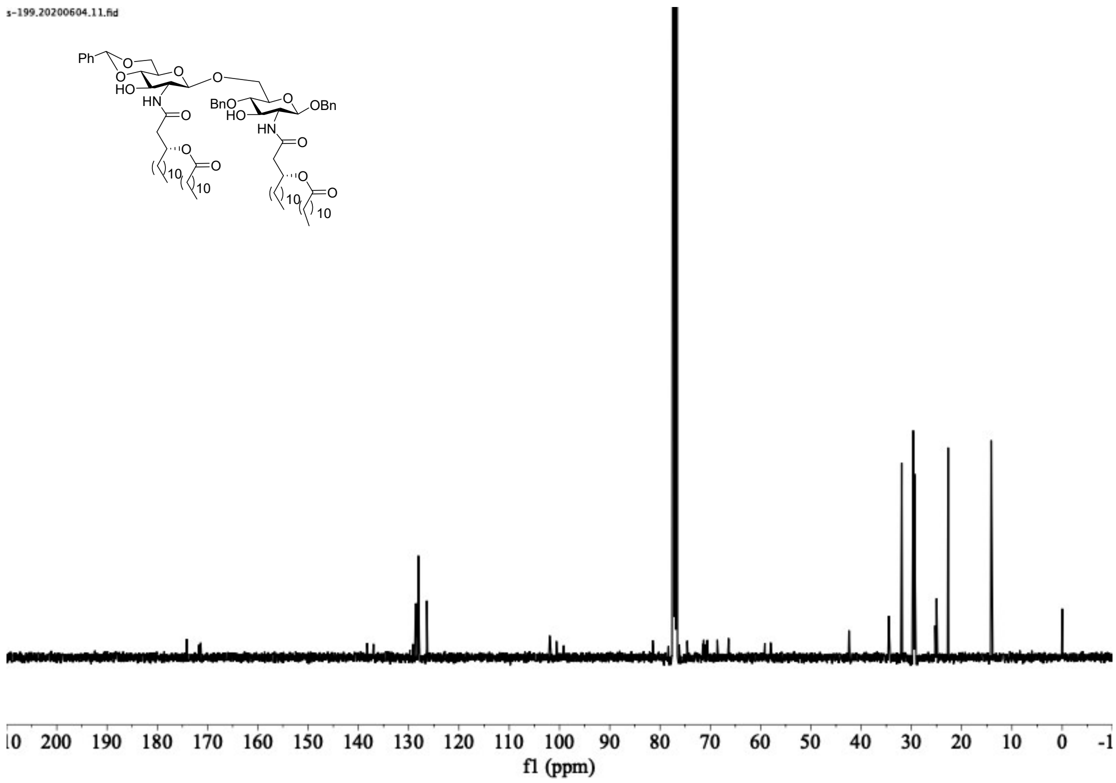
^1H-^{13}C HMQC spectrum of compound **31** ($CDCl_3$, 400/100 MHz)



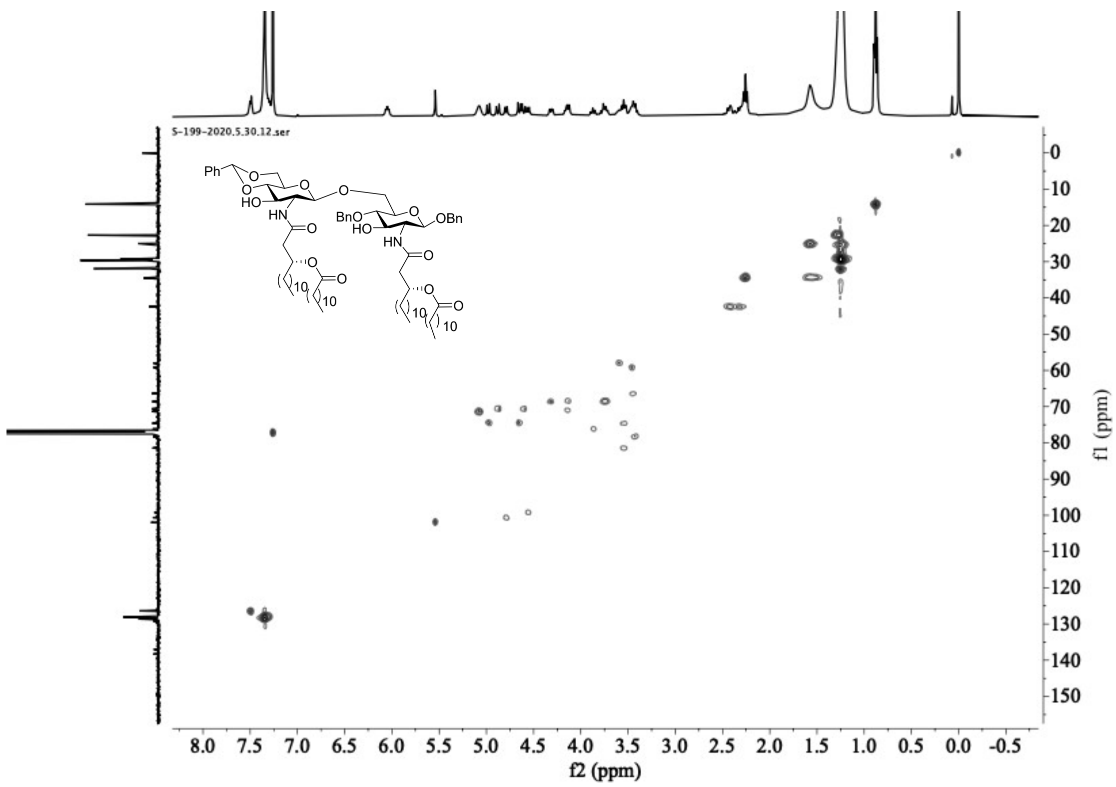
HRMS spectrum of compound **31**



[1]H NMR spectrum of compound **33** ($CDCl_3$, 400 MHz)

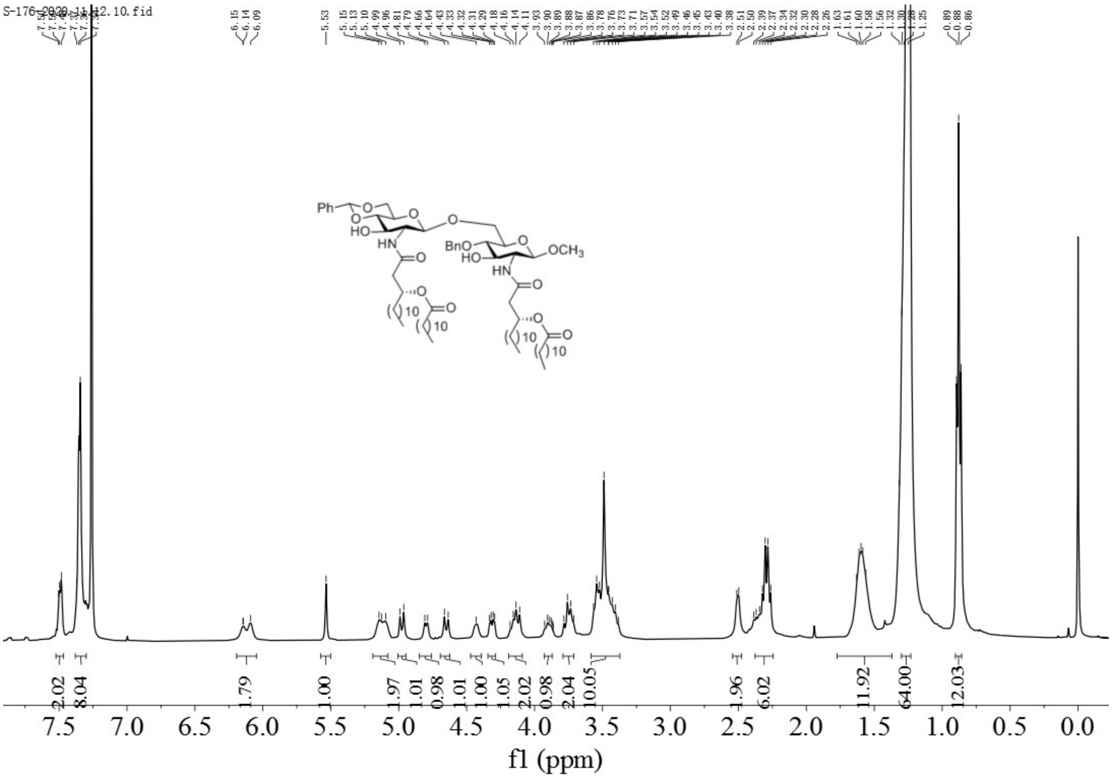


$^{13}C\{^{1}H\}$ NMR Spectrum of compound **33** ($CDCl_3$, 100 MHz)

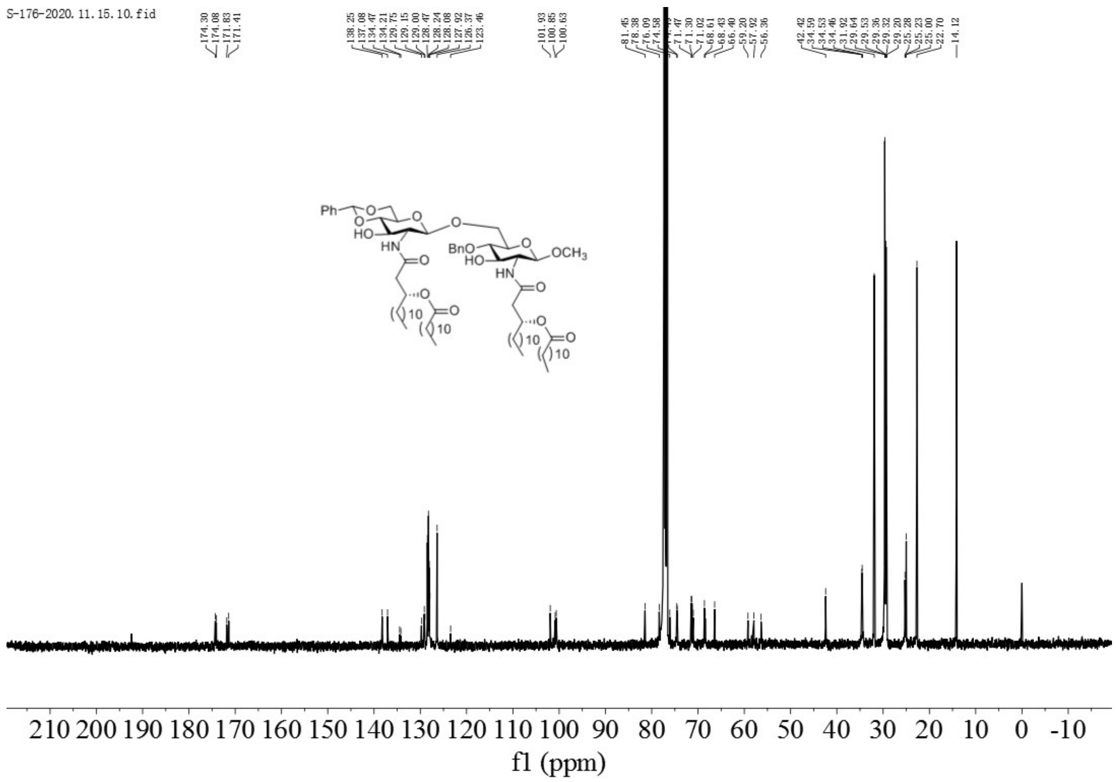


$^{1}H - {}^{1}H$ COSY spectrum of compound **33** ($CDCl_3$, 400 MHz)

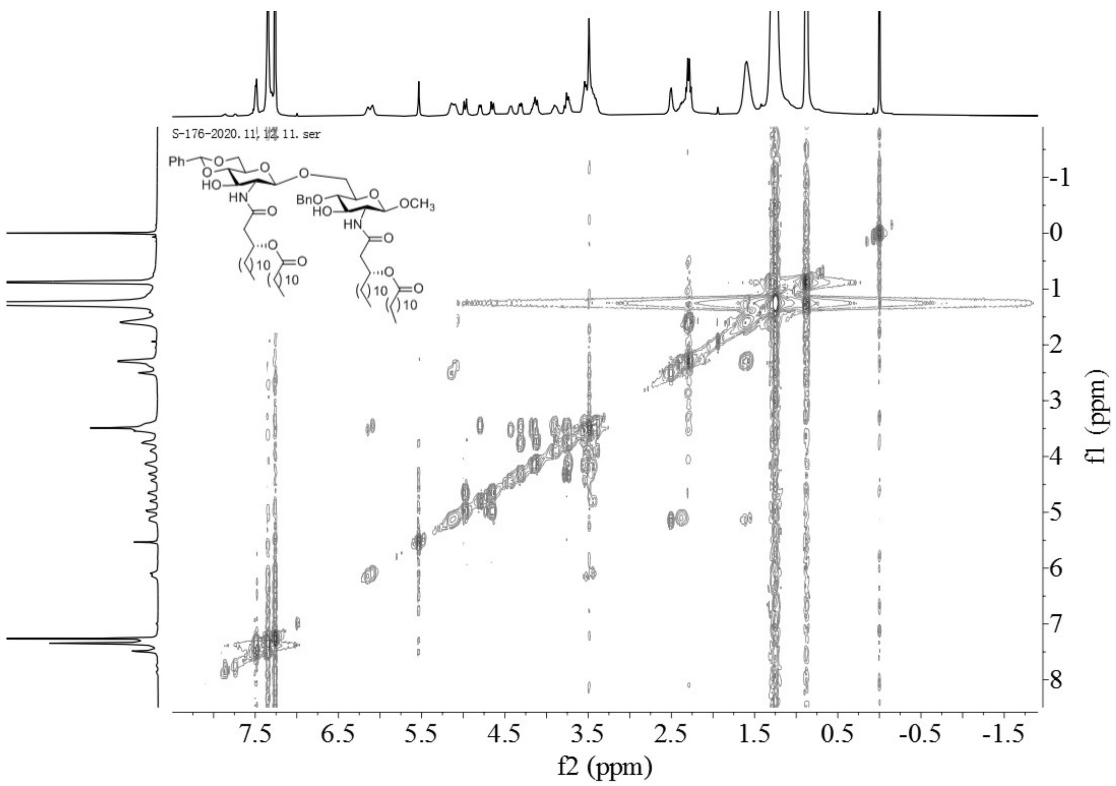
^1H – ^{13}C HMQC spectrum of compound **33** ($CDCl_3$, 400/100 MHz)



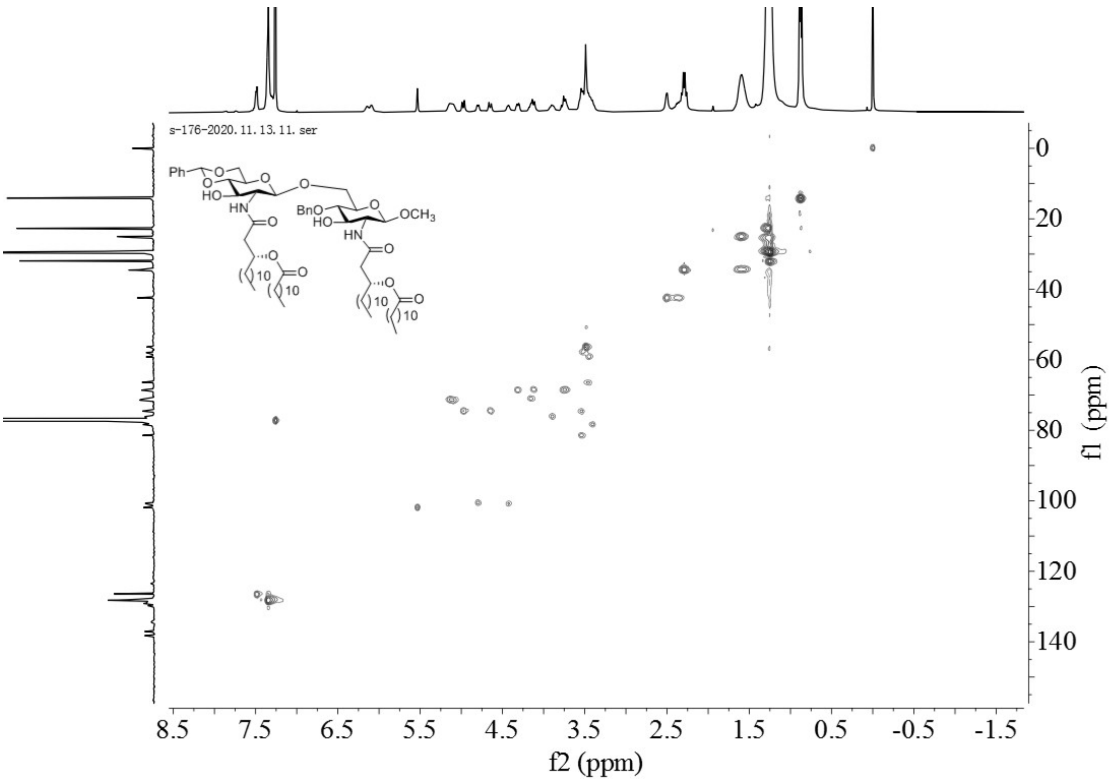
^1H NMR Spectrum of compound **34** ($CDCl_3$, 400 MHz)



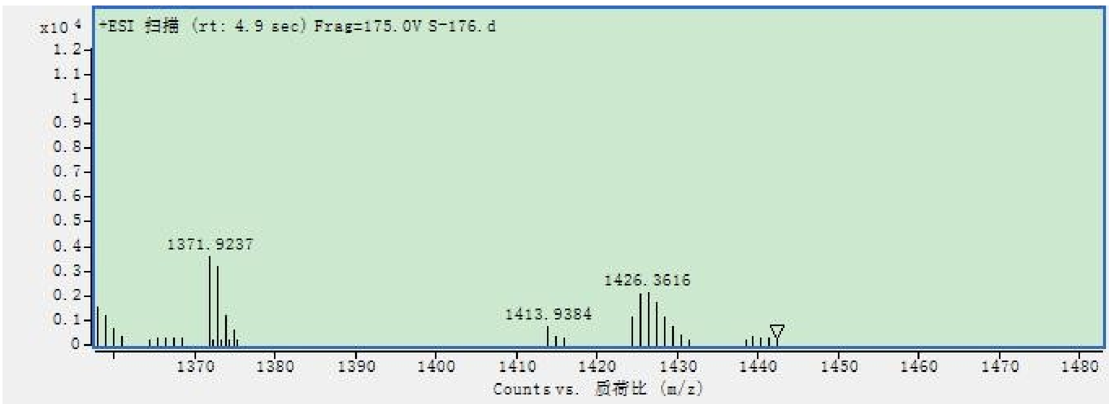
$^{13}C\{^{1}H\}$ NMR spectrum of compound **34** ($CDCl_3$, 100 MHz)



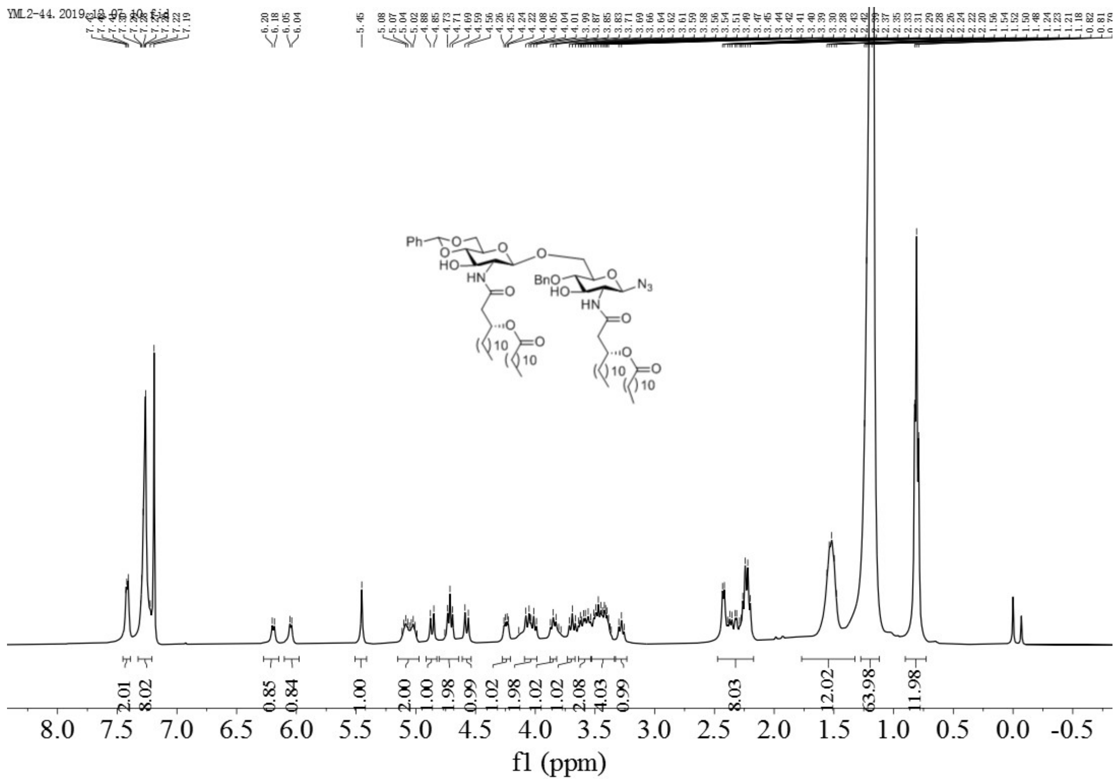
^{1}H-^{1}H COSY spectrum of compound **34** ($CDCl_3$, 400 MHz)



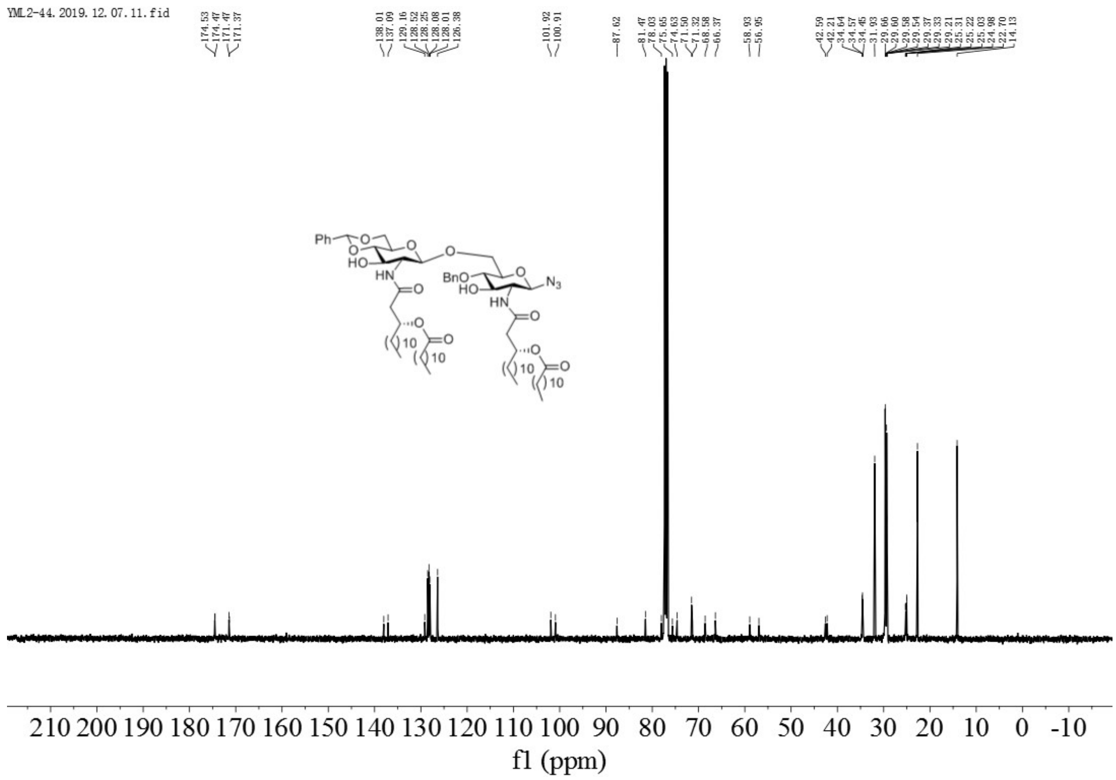
^{1}H-^{13}C HMQC spectrum of compound **34** ($CDCl_3$, 400/100 MHz)



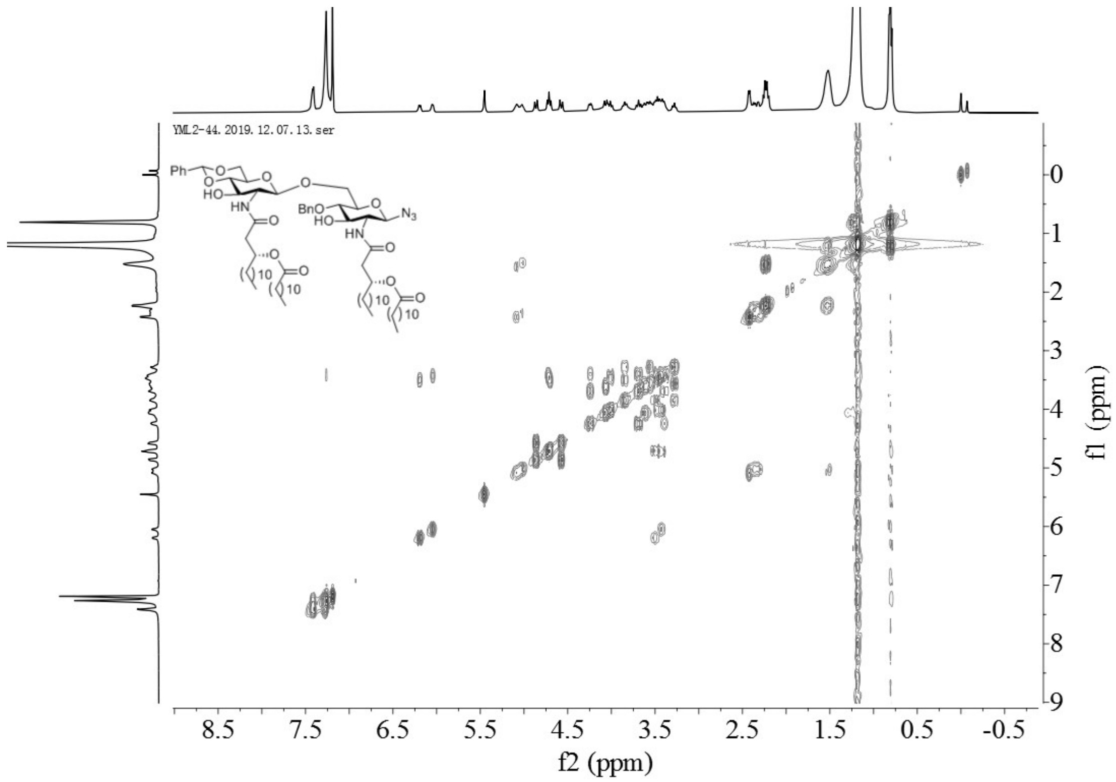
HRMS spectrum of compound **34**



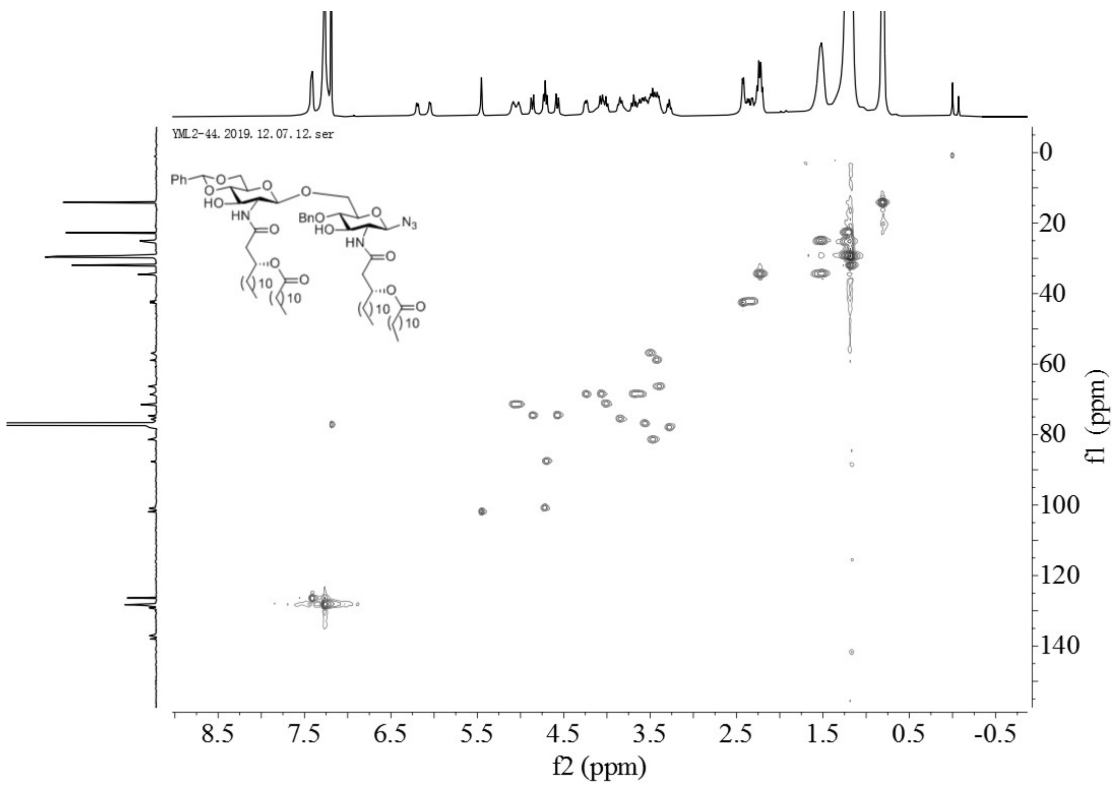
^{1}H NMR spectrum of compound **35** ($CDCl_3$, 400 MHz)



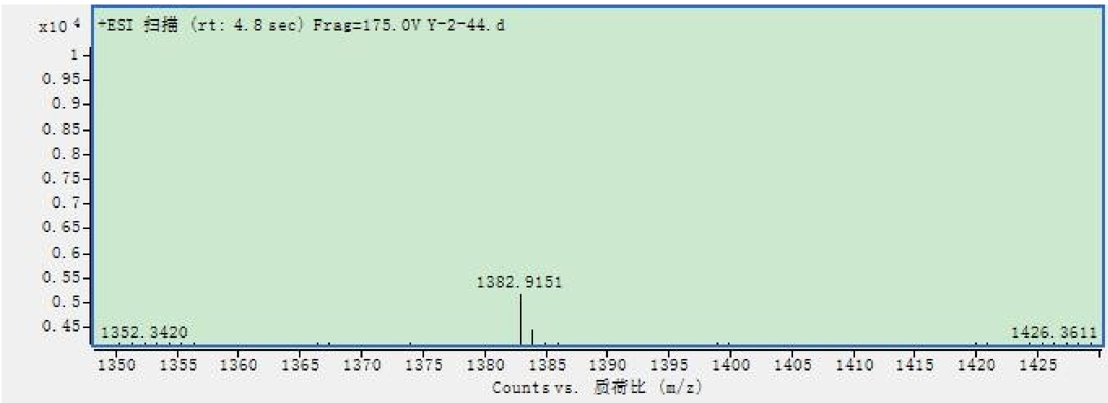
$^{13}C\{^{1}H\}$ NMR spectrum of compound **35** ($CDCl_3$, 100 MHz)



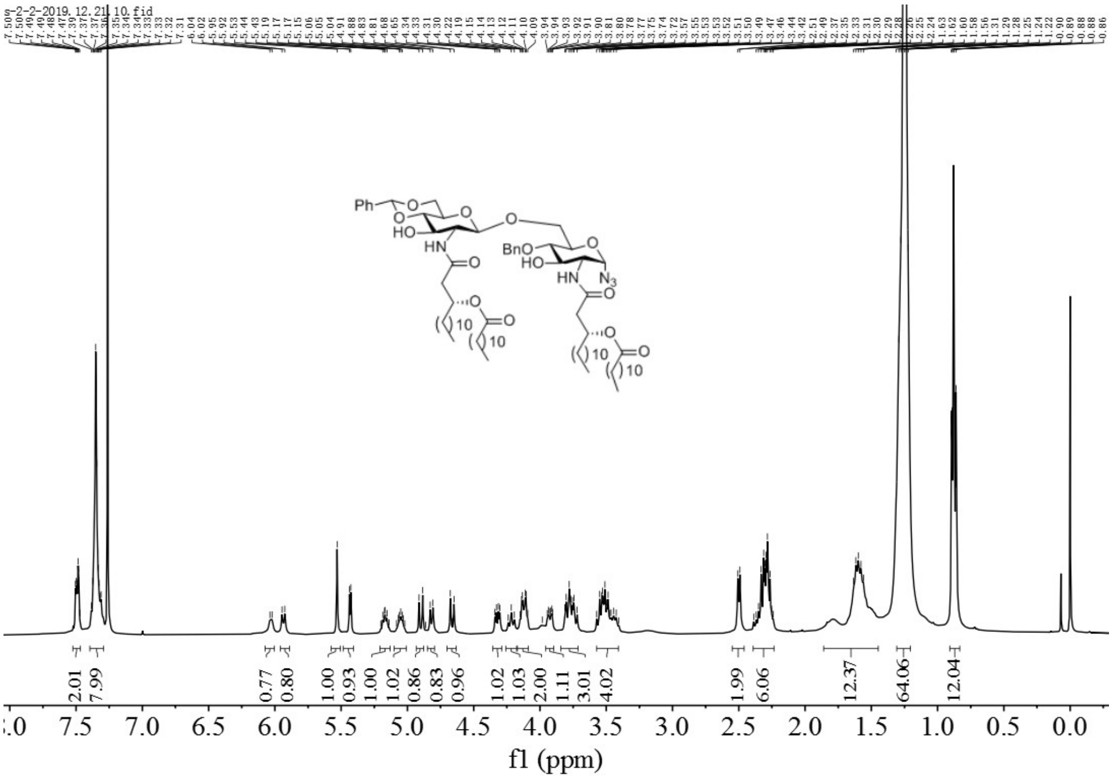
$^1H - ^1H$ COSY spectrum of compound **35** ($CDCl_3$, 400 MHz)



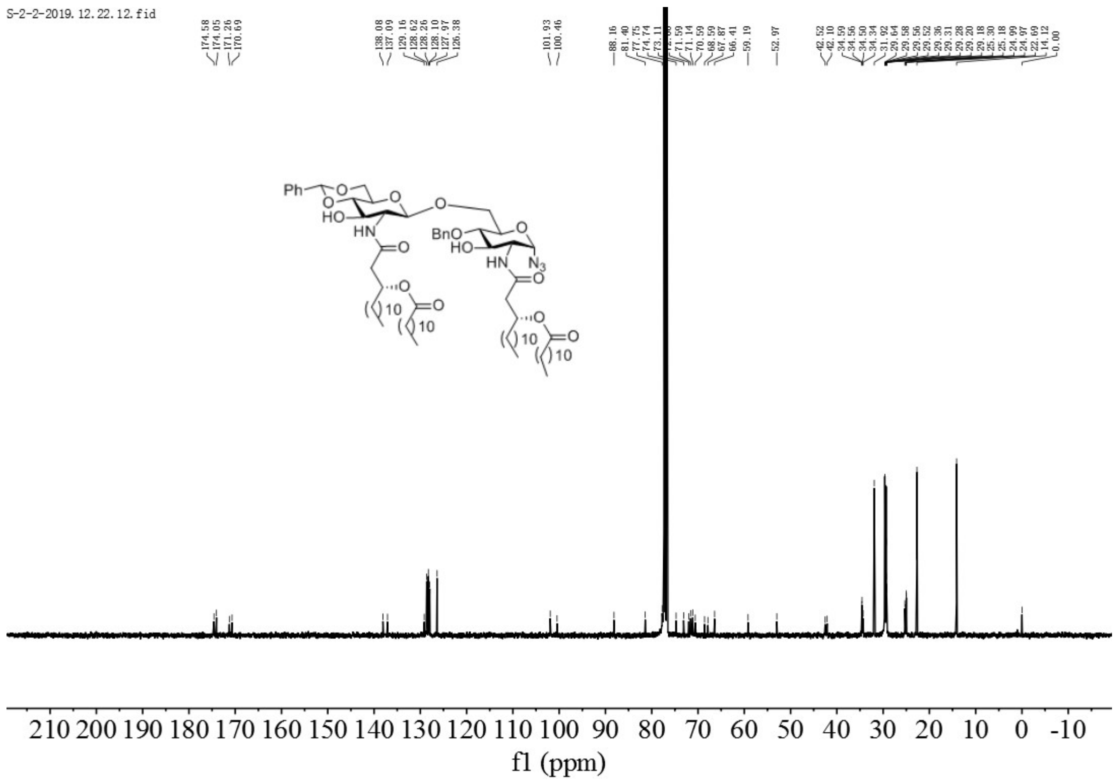
$^1H - ^{13}C$ HMQC spectrum of compound **35** ($CDCl_3$, 400/100 MHz)



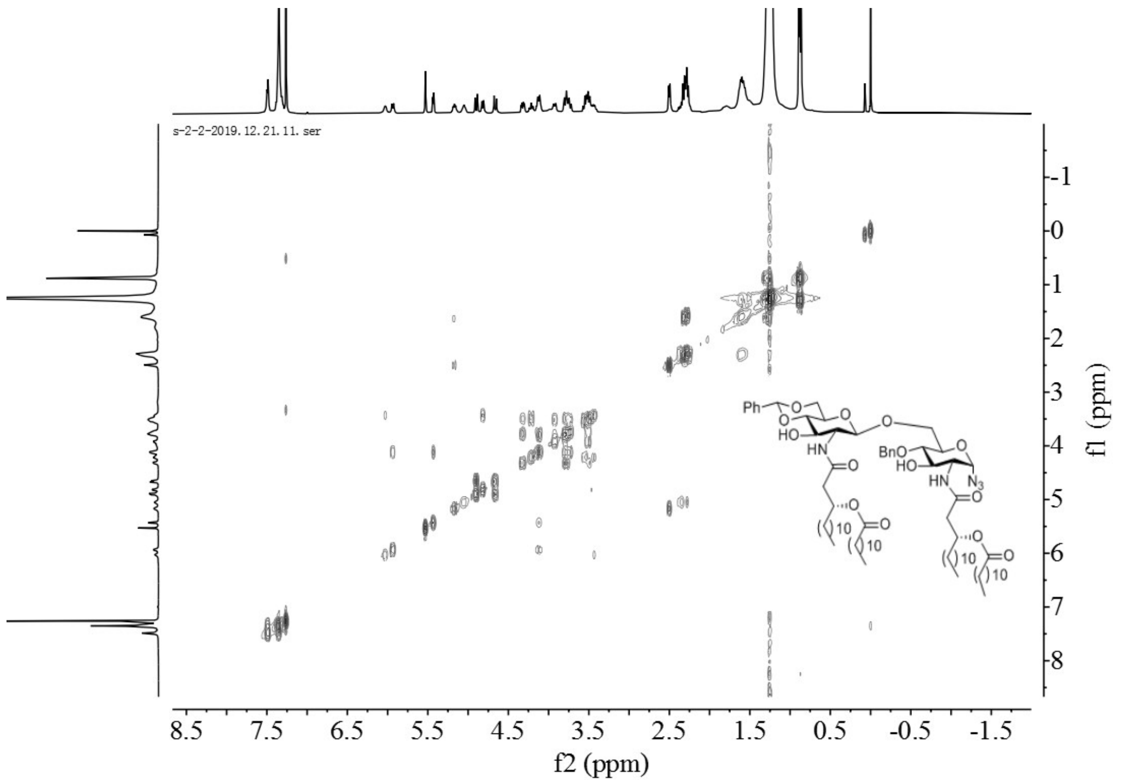
HRMS spectrum of compound **35**



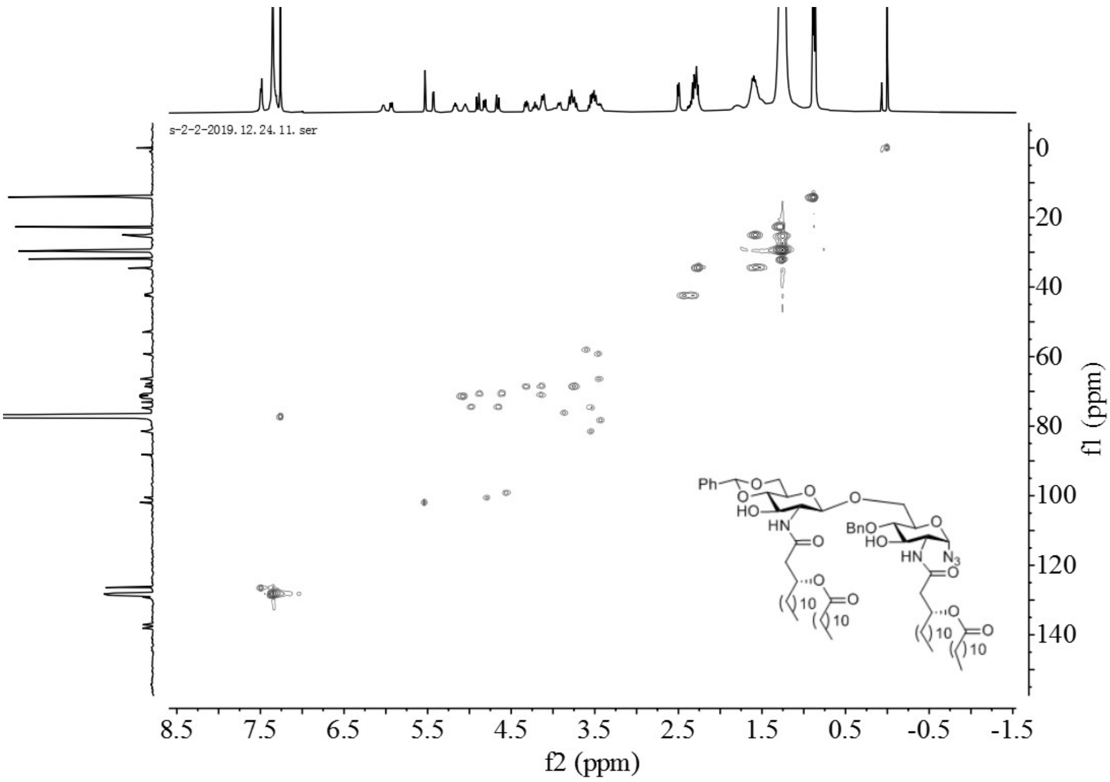
^{1}H NMR spectrum of compound **36** ($CDCl_3$, 400 MHz)



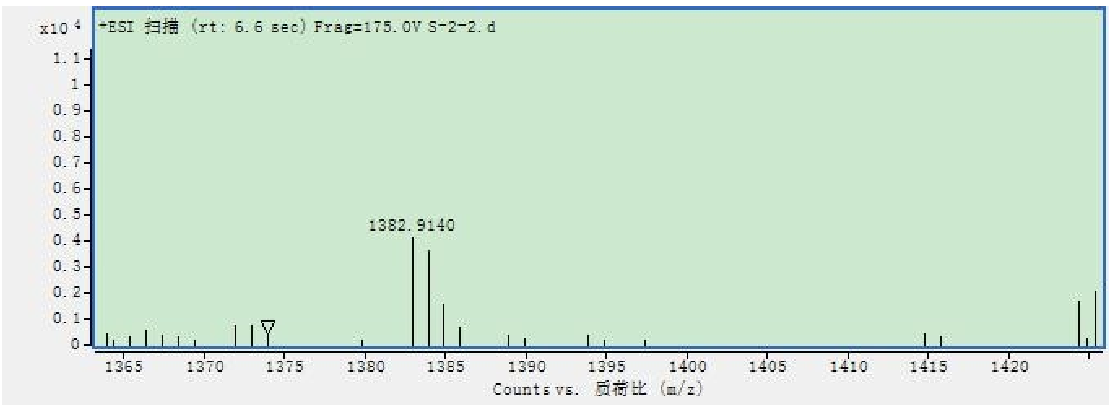
$^{13}C\{^1H\}$ NMR spectrum of compound **36** ($CDCl_3$, 100 MHz)



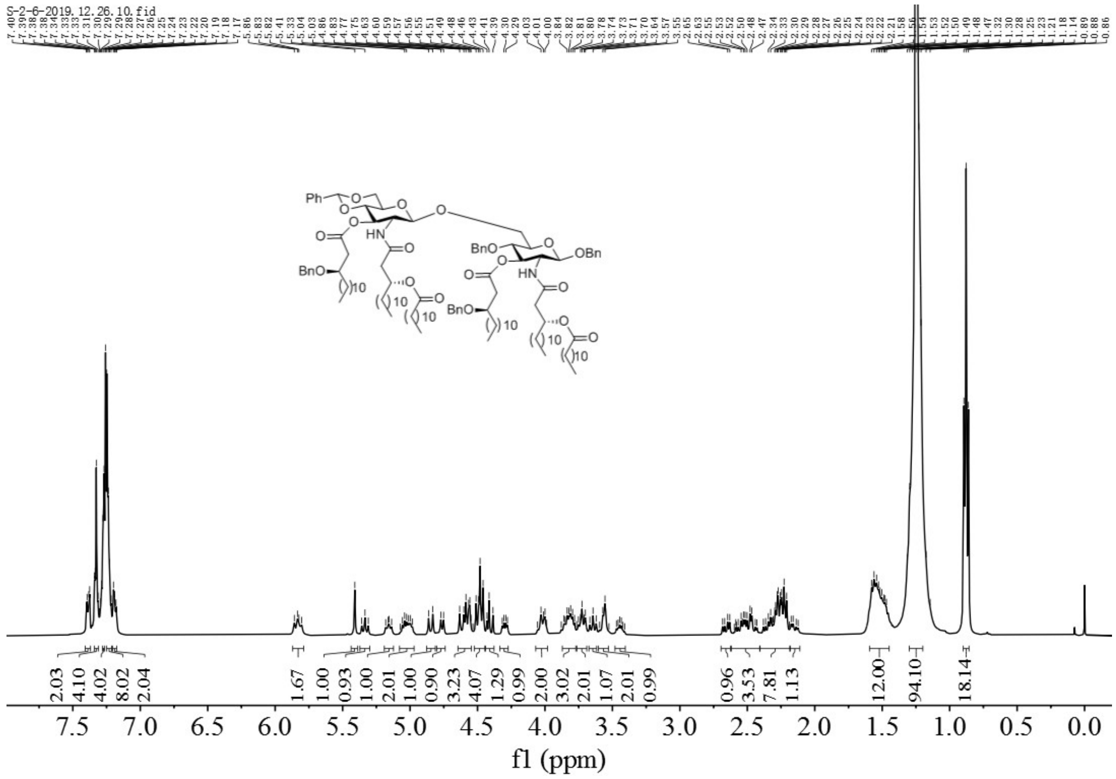
^1H-^1H COSY spectrum of compound **36** ($CDCl_3$, 400 MHz)



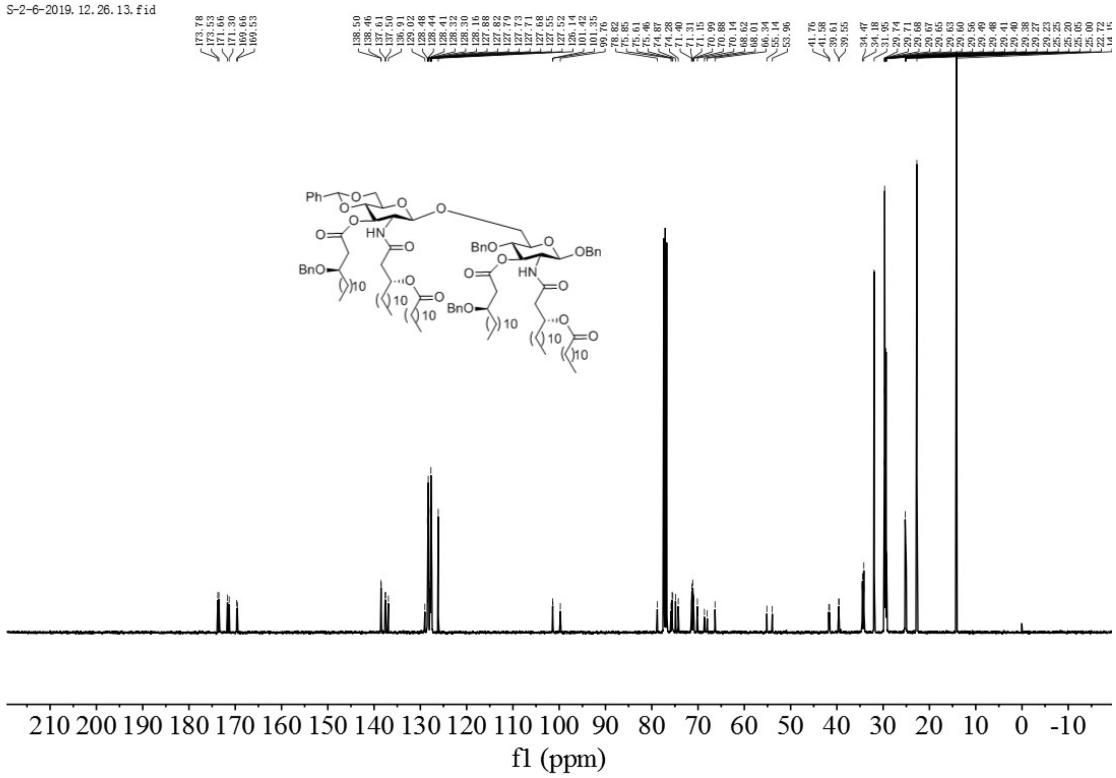
^{1}H-^{13}C HMQC spectrum of compound **36** ($CDCl_3$, 400/100 MHz)



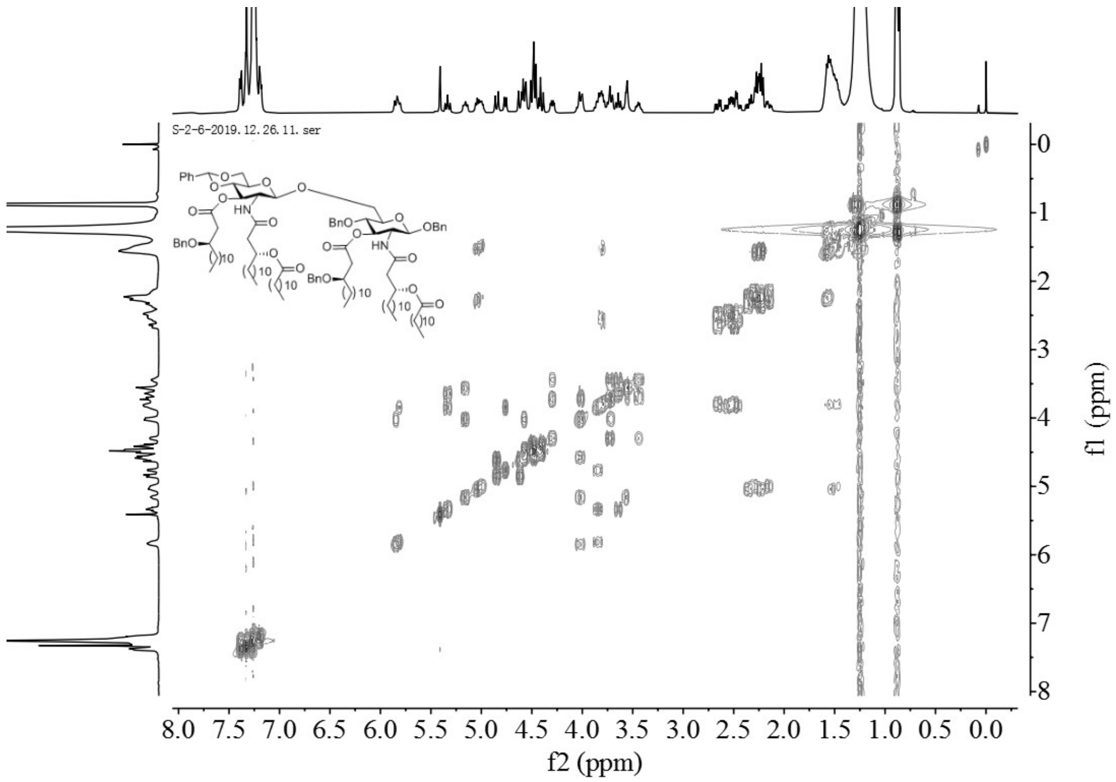
HRMS spectrum of compound **36**



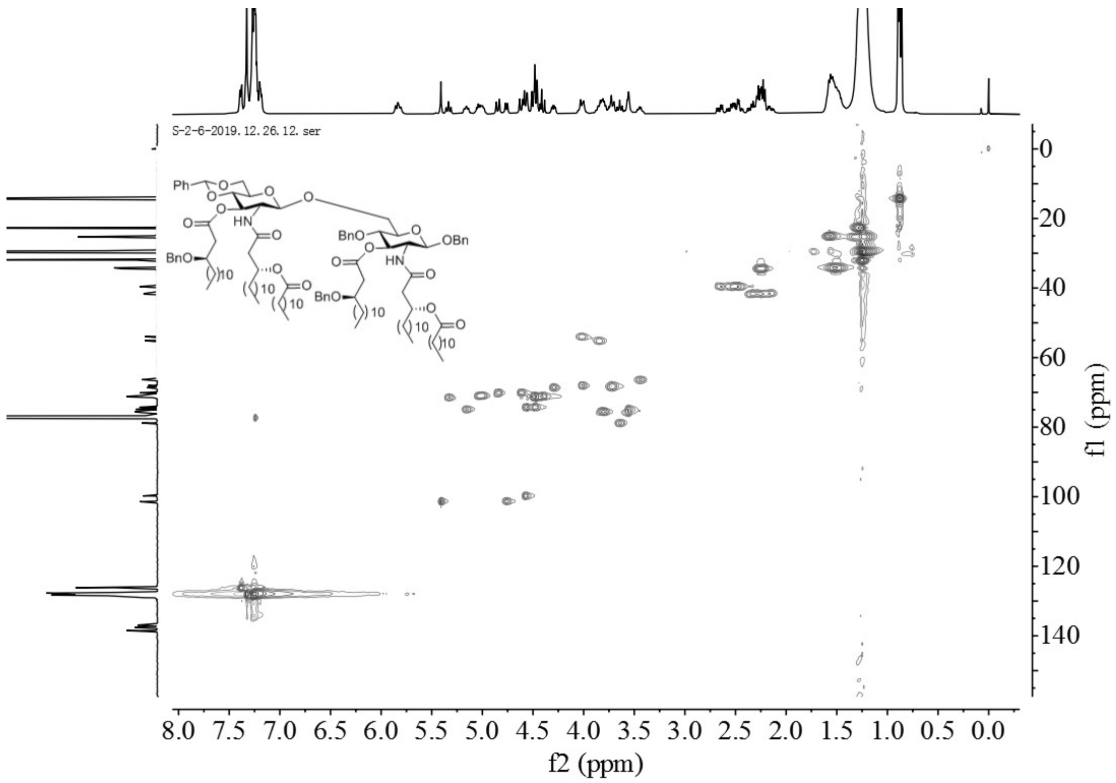
^{1}H NMR spectrum of compound **38** ($CDCl_3$, 400 MHz)



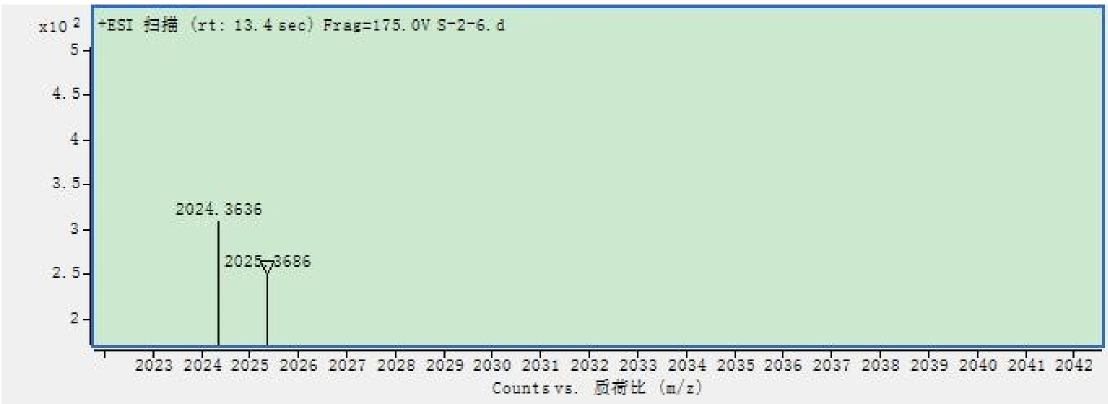
$^{13}C\{^{1}H\}$ NMR spectrum of compound **38** ($CDCl_3$, 100 MHz)



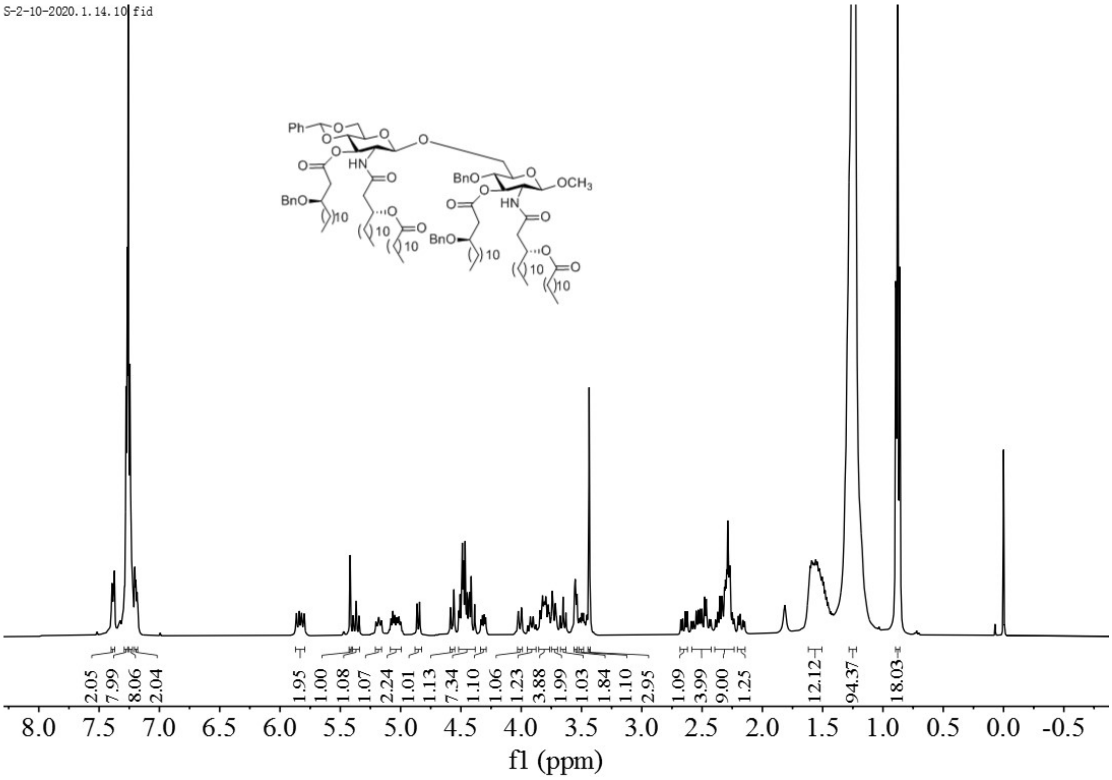
^{1}H-^{1}H COSY spectrum of compound **38** ($CDCl_3$, 400 MHz)



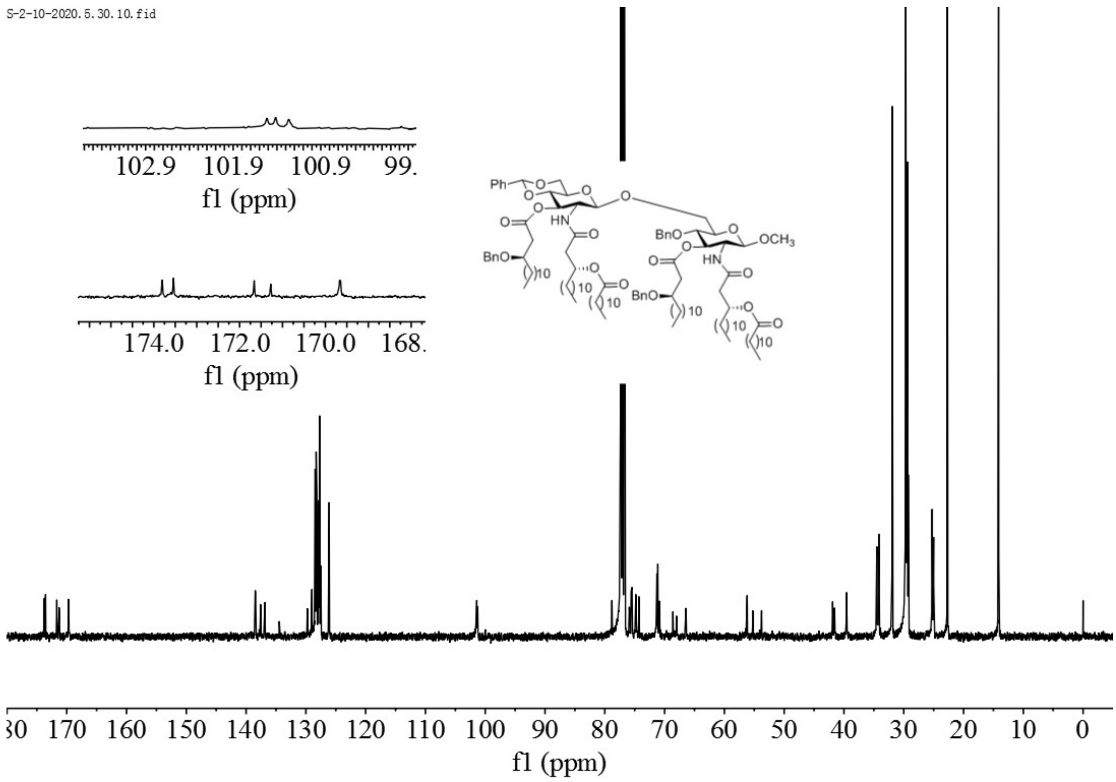
^{1}H-^{13}C HMQC spectrum of compound **38** ($CDCl_3$, 400/100 MHz)



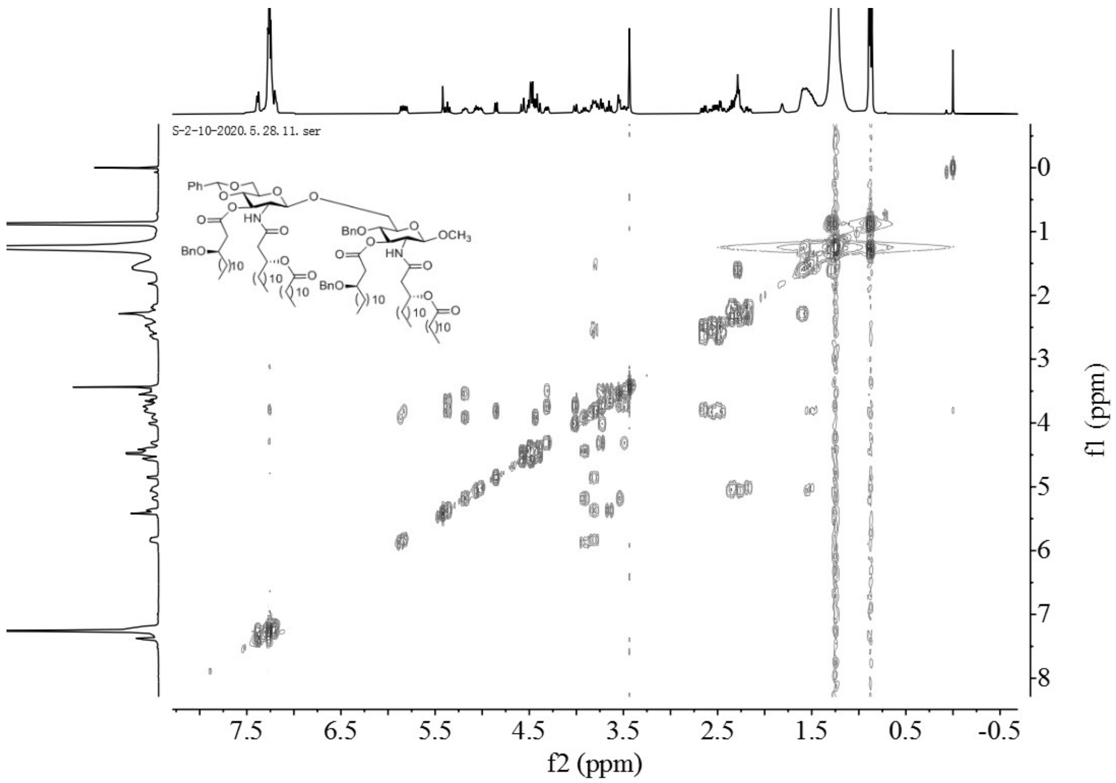
HRMS spectrum of compound **38**



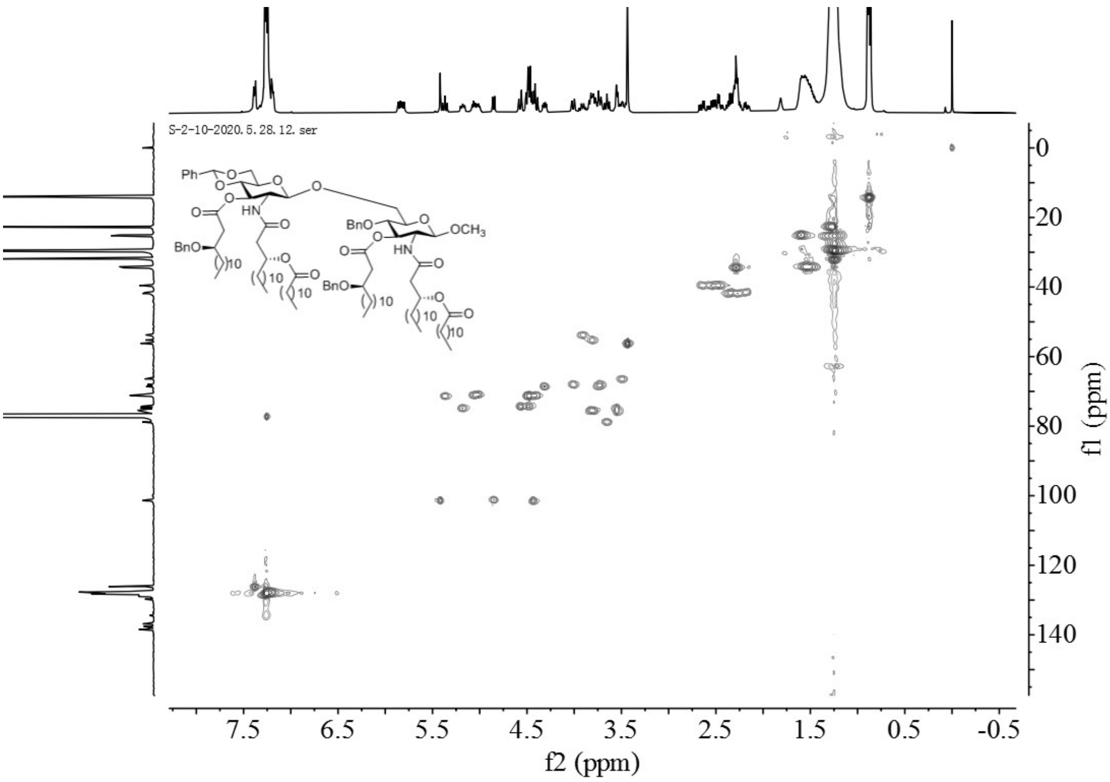
[1]H NMR spectrum of compound **39** ($CDCl_3$, 400 MHz)



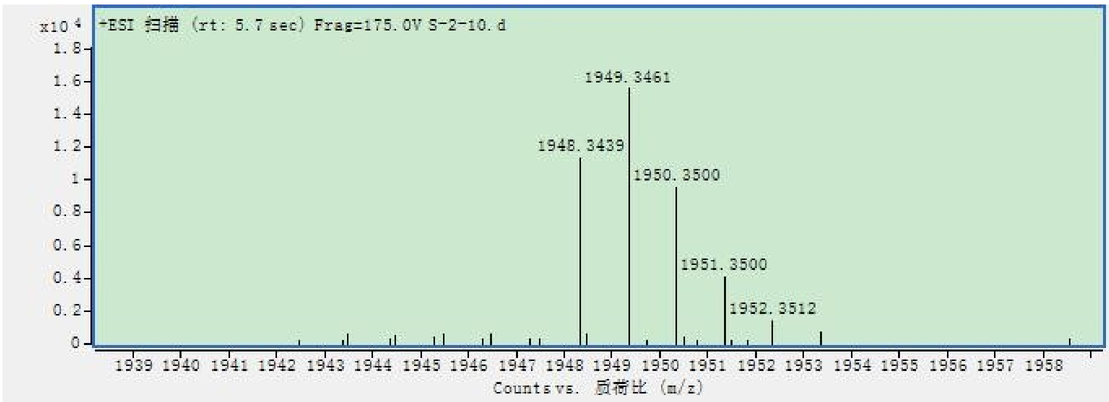
$^{13}C\{^1H\}$ NMR spectrum of compound **39** ($CDCl_3$, 100 MHz)



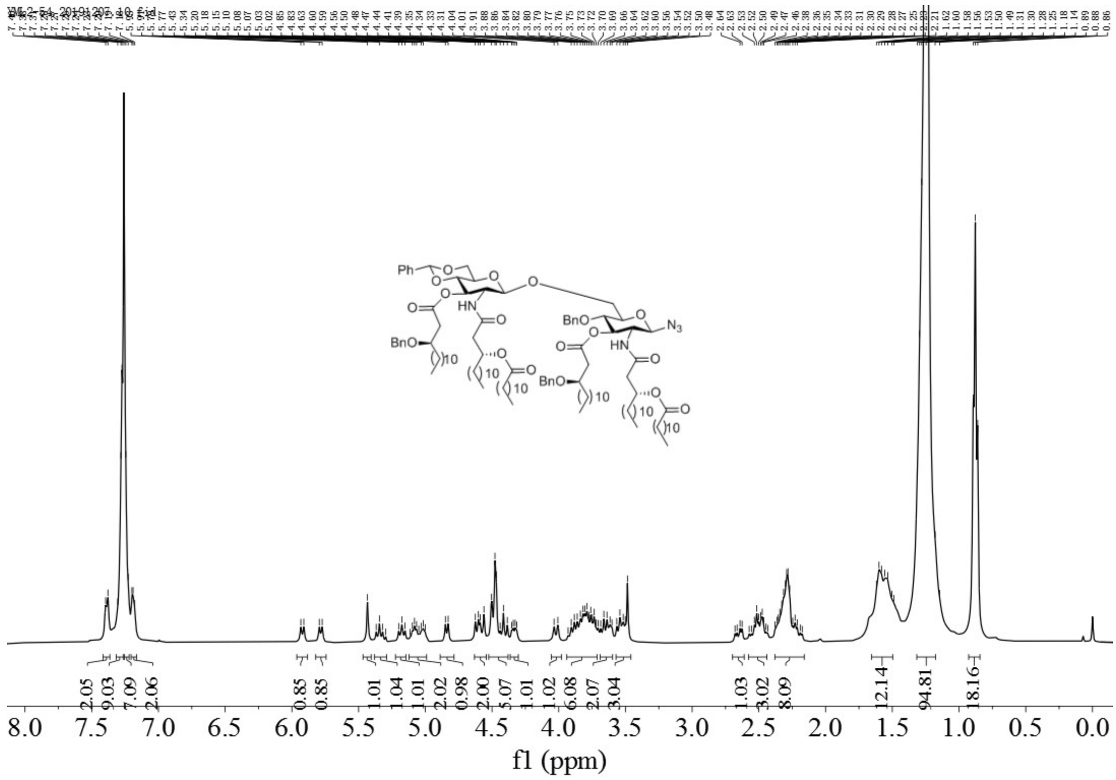
^1H-^1H COSY spectrum of compound **39** ($CDCl_3$, 400 MHz)



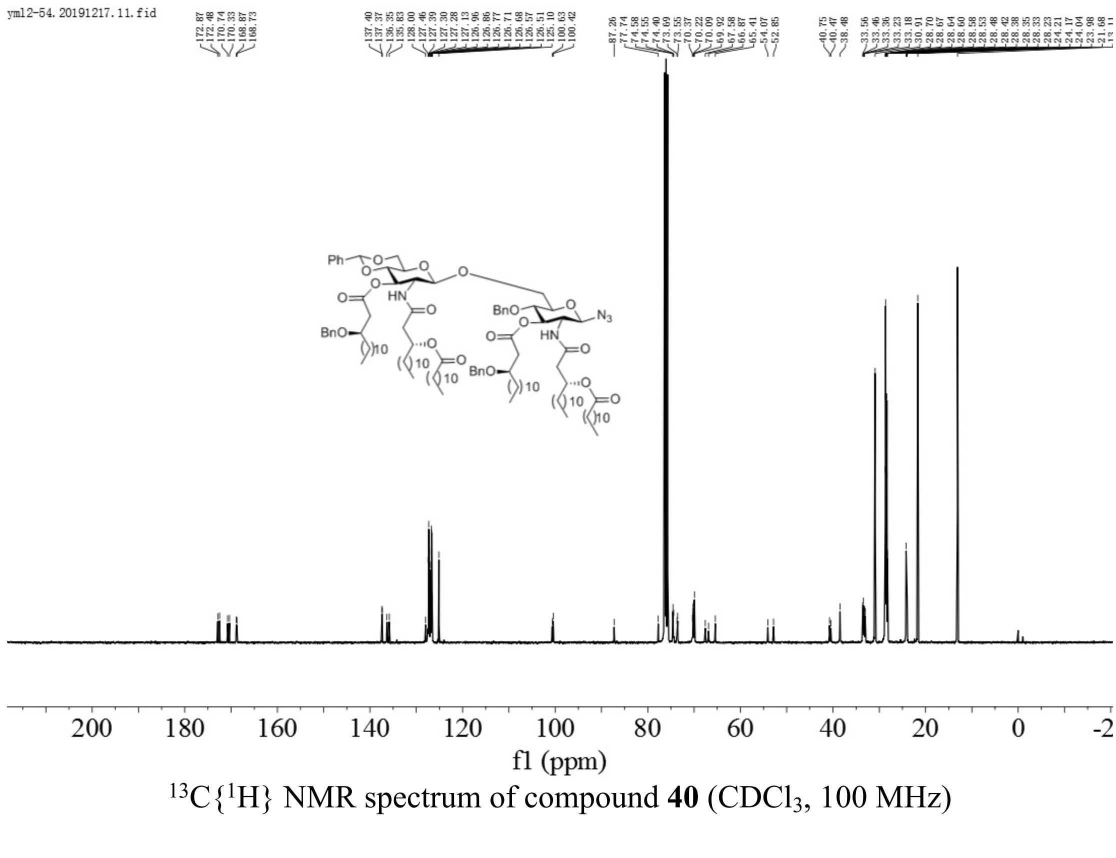
^{1}H-^{13}C HMQC spectrum of compound **39** ($CDCl_3$, 400/100 MHz)



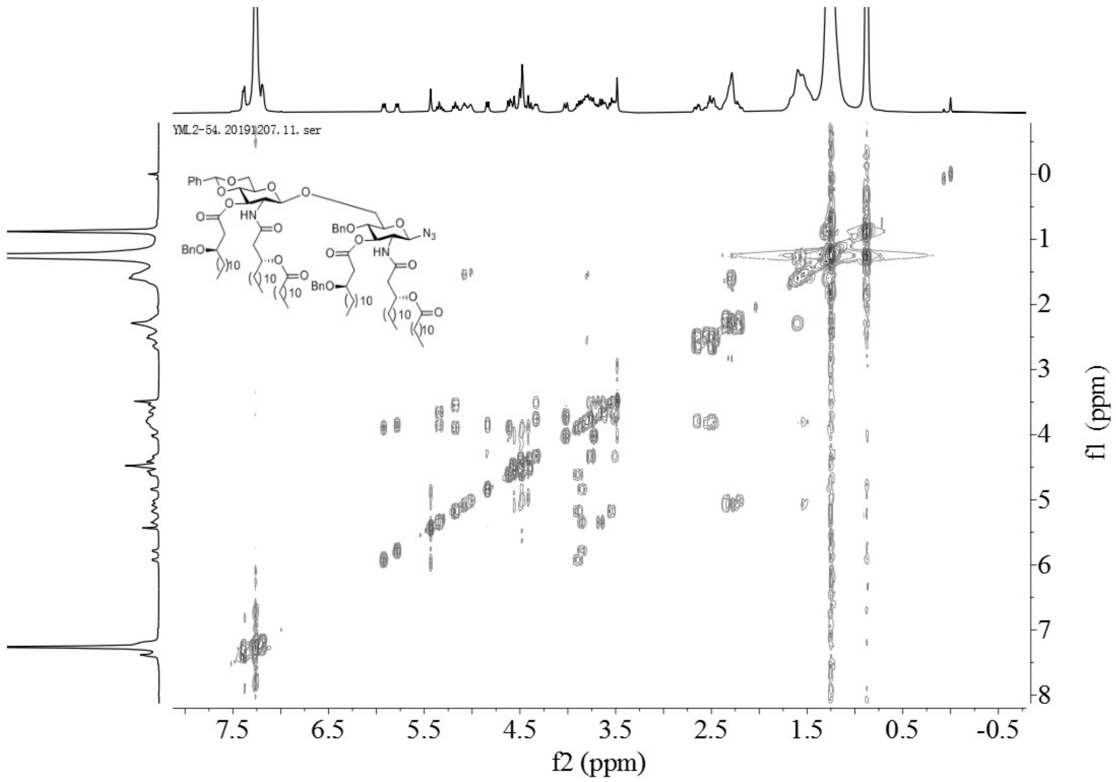
HRMS spectrum of compound **39**



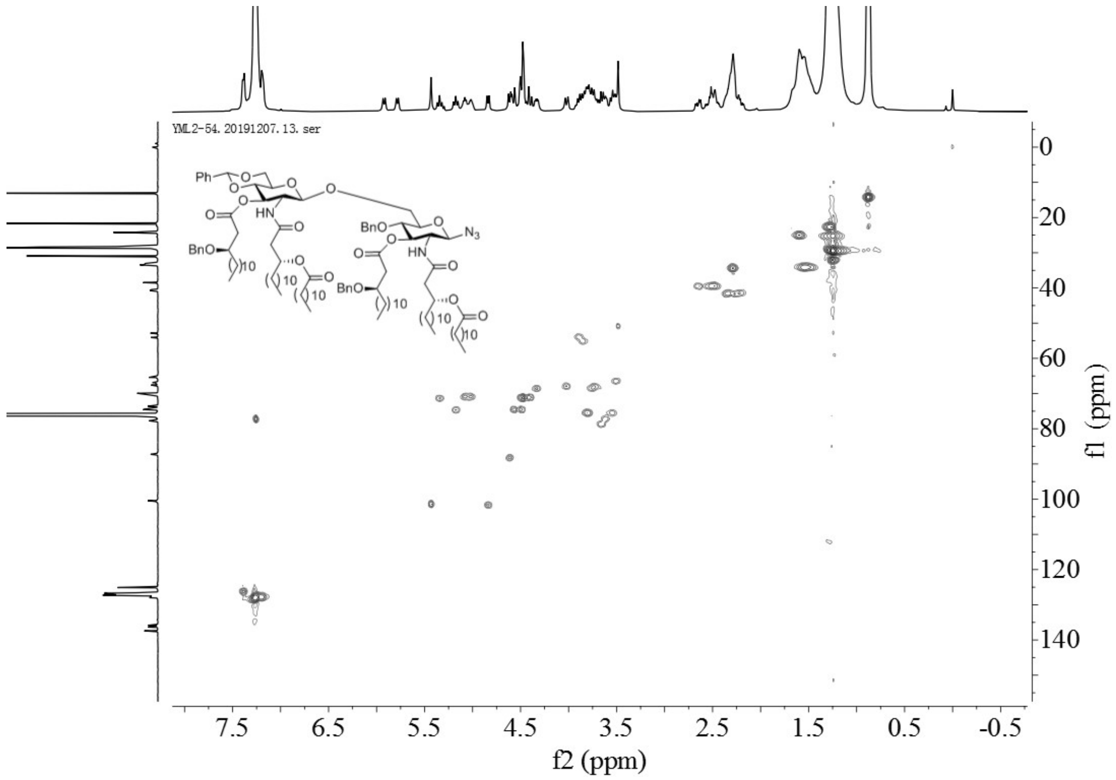
^{1}H NMR spectrum of compound **40** ($CDCl_3$, 400 MHz)



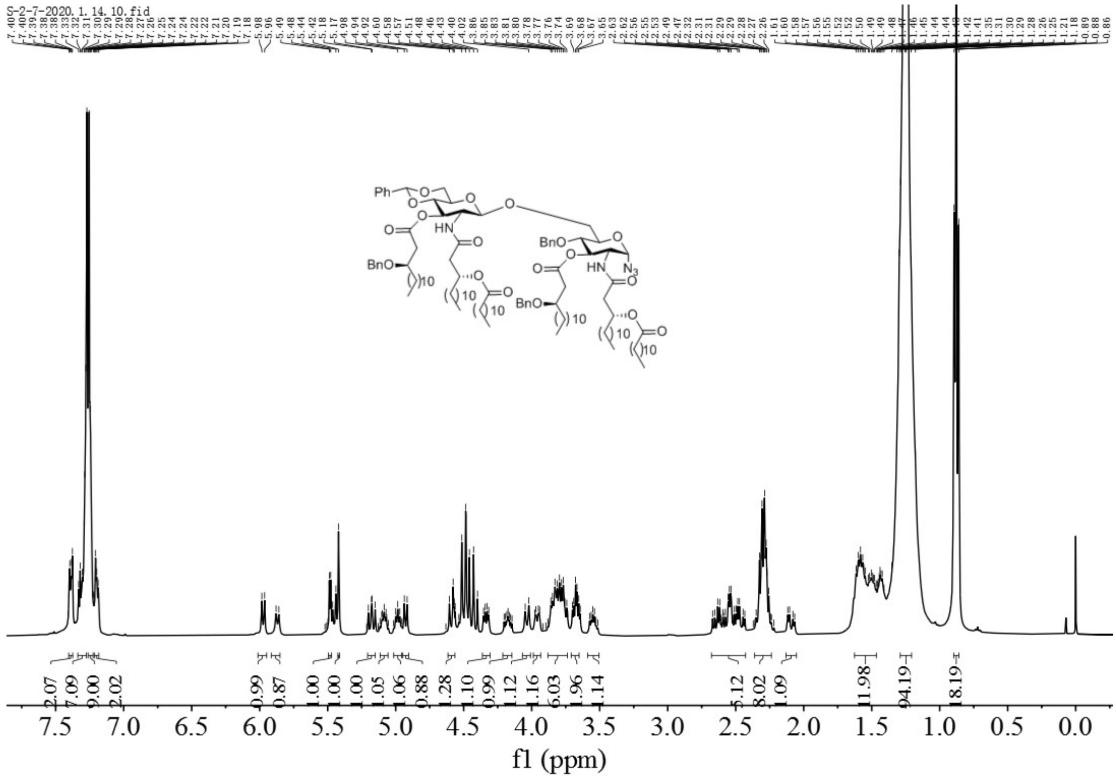
^{13}C{^{1}H} NMR spectrum of compound **40** ($CDCl_3$, 100 MHz)



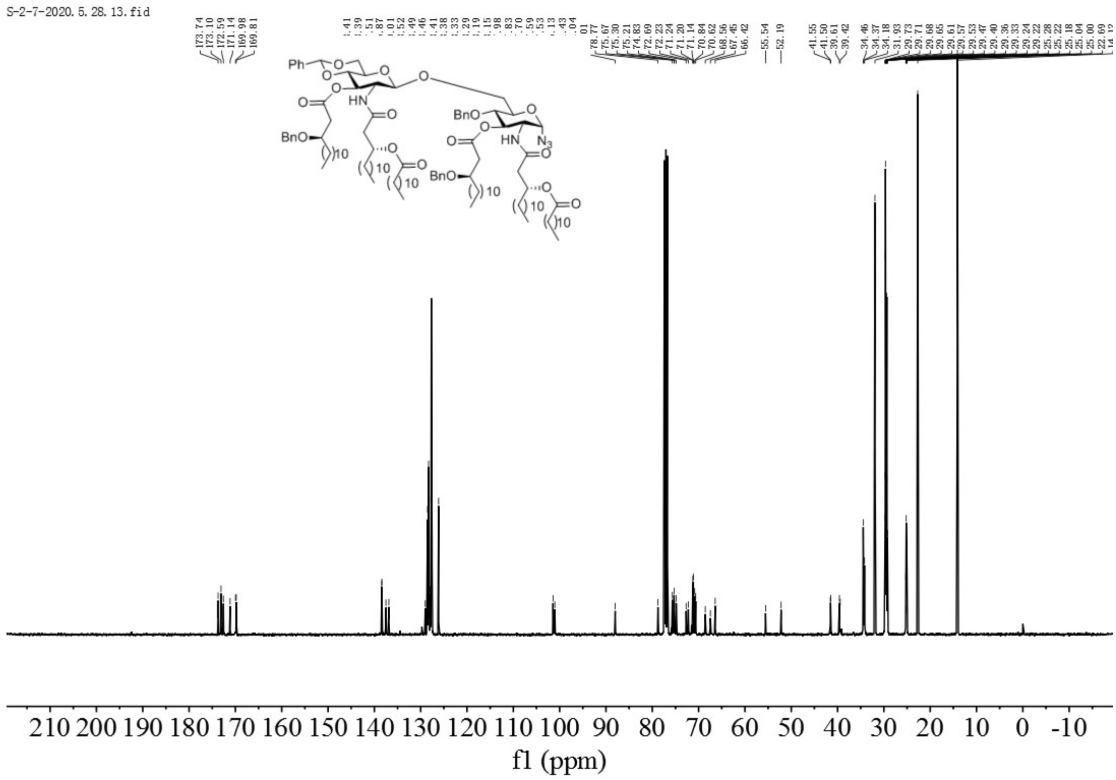
$^1H – ^1H$ COSY spectrum of compound **40** ($CDCl_3$, 400 MHz)



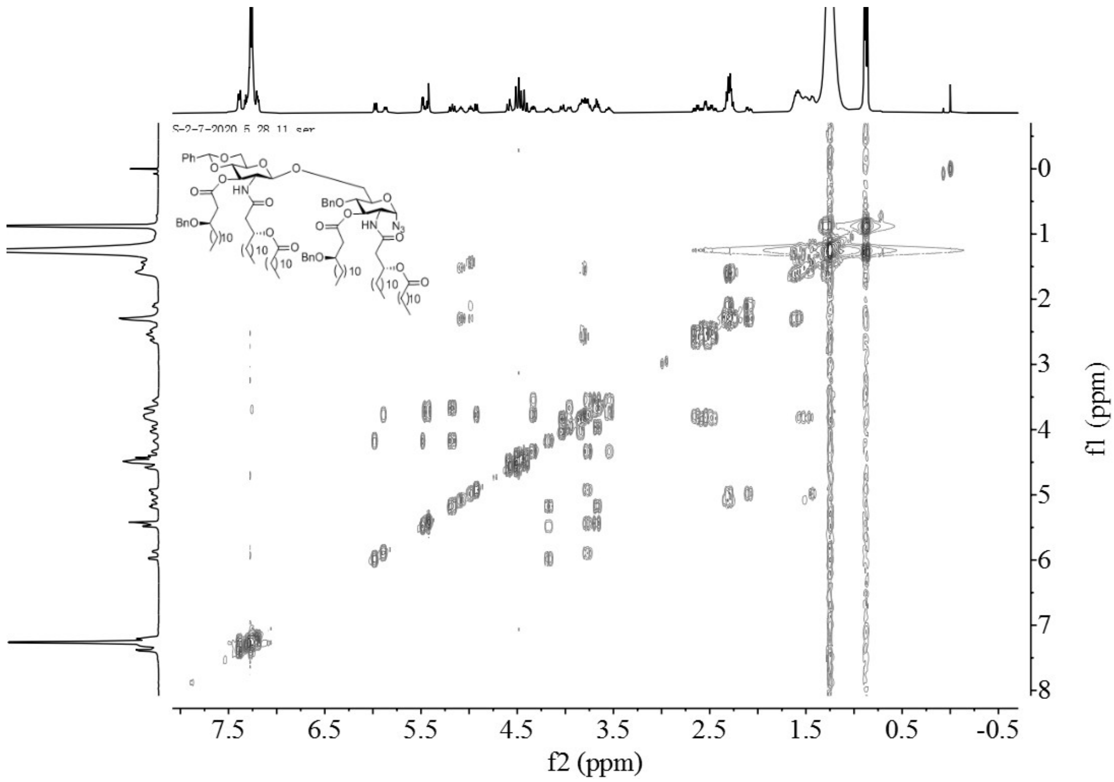
$^1H – ^{13}C$ HMQC spectrum of compound **40** ($CDCl_3$, 400/100 MHz)



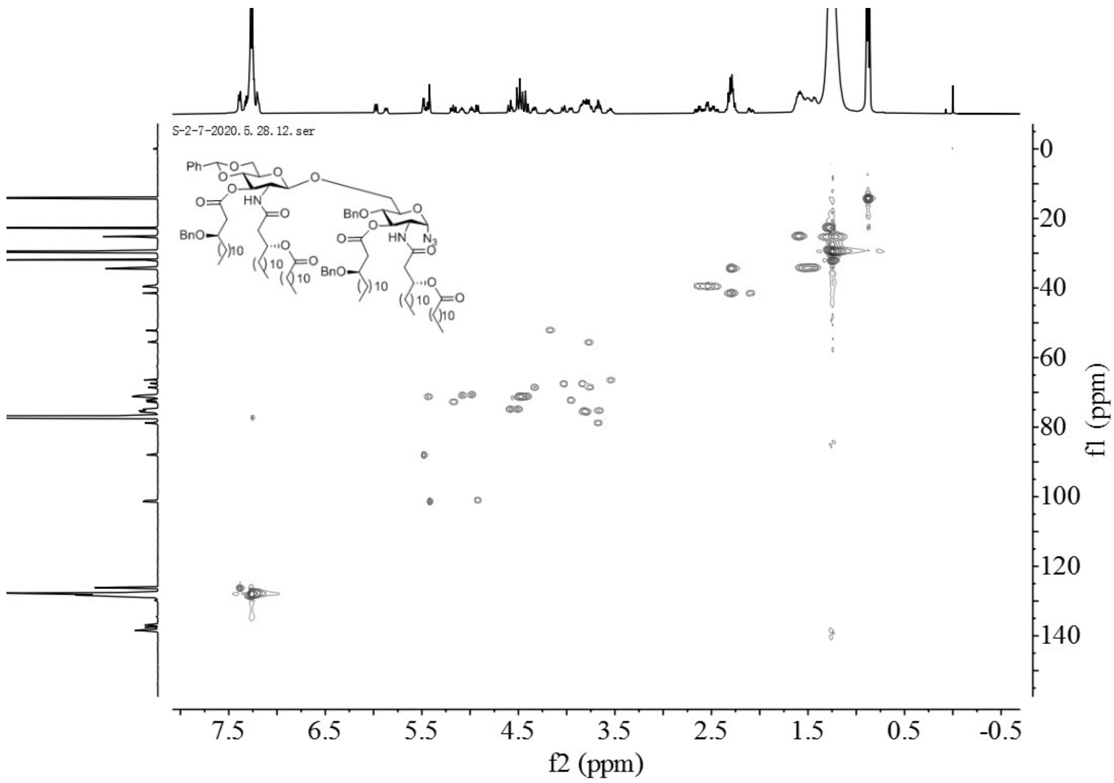
^{1}H NMR spectrum of compound **41** ($CDCl_3$, 400 MHz)



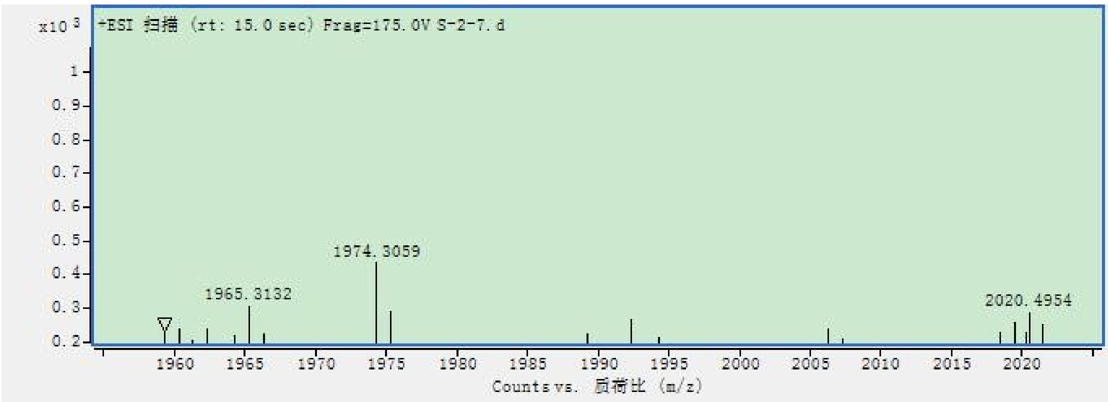
$^{13}C\{^{1}H\}$ NMR spectrum of compound **41** ($CDCl_3$, 100 MHz)



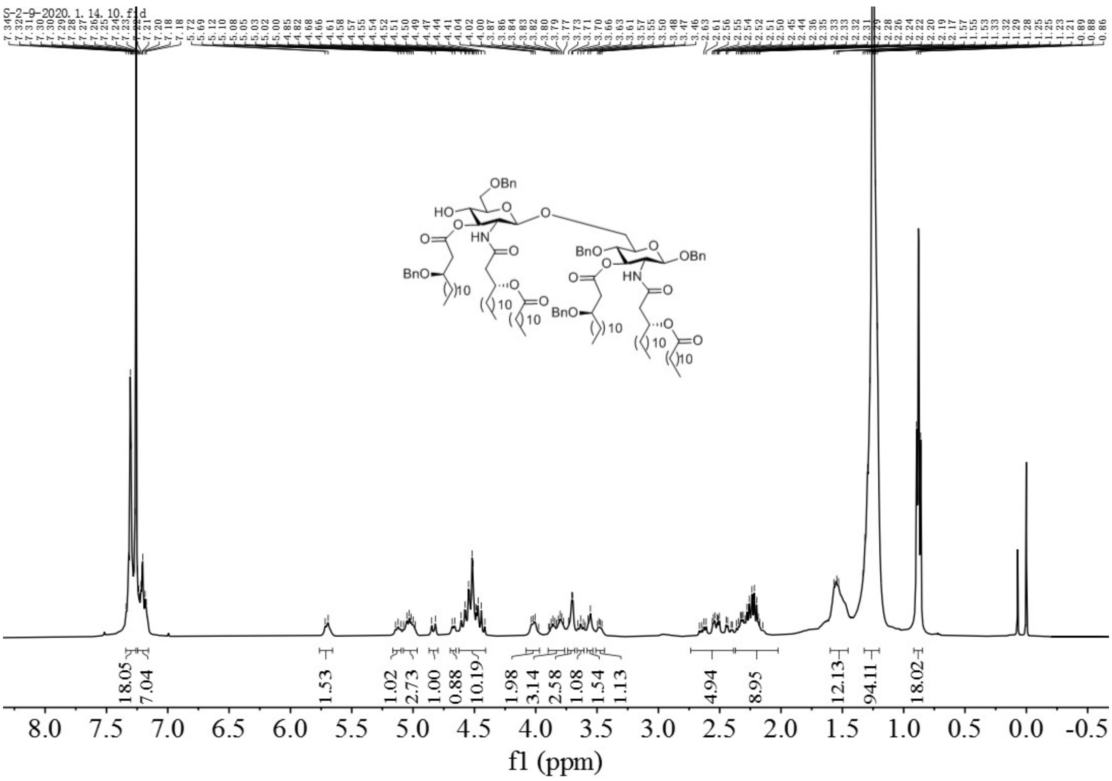
^{1}H-^{1}H COSY spectrum of compound **41** ($CDCl_3$, 400 MHz)



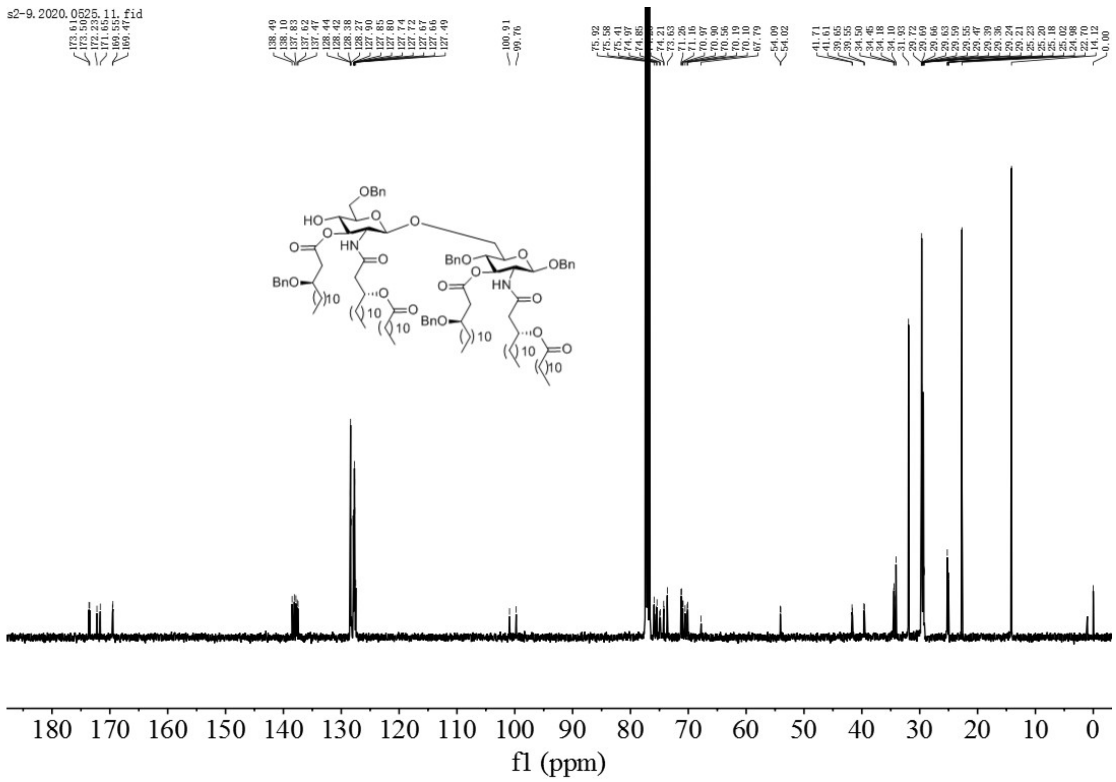
^{1}H-^{13}C HMQC spectrum of compound **41** ($CDCl_3$, 400/100 MHz)



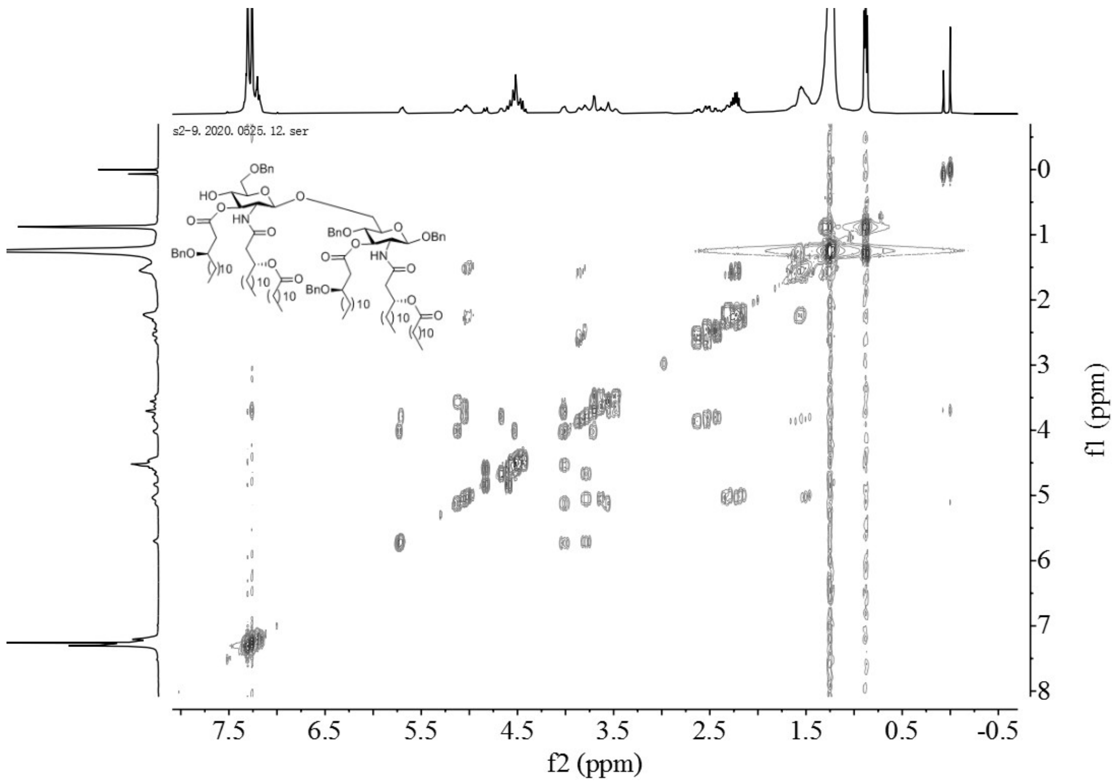
HRMS spectrum of compound **41**



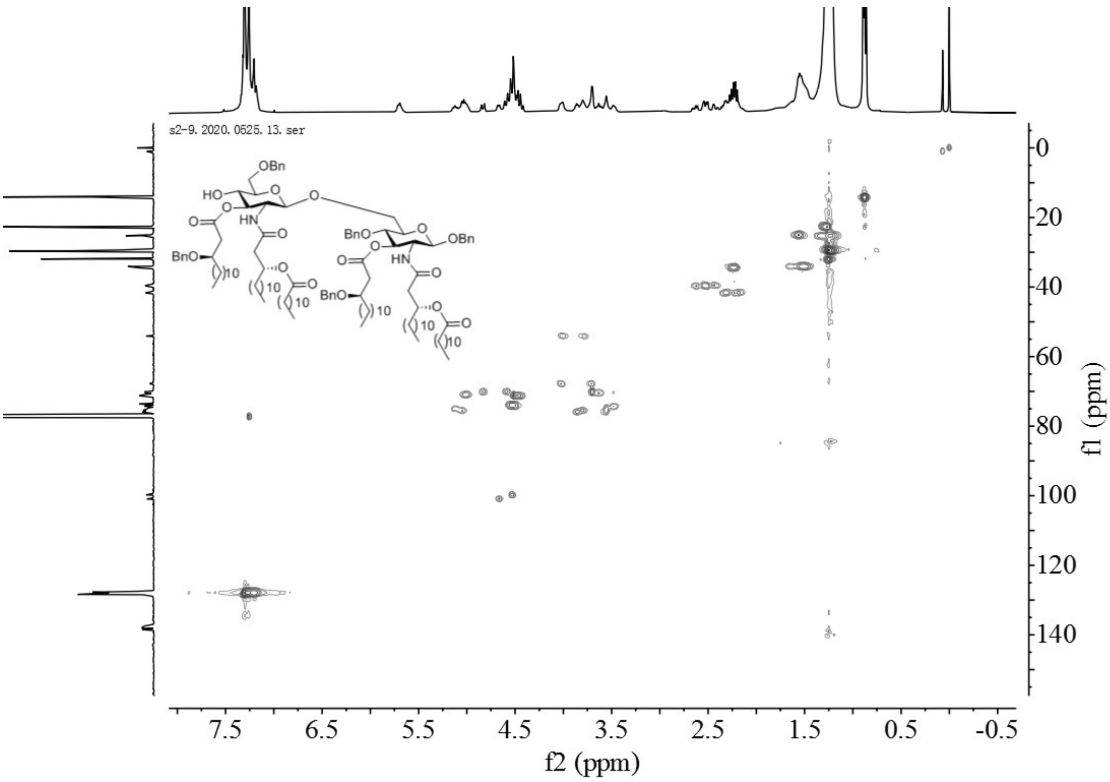
^{1}H NMR spectrum of compound **42** ($CDCl_3$, 400 MHz)



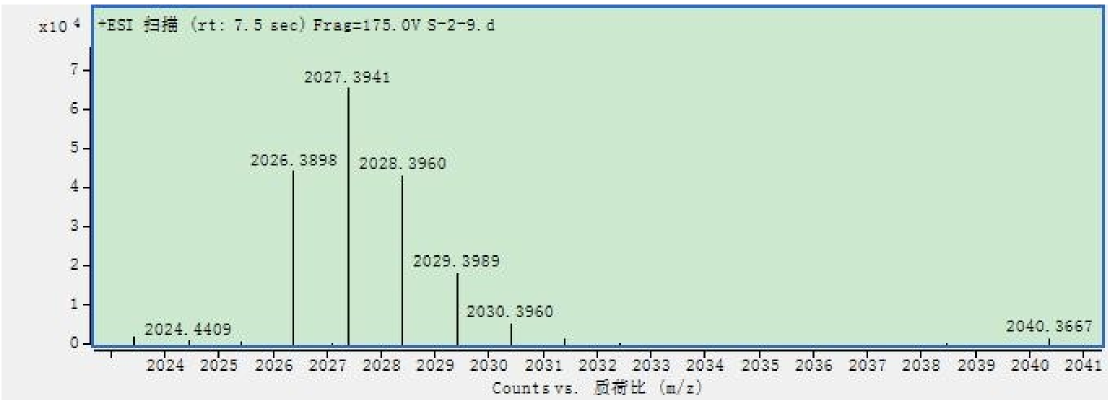
$^{13}C\{^{1}H\}$ NMR spectrum of compound **42** ($CDCl_3$, 100 MHz)



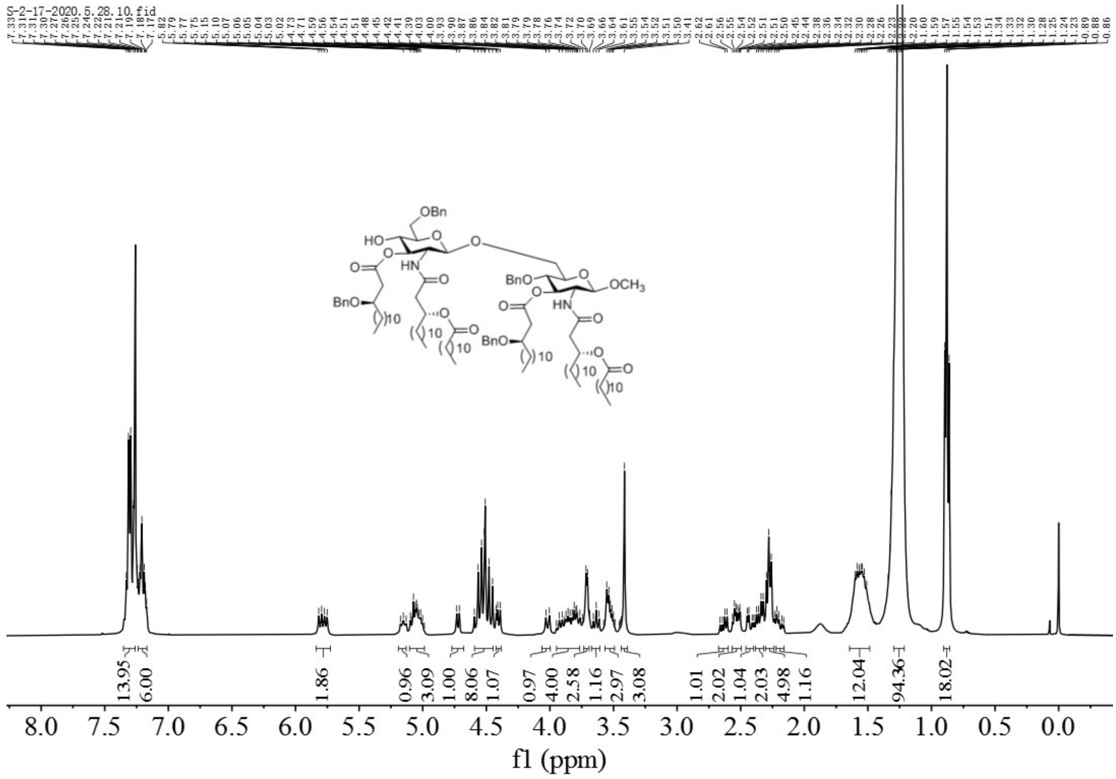
^{1}H-^{1}H COSY spectrum of compound **42** ($CDCl_3$, 400 MHz)



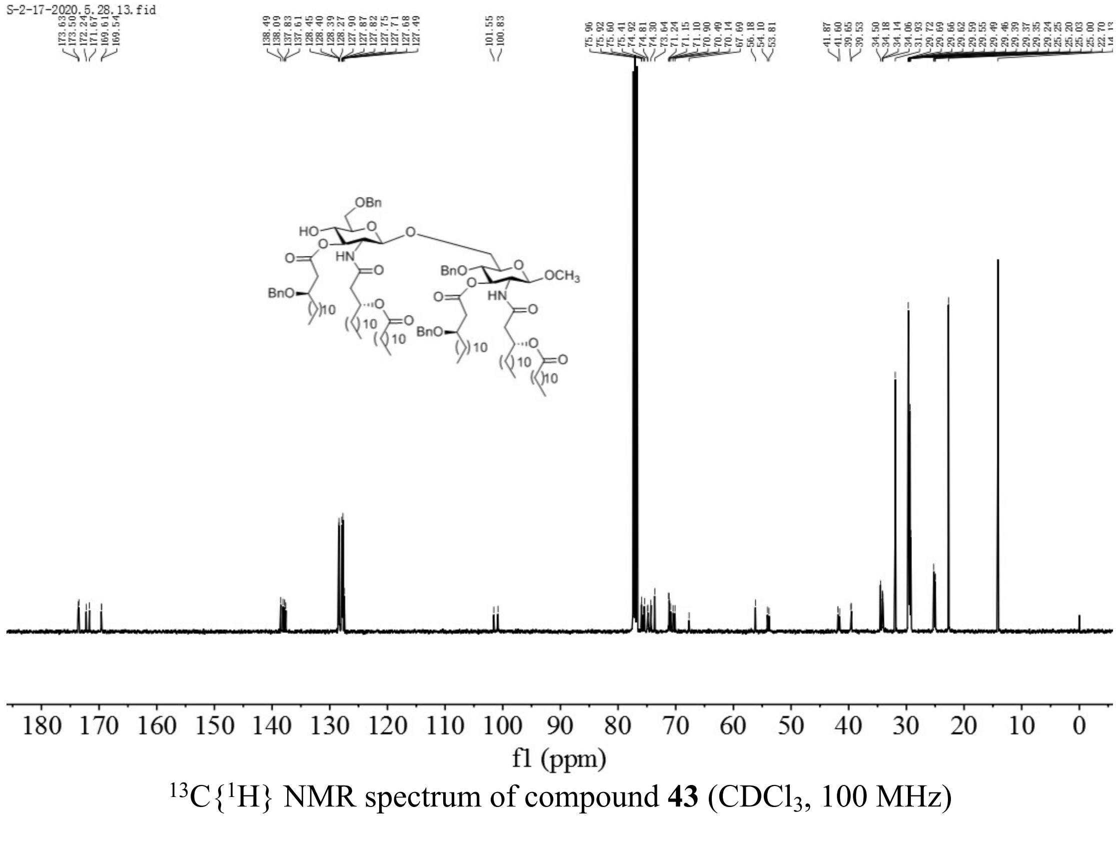
^{1}H-^{13}C HMQC spectrum of compound **42** ($CDCl_3$, 400/100 MHz)



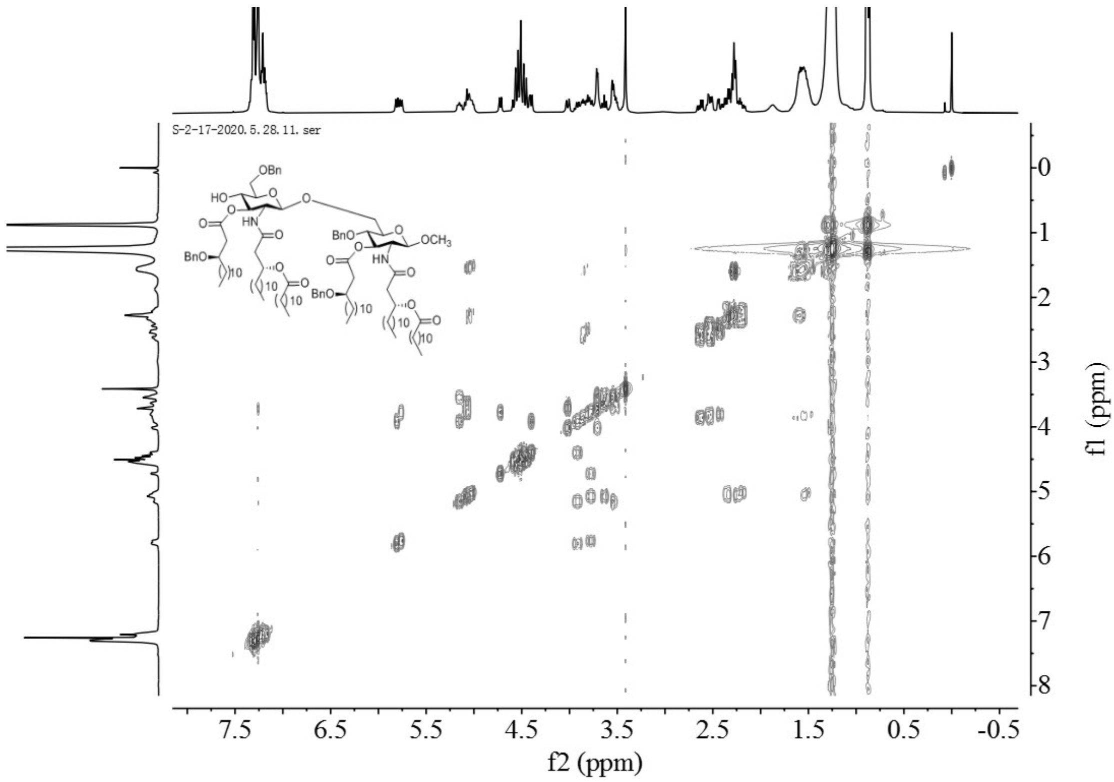
HRMS spectrum of compound **42**



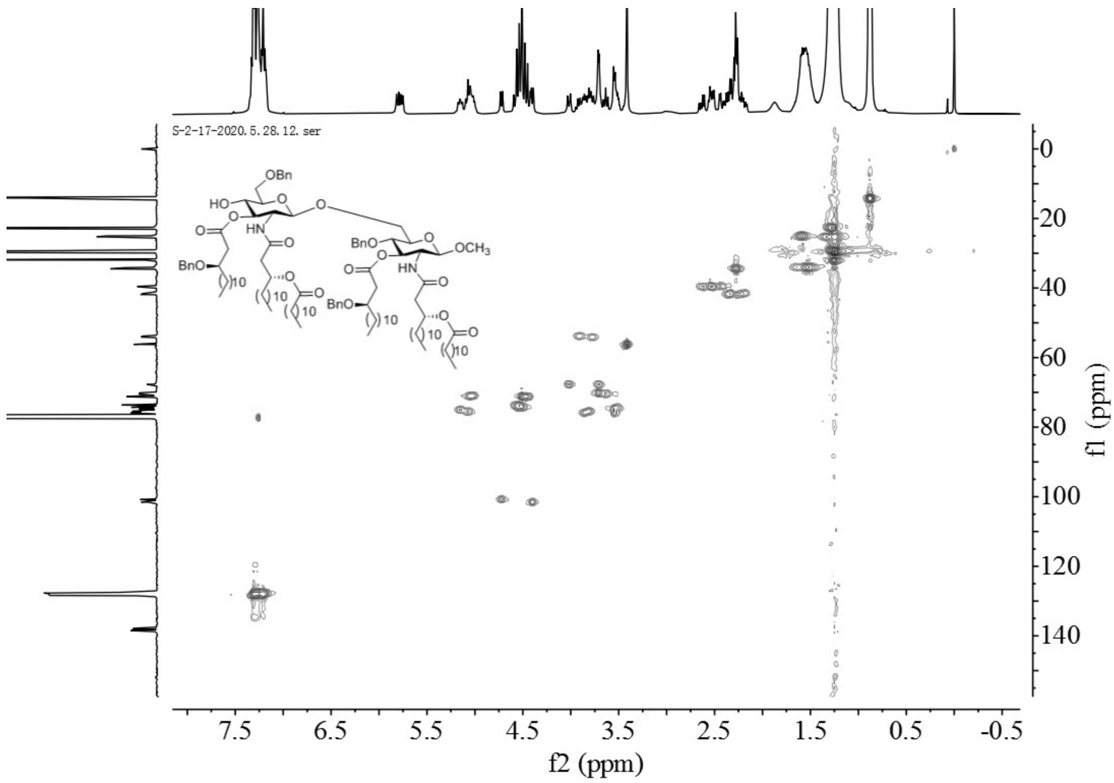
^{1}H NMR spectrum of compound **43** ($CDCl_3$, 400 MHz)



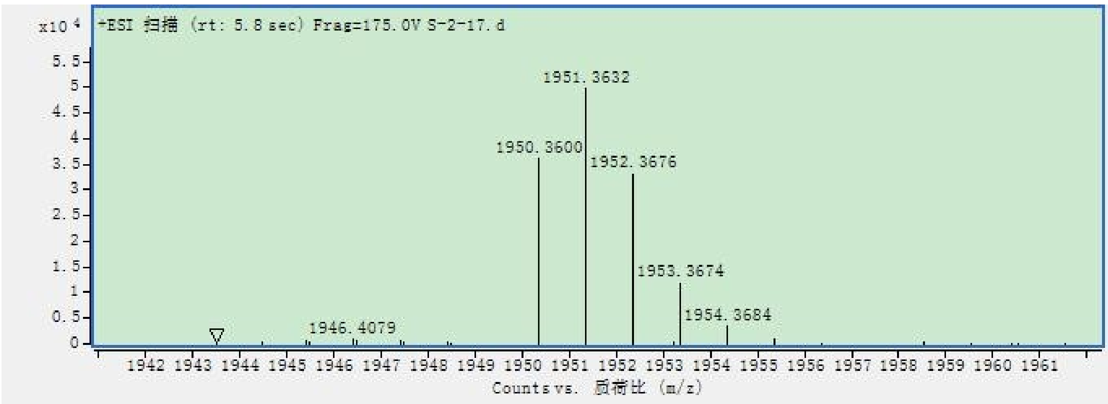
$^{13}C\{^1H\}$ NMR spectrum of compound **43** ($CDCl_3$, 100 MHz)



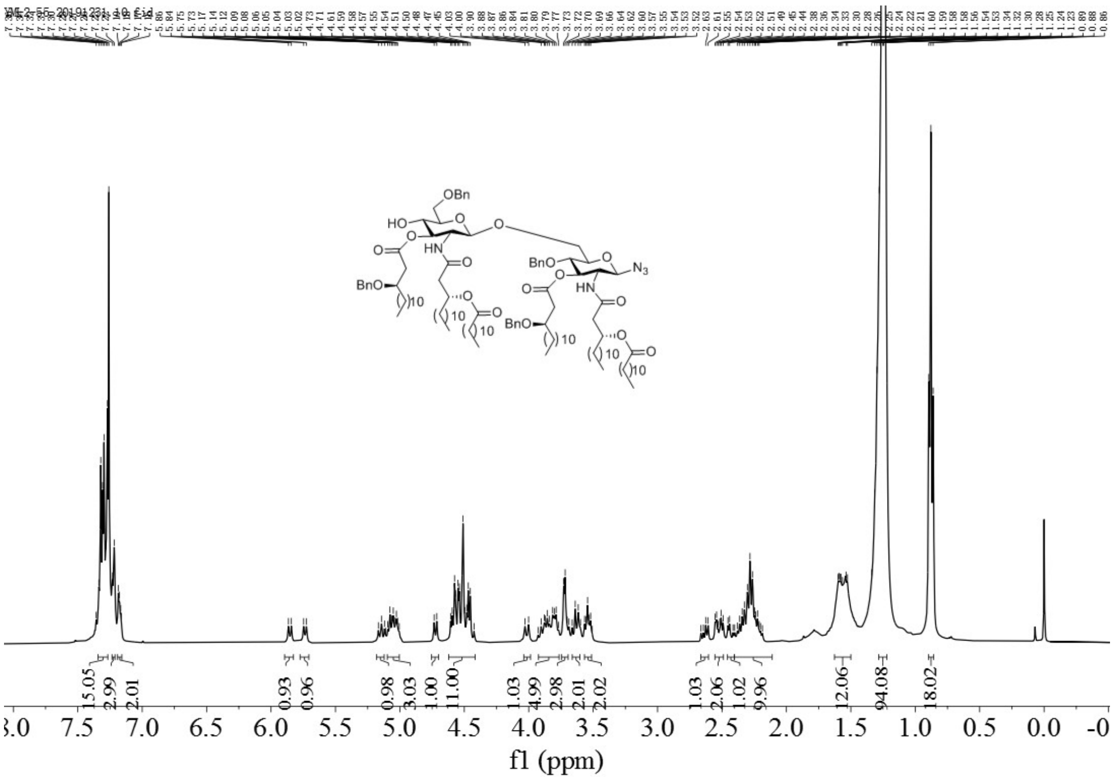
^{1}H-^{1}H COSY spectrum of compound **43** ($CDCl_3$, 400 MHz)



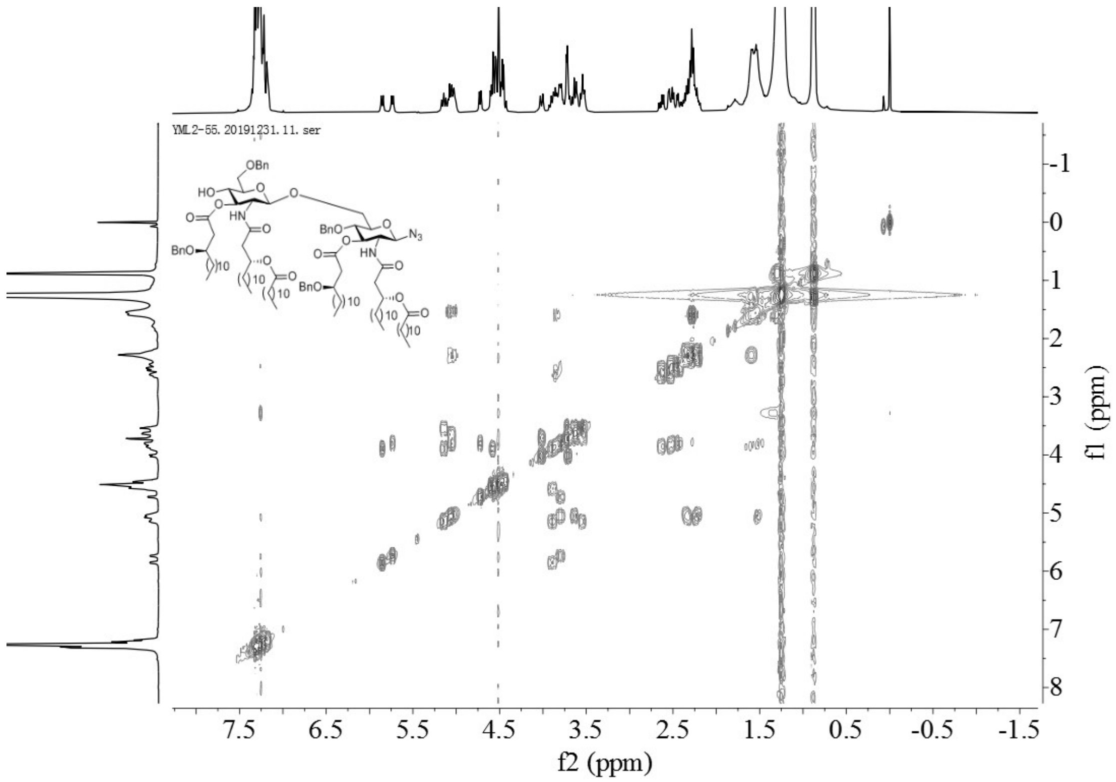
^{1}H-^{13}C HMQC spectrum of compound **43** ($CDCl_3$, 400/100 MHz)



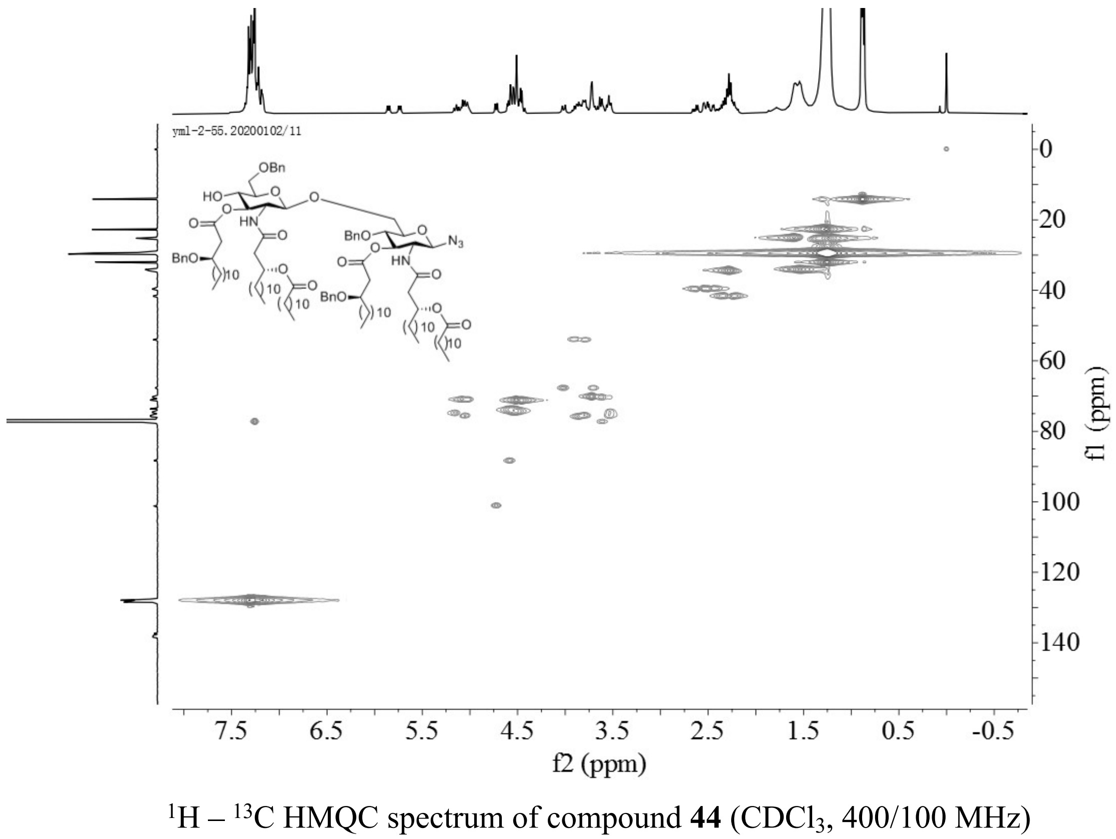
HRMS spectrum of compound **43**



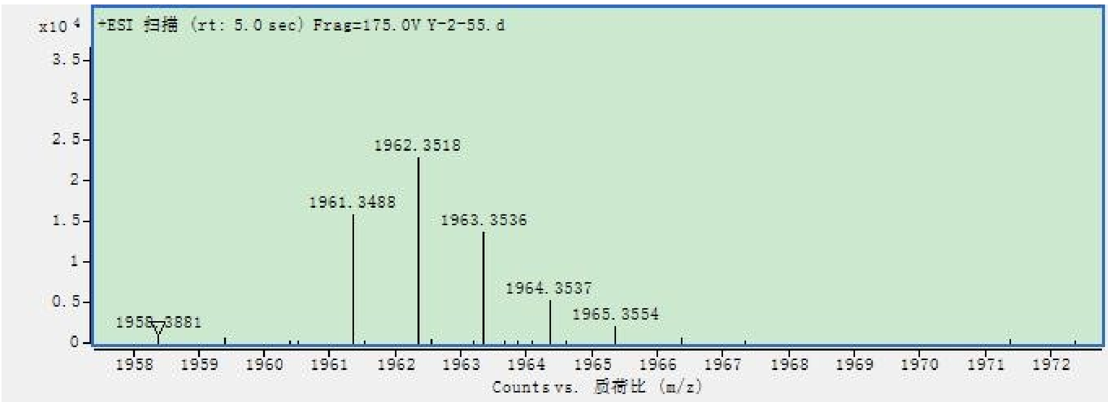
[1]H NMR spectrum of compound **44** ($CDCl_3$, 400 MHz)



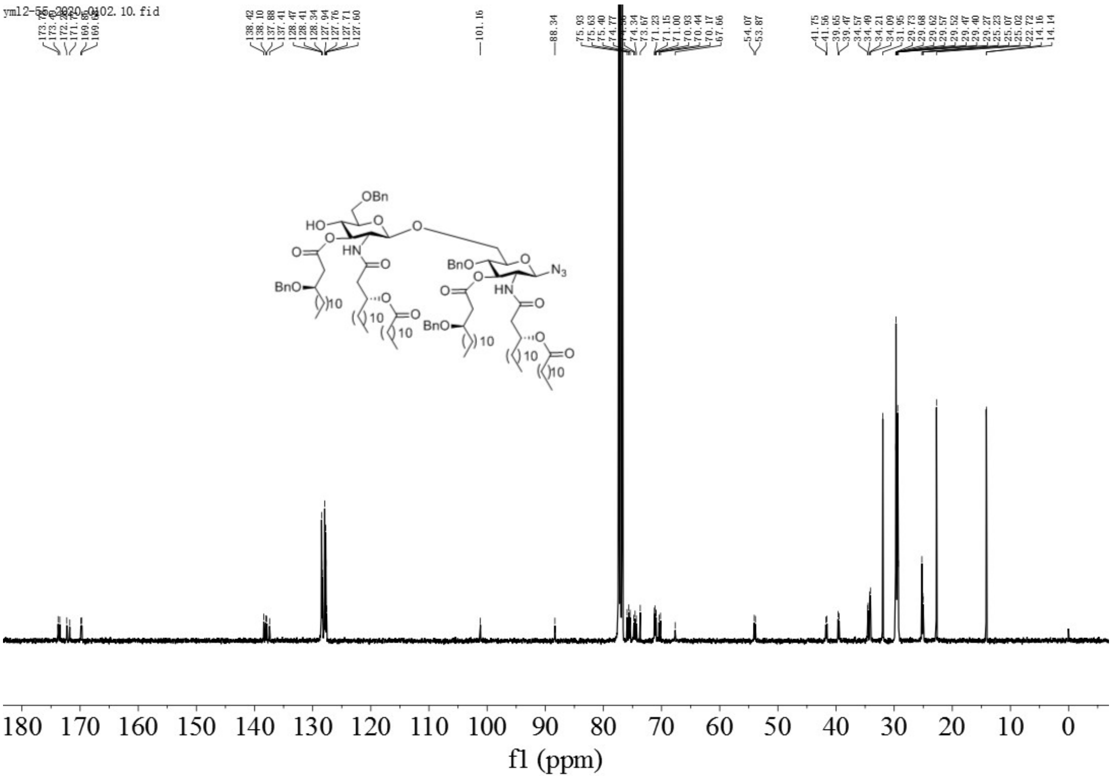
$^1H - ^1H$ COSY spectrum of compound **44** ($CDCl_3$, 400 MHz)



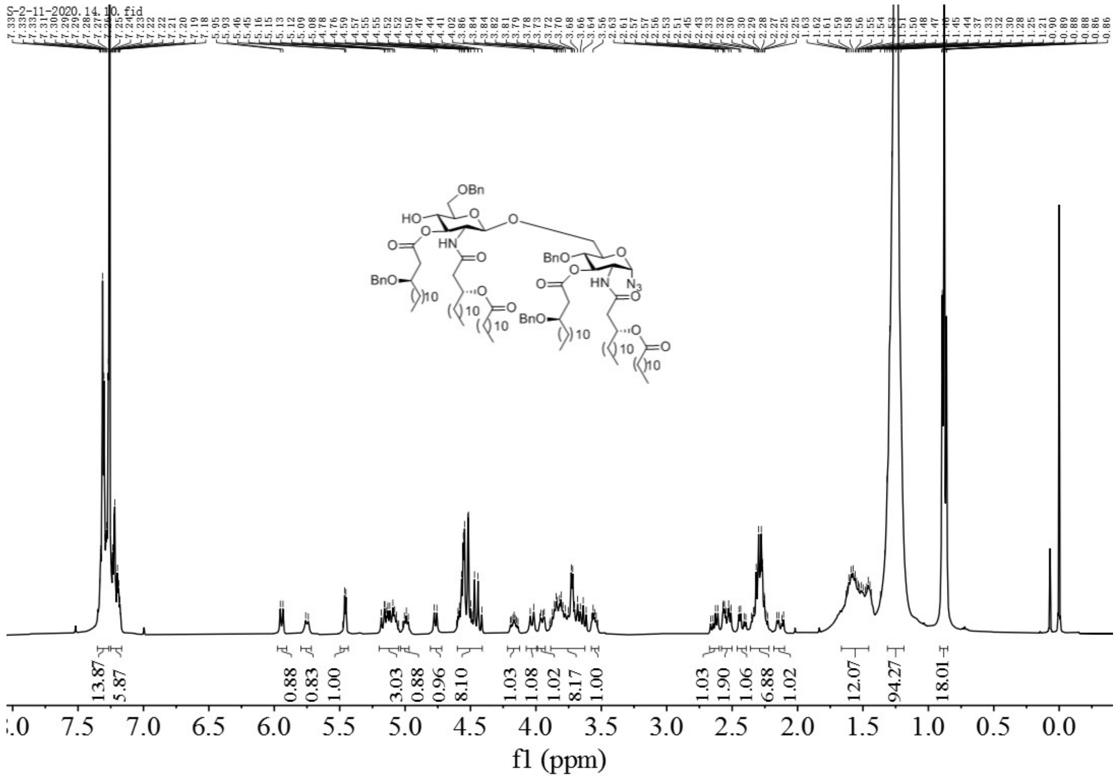
$^1H - ^{13}C$ HMQC spectrum of compound **44** ($CDCl_3$, 400/100 MHz)



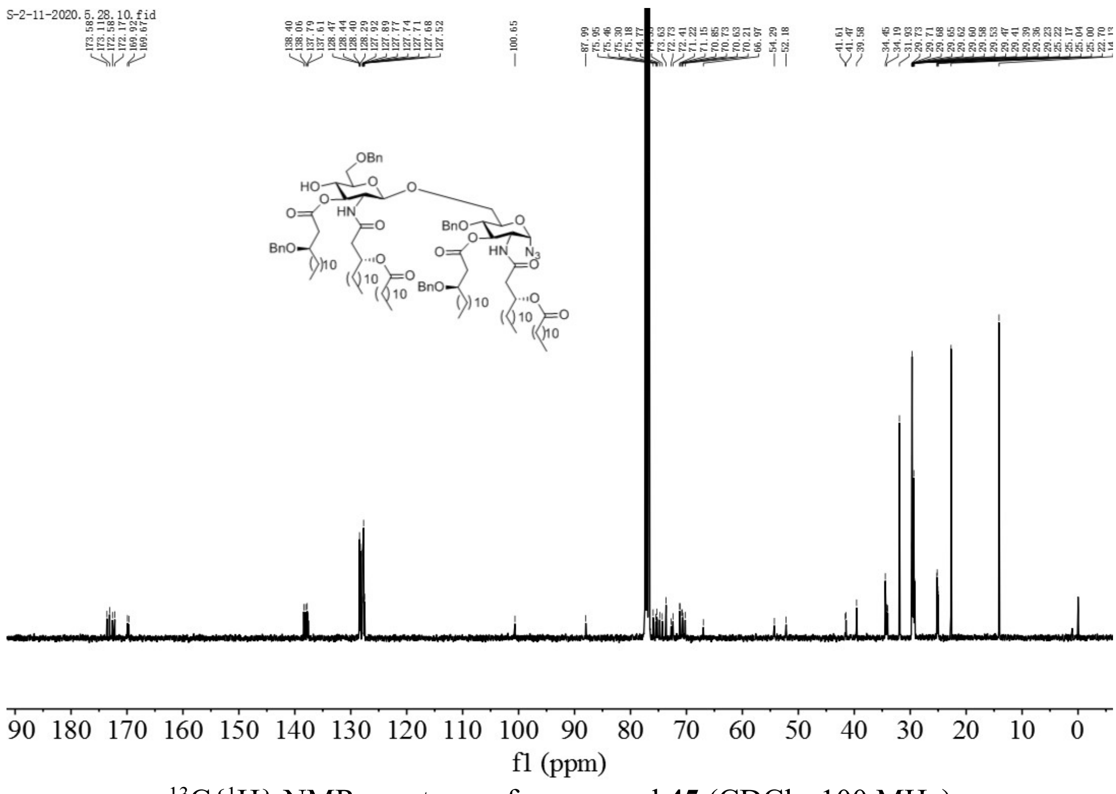
HRMS spectrum of compound **44**



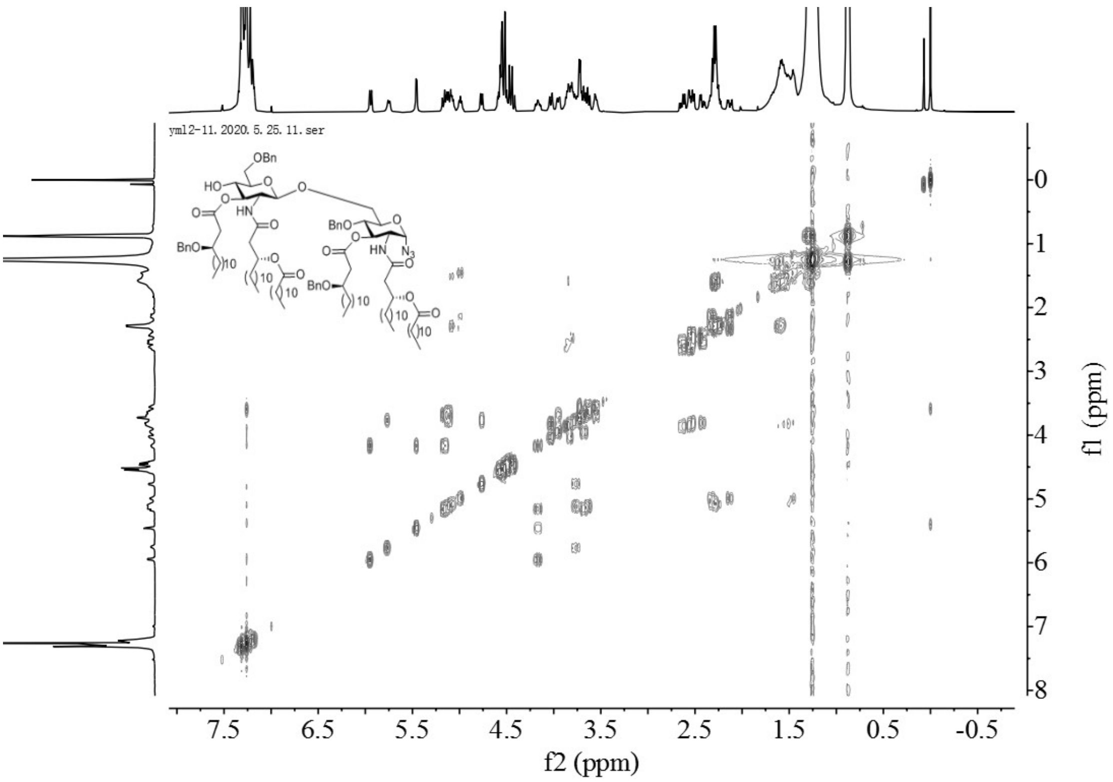
$^{13}C\{^{1}H\}$ NMR spectrum of compound **44** ($CDCl_3$, 100 MHz)



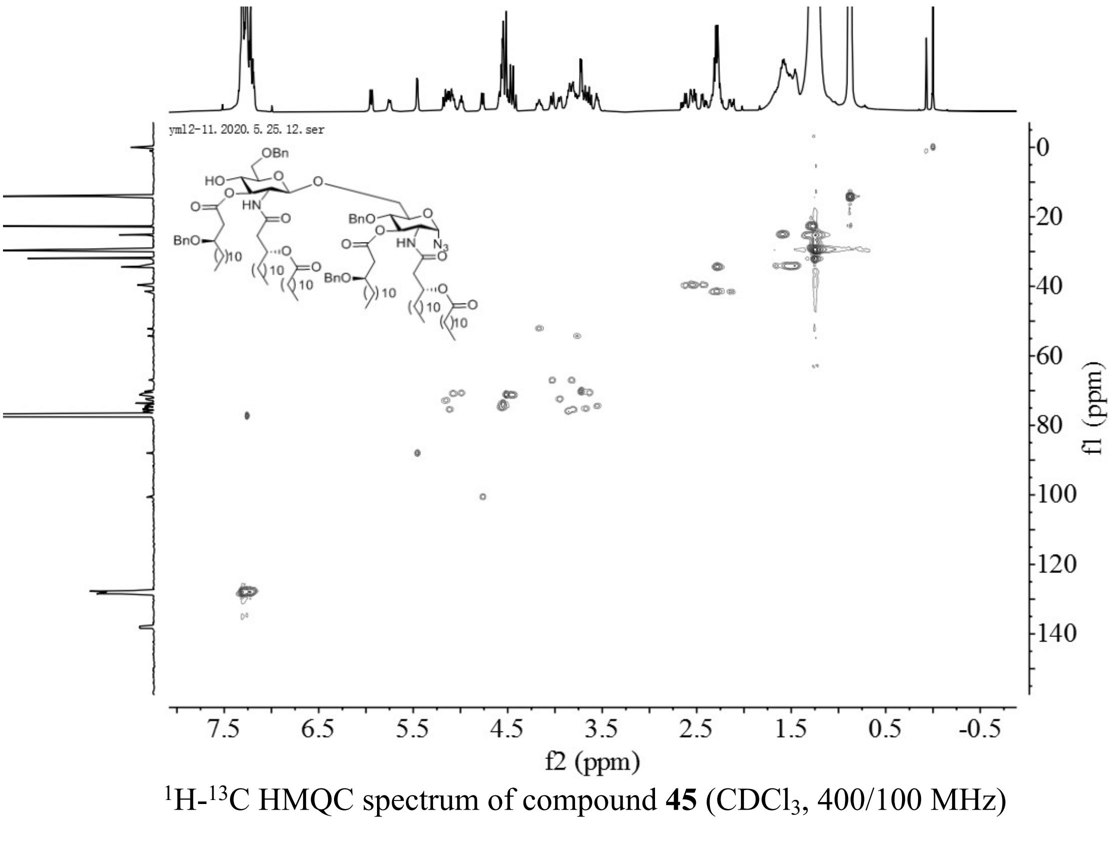
[1]H NMR spectrum of compound **45** ($CDCl_3$, 400 MHz)



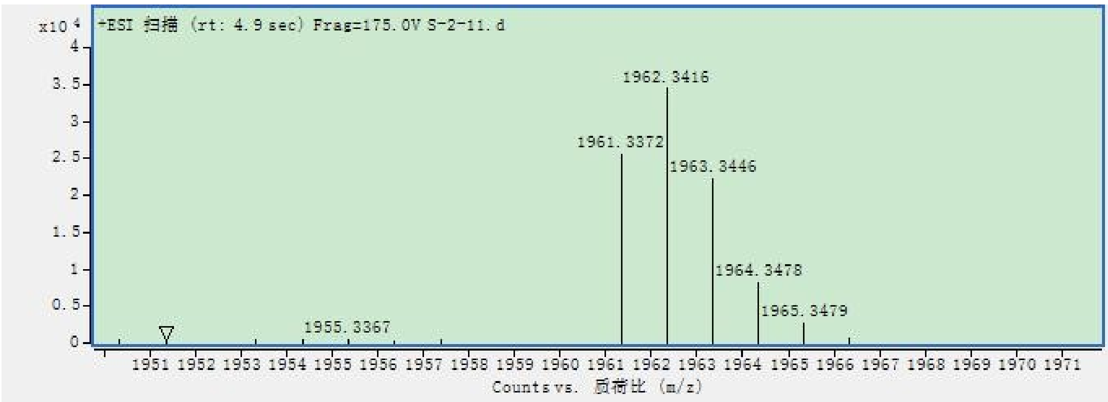
[13]C{[1]H} NMR spectrum of compound **45** ($CDCl_3$, 100 MHz)



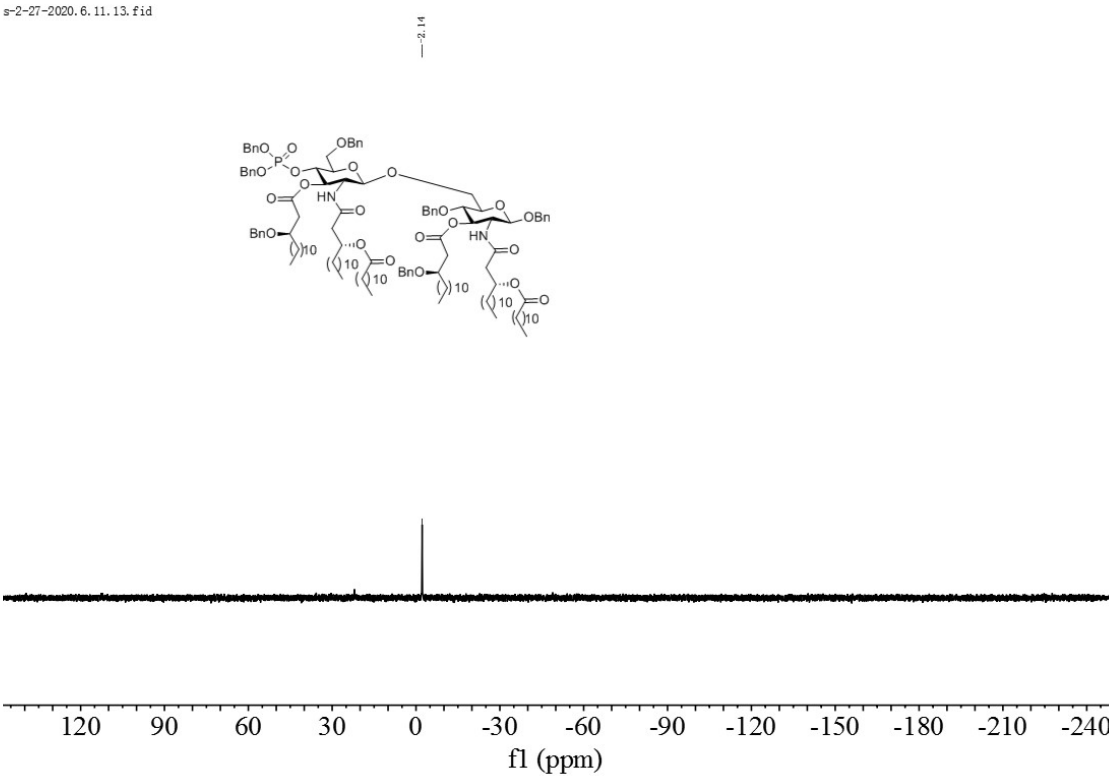
^{1}H-^{1}H COSY spectrum of compound **45** ($CDCl_3$, 400 MHz)



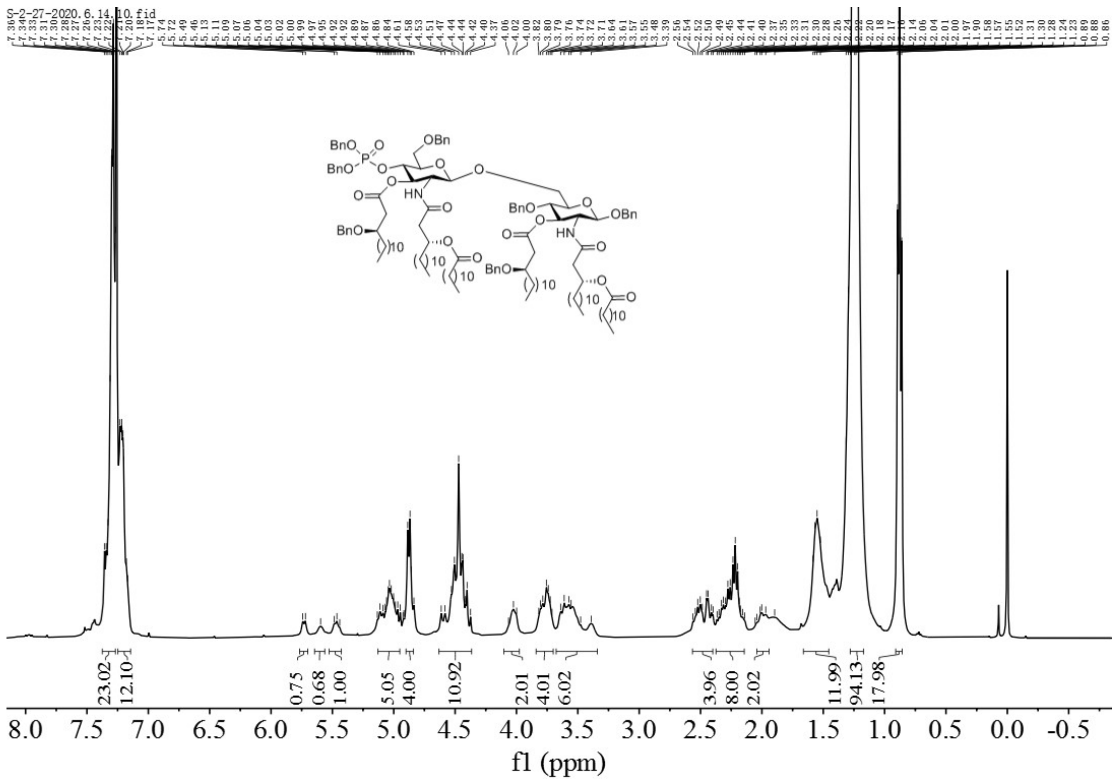
^{1}H-^{13}C HMQC spectrum of compound **45** ($CDCl_3$, 400/100 MHz)



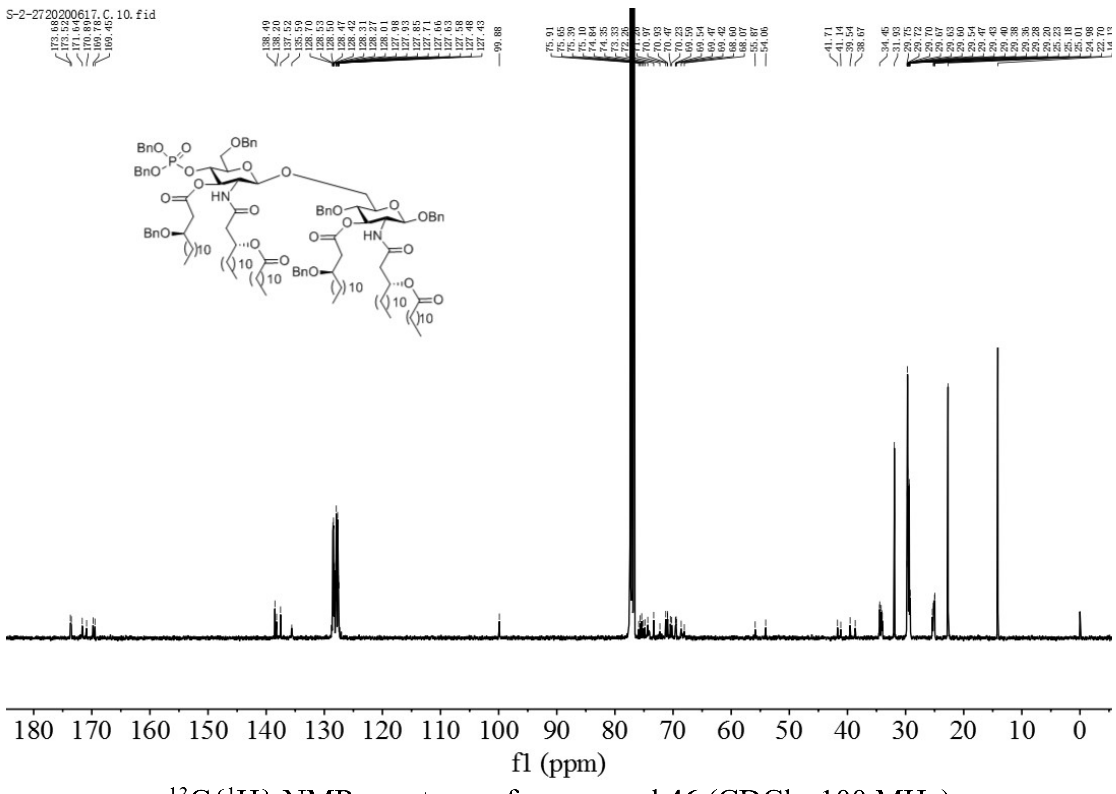
HRMS spectrum of compound **45**



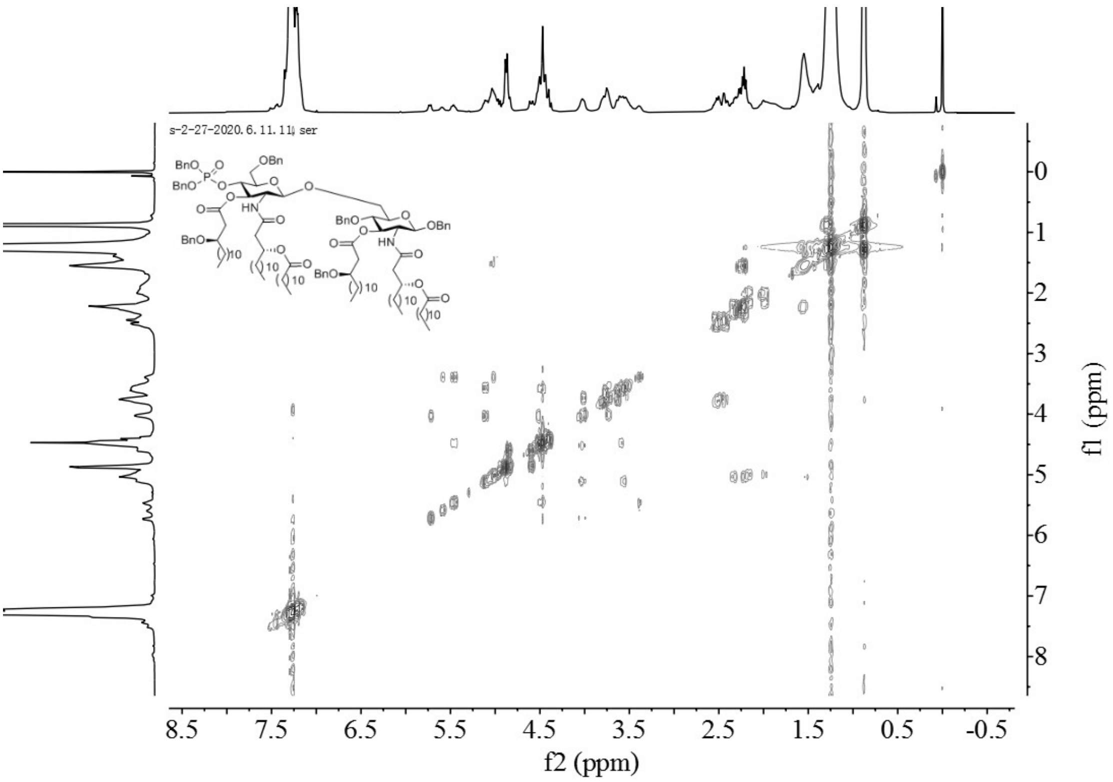
[31]P NMR spectrum of compound **46** ($CDCl_3$, 162 MHz)



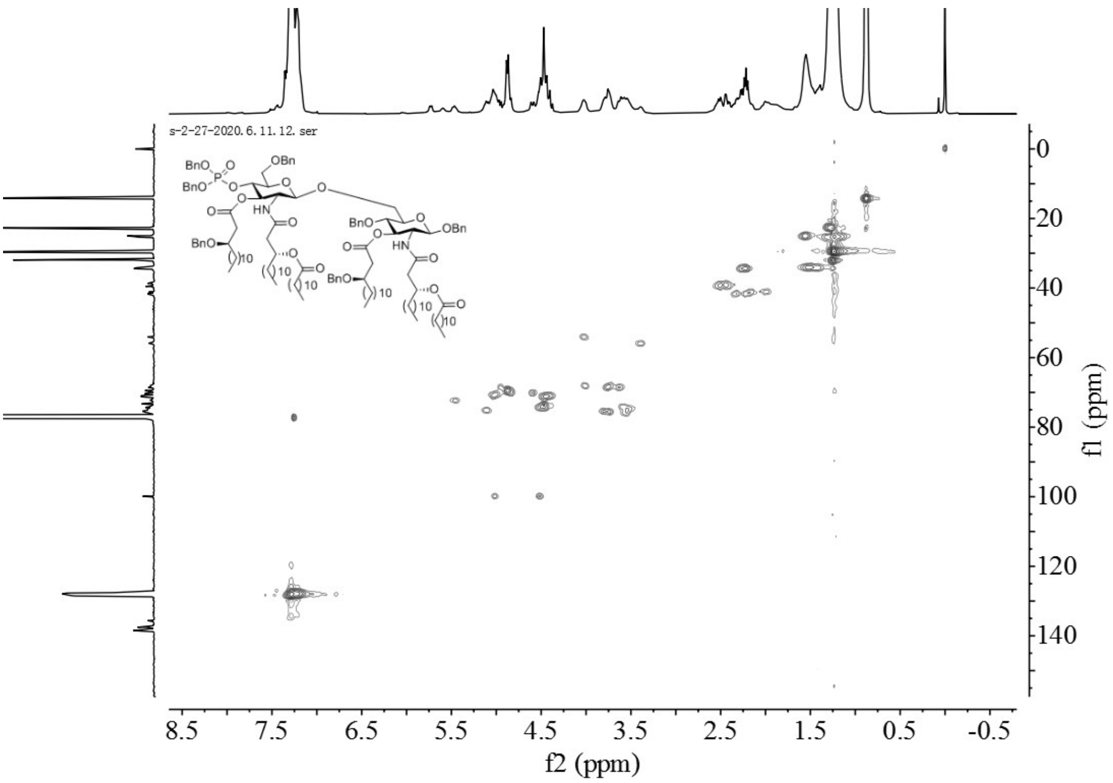
^{1}H NMR spectrum of compound **46** ($CDCl_3$, 400 MHz)



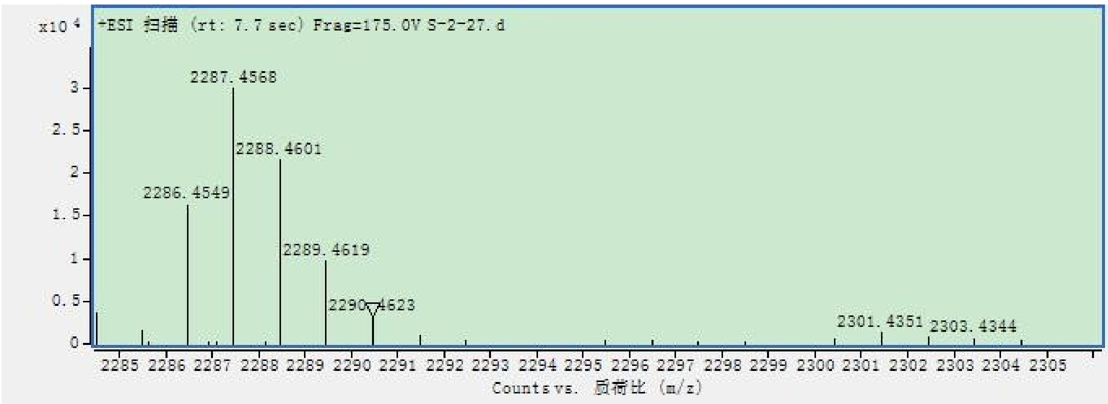
$^{13}C\{^1H\}$ NMR spectrum of compound **46** ($CDCl_3$, 100 MHz)



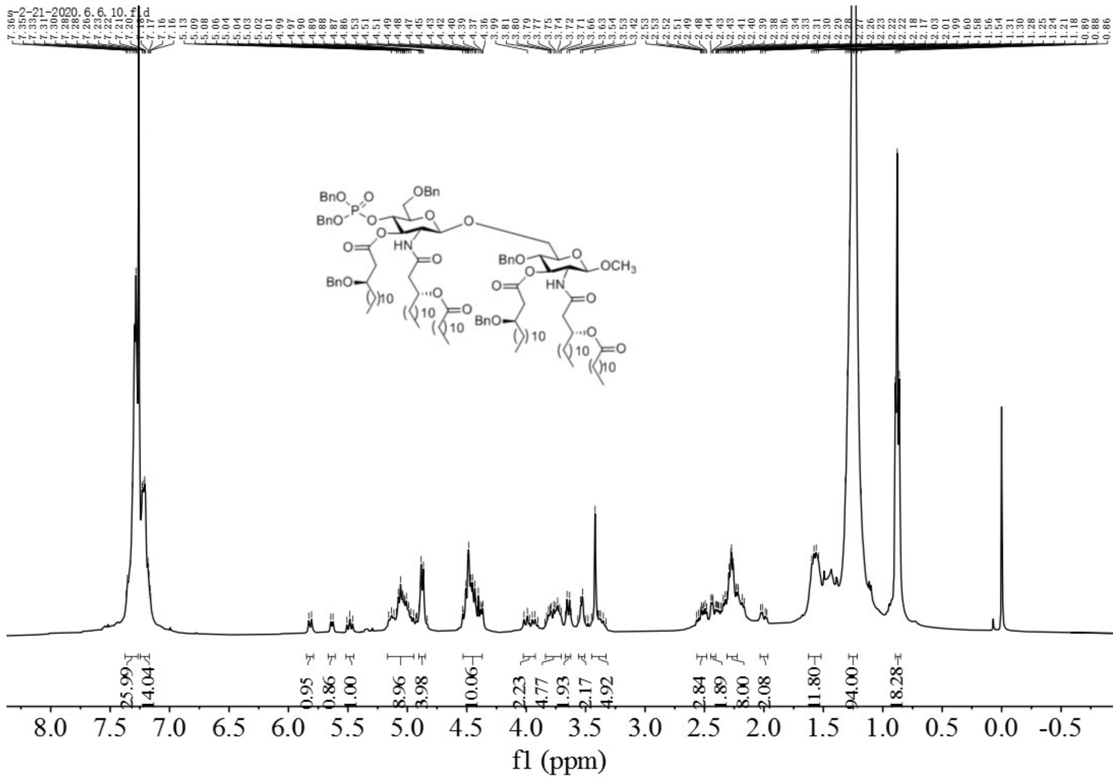
^{1}H-^{1}H COSY spectrum of compound **46** ($CDCl_3$, 400 MHz)



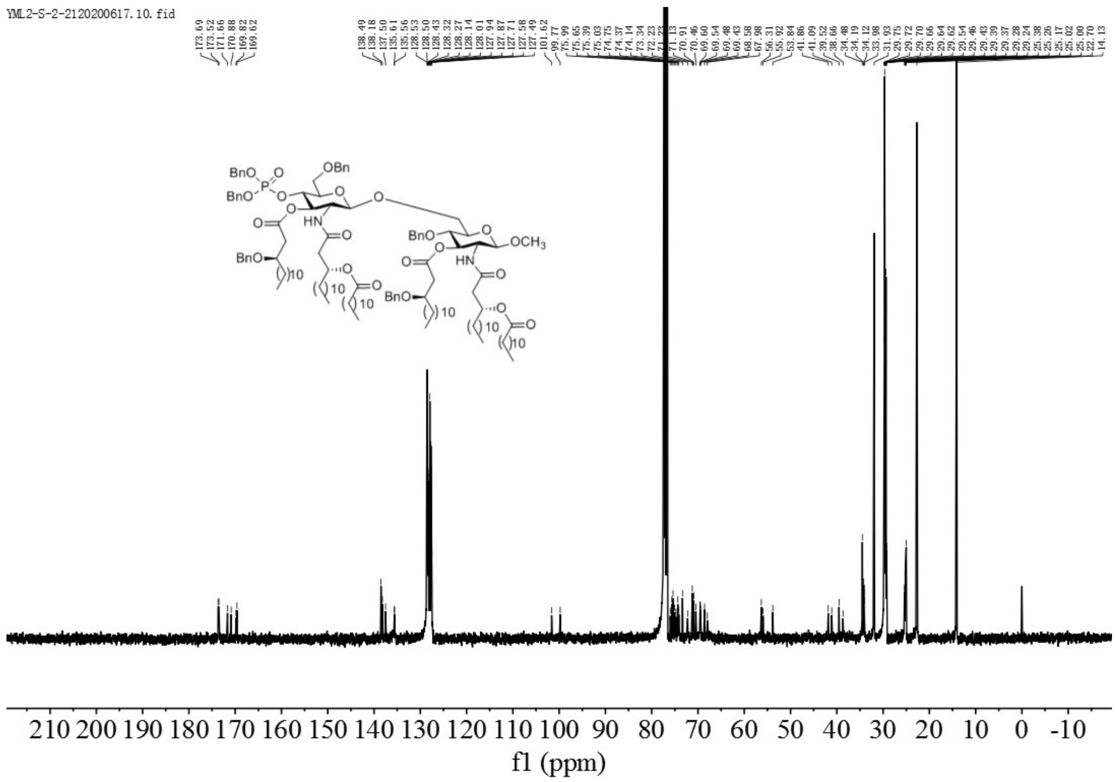
^{1}H-^{13}C HMQC spectrum of compound **46** ($CDCl_3$, 400/100 MHz)



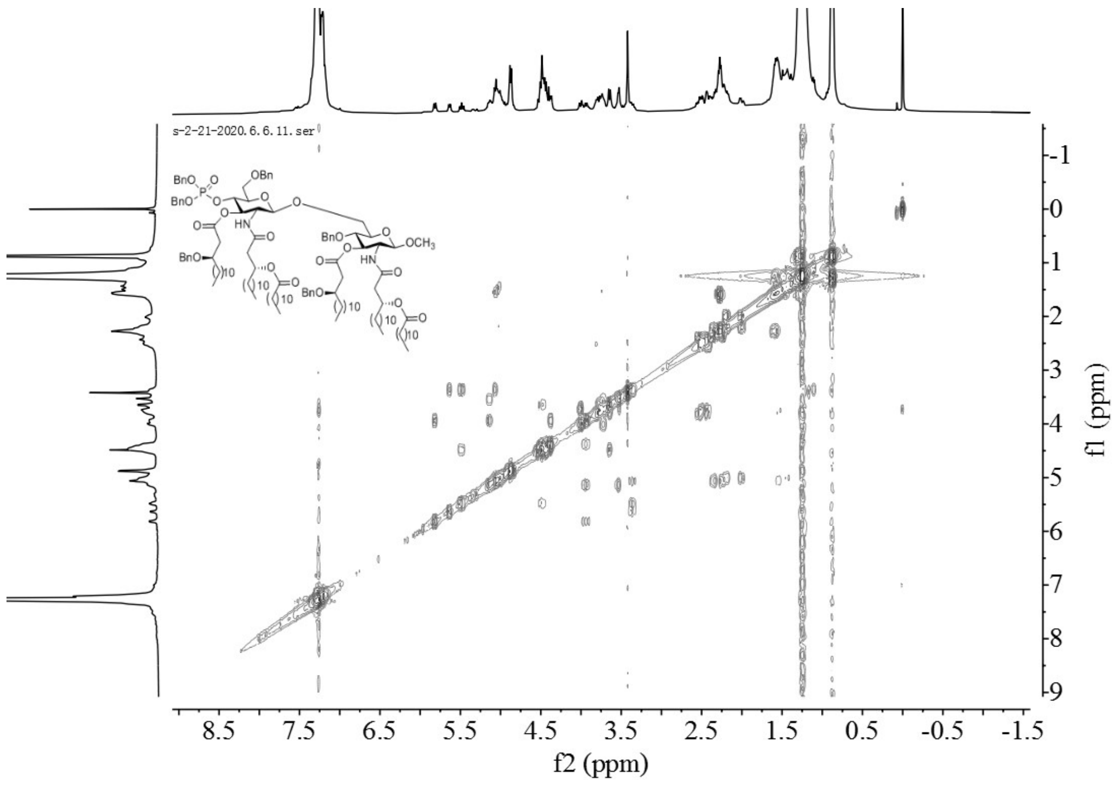
HRMS spectrum of compound **46**



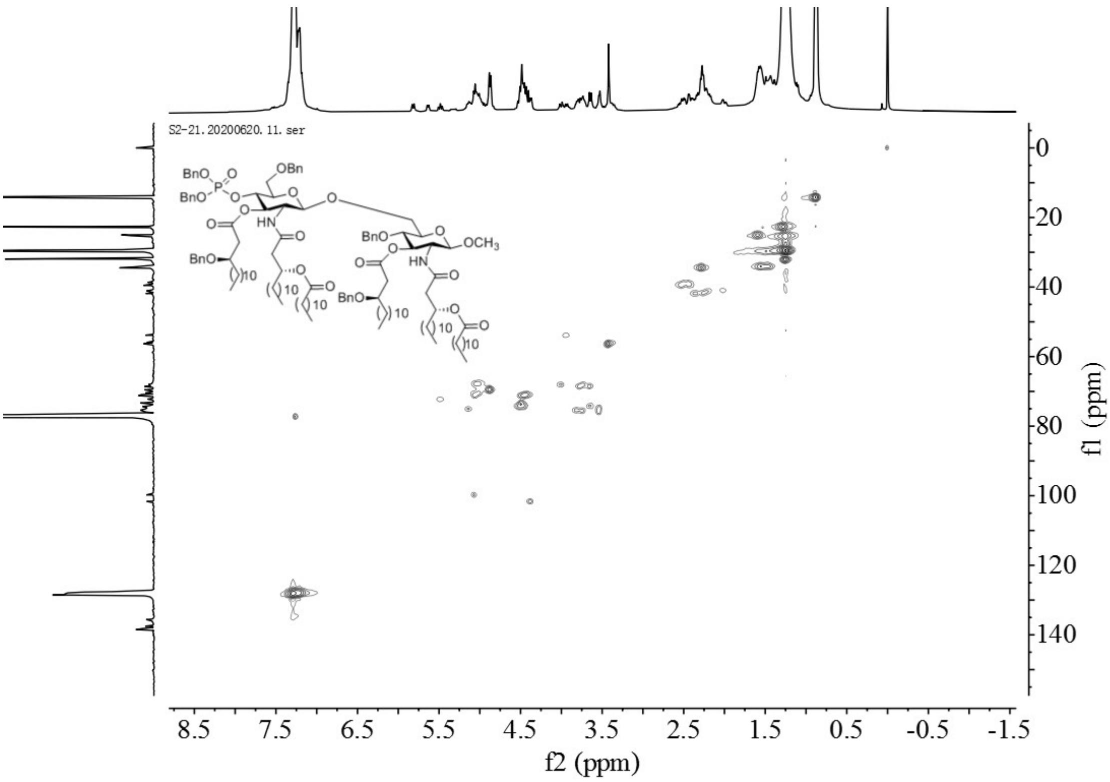
^{1}H NMR spectrum of compound **47** ($CDCl_3$, 400 MHz)



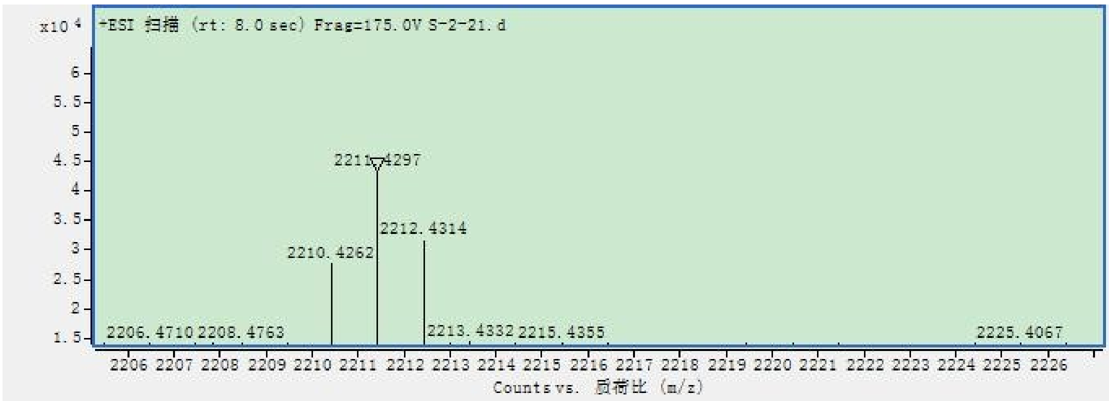
$^{13}C\{^{1}H\}$ NMR spectrum of compound **47** ($CDCl_3$, 100 MHz)



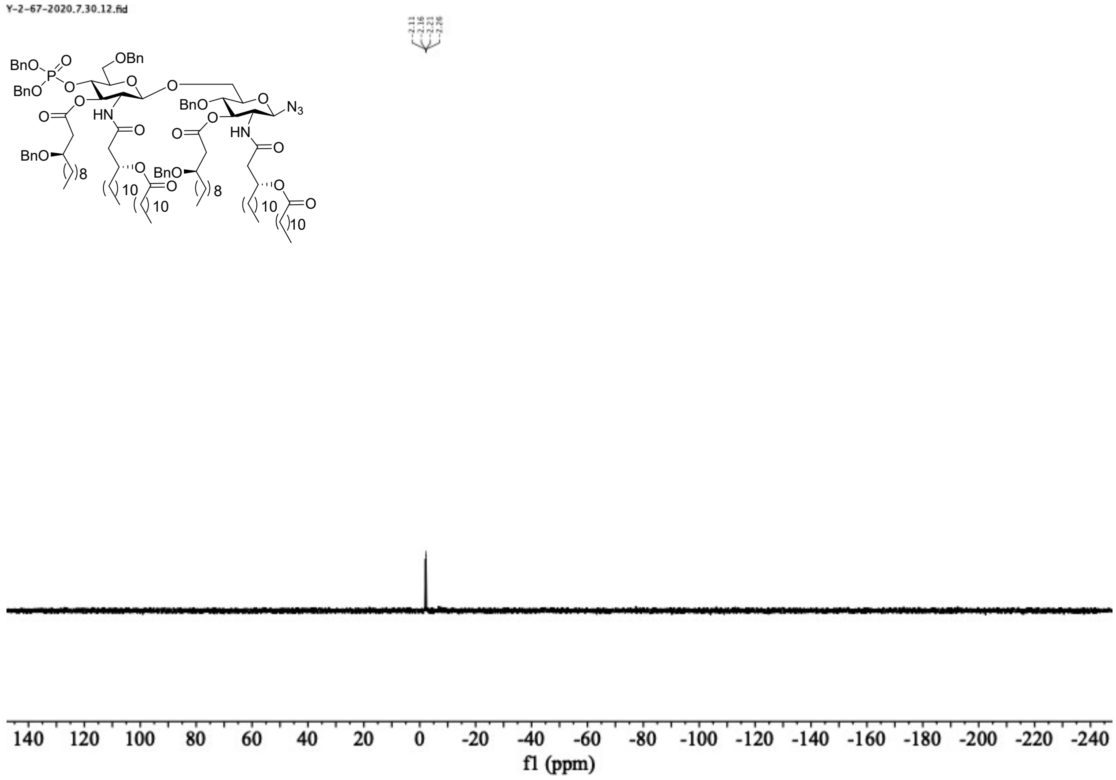
^{1}H-^{1}H COSY spectrum of compound **47** ($CDCl_3$, 400 MHz)



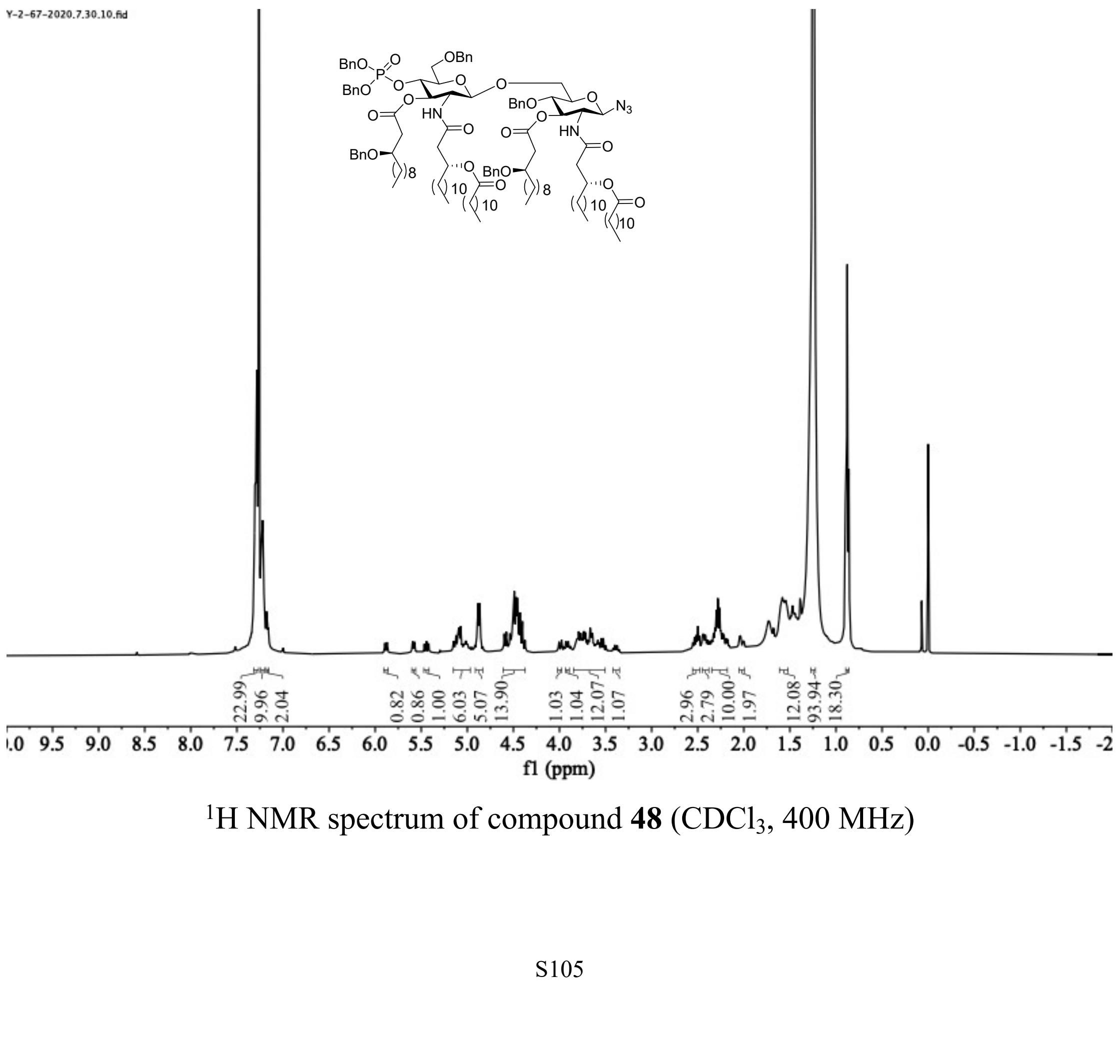
^{1}H-^{13}C HMQC spectrum of compound **47** ($CDCl_3$, 400/100 MHz)



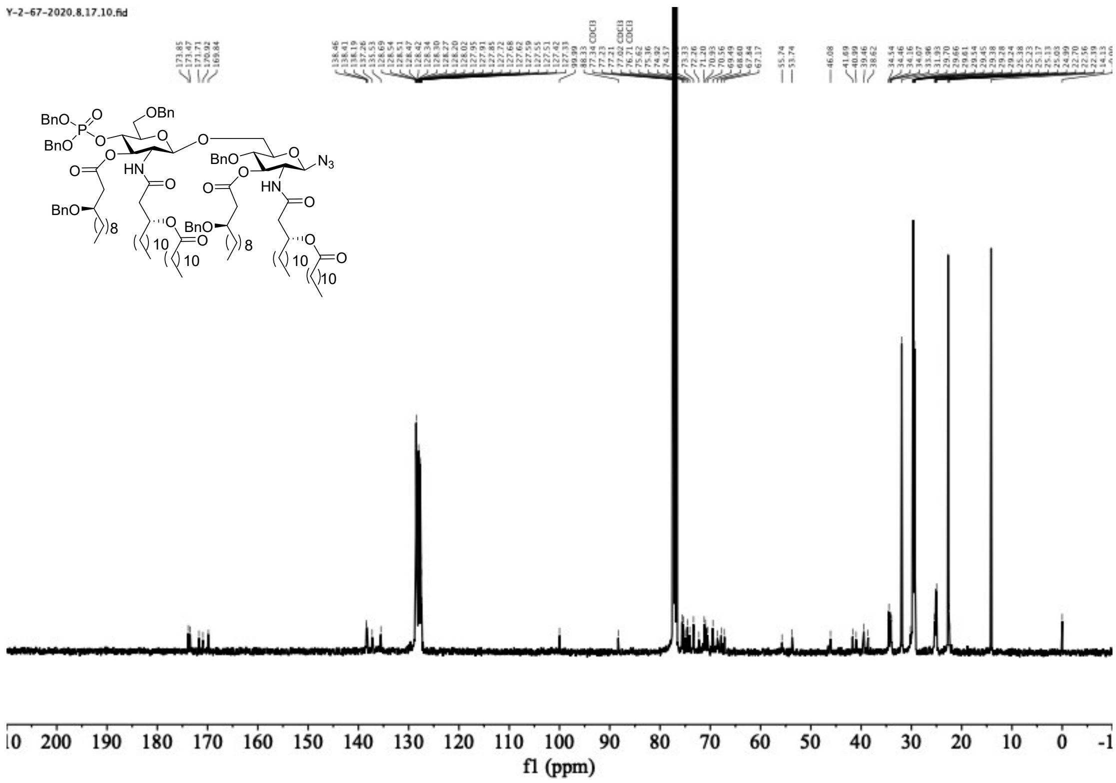
HRMS spectrum of compound **47**



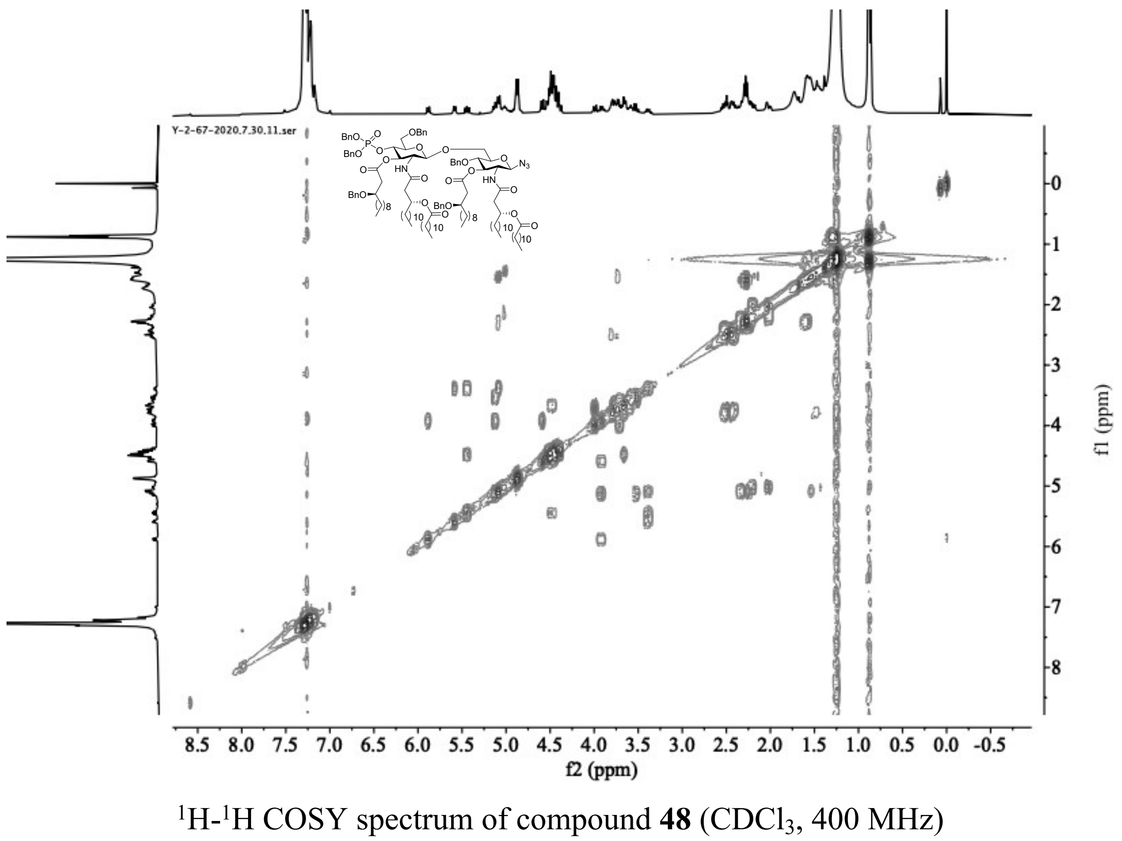
^{31}P NMR spectrum of compound **48** ($CDCl_3$, 162 MHz)



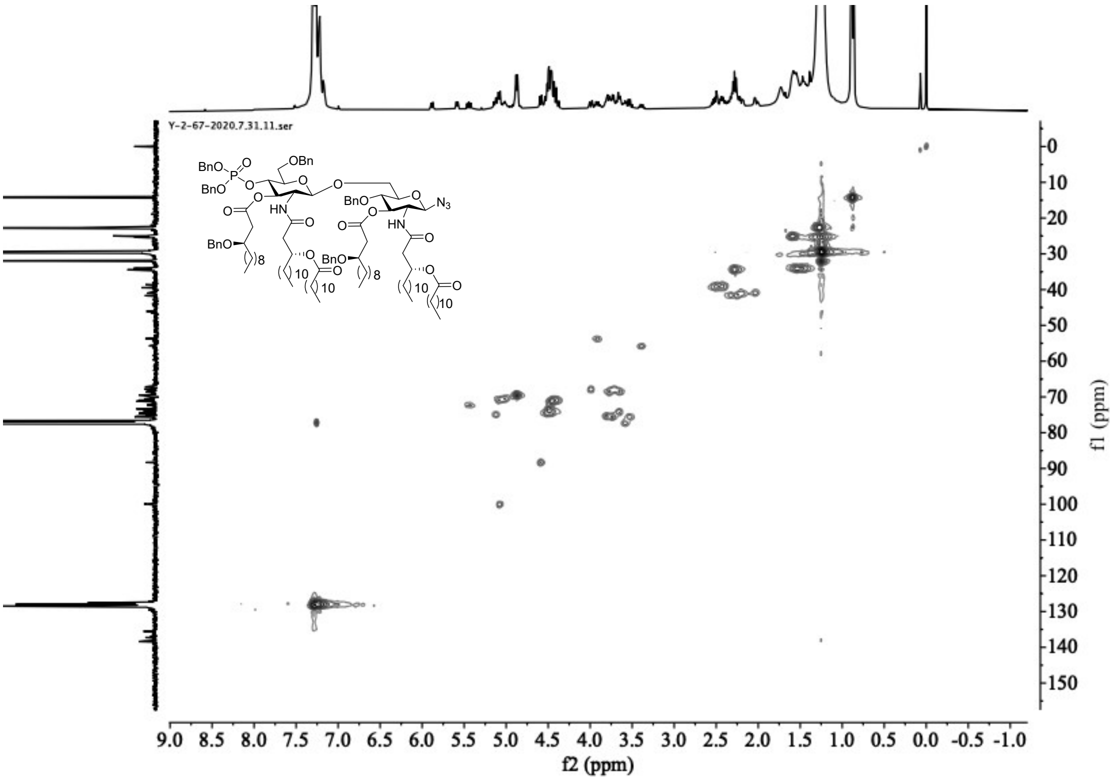
^{1}H NMR spectrum of compound **48** ($CDCl_3$, 400 MHz)



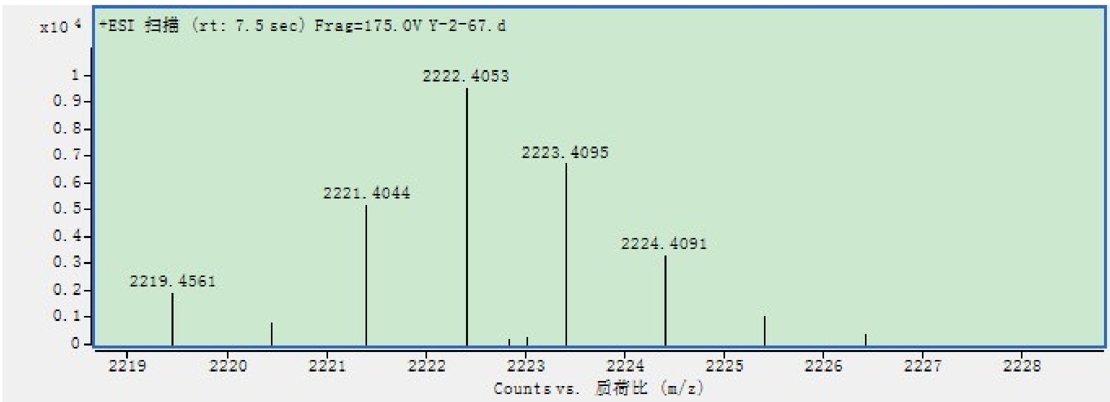
$^{13}C\{^{1}H\}$ NMR spectrum of compound **48** ($CDCl_3$, 100 MHz)



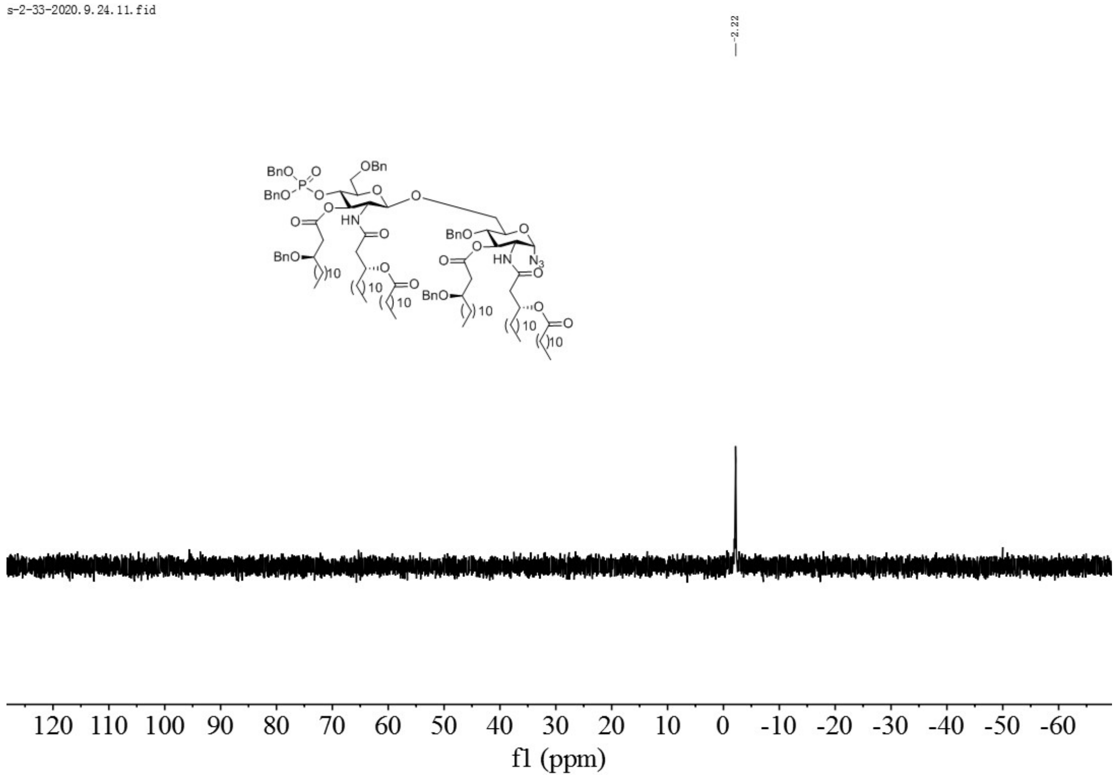
^{1}H-^{1}H COSY spectrum of compound **48** ($CDCl_3$, 400 MHz)



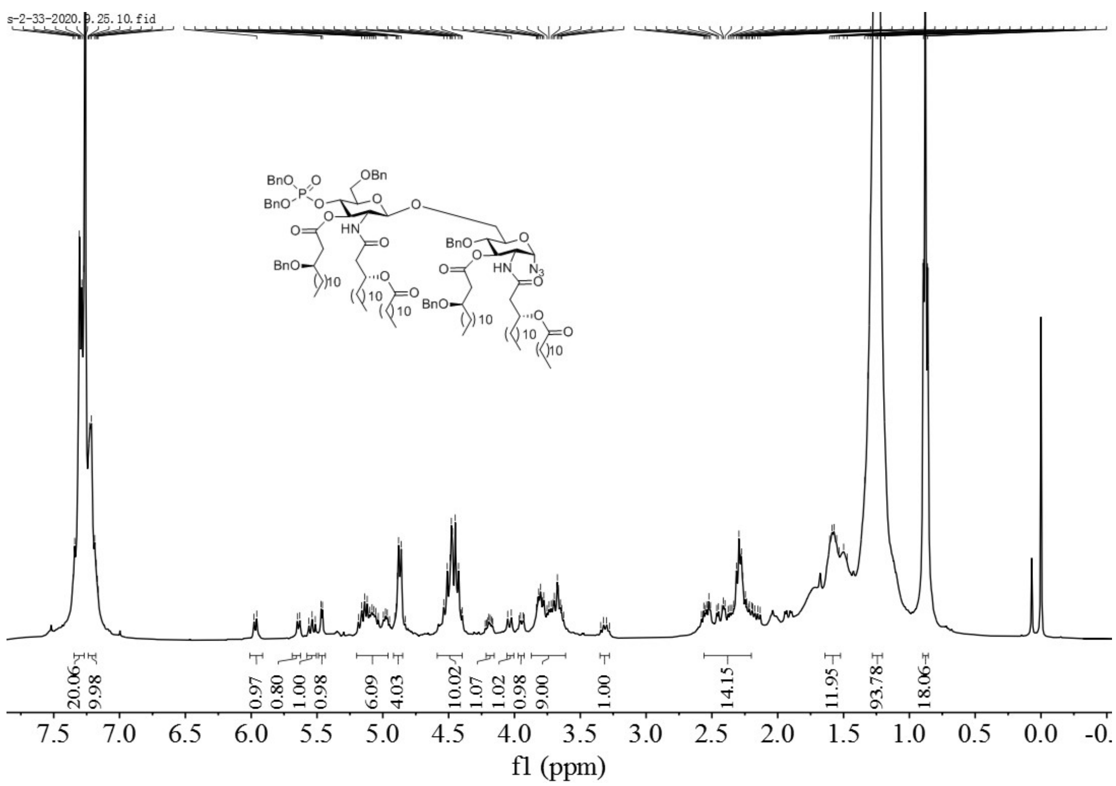
^{1}H-^{13}C HMQC spectrum of compound **48** ($CDCl_3$, 400/100 MHz)



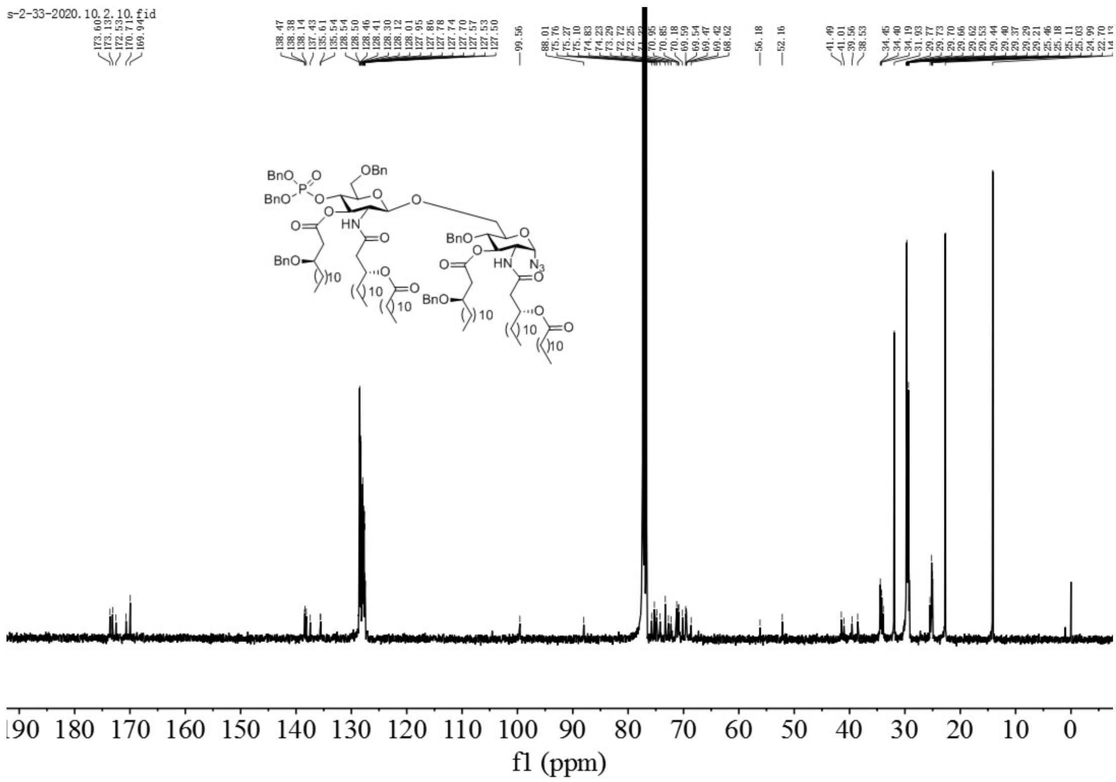
HRMS spectrum of compound **48**



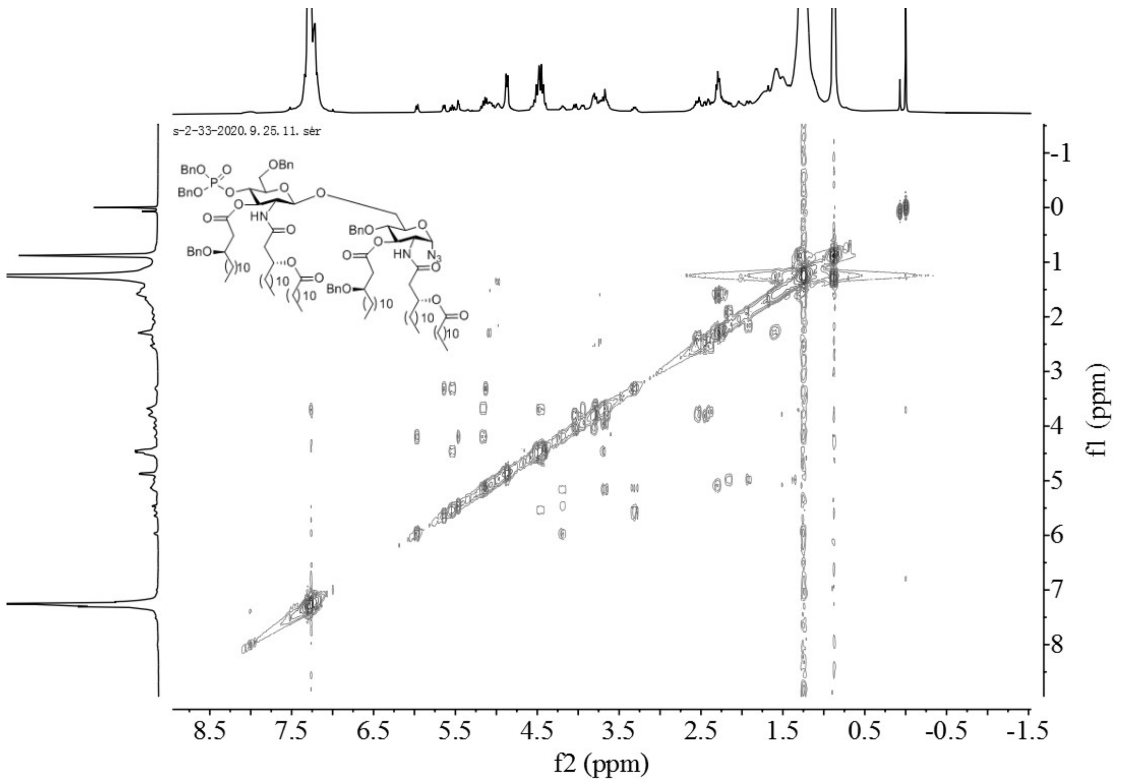
^{31}P NMR spectrum of compound **49** ($CDCl_3$, 162 MHz)



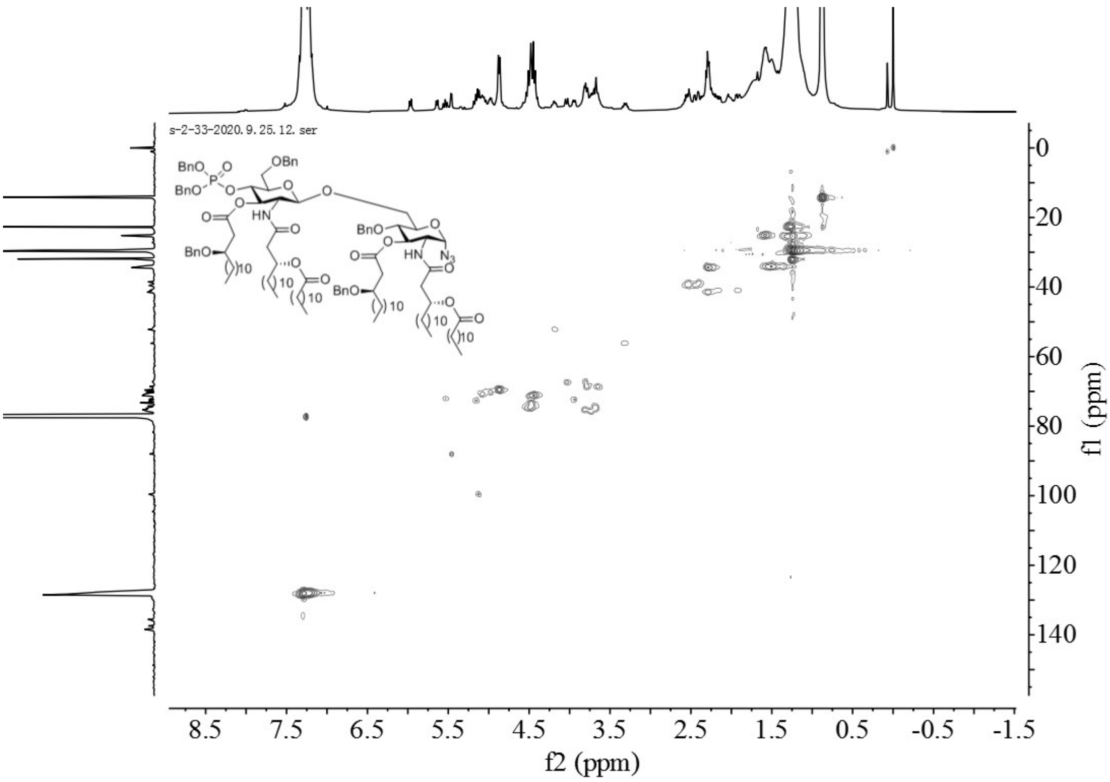
^{1}H NMR spectrum of compound **49** ($CDCl_3$, 400 MHz)



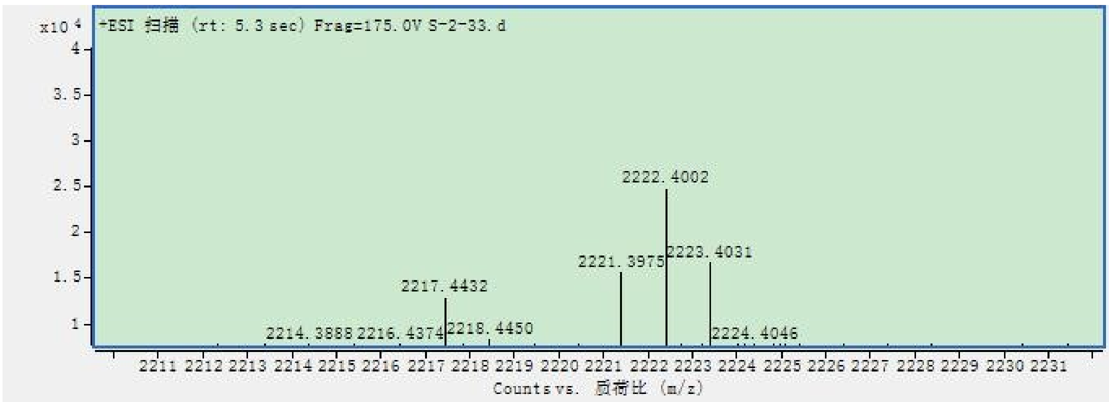
$^{13}C\{^{1}H\}$ NMR spectrum of compound **49** ($CDCl_3$, 100 MHz)



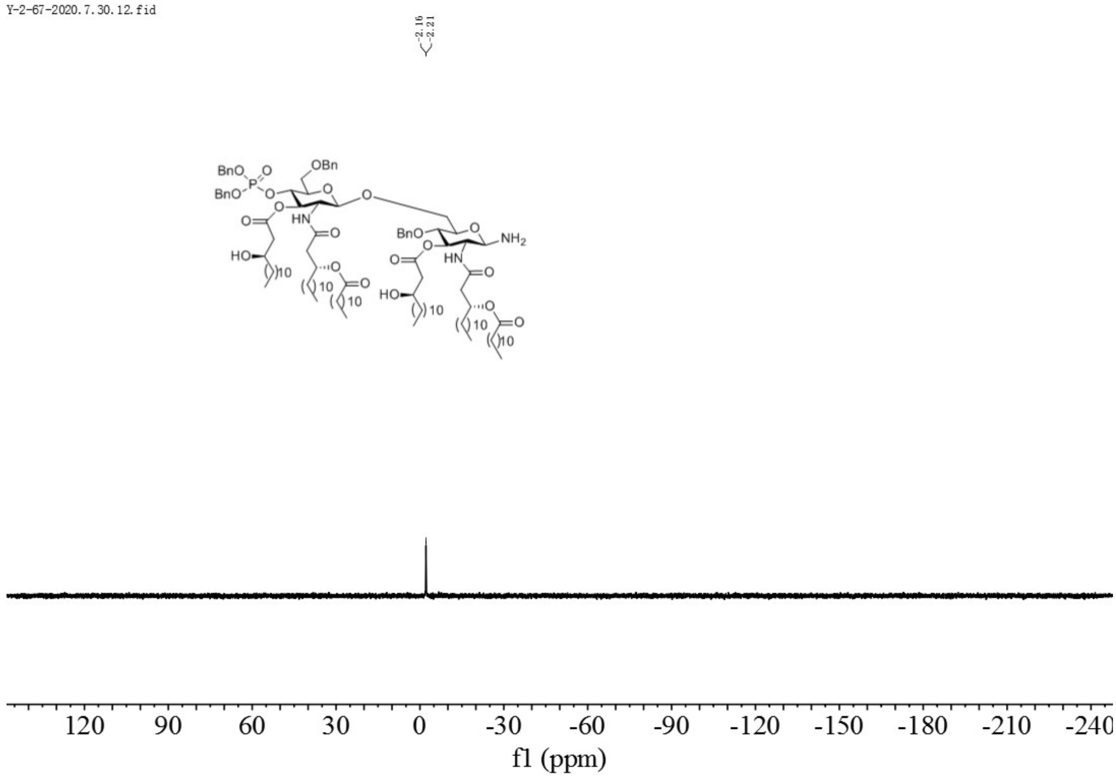
^{1}H-^{1}H COSY spectrum of compound **49** ($CDCl_3$, 400 MHz)



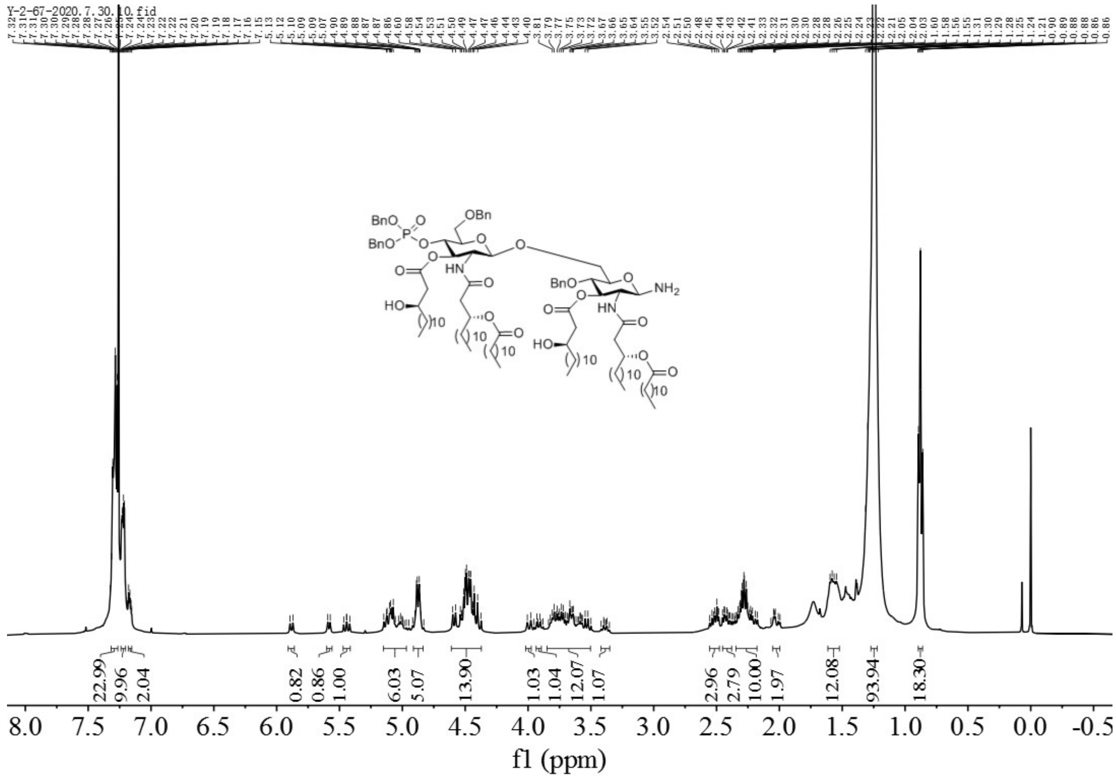
^{1}H-^{13}C HMQC spectrum of compound **49** ($CDCl_3$, 400/100 MHz)



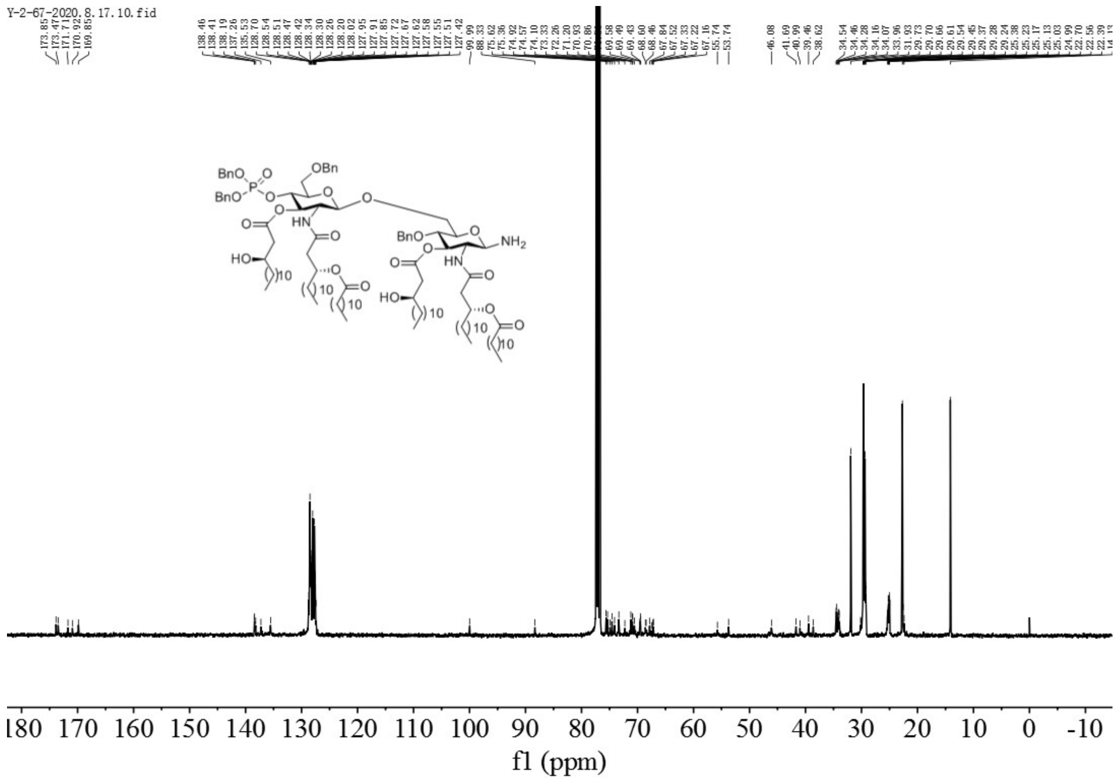
HRMS spectrum of compound **49**



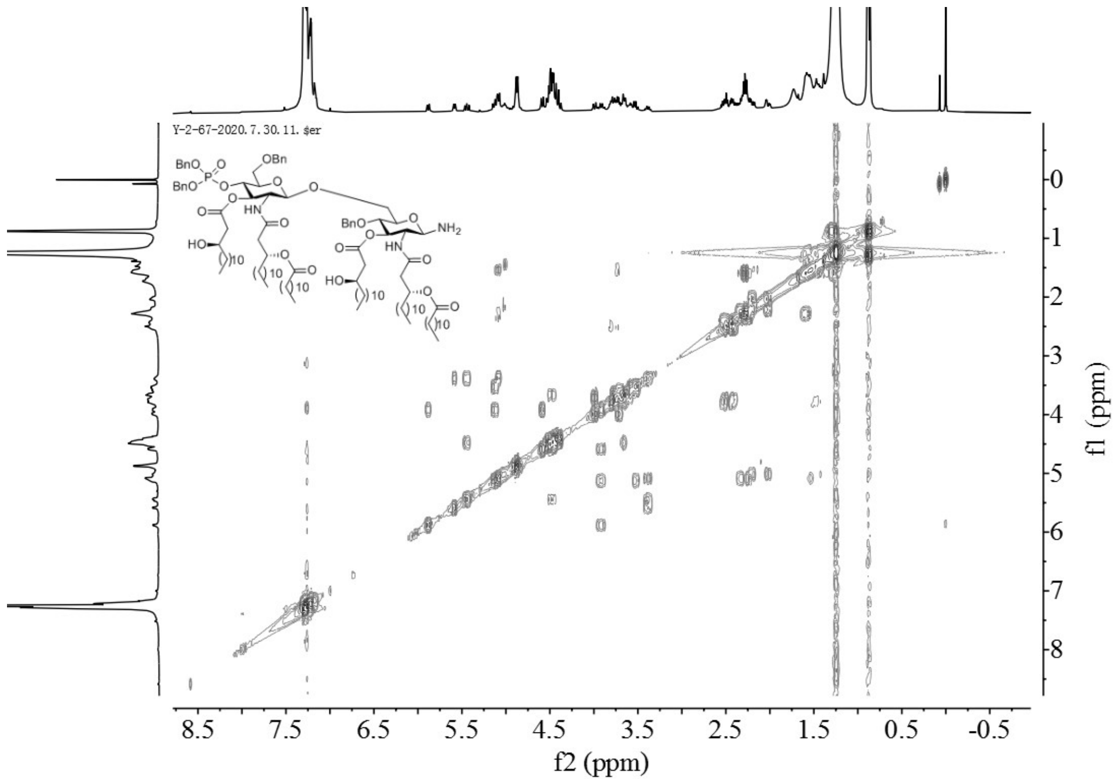
^{31}P NMR spectrum of compound **50** ($CDCl_3$, 162 MHz)



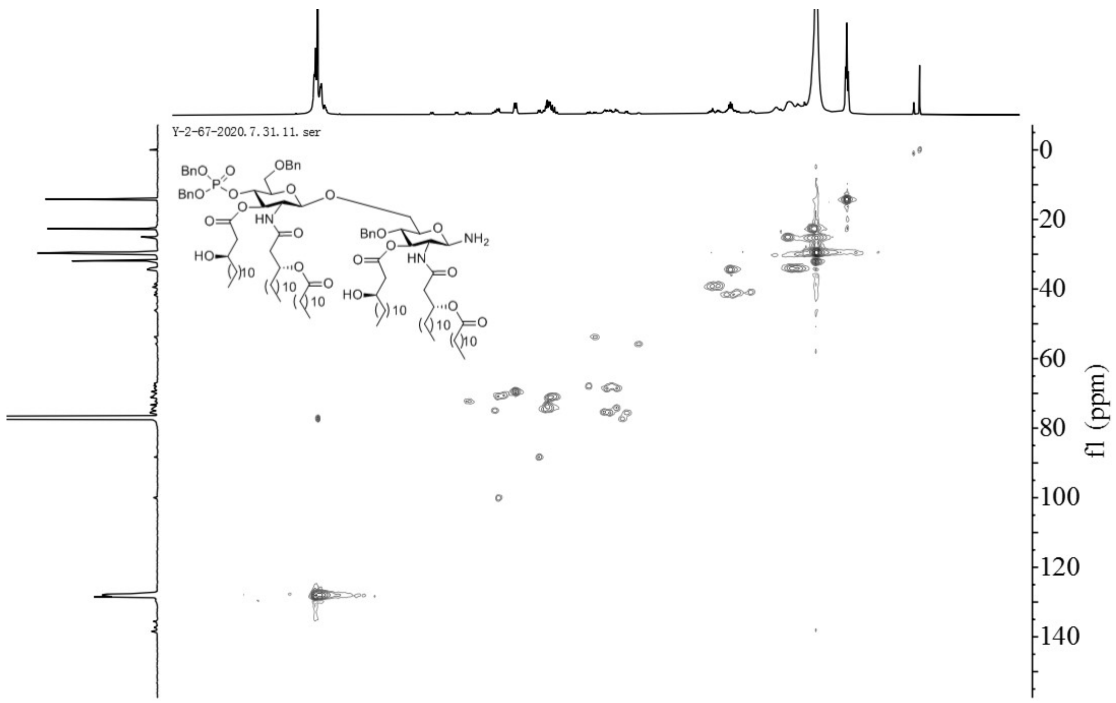
[1]H NMR spectrum of compound **50** ($CDCl_3$, 400 MHz)



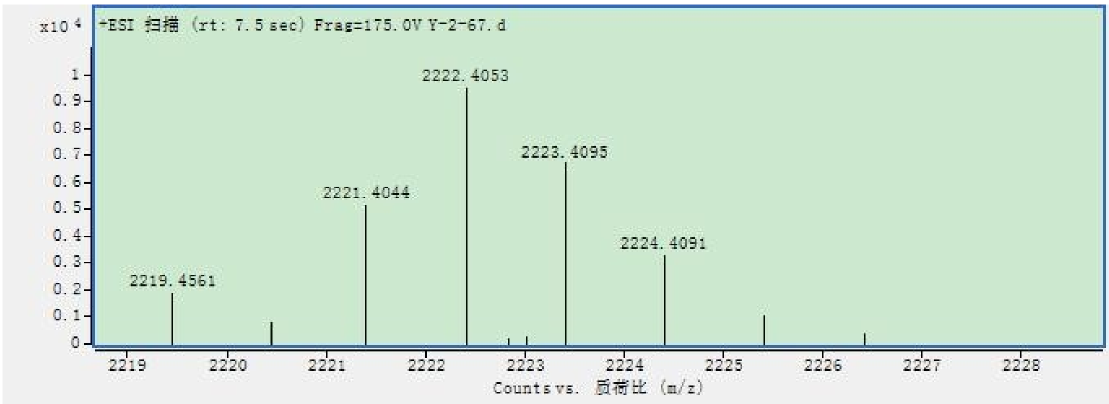
[13]C{[1]H} NMR spectrum of compound **50** ($CDCl_3$, 100 MHz)



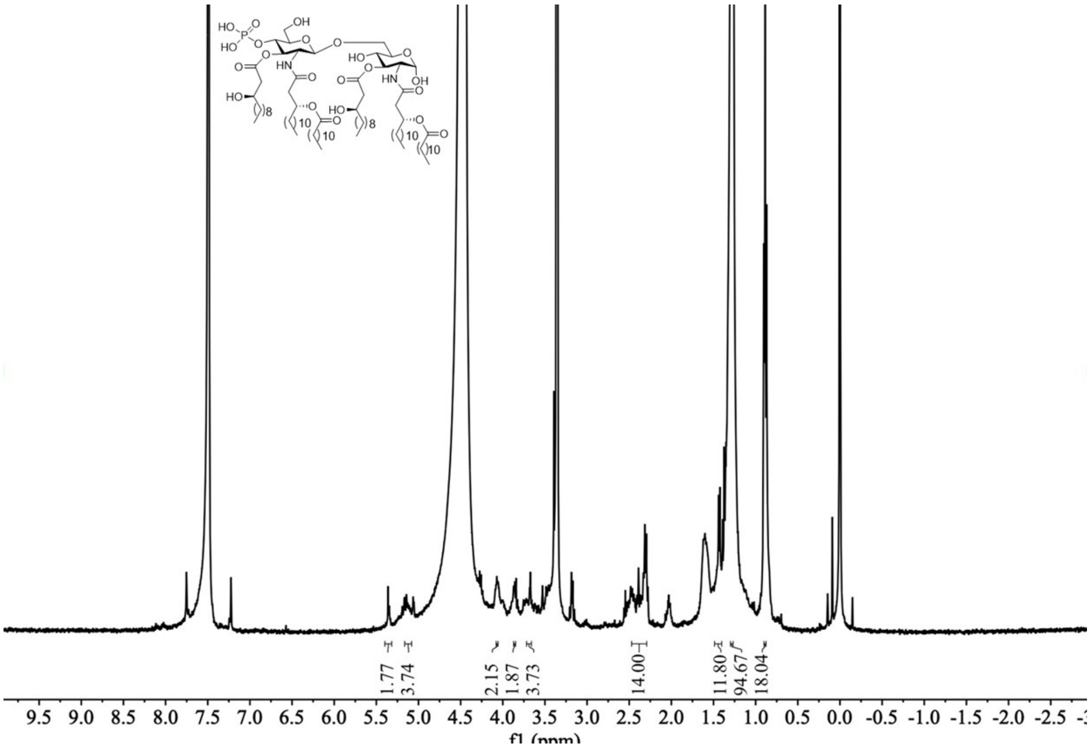
$^{1}H - ^{1}H$ COSY spectrum of compound **50** ($CDCl_3$, 400 MHz)



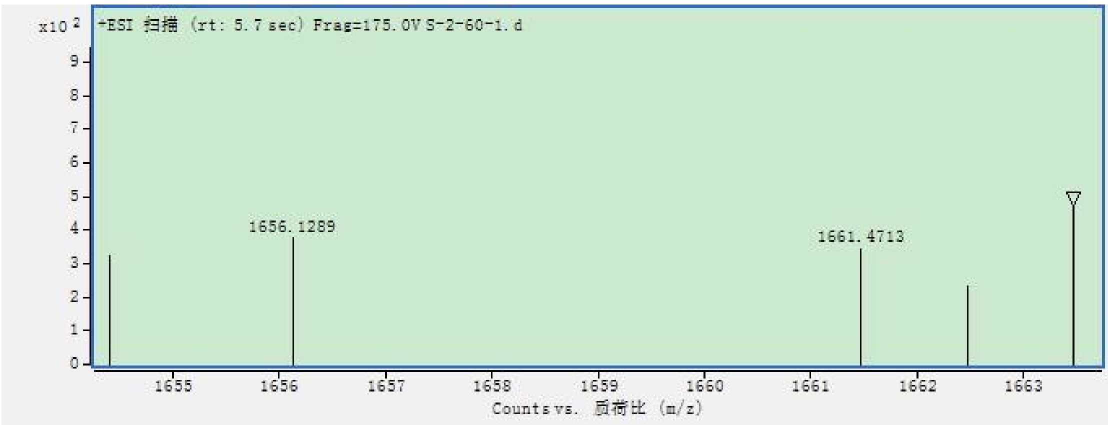
$^{1}H - ^{13}C$ HMQC spectrum of compound **50** ($CDCl_3$, 400/100 MHz)



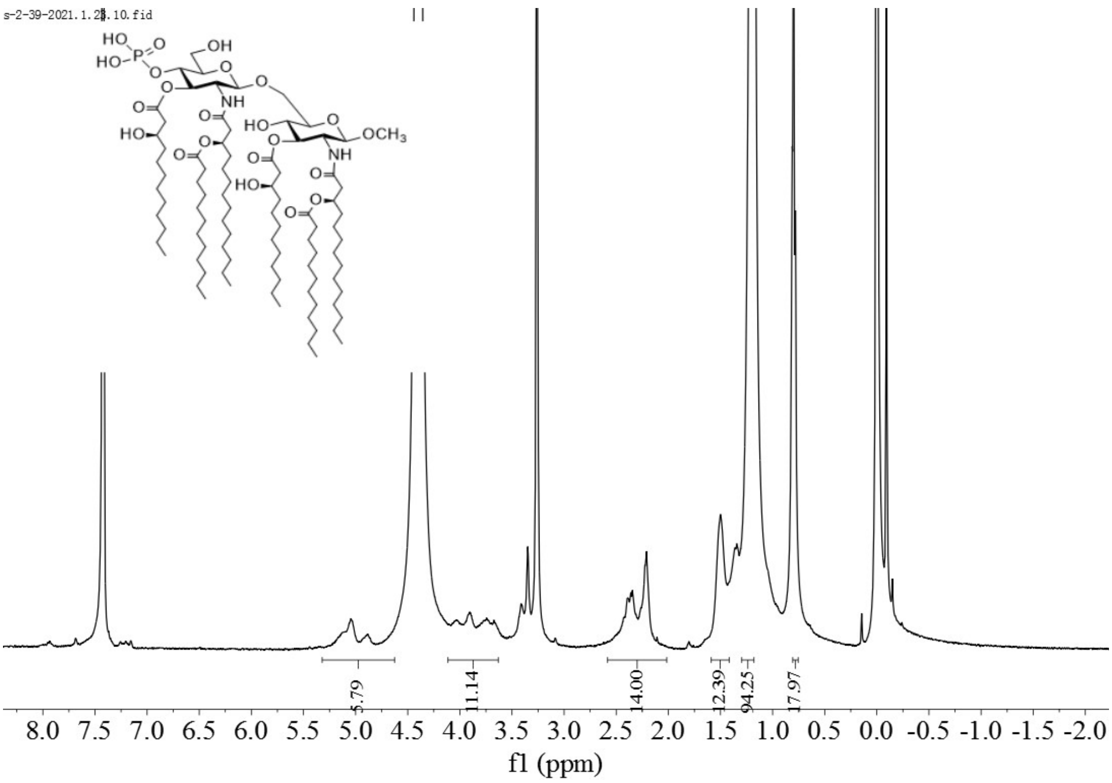
HRMS spectrum of compound **50**



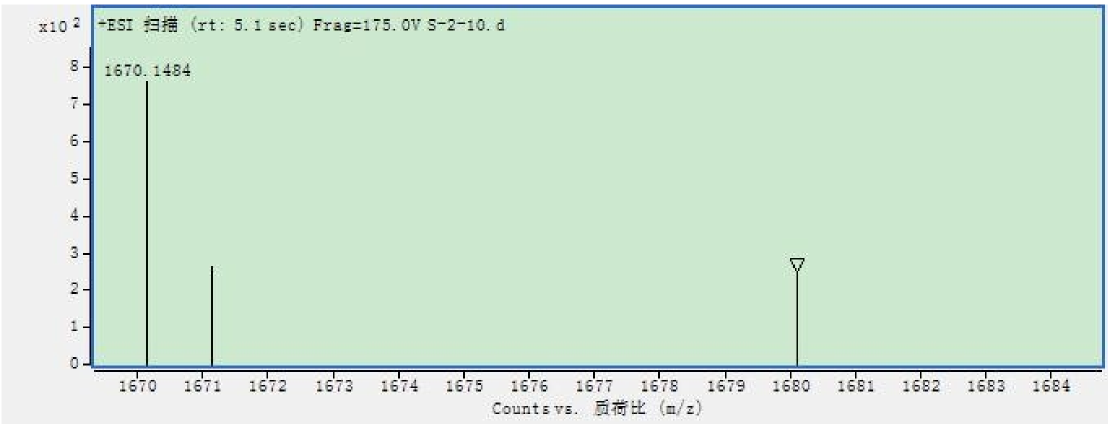
^{1}H NMR spectrum of compound **1** ($CDCl_3/CD_3OD$, 400 MHz)



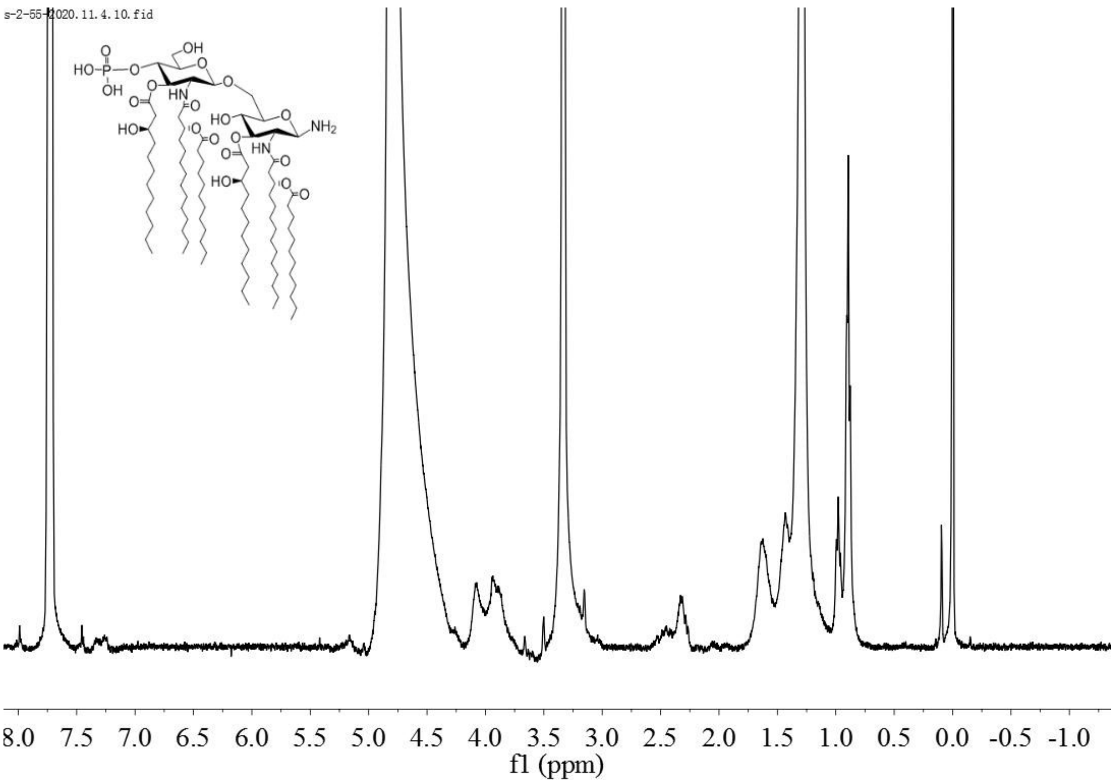
HRMS spectrum of compound **1**



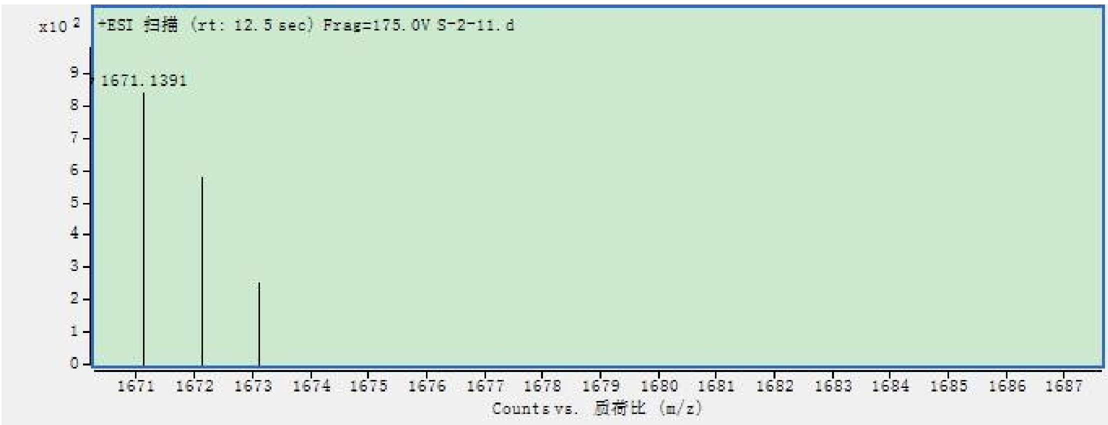
[1]H NMR spectrum of compound **2** ($CDCl_3/CD_3OD$, 400 MHz)



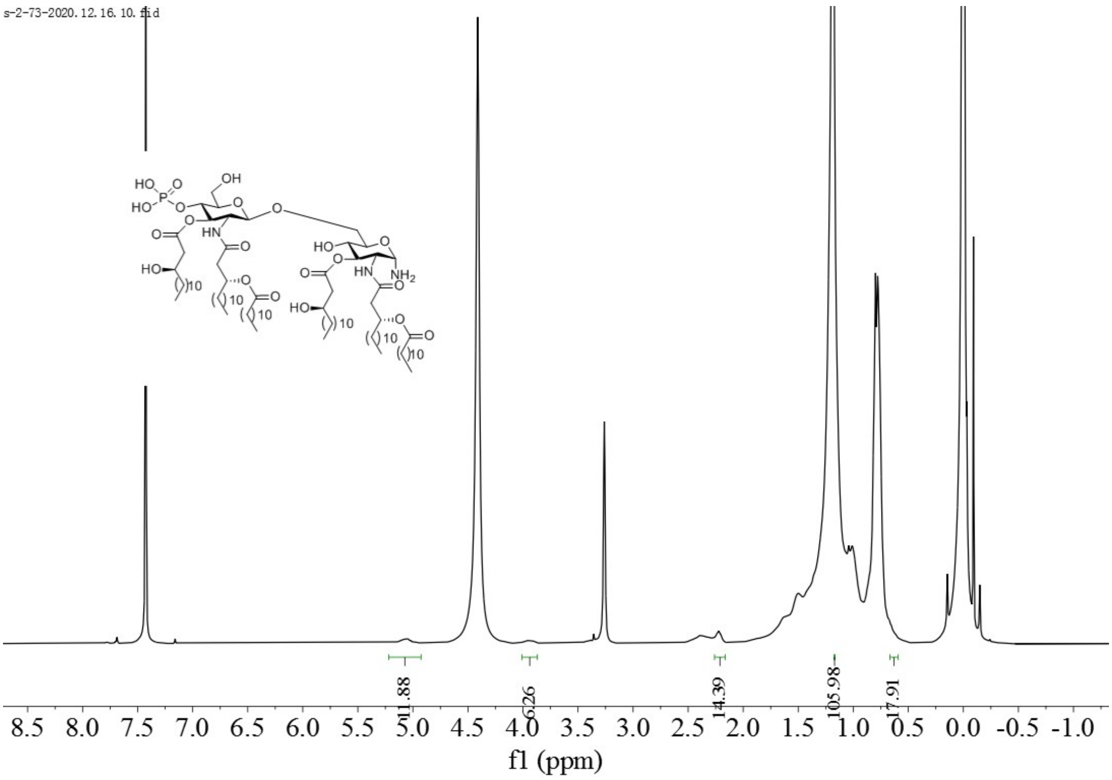
HRMS spectrum of compound **2**



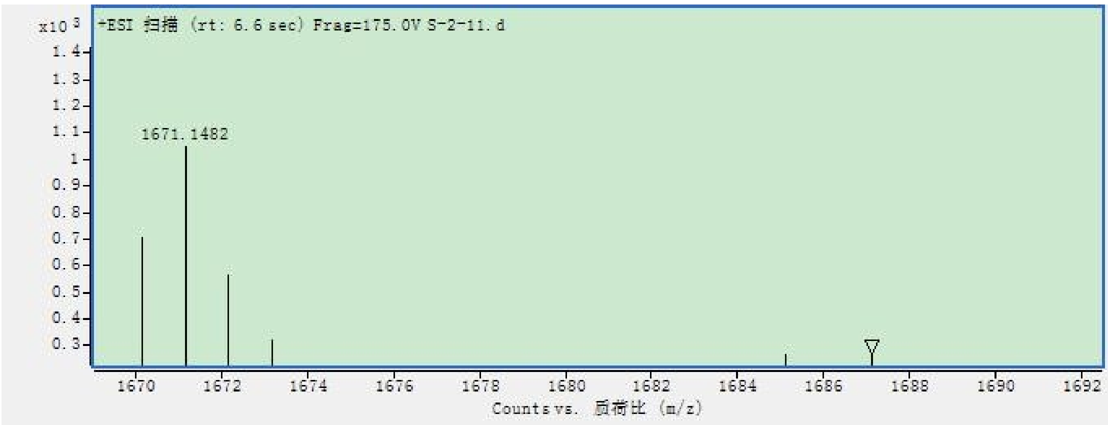
^{1}H NMR spectrum of compound **3** ($CDCl_3/CD_3OD$, 400 MHz)



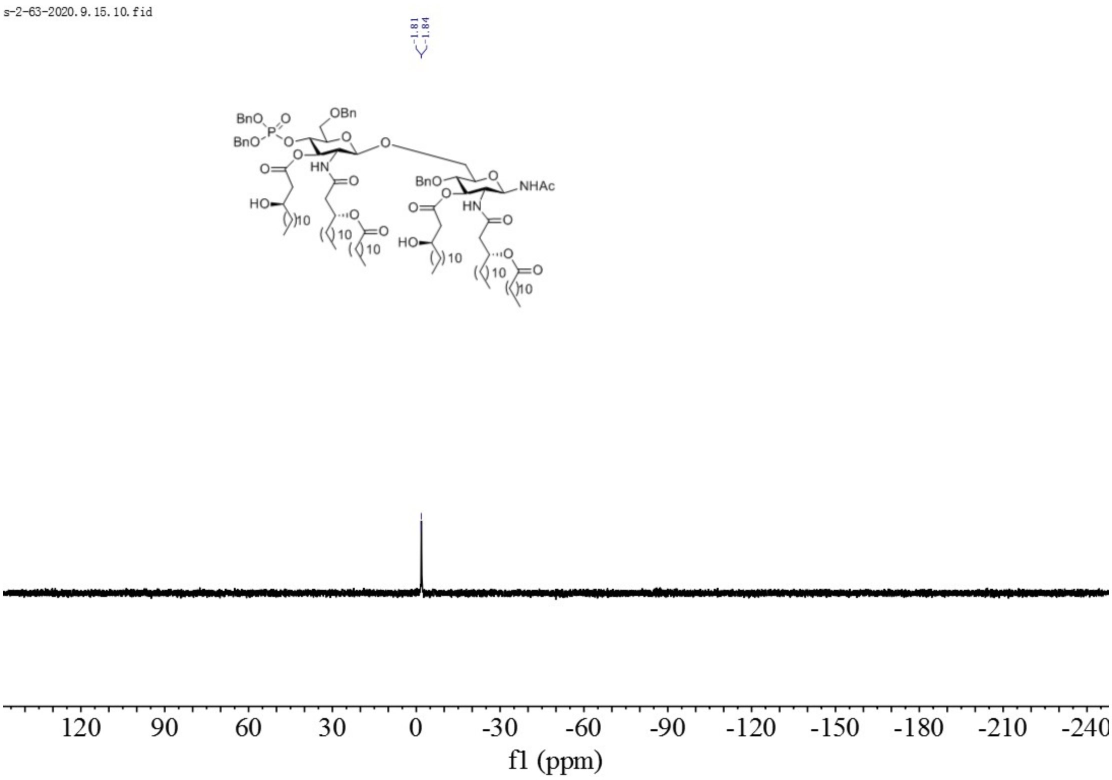
HRMS spectrum of compound **3**



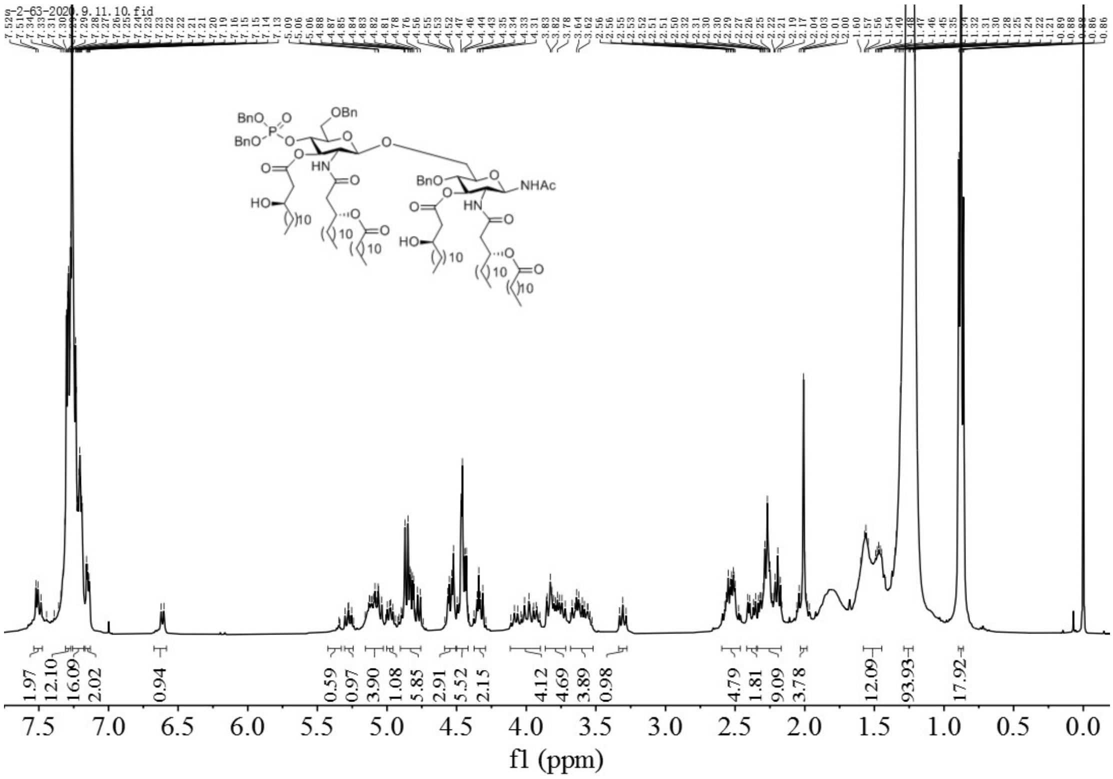
[1]H NMR spectrum of compound **4** ($CDCl_3/CD_3OD$, 400 MHz)



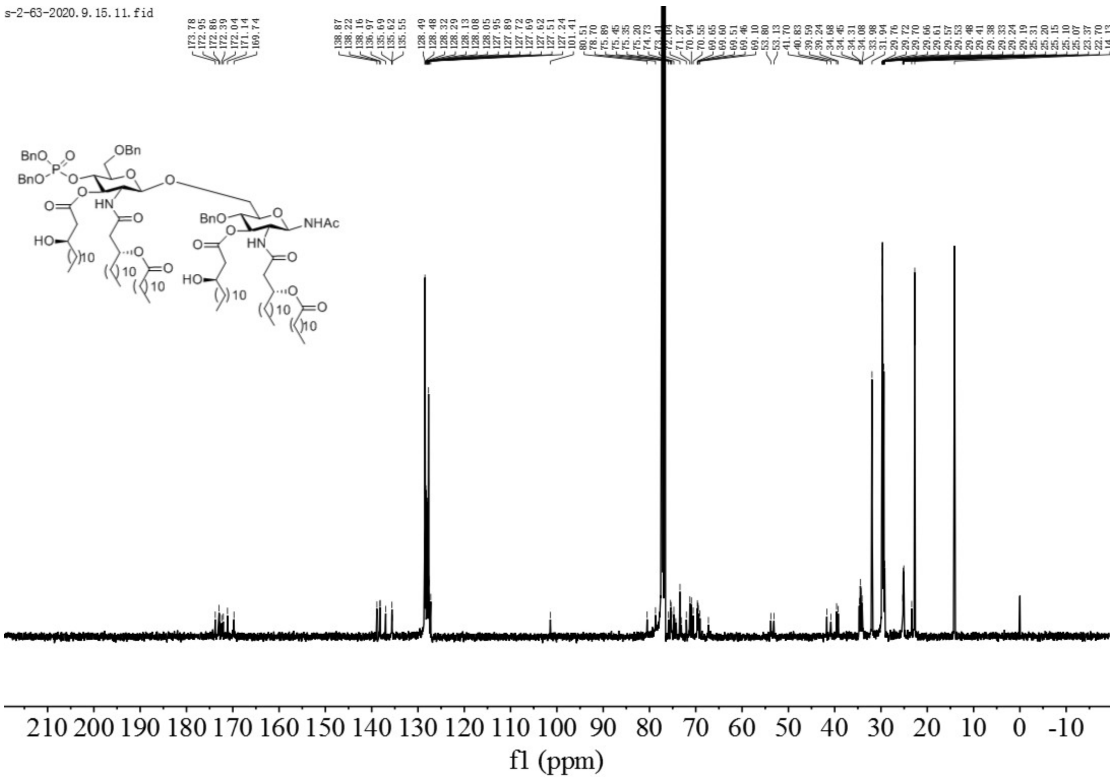
HRMS spectrum of compound **4**



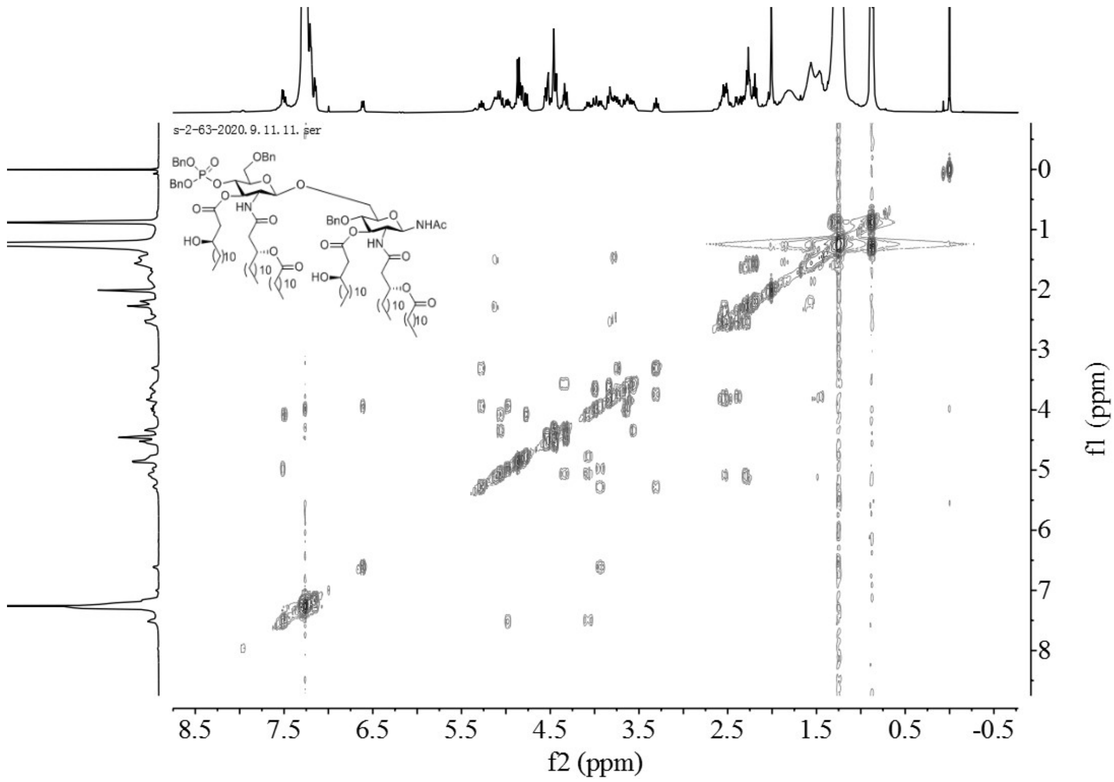
^{31}P NMR spectrum of compound **52** ($CDCl_3$, 162 MHz)



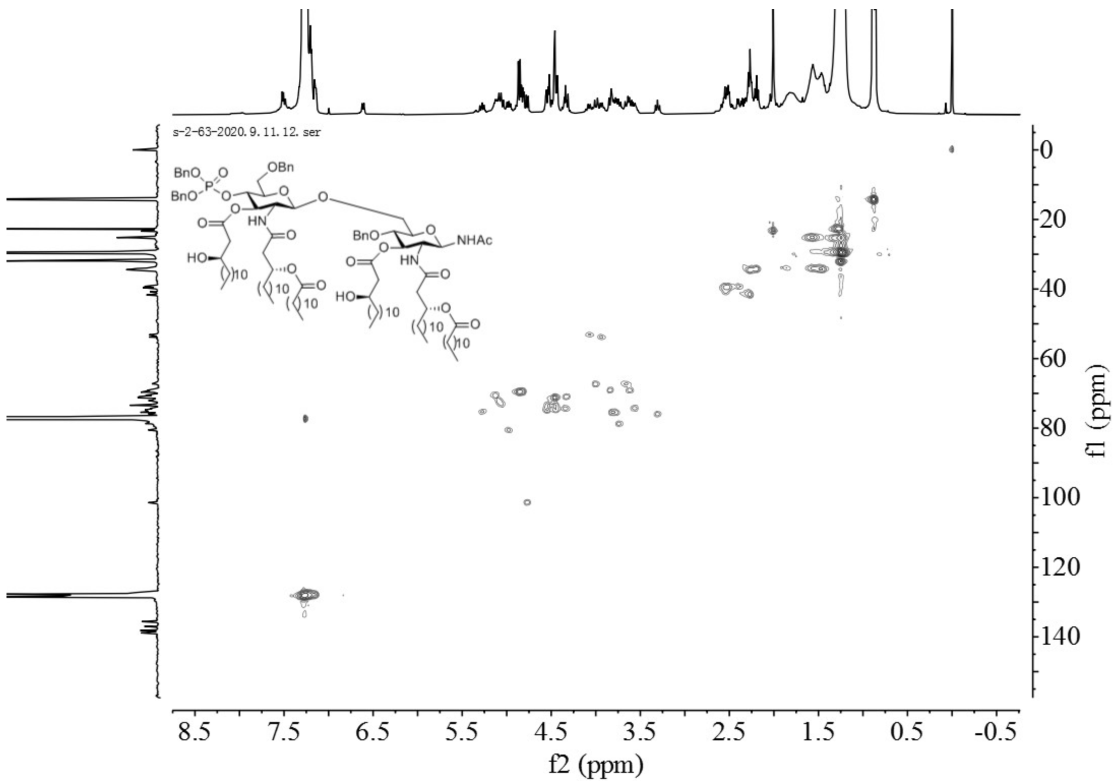
^{1}H NMR spectrum of compound **52** ($CDCl_3$, 400 MHz)



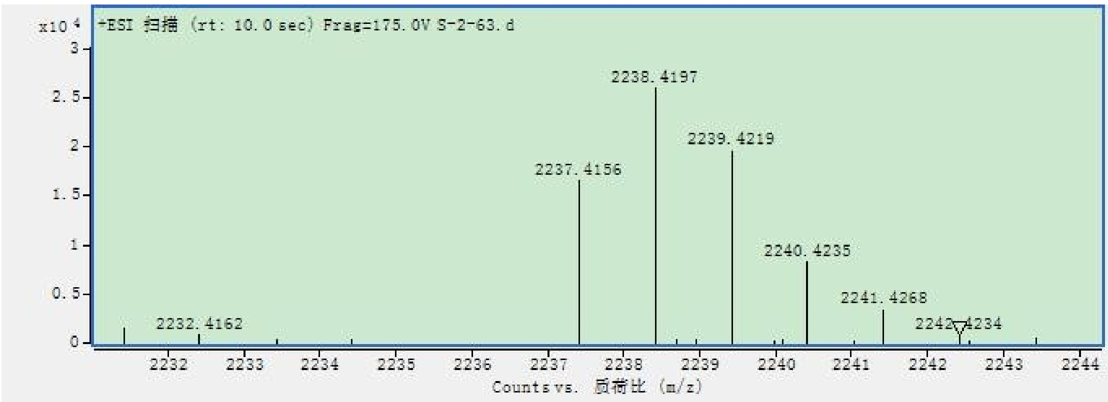
$^{13}C\{^{1}H\}$ NMR spectrum of compound **52** ($CDCl_3$, 100 MHz)



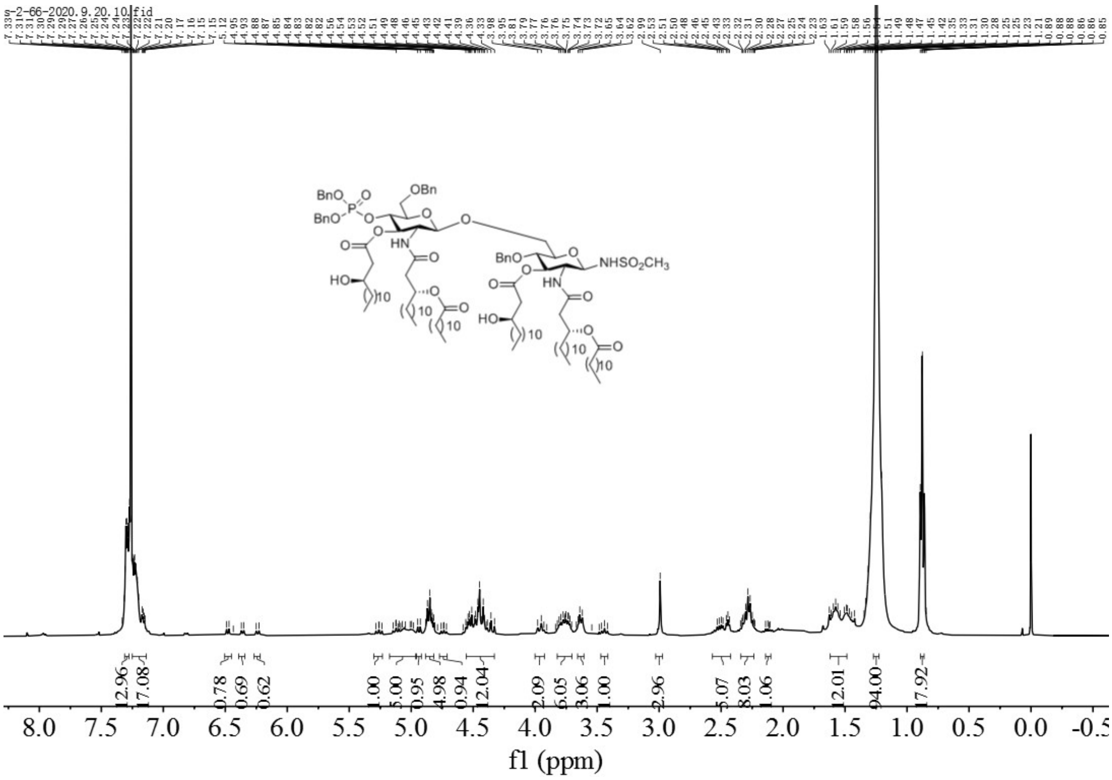
$^{1}H - ^{1}H$ COSY spectrum of compound **52** ($CDCl_3$, 400 MHz)



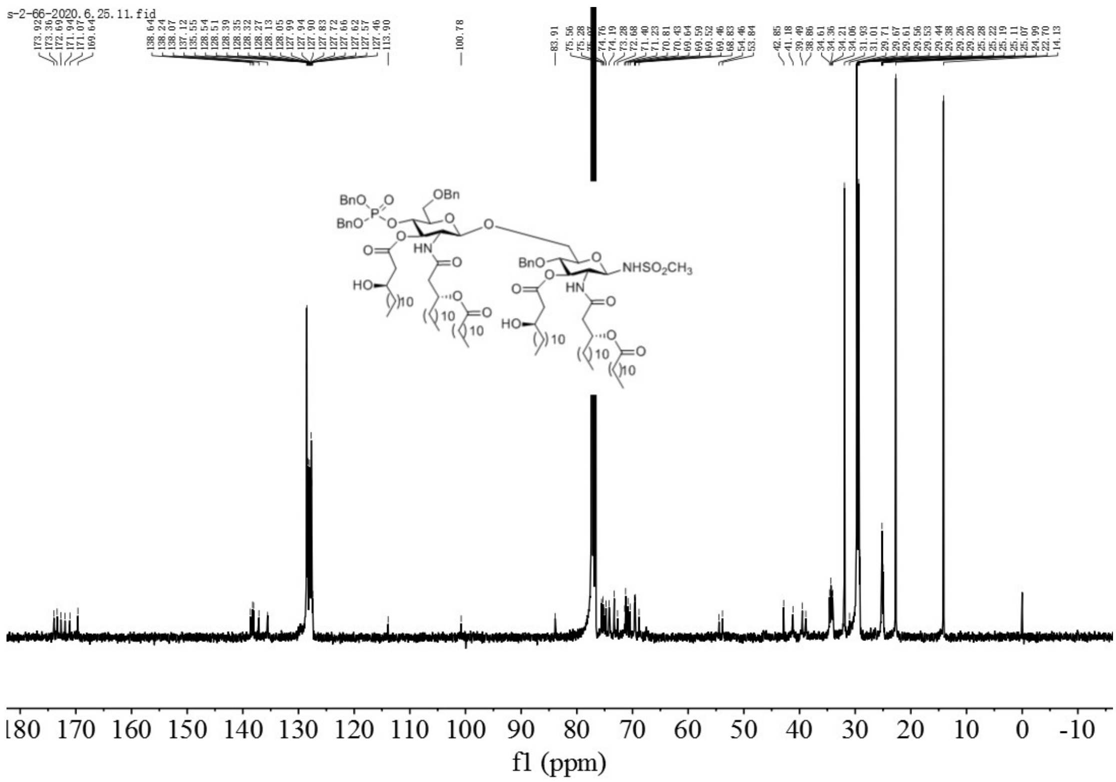
$^{1}H - ^{13}C$ HMQC spectrum of compound **52** ($CDCl_3$, 400/100 MHz)



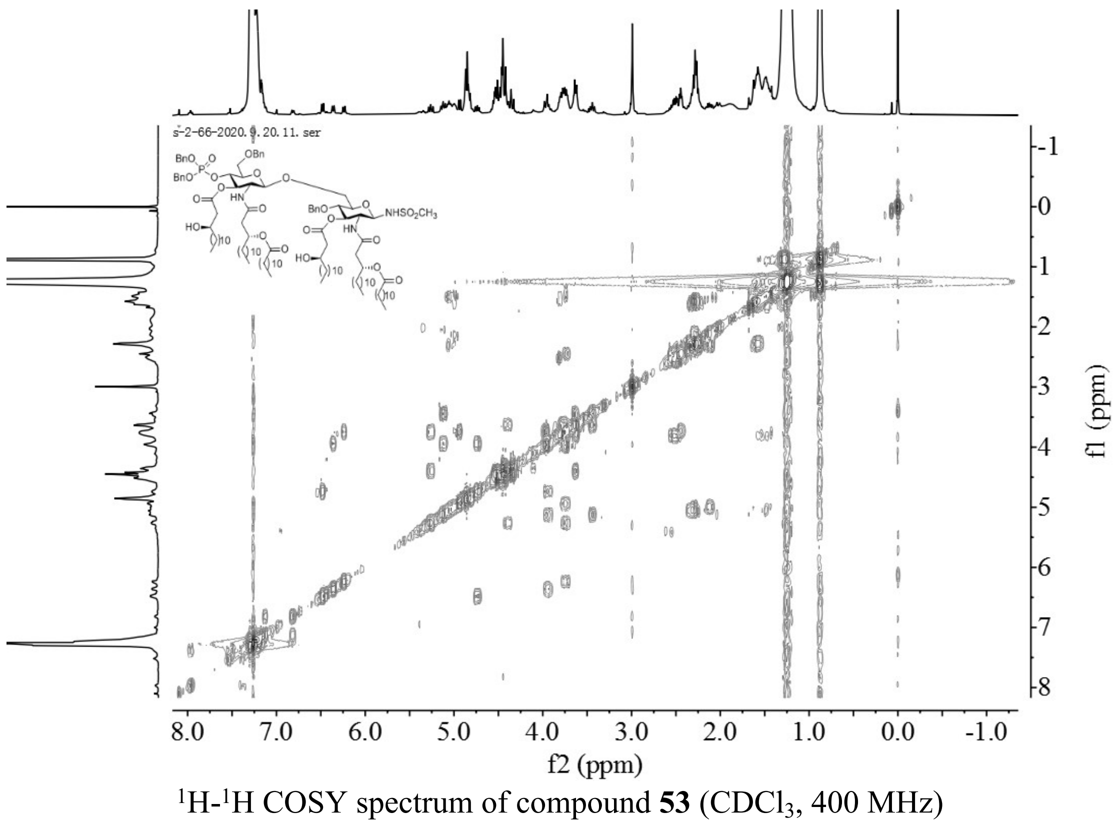
HRMS spectrum of compound **52**



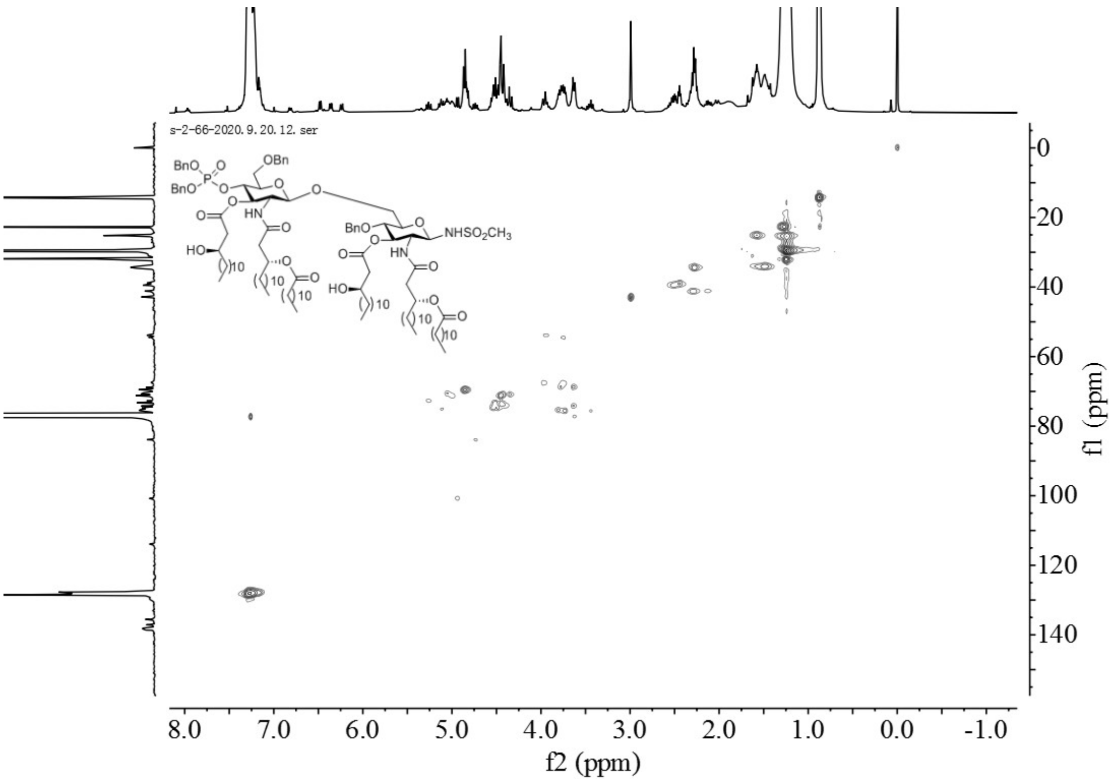
^{1}H NMR spectrum of compound **53** ($CDCl_3$, 400 MHz)



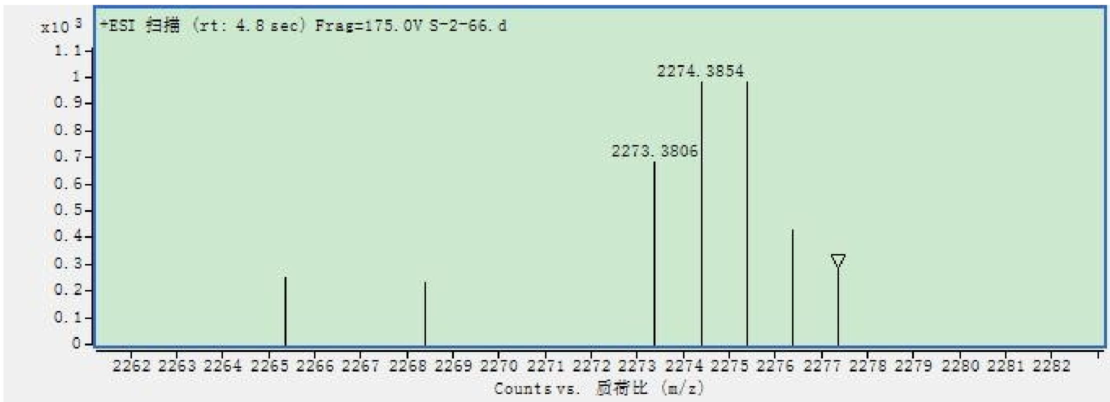
$^{13}C\{^1H\}$ NMR spectrum of compound **53** ($CDCl_3$, 100 MHz)



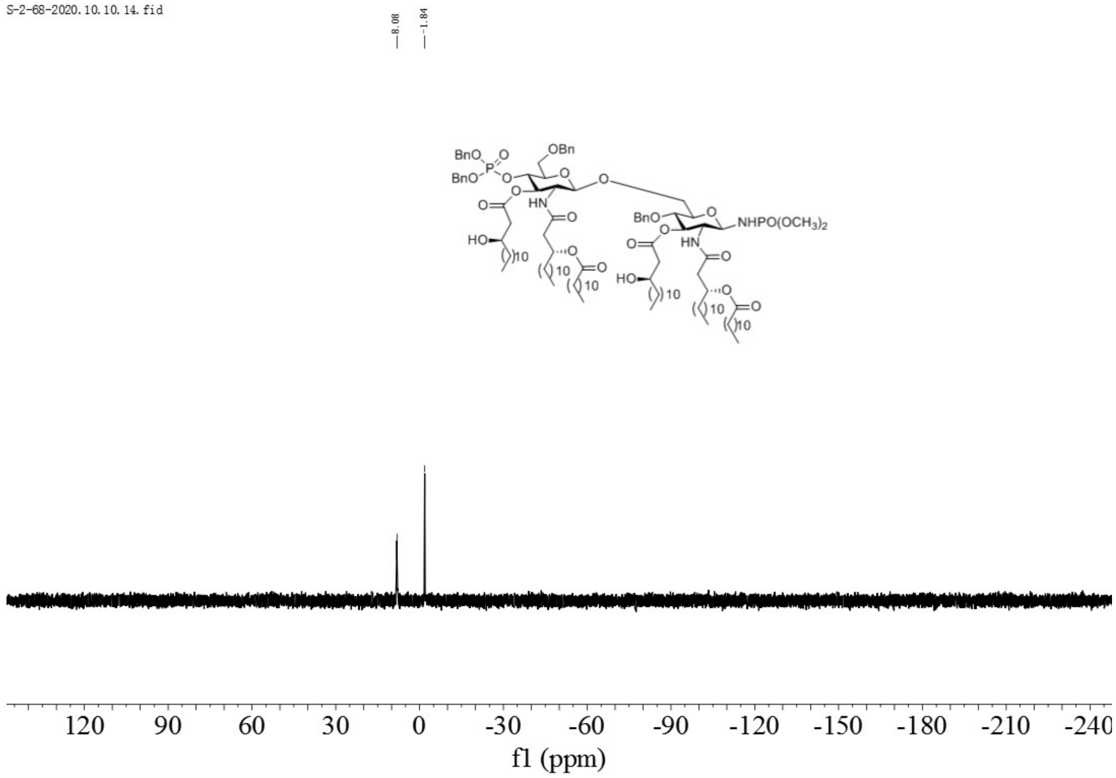
^1H-^1H COSY spectrum of compound **53** ($CDCl_3$, 400 MHz)



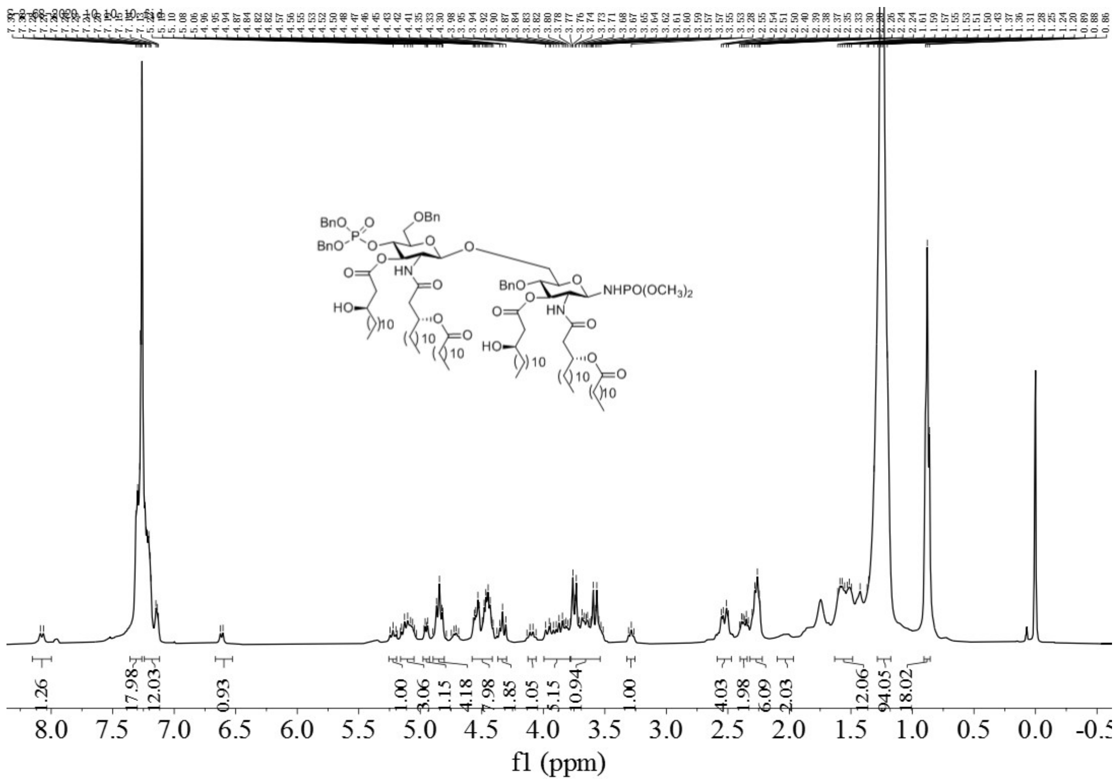
^1H-^{13}C HMQC spectrum of compound **53** ($CDCl_3$, 400/100 MHz)



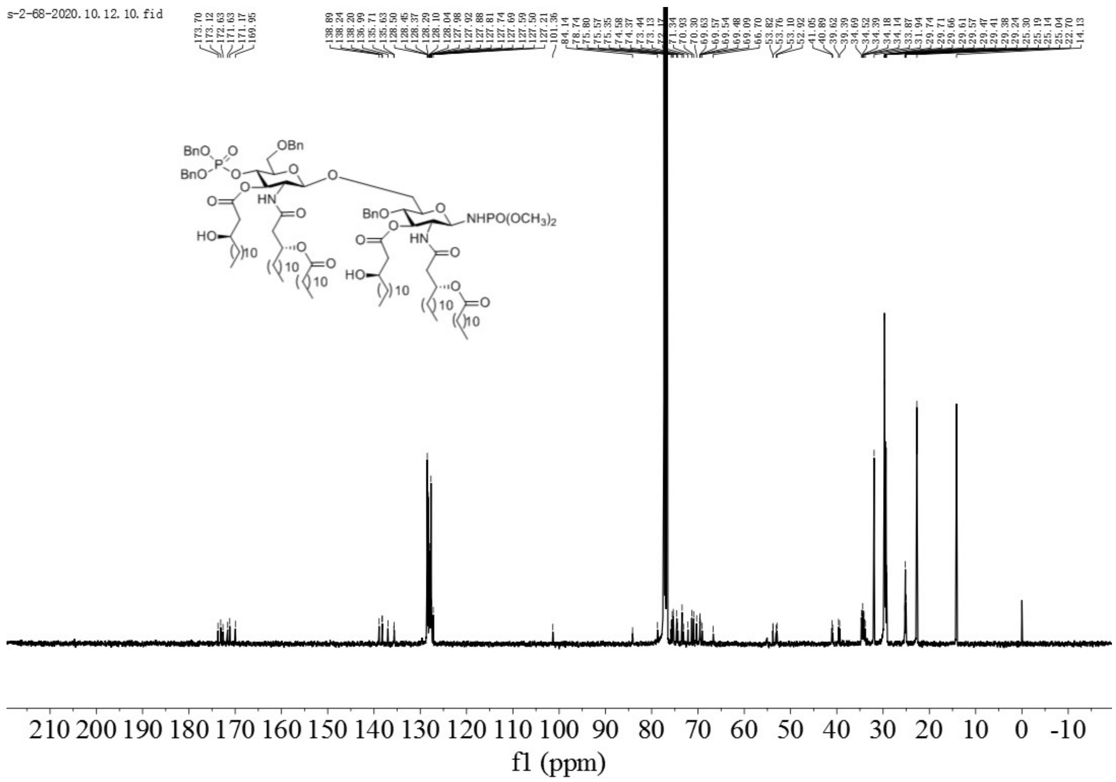
HRMS spectrum of compound **53**



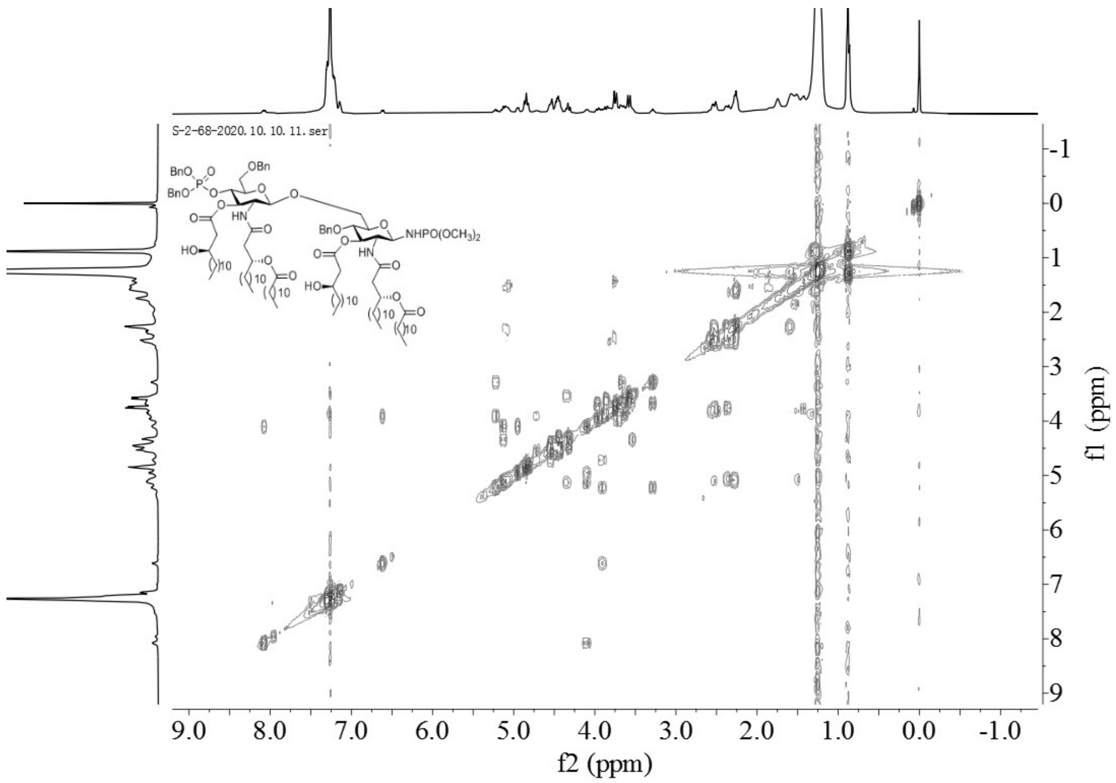
^{31}P NMR spectrum of compound **54** ($CDCl_3$, 162 MHz)



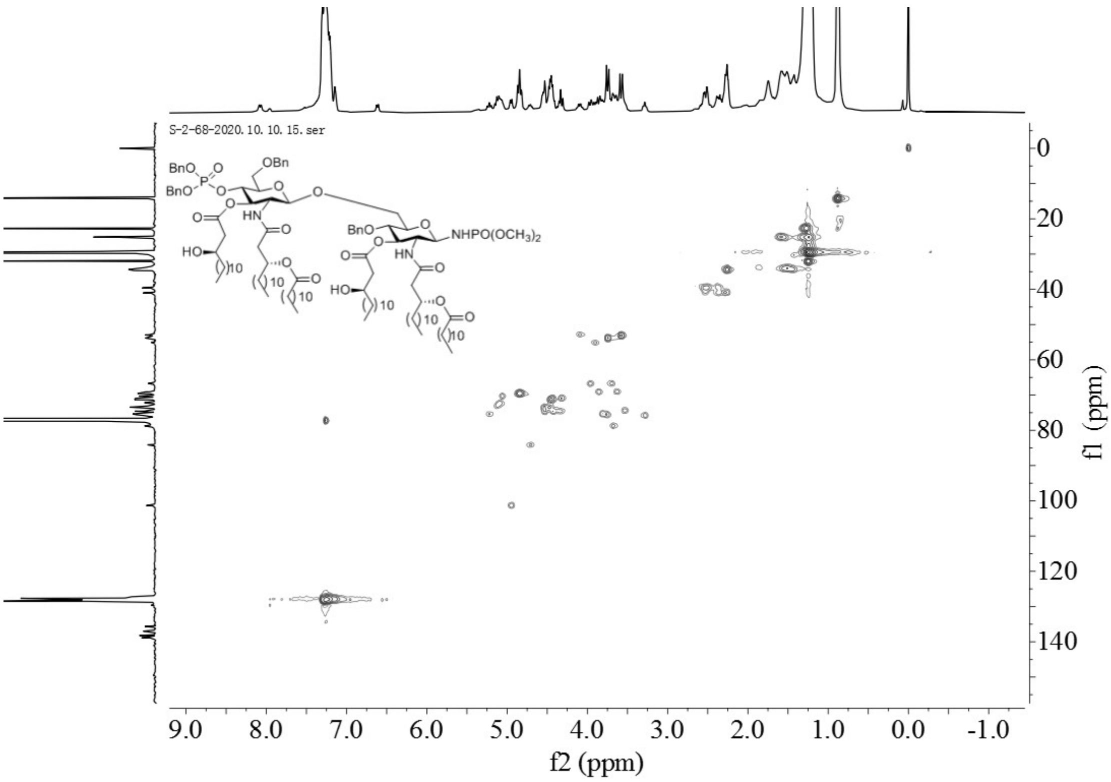
^{1}H NMR spectrum of compound **54** ($CDCl_3$, 400 MHz)



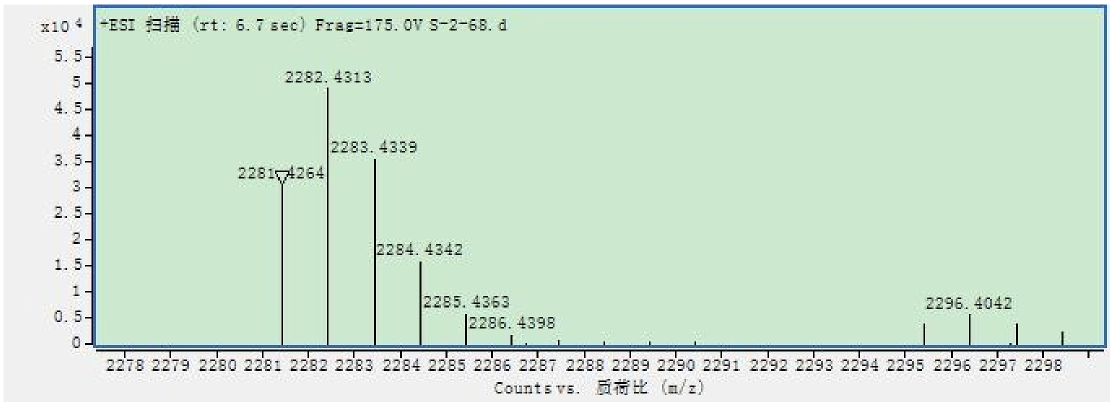
$^{13}C\{^{1}H\}$ NMR spectrum of compound **54** ($CDCl_3$, 100 MHz)



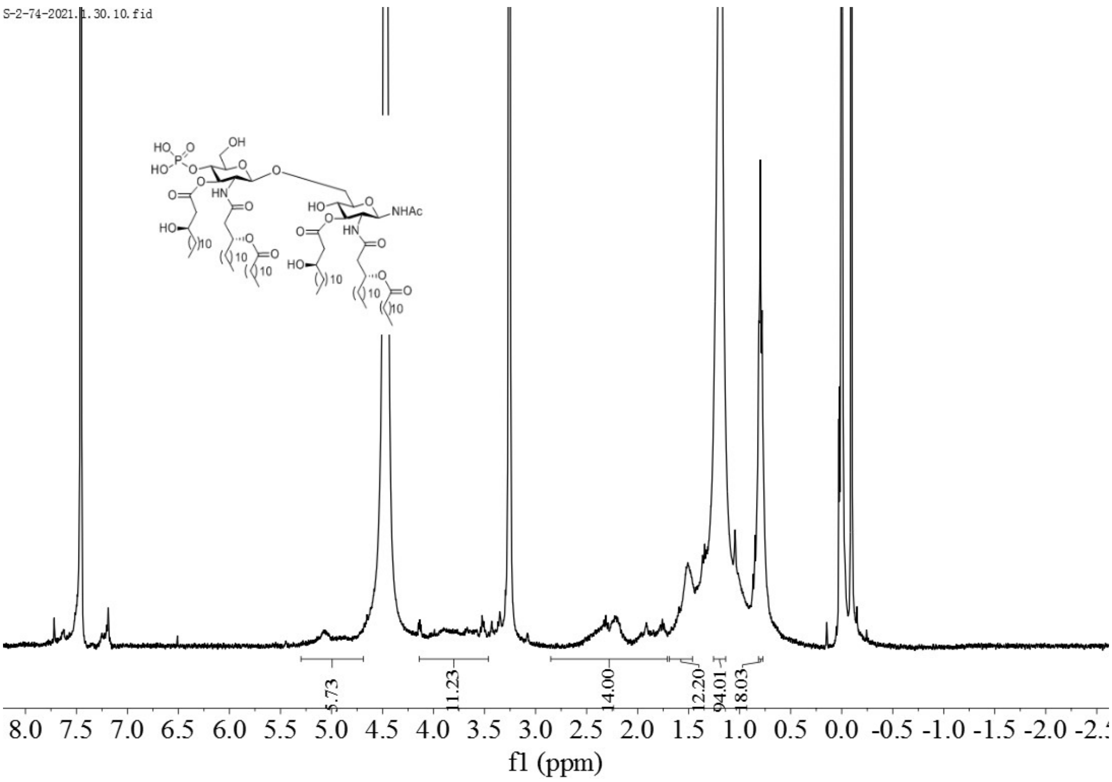
^{1}H-^{1}H COSY spectrum of compound **54** ($CDCl_3$, 400 MHz)



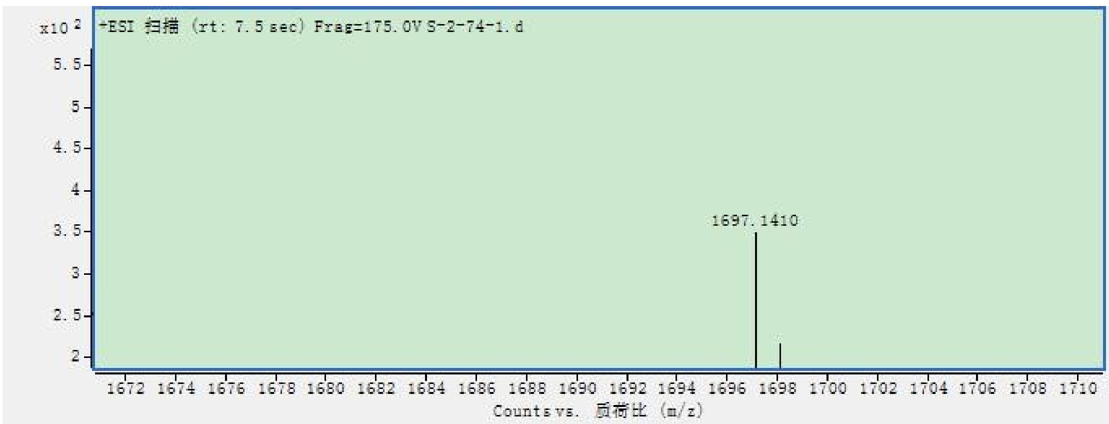
^{1}H-^{13}C HMQC spectrum of compound **54** ($CDCl_3$, 400/100 MHz)



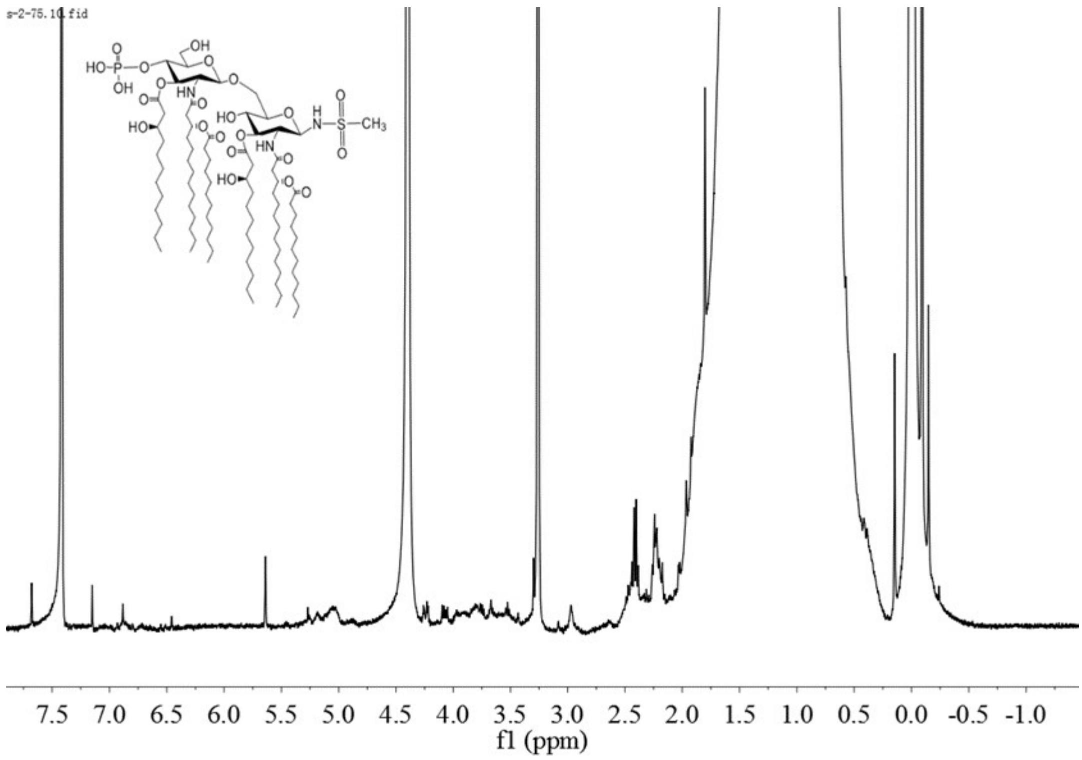
HRMS spectrum of compound **54**



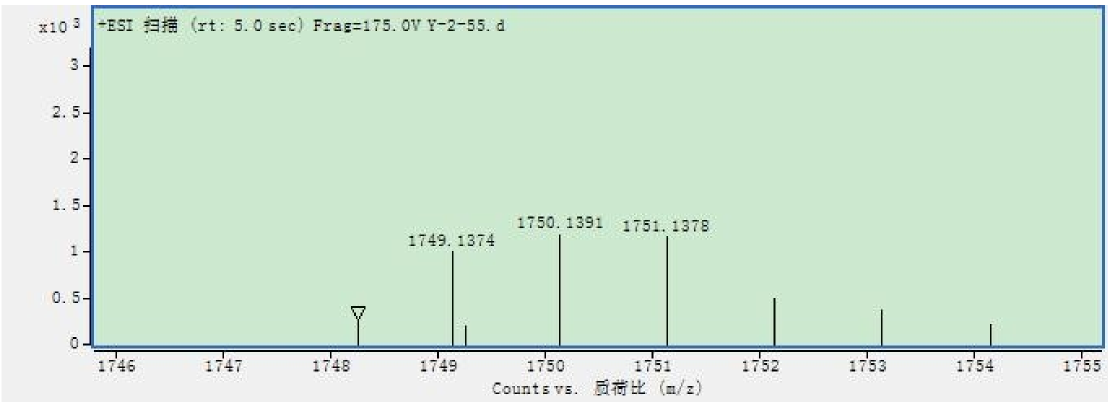
^{1}H NMR spectrum of compound **5** ($CDCl_3$/CD_3OD, 400 MHz)



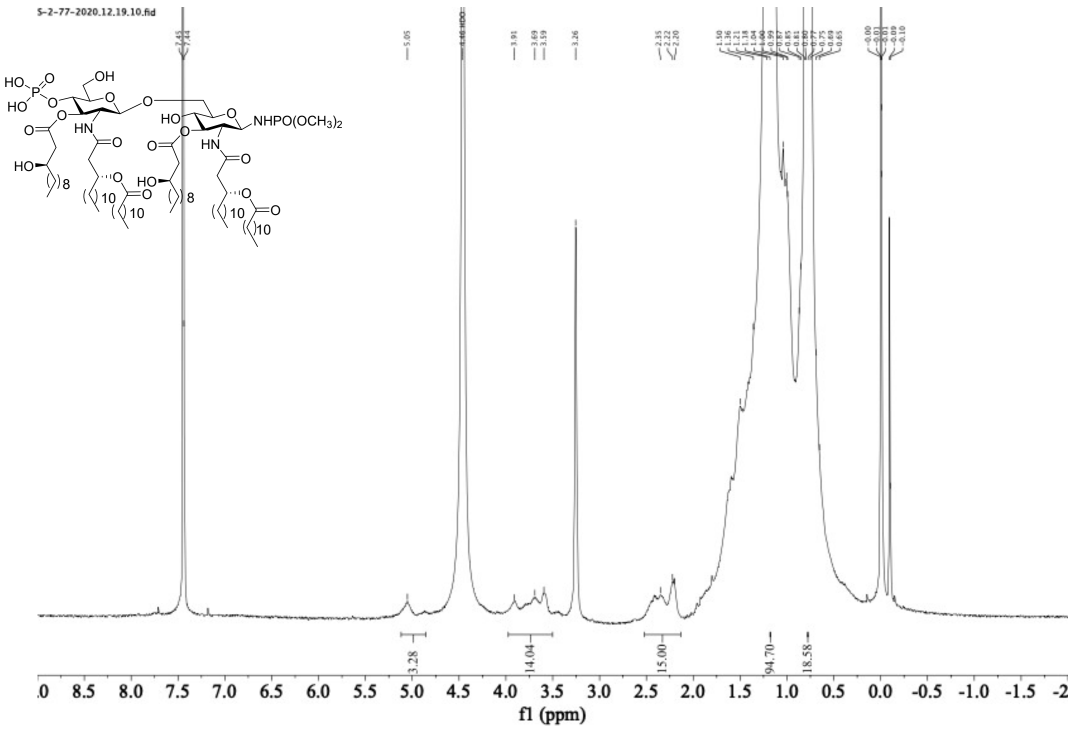
HRMS spectrum of compound **5**



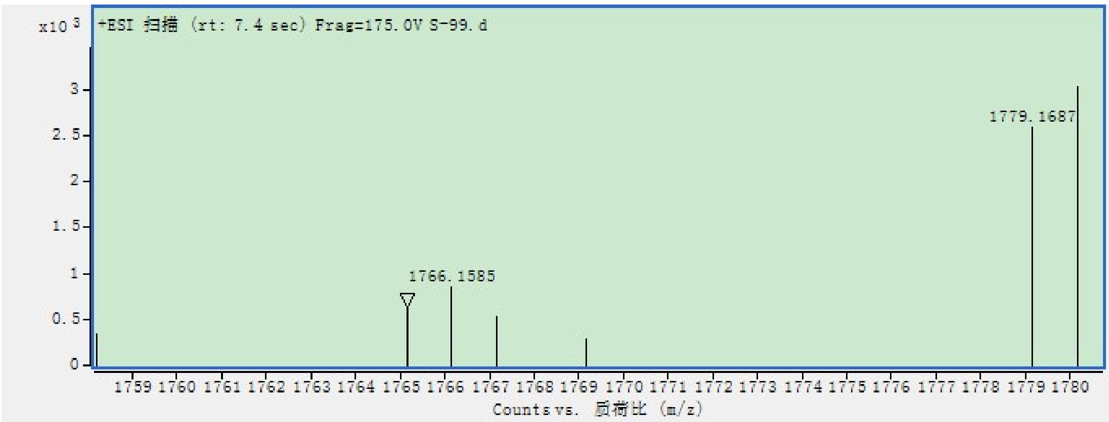
[1]H NMR spectrum of compound **6** ($CDCl_3/CD_3OD$, 400 MHz)



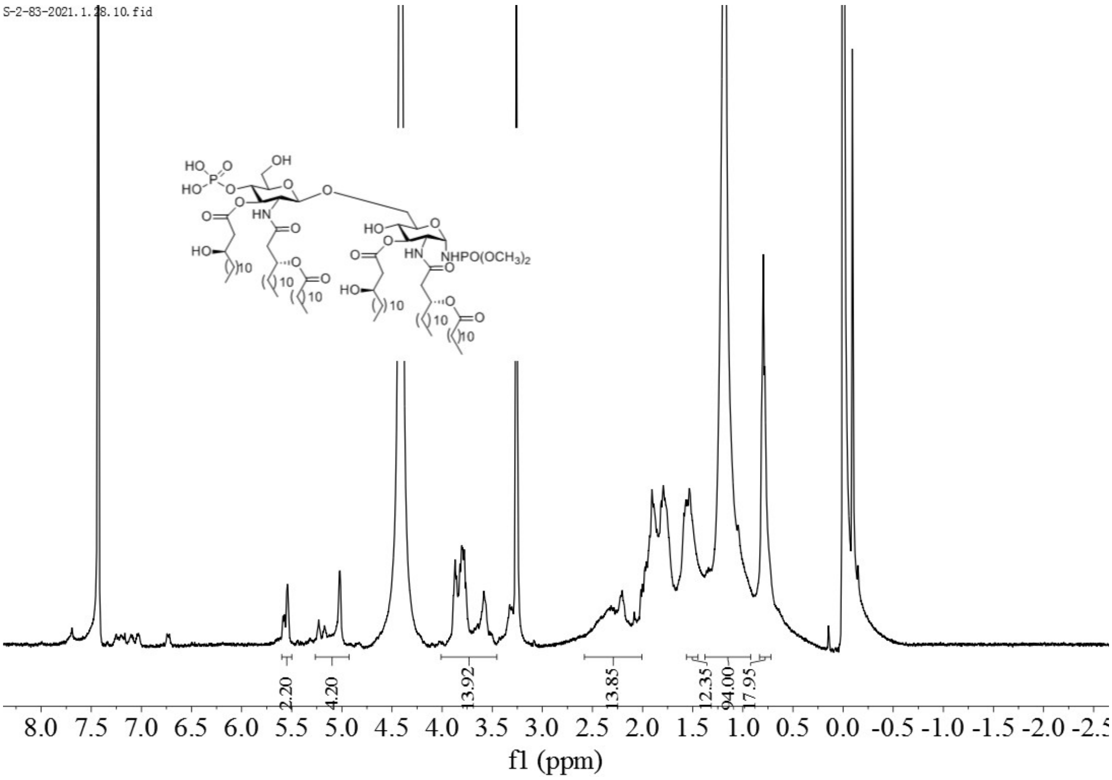
HRMS spectrum of compound **6**



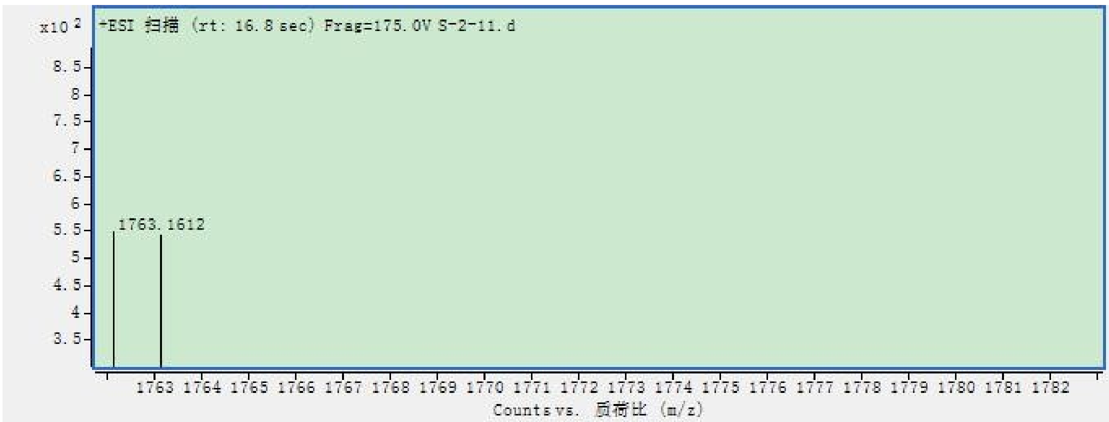
^{1}H NMR spectrum of compound **7** ($CDCl_3/CD_3OD$, 400 MHz)



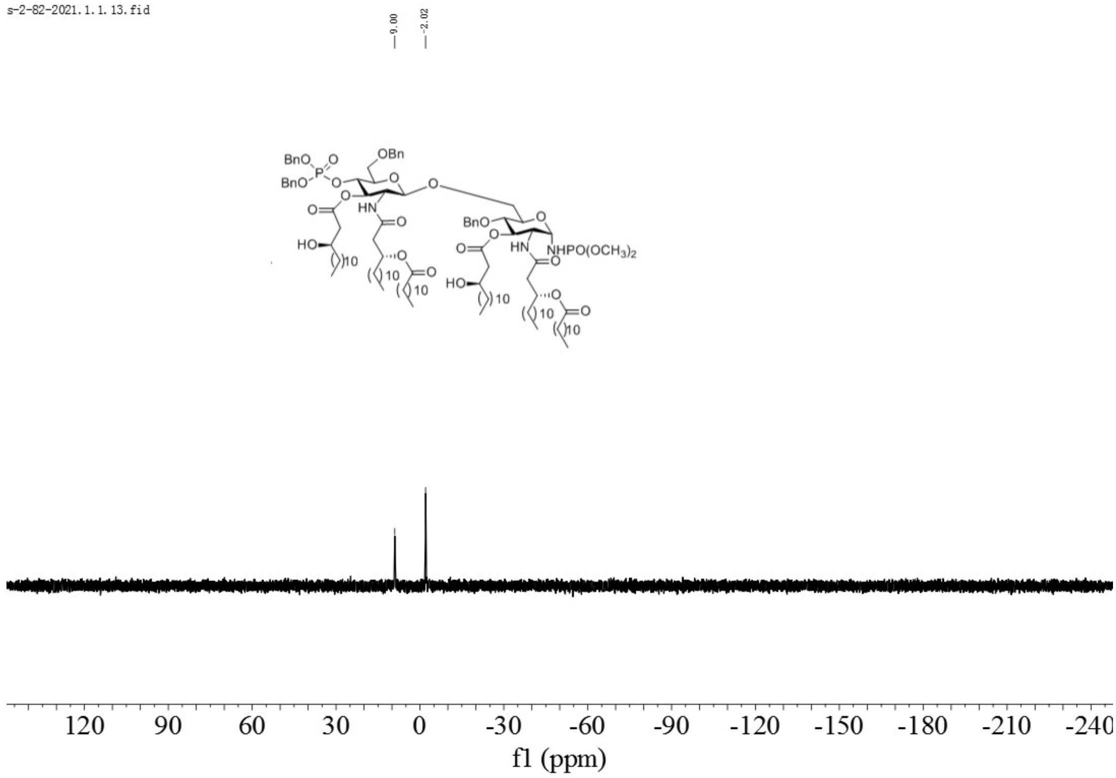
HRMS spectrum of compound **7**



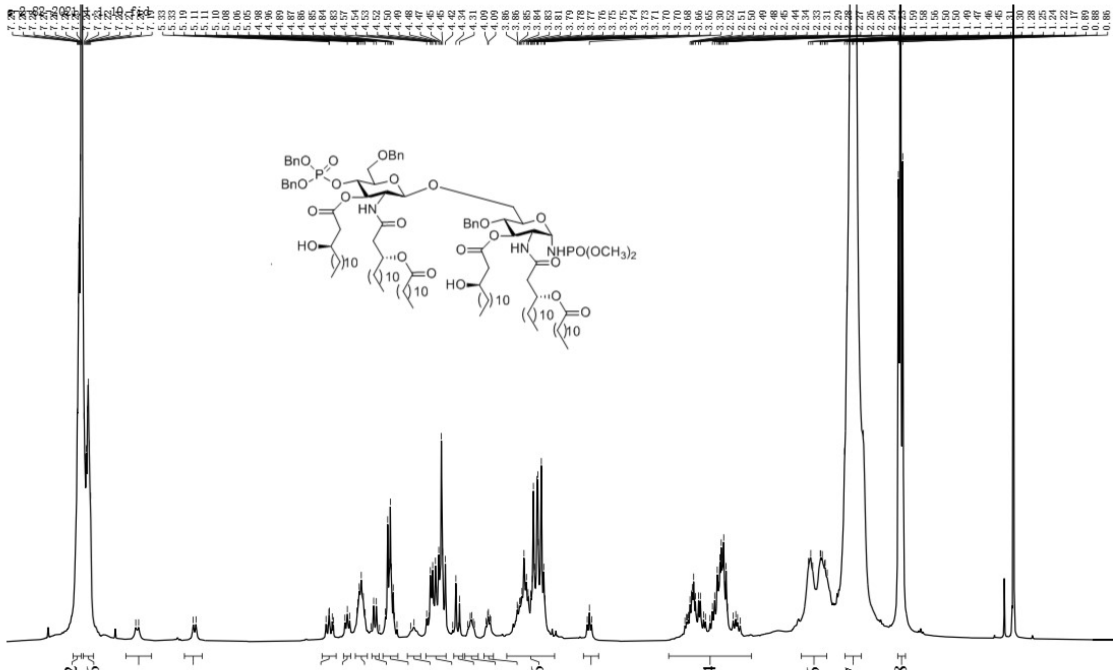
[1]H NMR spectrum of compound **8** ($CDCl_3/CD_3OD$, 400 MHz)



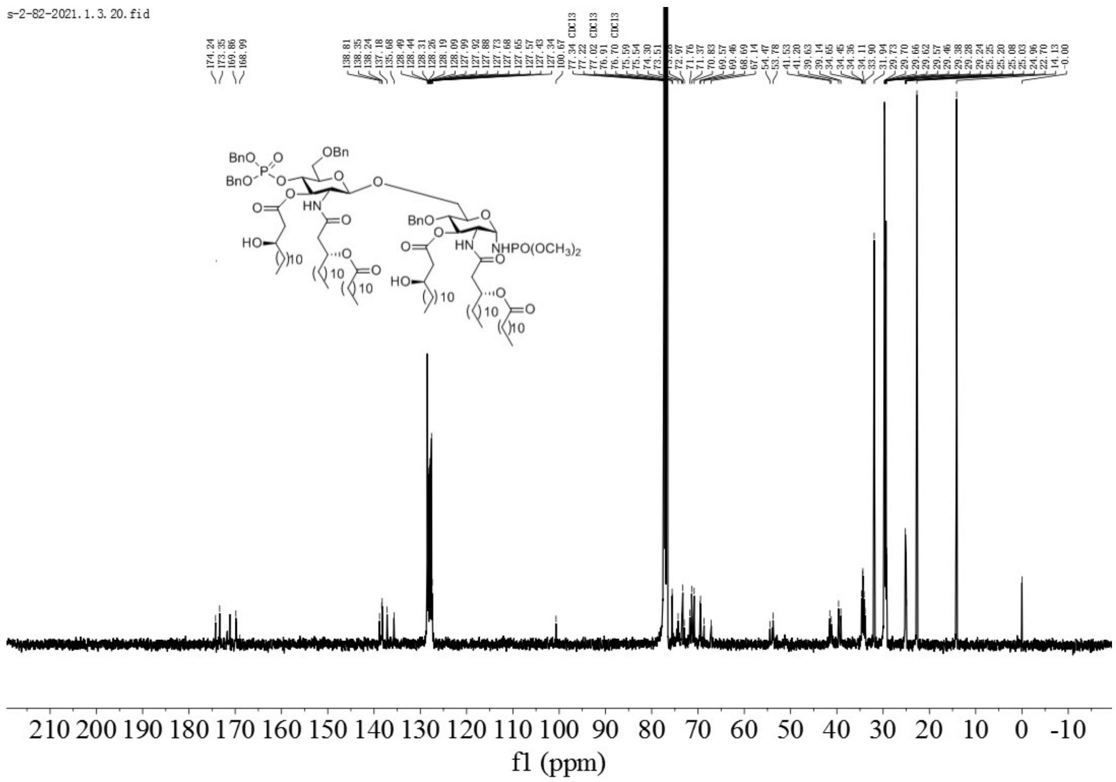
HRMS spectrum of compound **8**



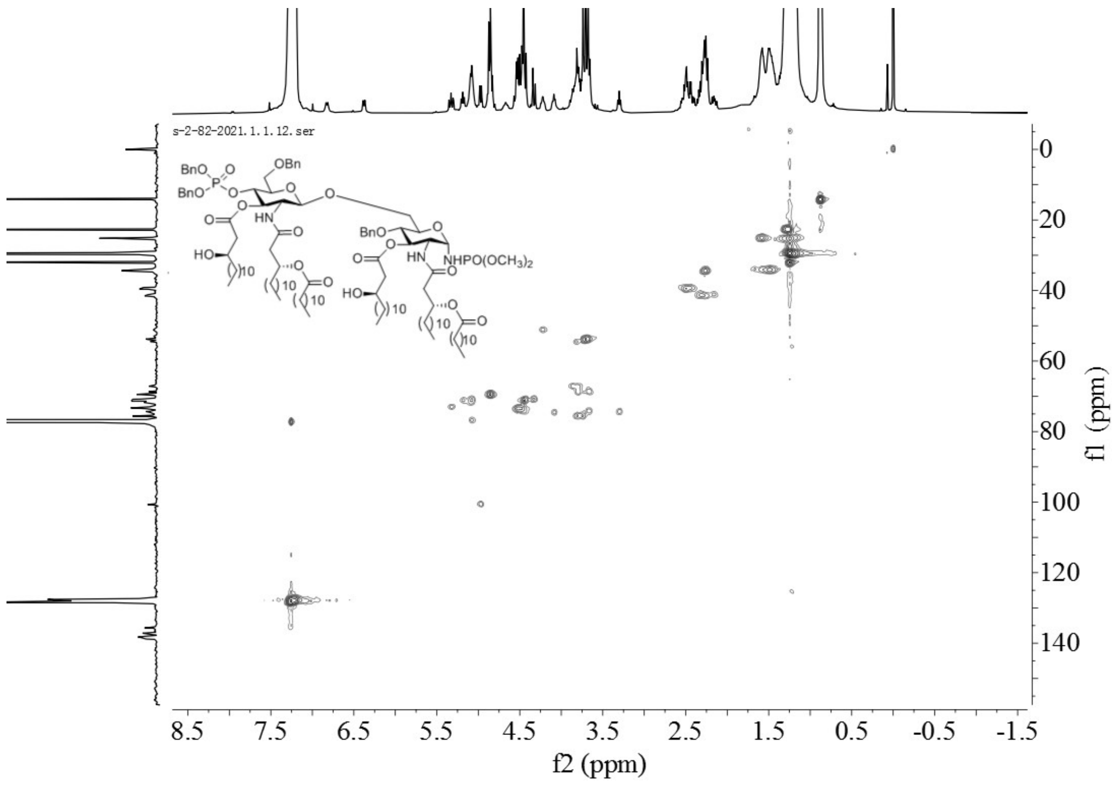
^{31}P NMR spectrum of compound **55** ($CDCl_3$, 162 MHz)



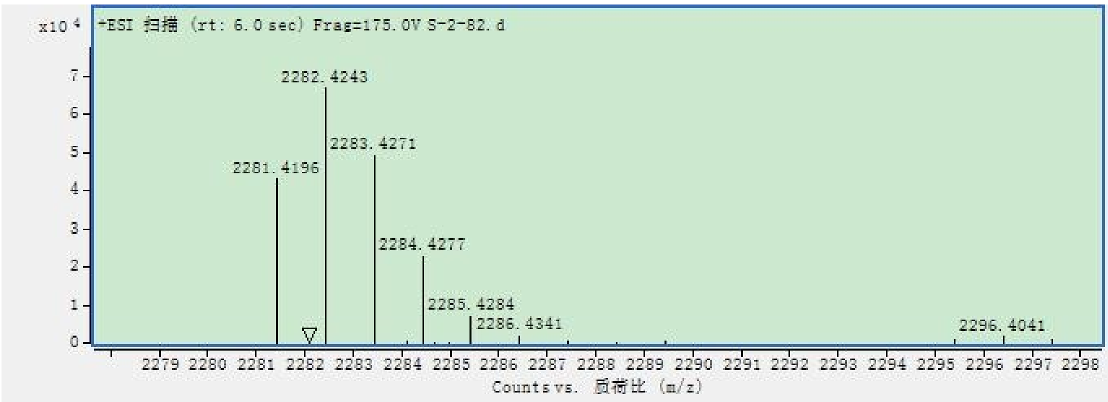
^{1}H NMR spectrum of compound **55** ($CDCl_3$, 400 MHz)



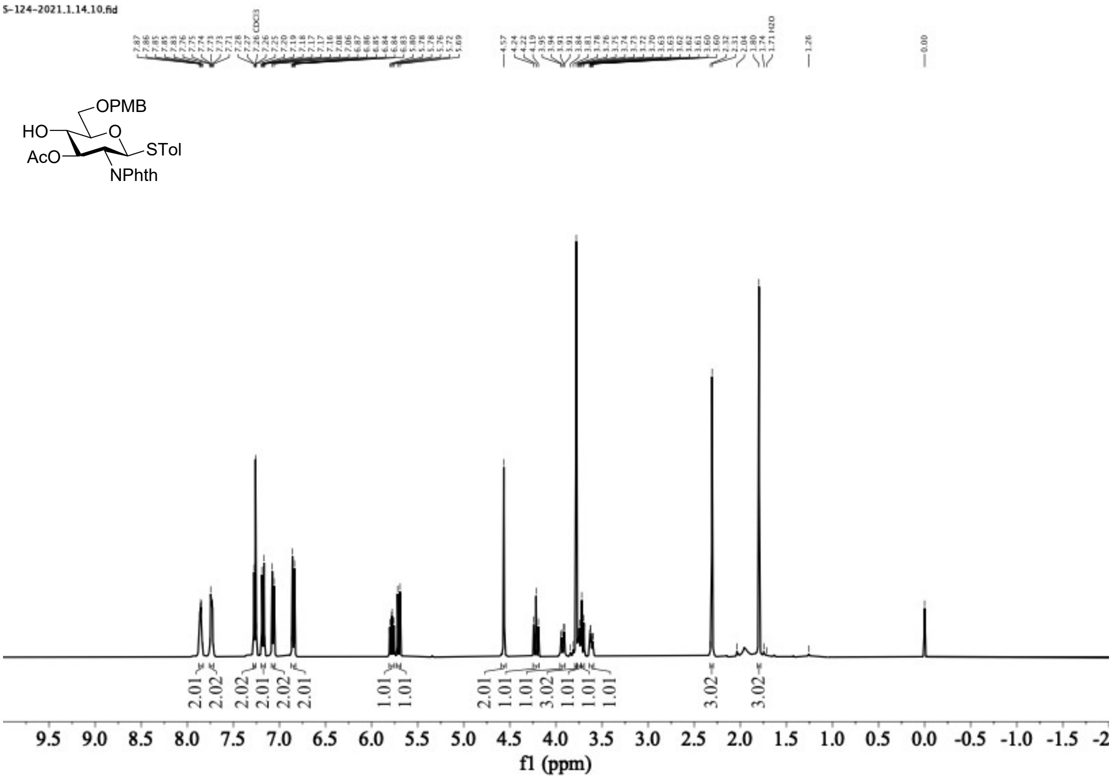
$^{13}C\{^{1}H\}$ NMR spectrum of compound **55** ($CDCl_3$, 100 MHz)



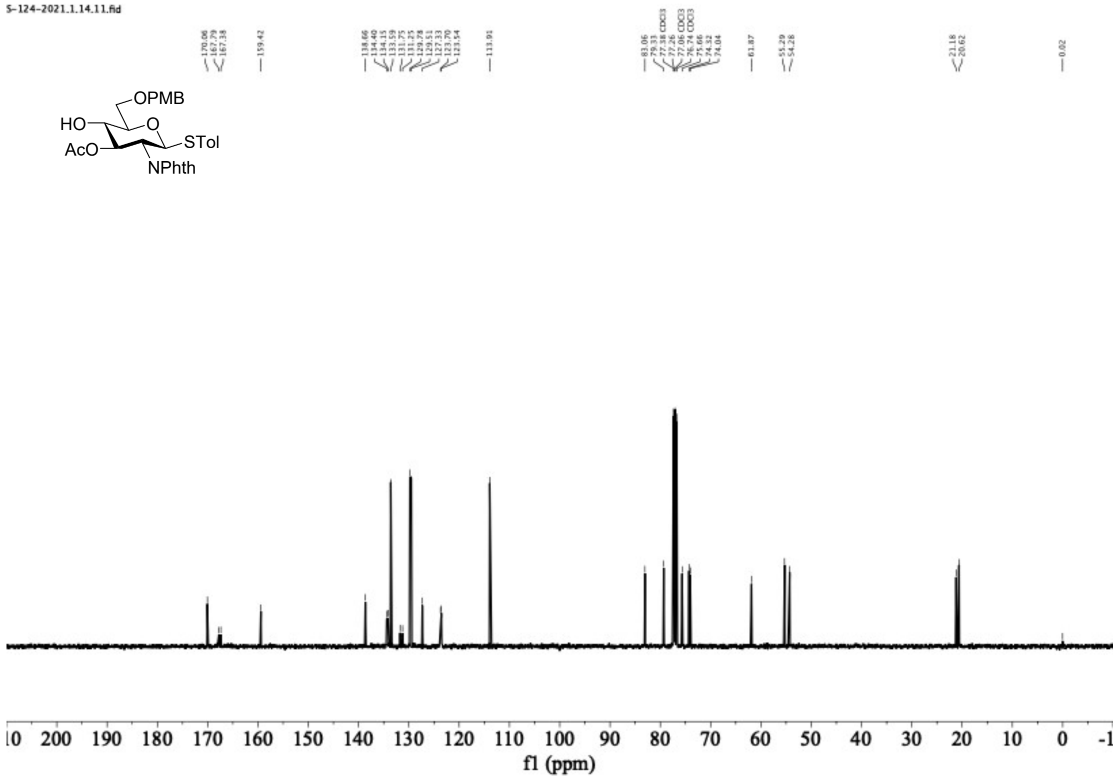
^{1}H – ^{13}C HMQC spectrum of compound **55** ($CDCl_3$, 400/100 MHz)



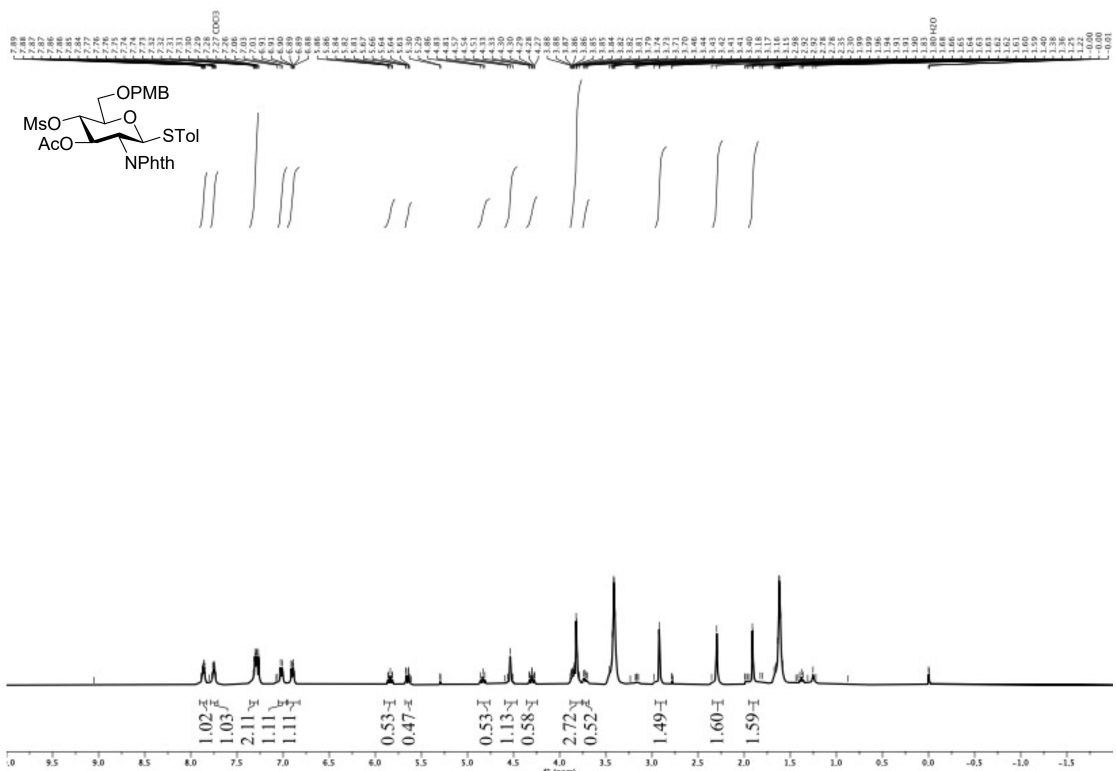
HRMS spectrum of compound **55**



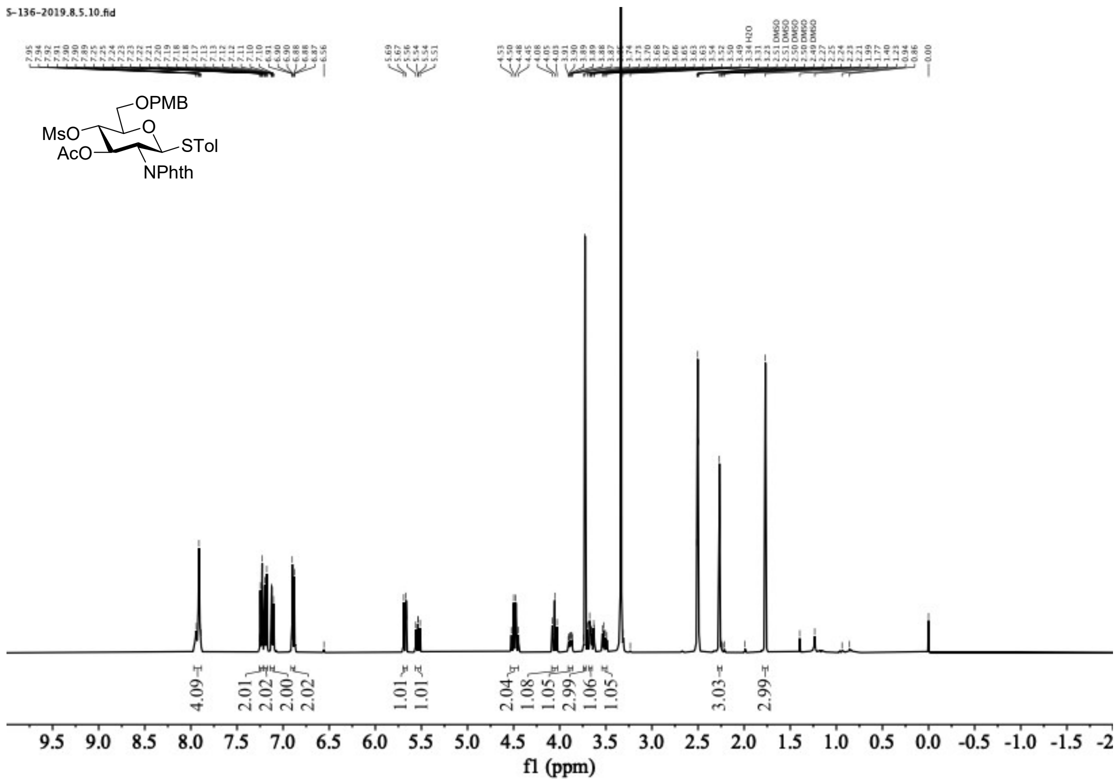
^{1}H NMR spectrum of compound **56** ($CDCl_3$, 400 MHz)



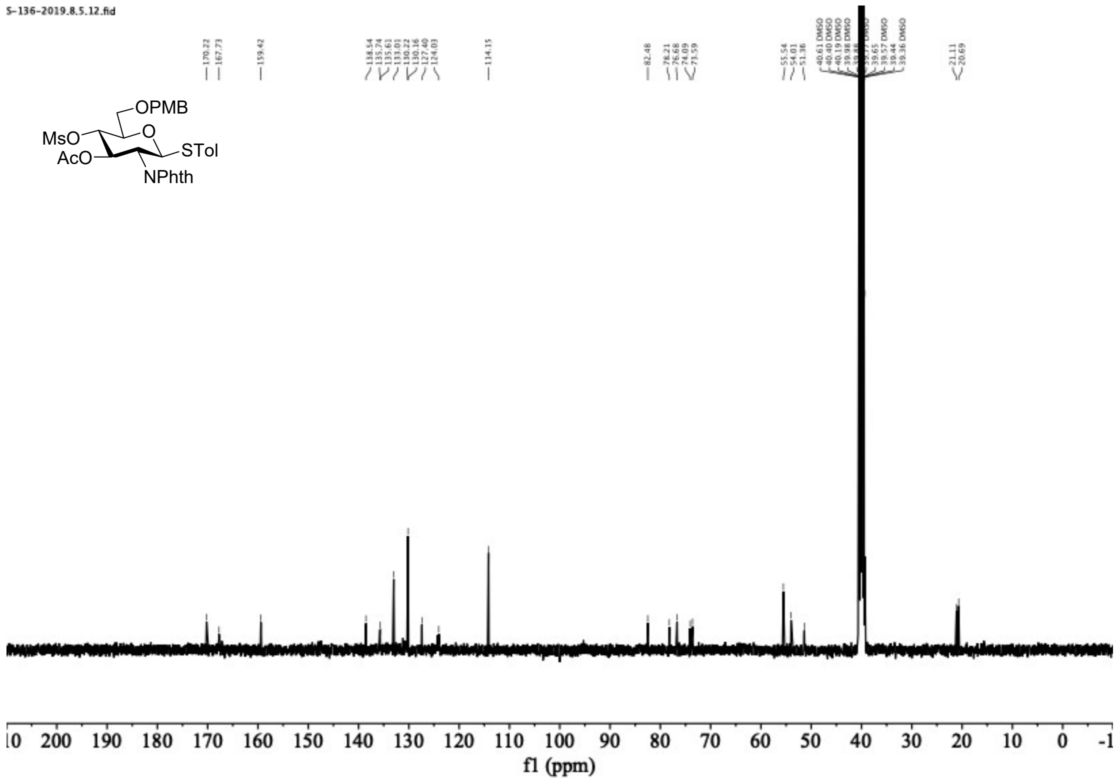
$^{13}C\{^{1}H\}$ NMR spectrum of compound **56** ($CDCl_3$, 100 MHz)



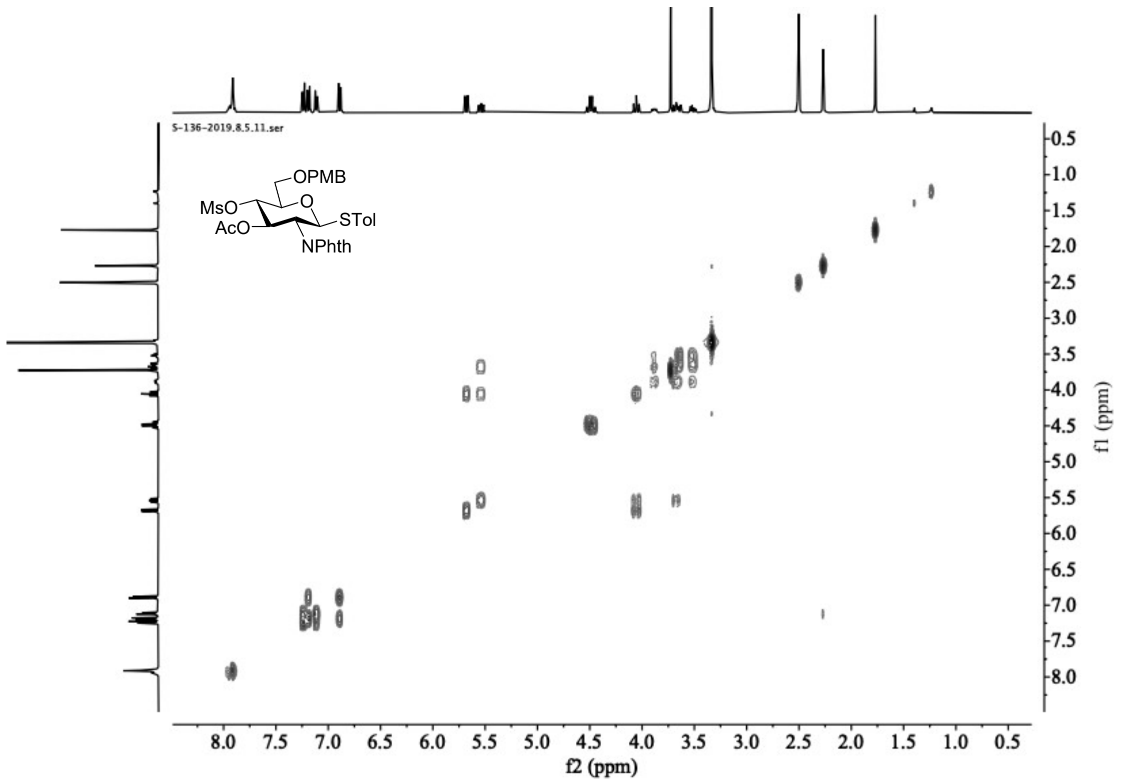
^{1}H NMR spectrum of compound **57** ($CDCl_3$, 400 MHz)



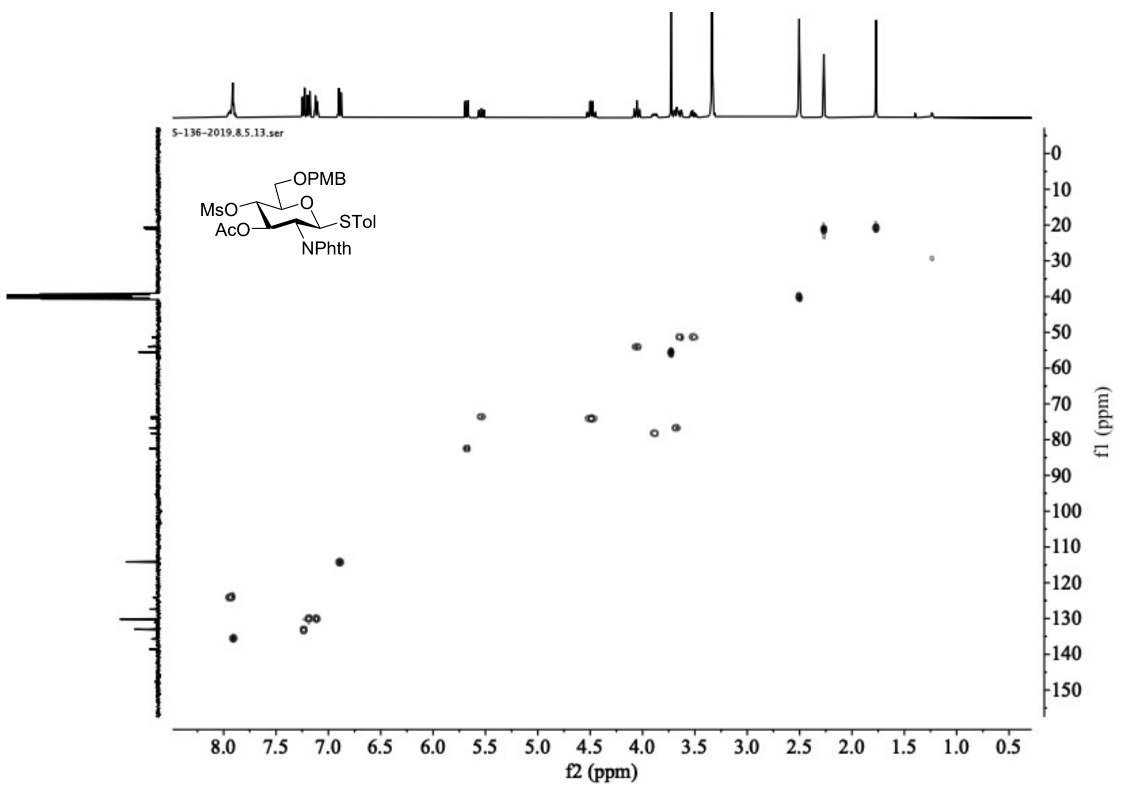
^{1}H NMR spectrum of compound **58** ($CDCl_3$, 400 MHz)



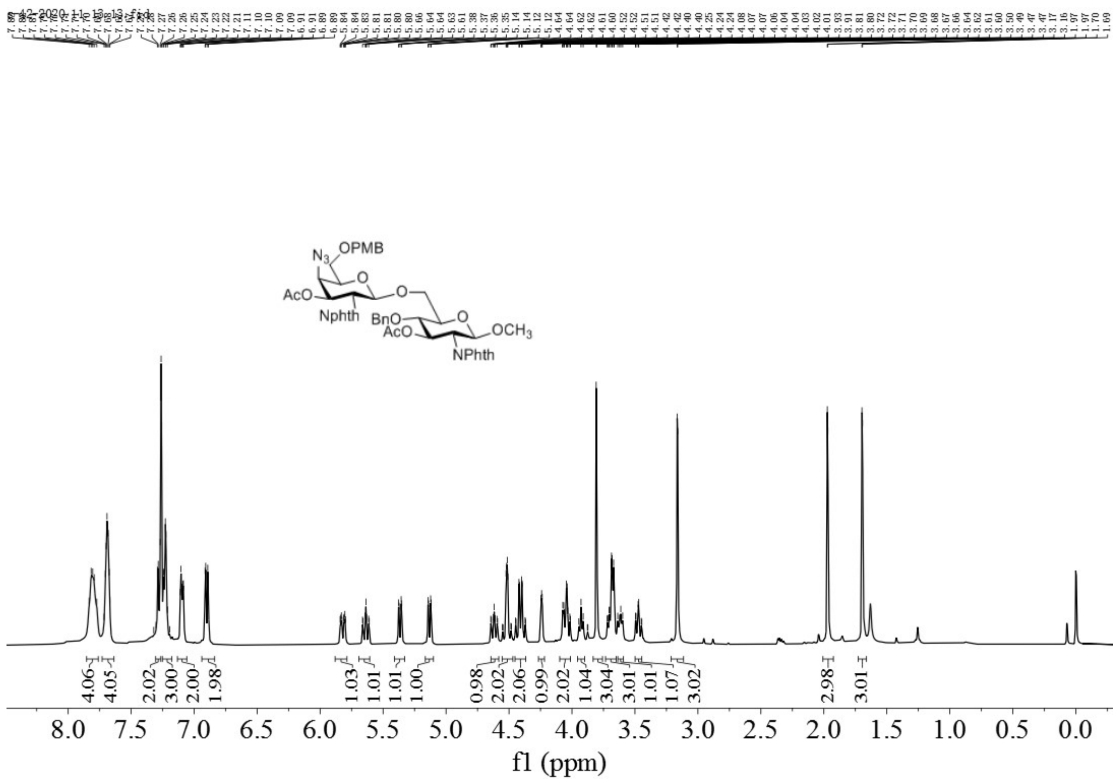
$^{13}C\{^{1}H\}$ NMR spectrum of compound **58** ($CDCl_3$, 100 MHz)



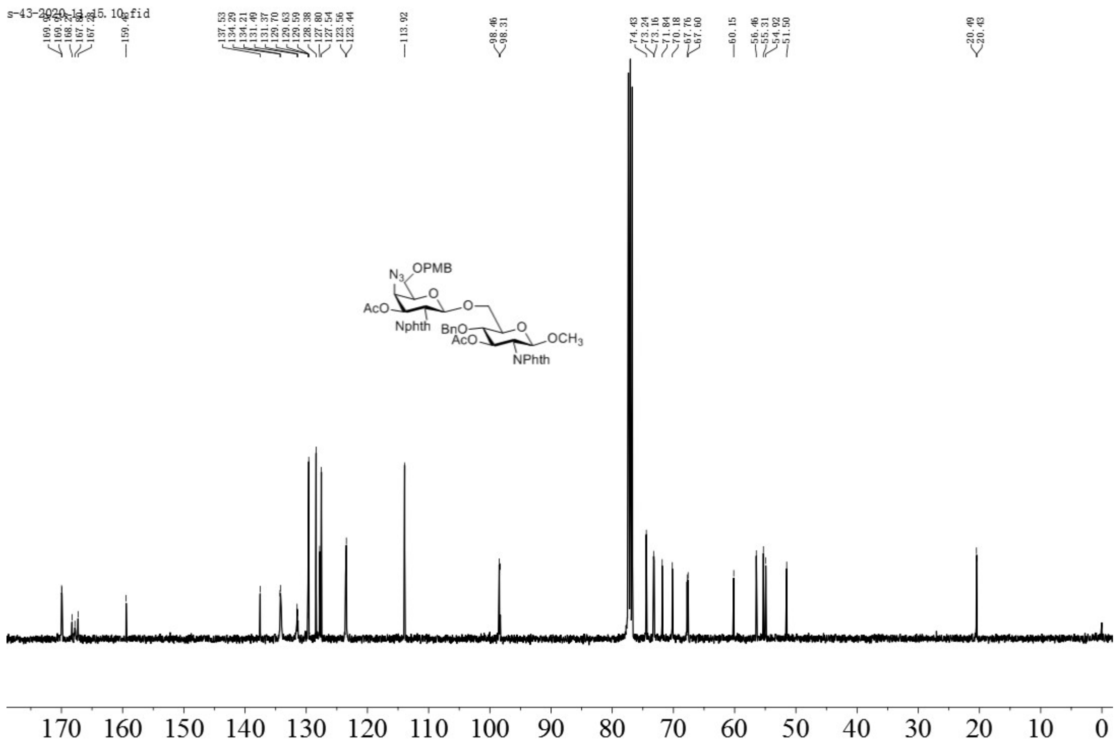
^1H – ^1H COSY spectrum of compound **58** ($CDCl_3$, 400 MHz)



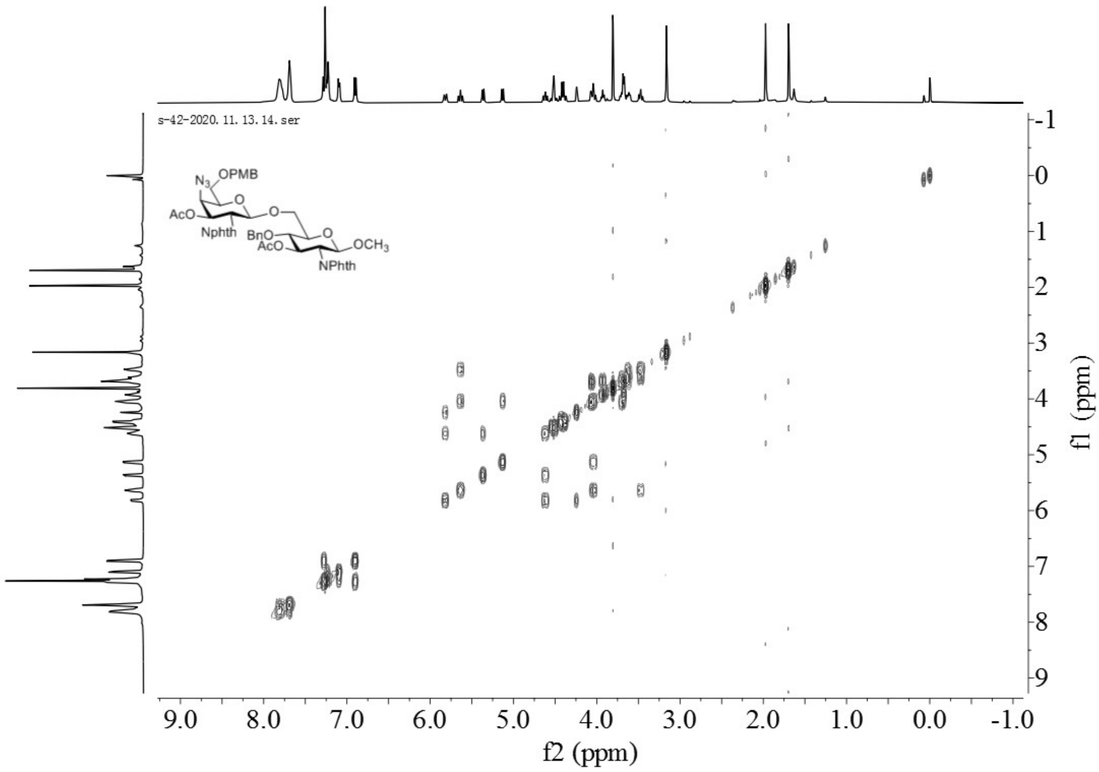
^1H – ^{13}C HMQC spectrum of compound **58** ($CDCl_3$, 400/100 MHz)



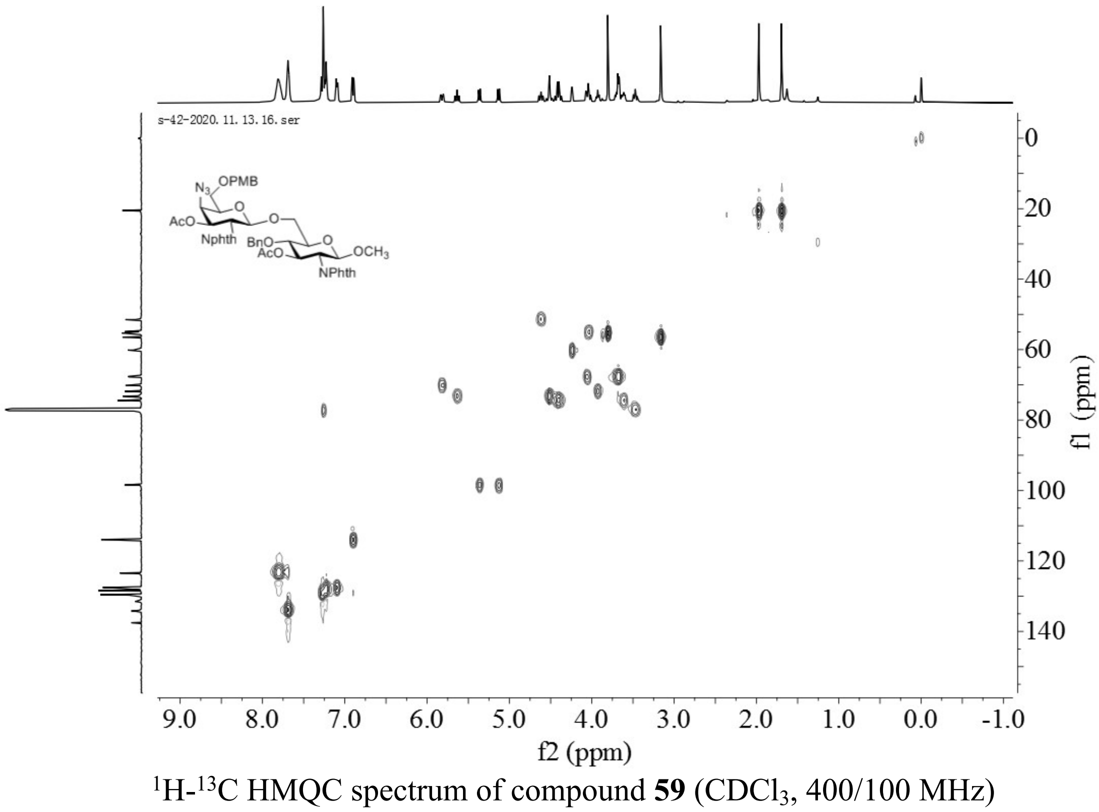
^{1}H NMR spectrum of compound **59** ($CDCl_3$, 400 MHz)



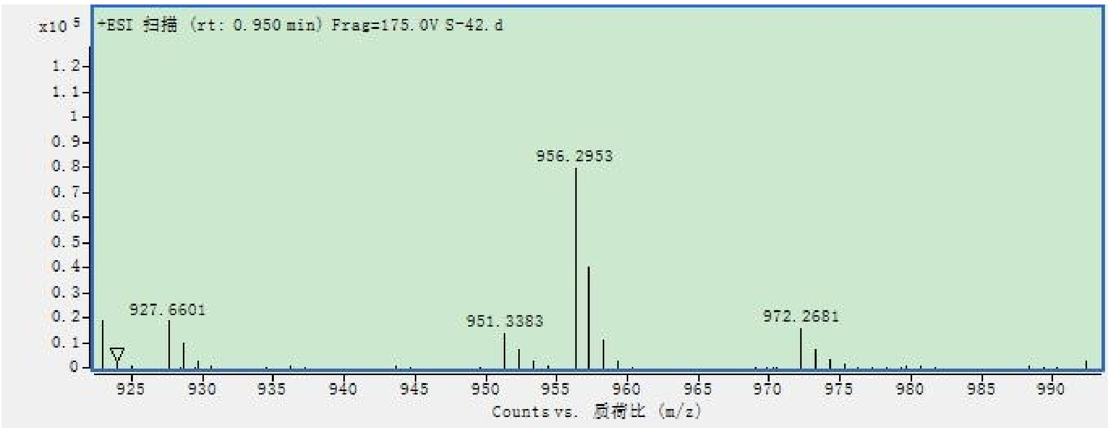
$^{13}C\{^{1}H\}$ NMR spectrum of compound **59** ($CDCl_3$, 100 MHz)



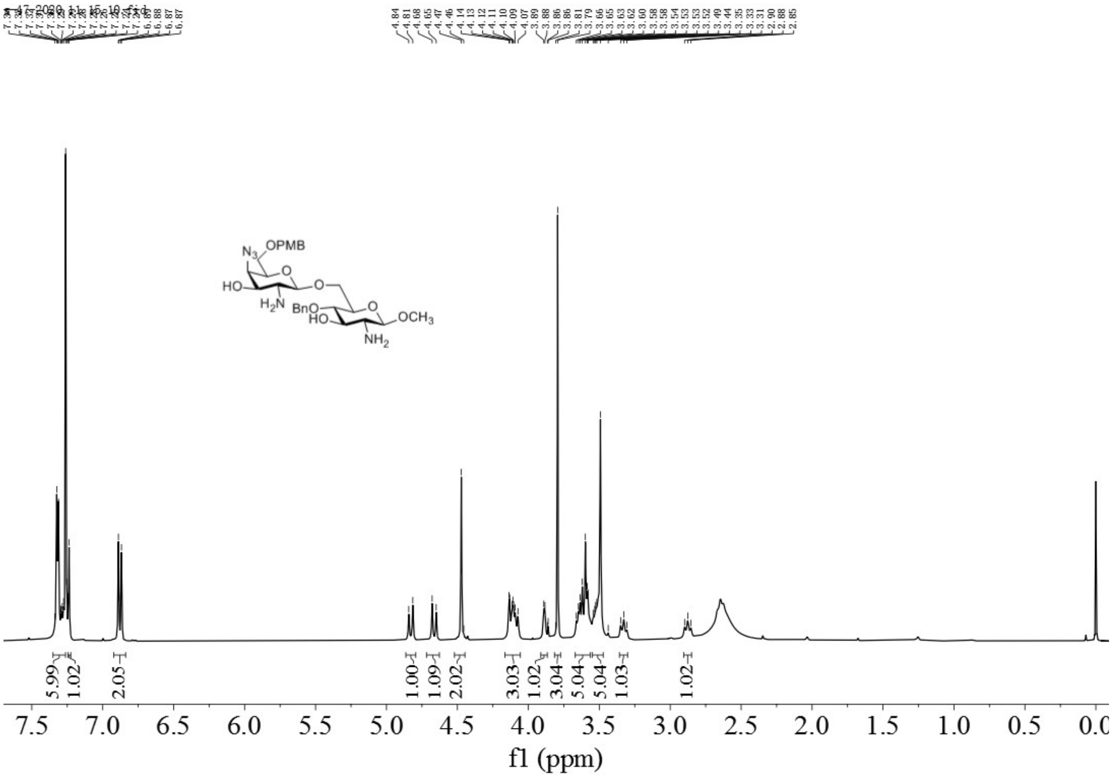
^1H-^1H COSY spectrum of compound **59** ($CDCl_3$, 400 MHz)



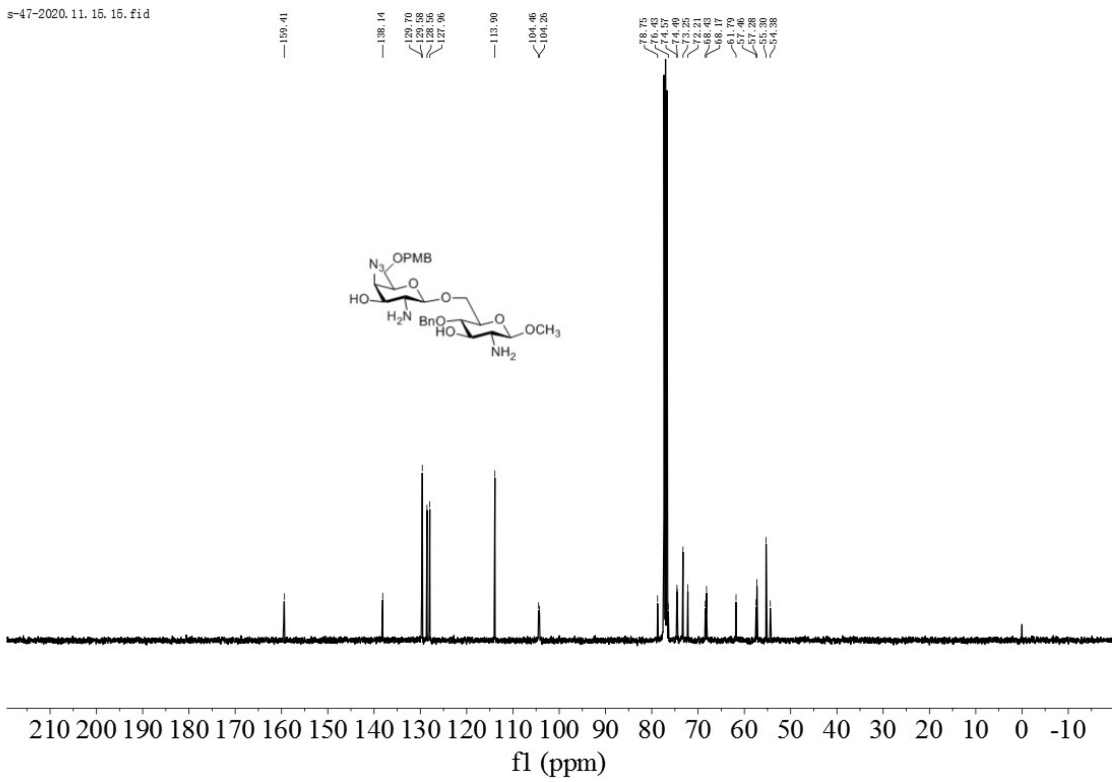
^1H-^{13}C HMQC spectrum of compound **59** ($CDCl_3$, 400/100 MHz)



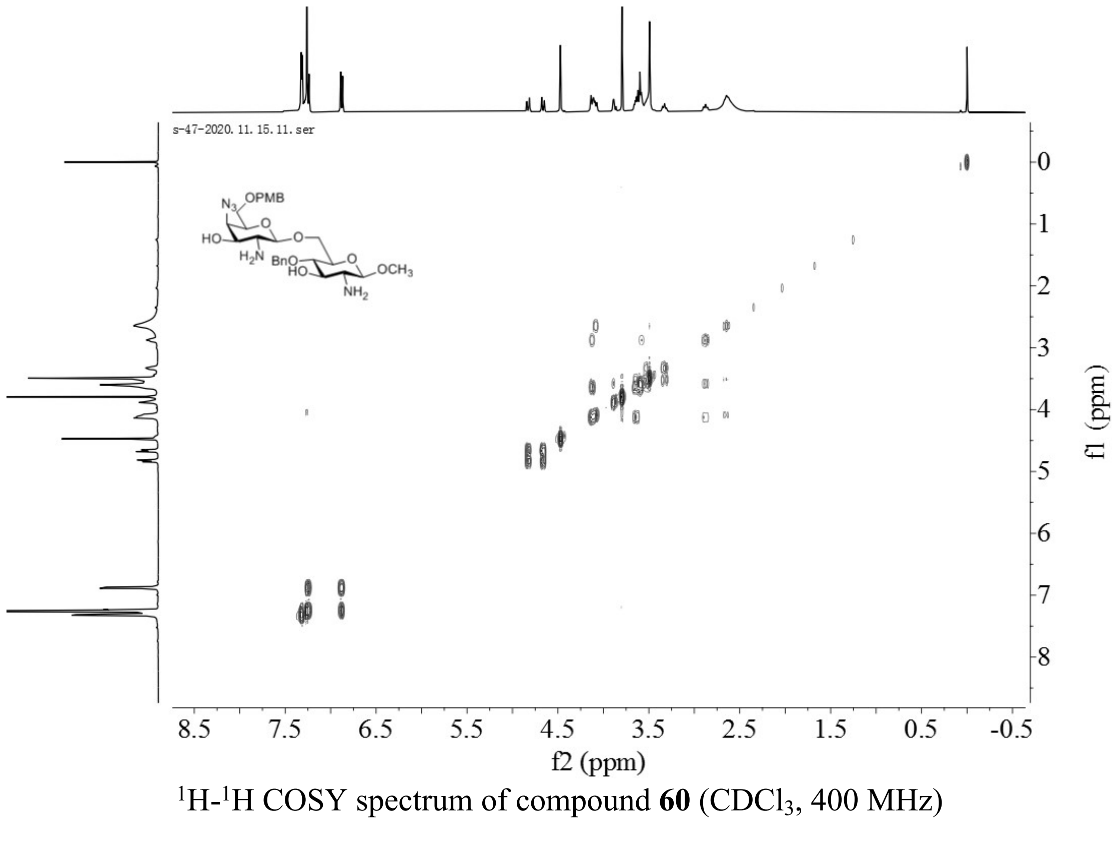
HRMS spectrum of Compound **59**



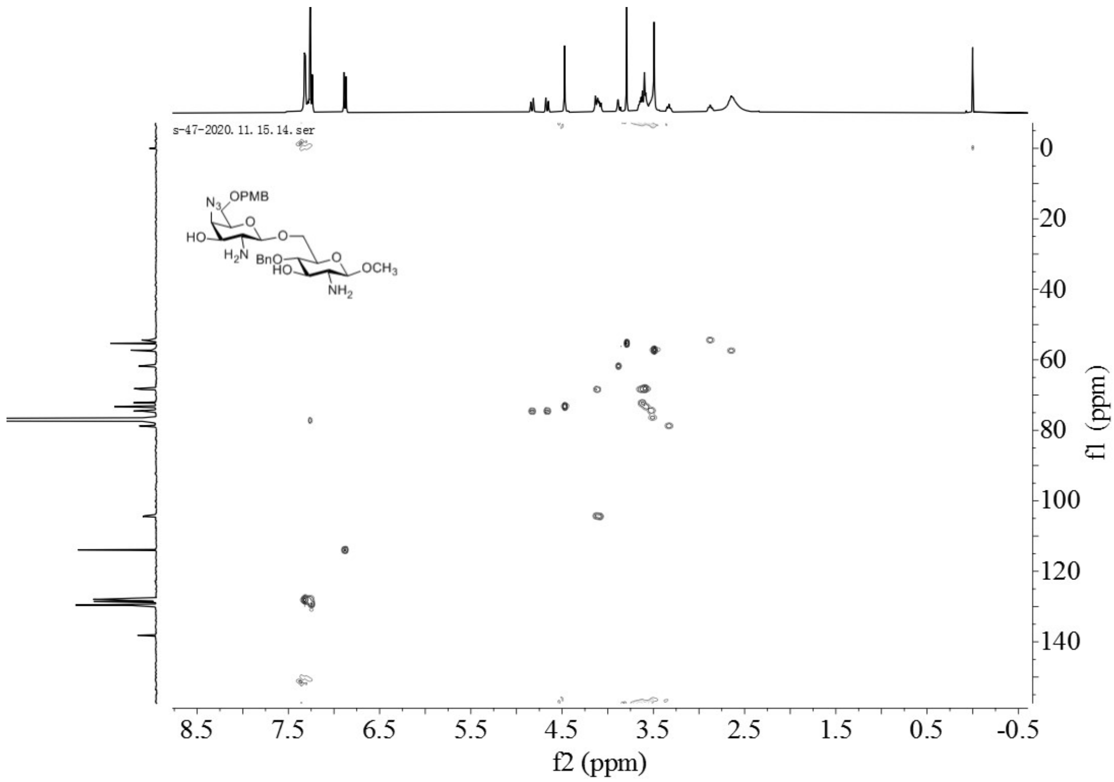
[1]H NMR spectrum of compound **60** ($CDCl_3$, 400 MHz)



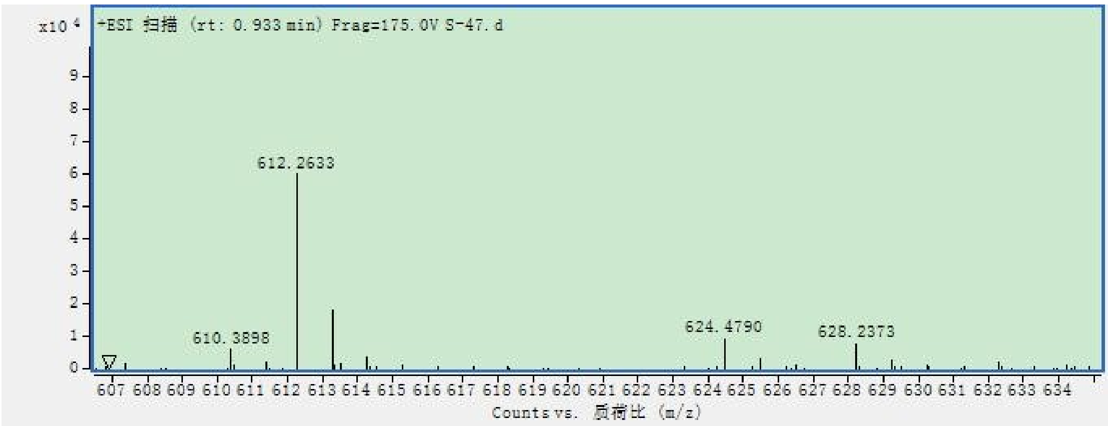
$^{13}C\{^{1}H\}$ NMR spectrum of compound **60** ($CDCl_3$, 100 MHz)



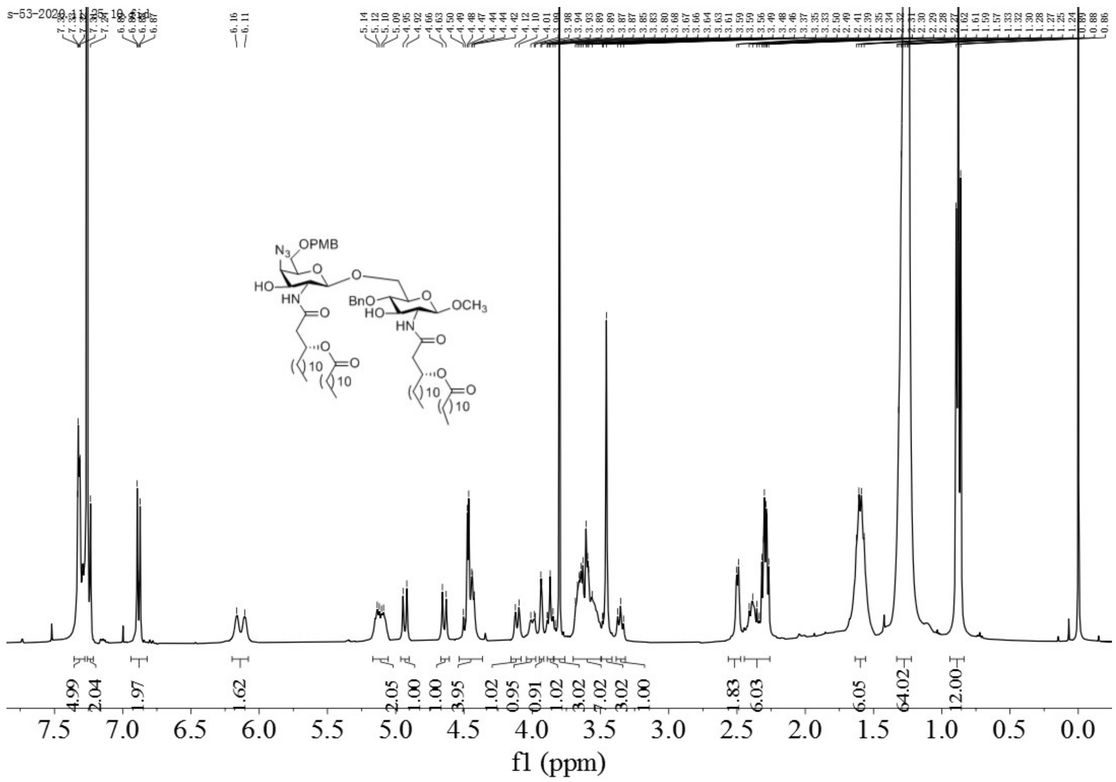
^{1}H-^{1}H COSY spectrum of compound **60** ($CDCl_3$, 400 MHz)



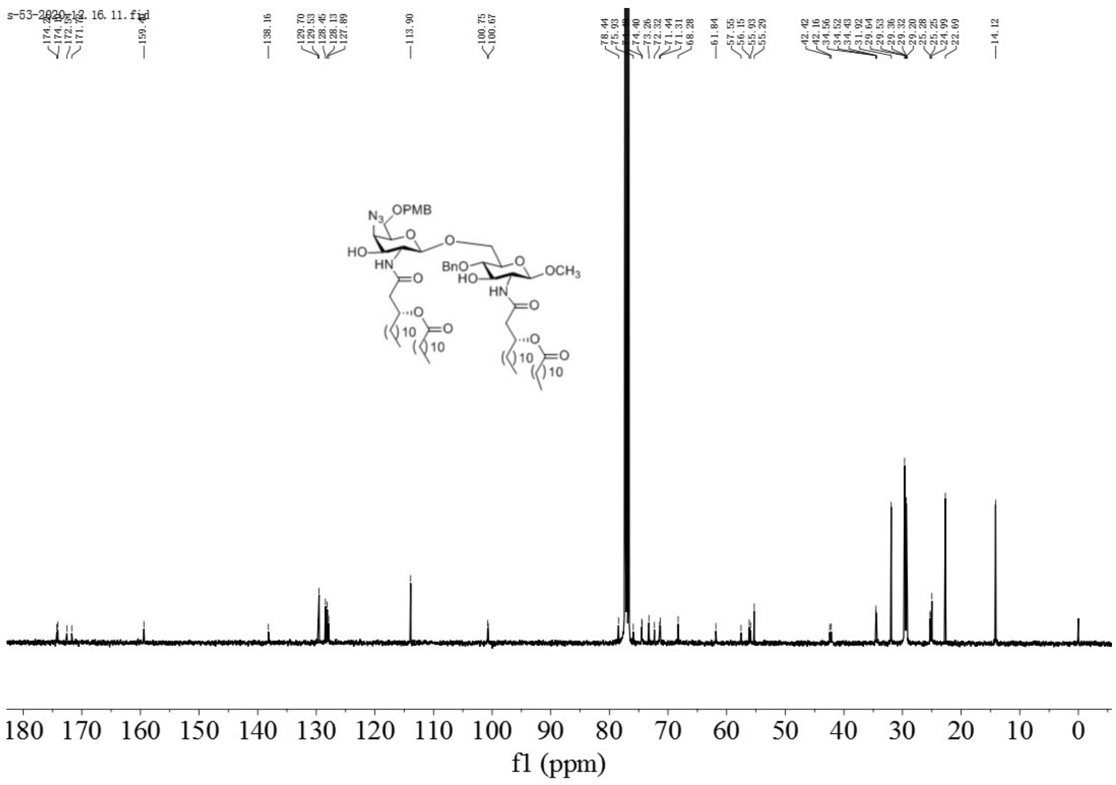
^{1}H-^{13}C HMQC spectrum of compound **60** ($CDCl_3$, 400/100 MHz)



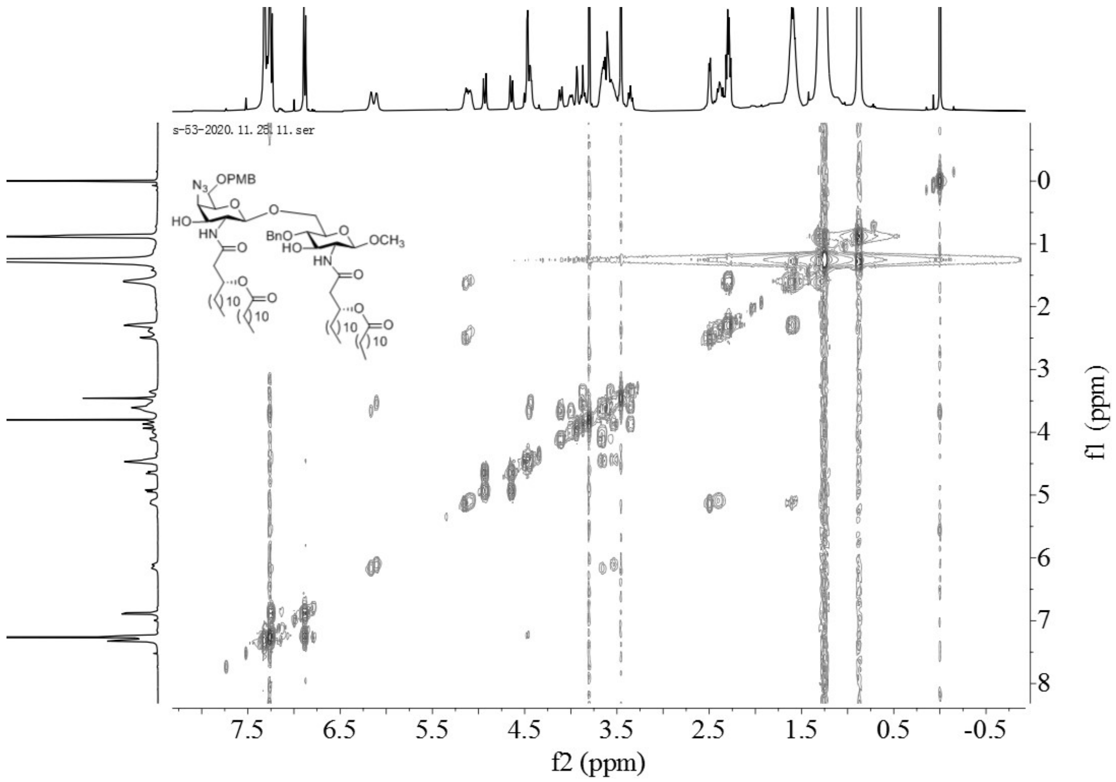
HRMS spectrum of compound **60**



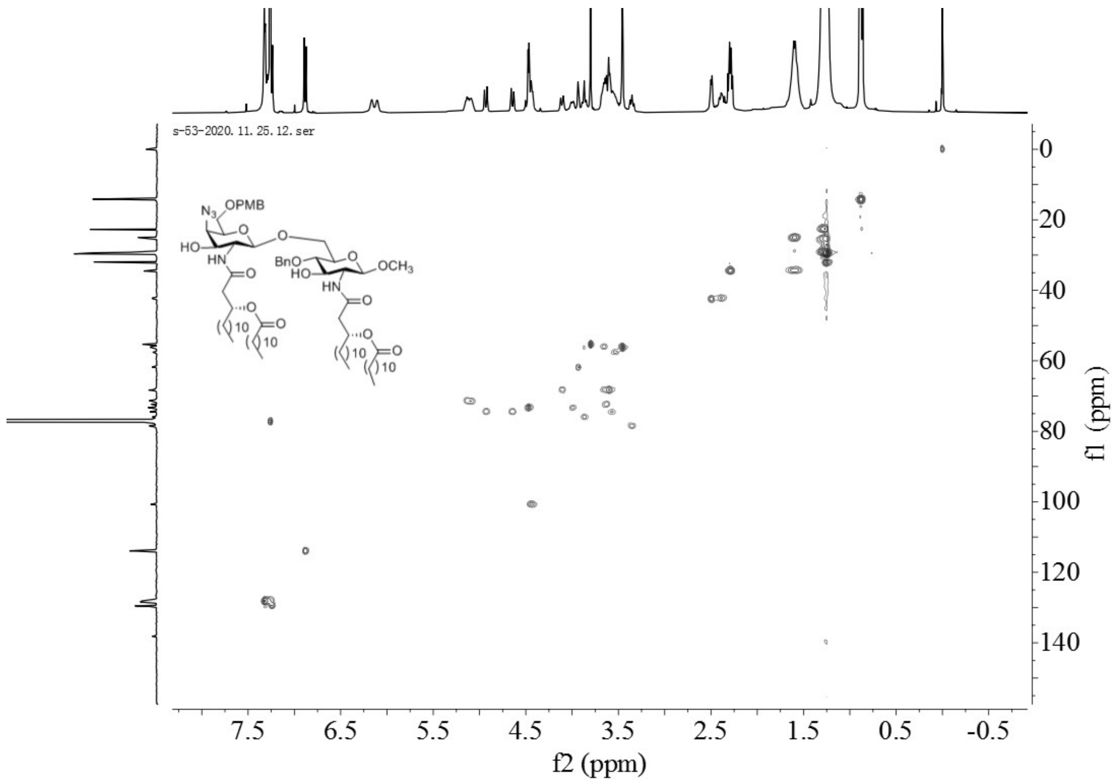
[1]H NMR spectrum of compound **61** ($CDCl_3$, 400 MHz)



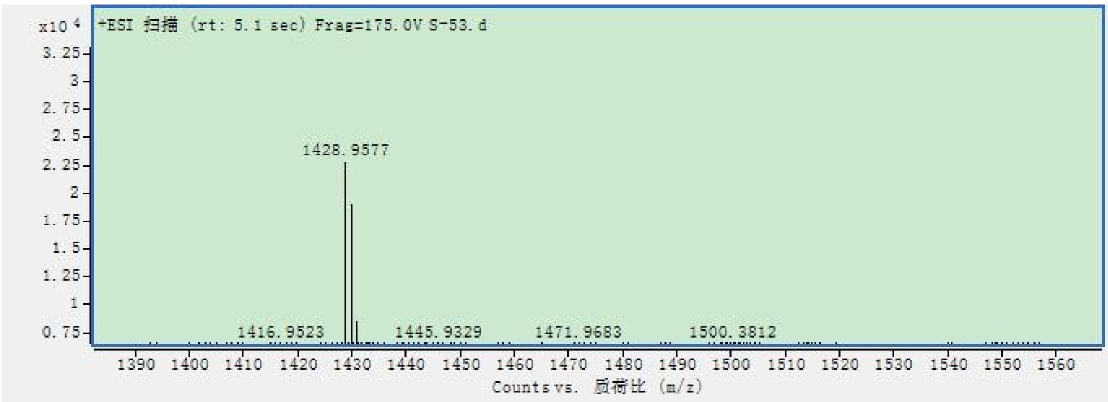
$^{13}C\{^1H\}$ NMR spectrum of compound **61** ($CDCl_3$, 100 MHz)



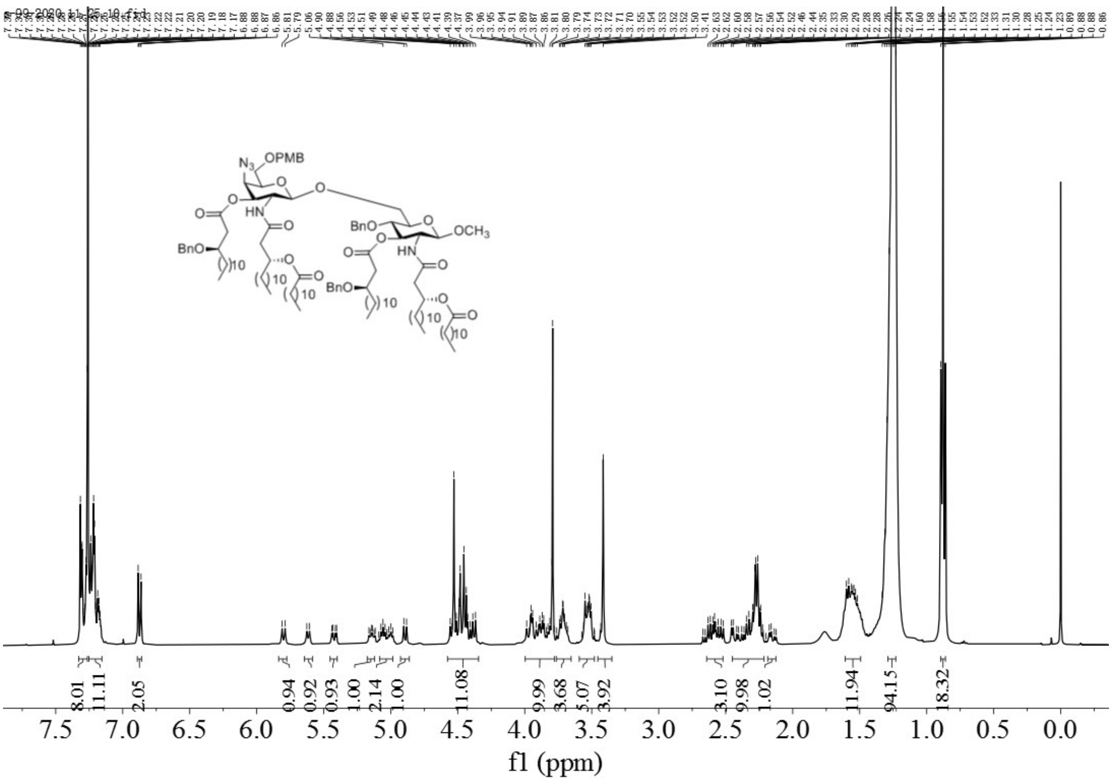
^{1}H-^{1}H COSY spectrum of compound **61** ($CDCl_3$, 400 MHz)



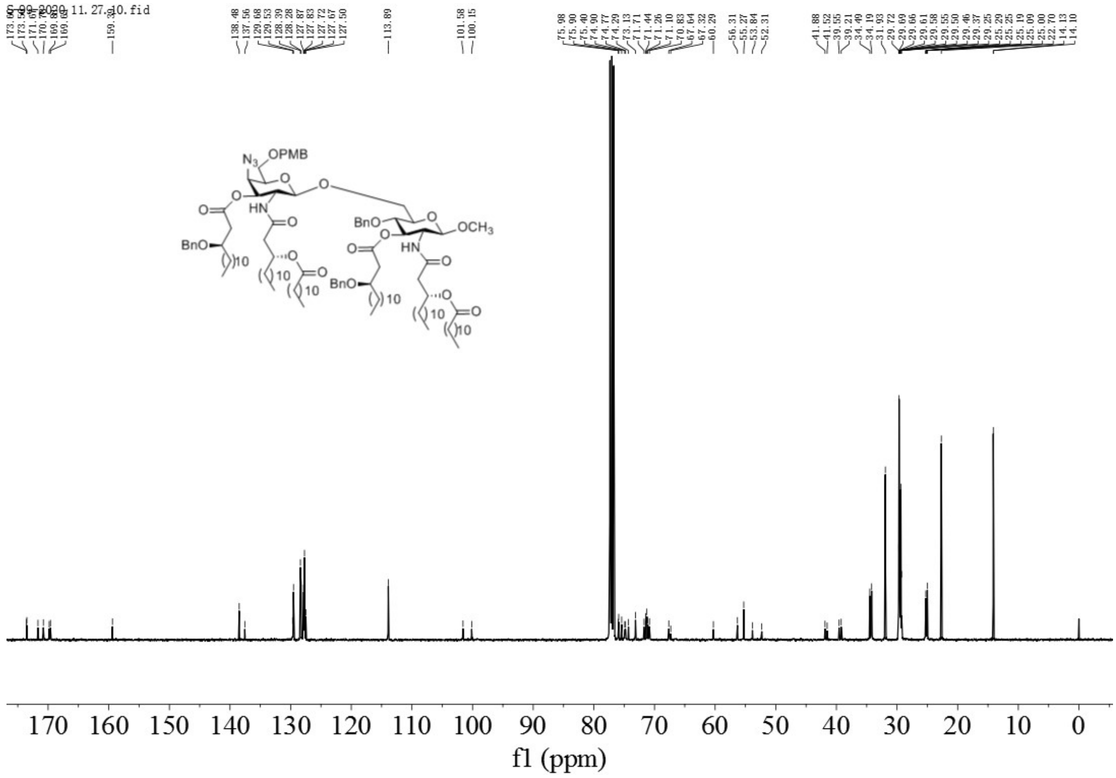
^{1}H-^{13}C HMQC spectrum of compound **61** ($CDCl_3$, 400/100 MHz)



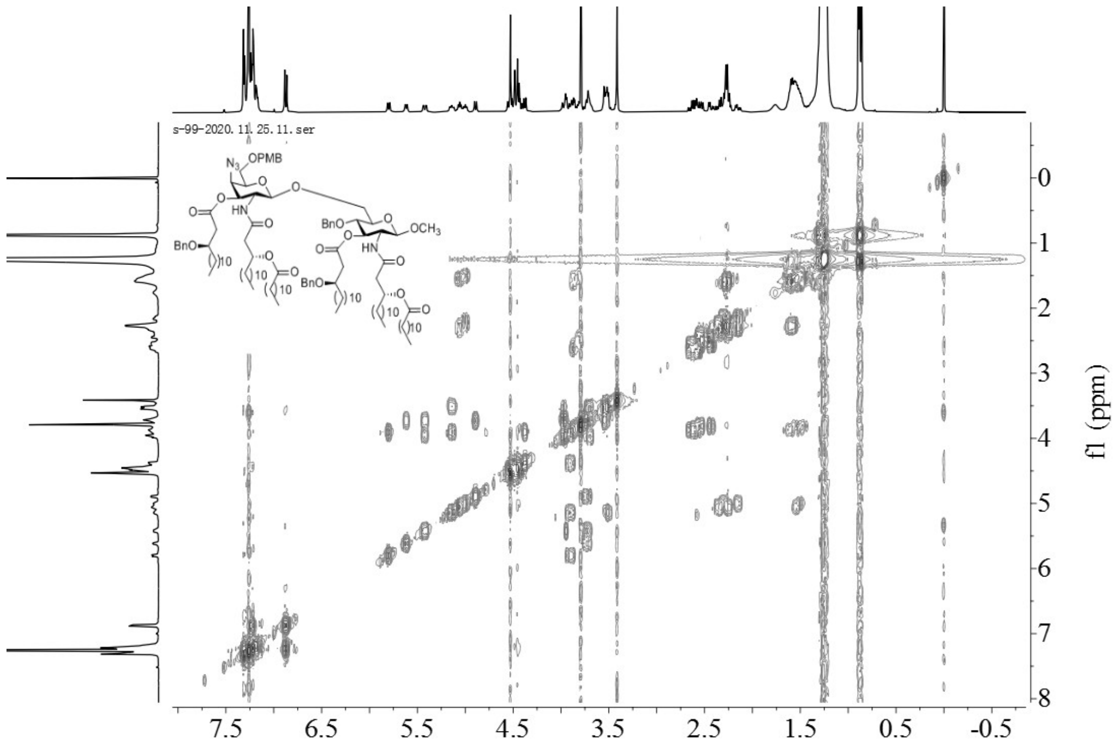
HRMS spectrum of compound **61**



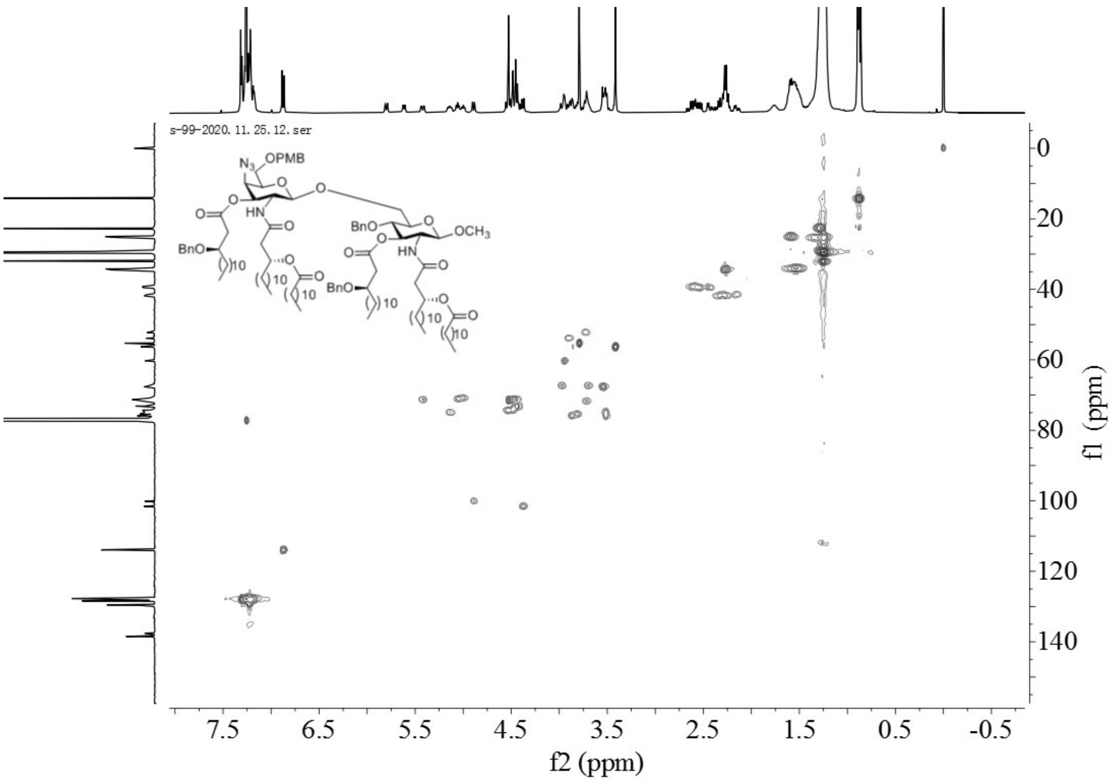
[1]H NMR spectrum of compound **62**($CDCl_3$, 400 MHz)



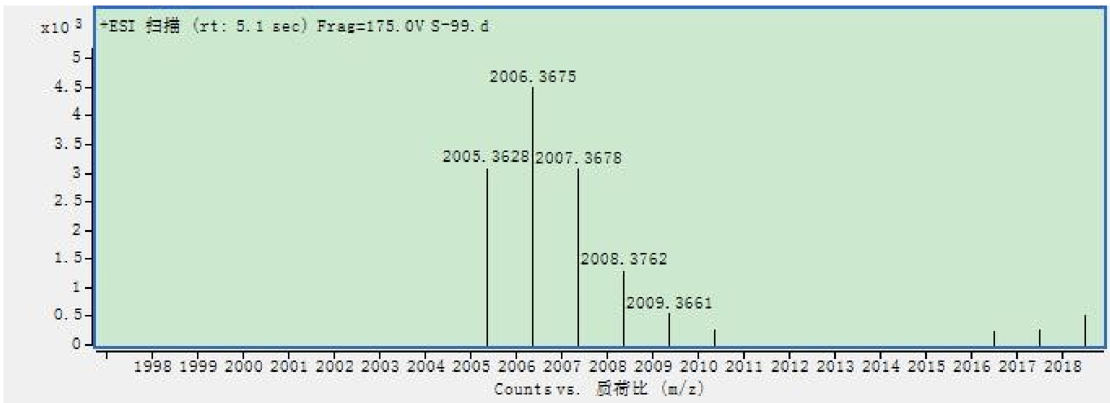
$^{13}C\{^1H\}$ NMR spectrum of compound **62** ($CDCl_3$, 100 MHz)



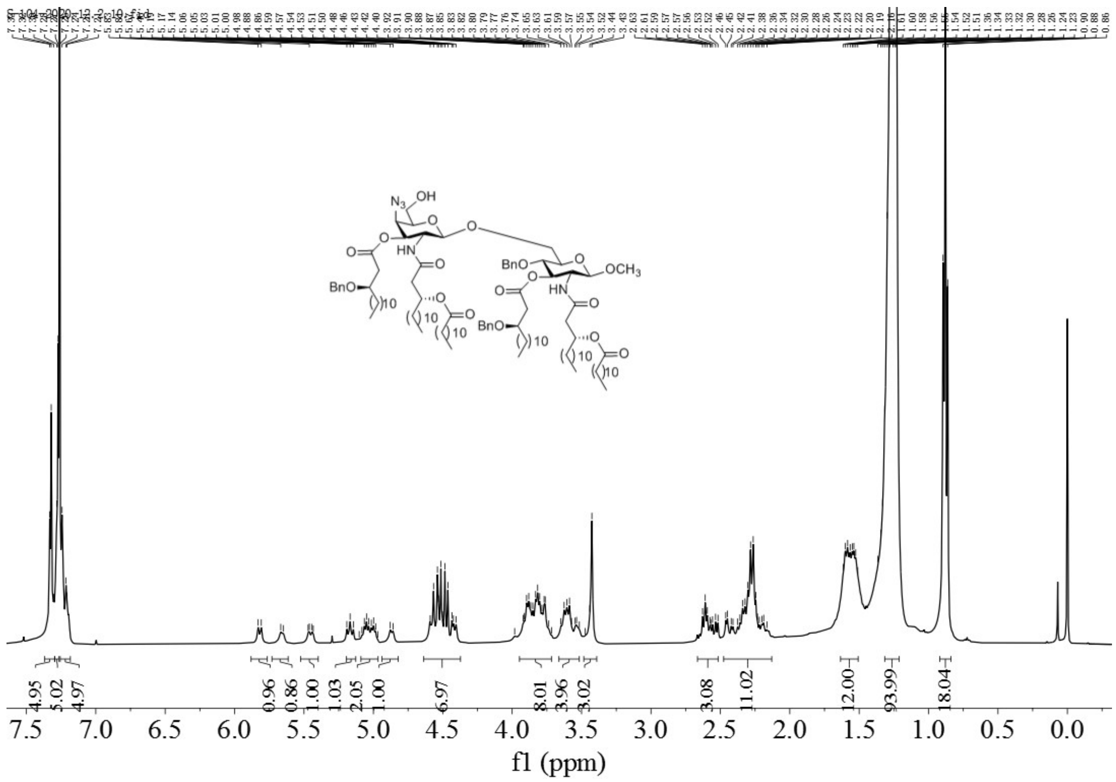
^1H-^1H COSY spectrum of compound **62** ($CDCl_3$, 400 MHz)



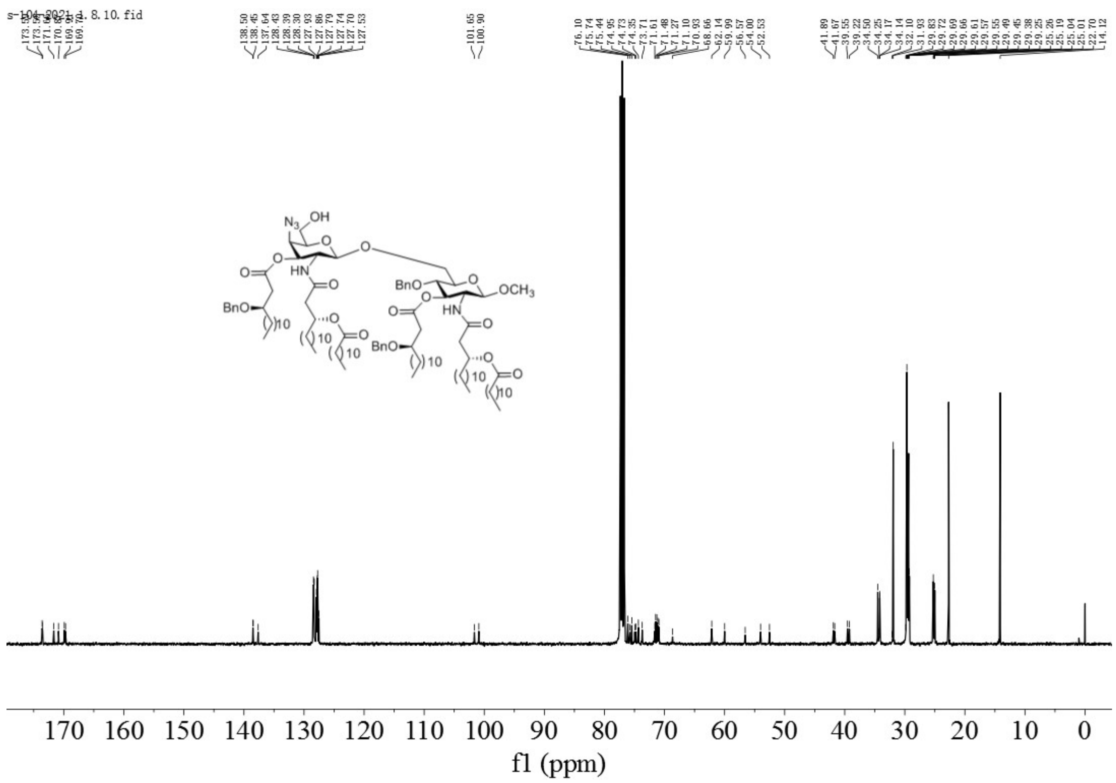
^{1}H-^{13}C HMQC spectrum of compound **62** ($CDCl_3$, 400/100 MHz)



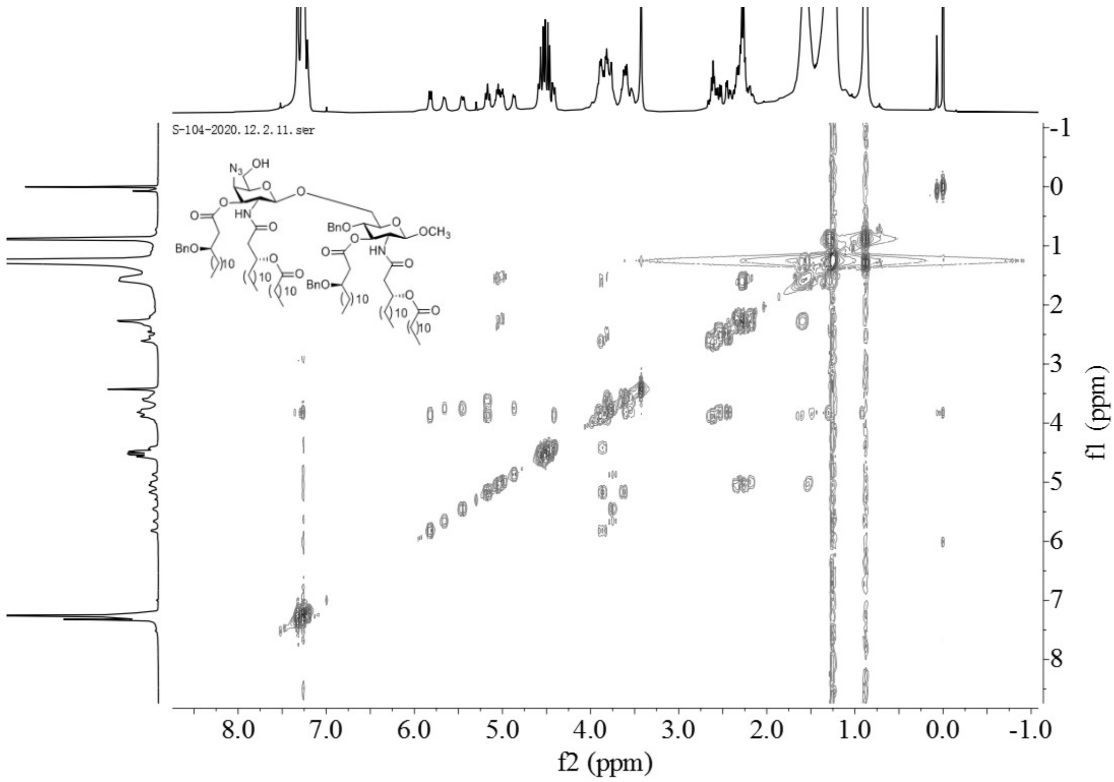
HRMS spectrum of compound **62**



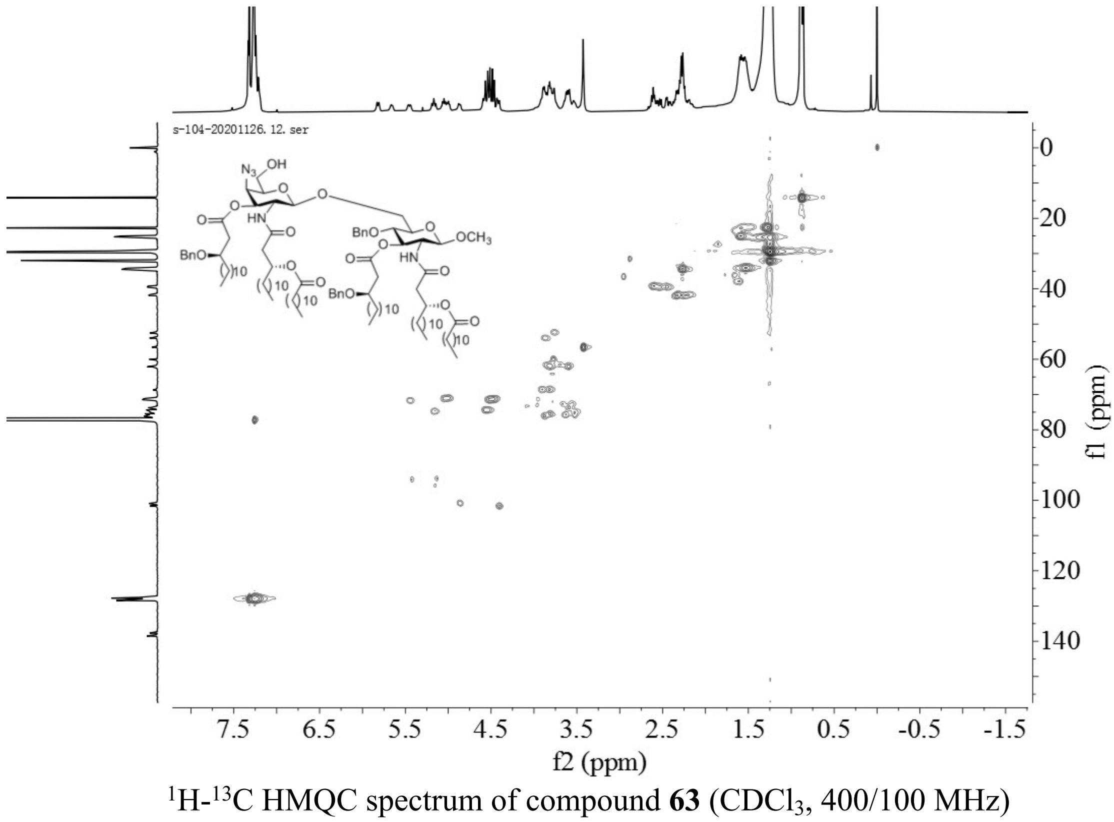
[1]H NMR spectrum of compound **63** ($CDCl_3$, 400 MHz)



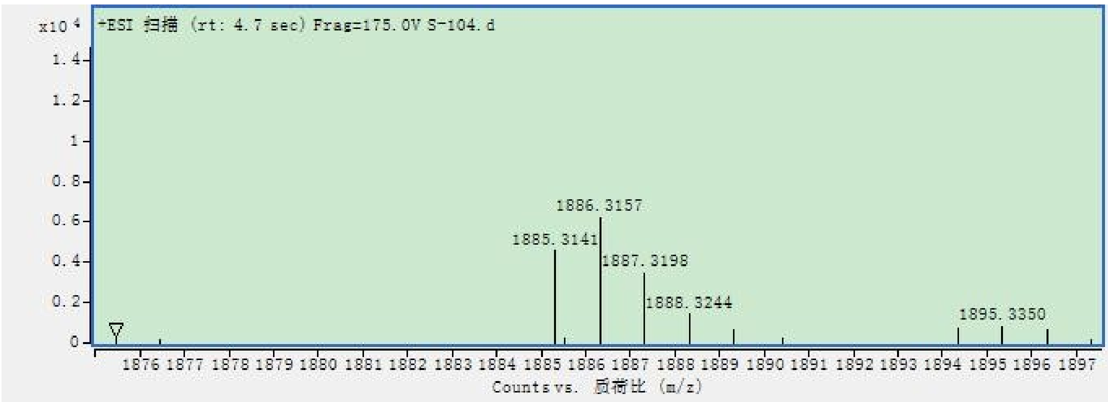
$^{13}C\{^1H\}$ NMR spectrum of compound **63** ($CDCl_3$, 100 MHz)



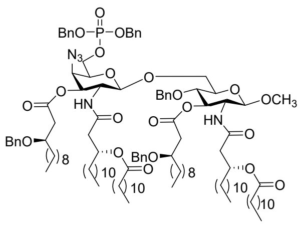
^{1}H-^{1}H COSY spectrum of compound **63** ($CDCl_3$, 400 MHz)

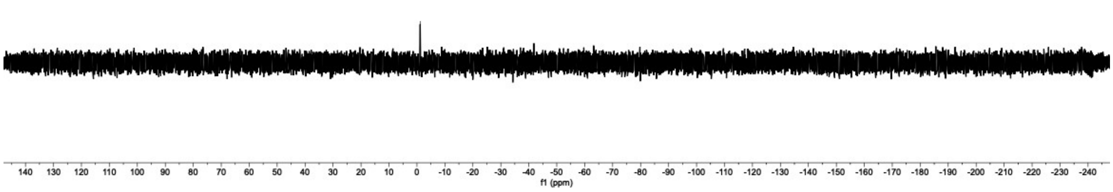


^{1}H-^{13}C HMQC spectrum of compound **63** ($CDCl_3$, 400/100 MHz)

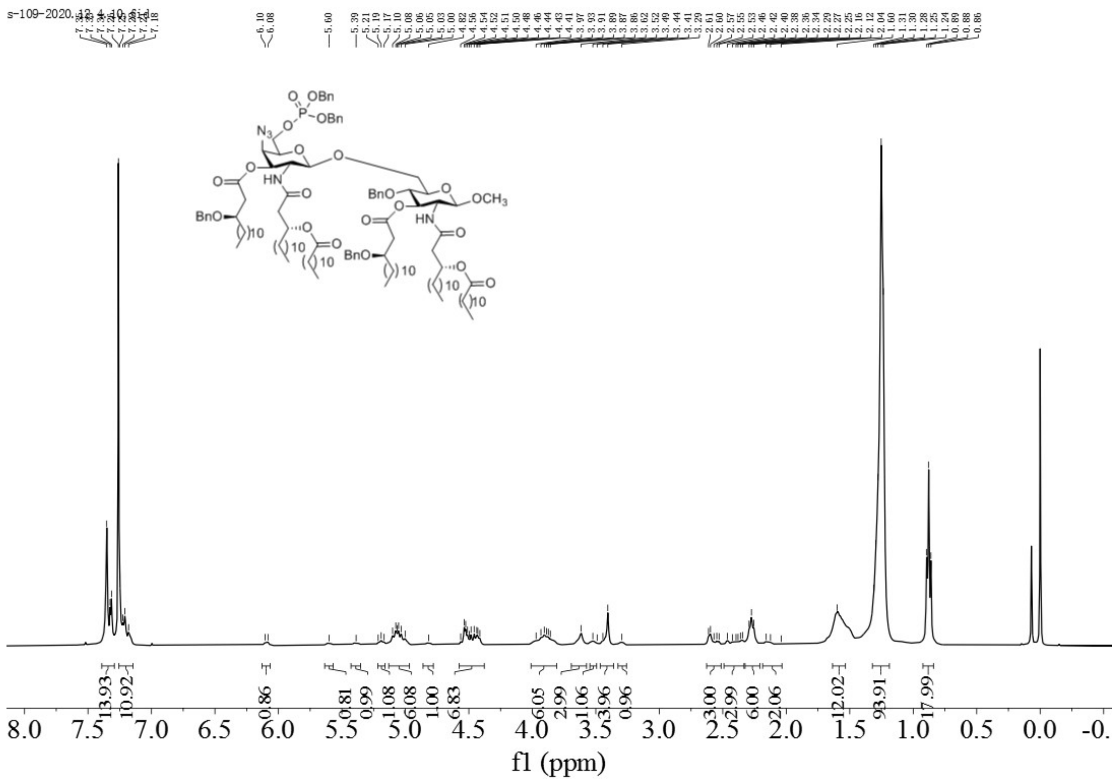


HRMS spectrum of compound **63**

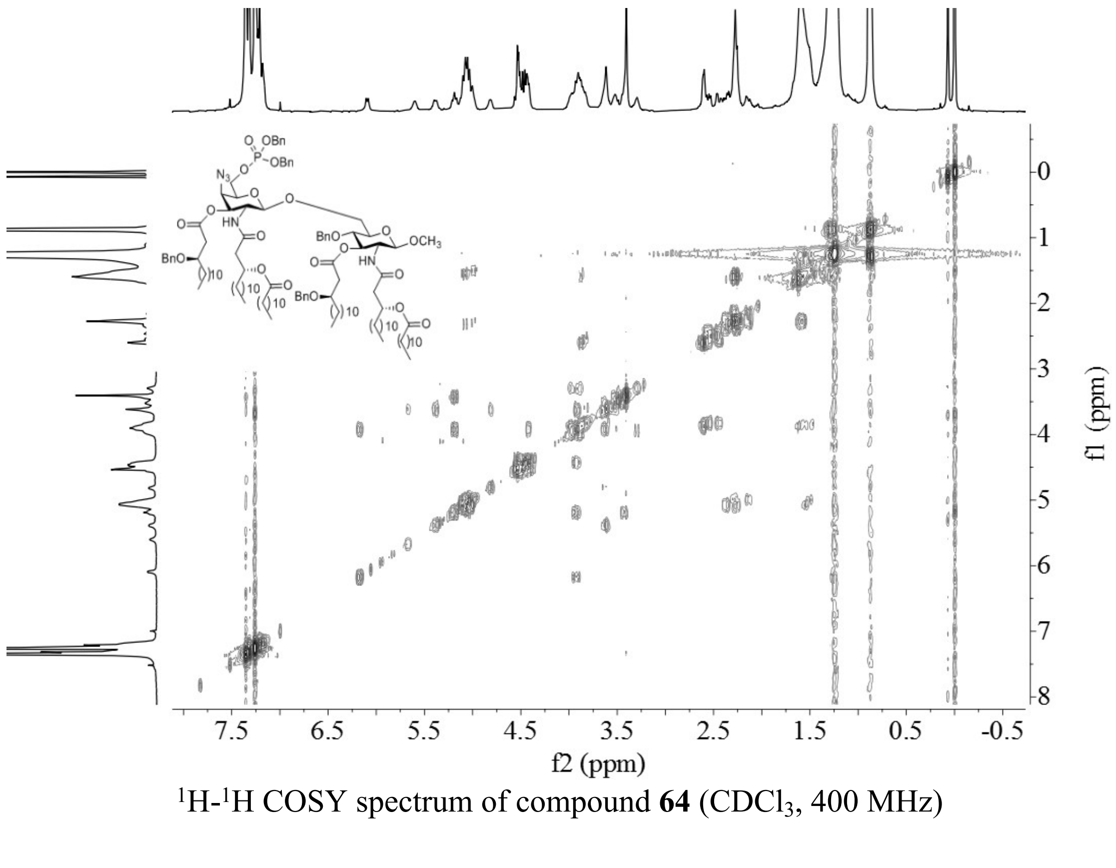




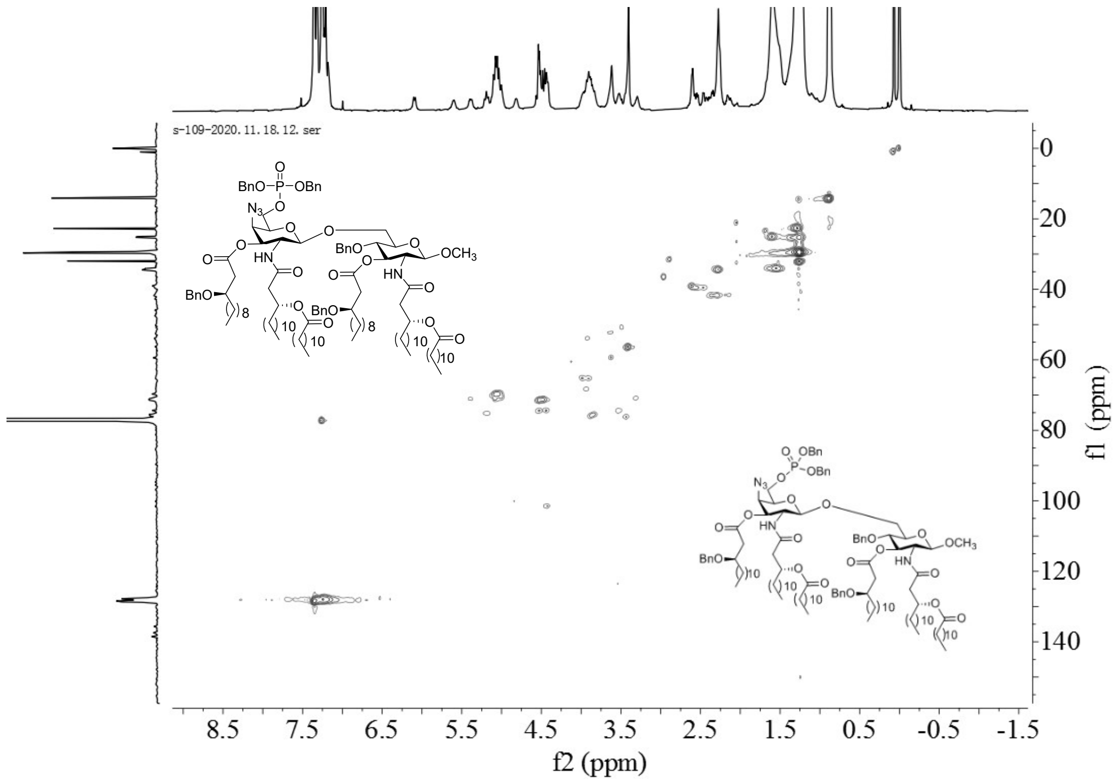
^{31}P NMR spectrum of compound **64** ($CDCl_3$, 162 MHz)



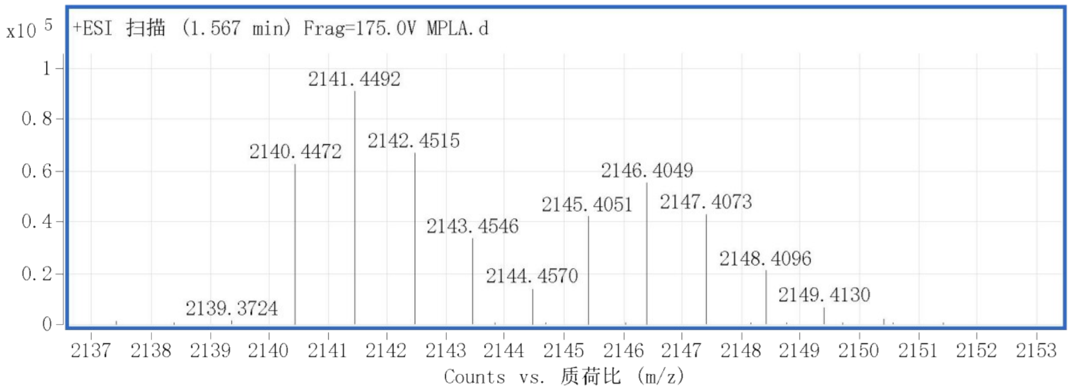
[1]H NMR spectrum of compound **64** ($CDCl_3$, 400 MHz)



[1]H-[1]H COSY spectrum of compound **64** ($CDCl_3$, 400 MHz)

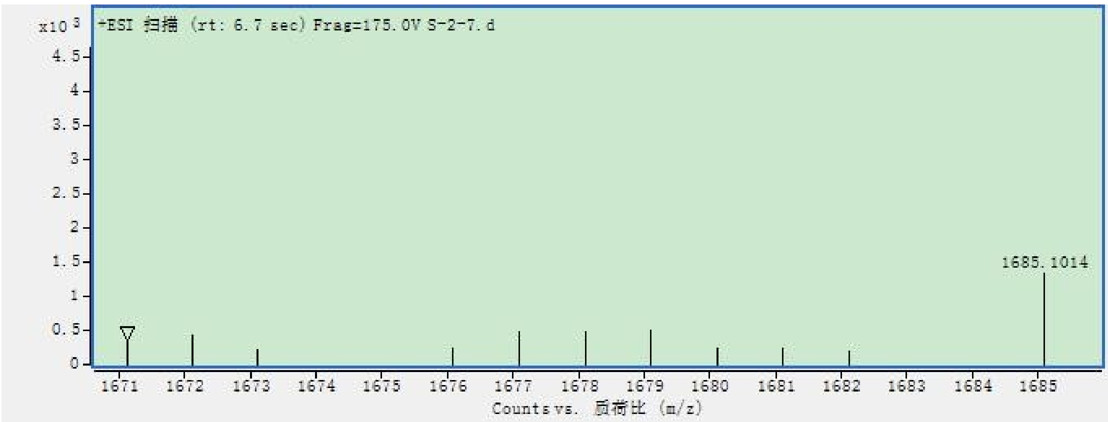


^{1}H-^{13}C HMQC spectrum of compound **64** ($CDCl_3$, 400/100 MHz)

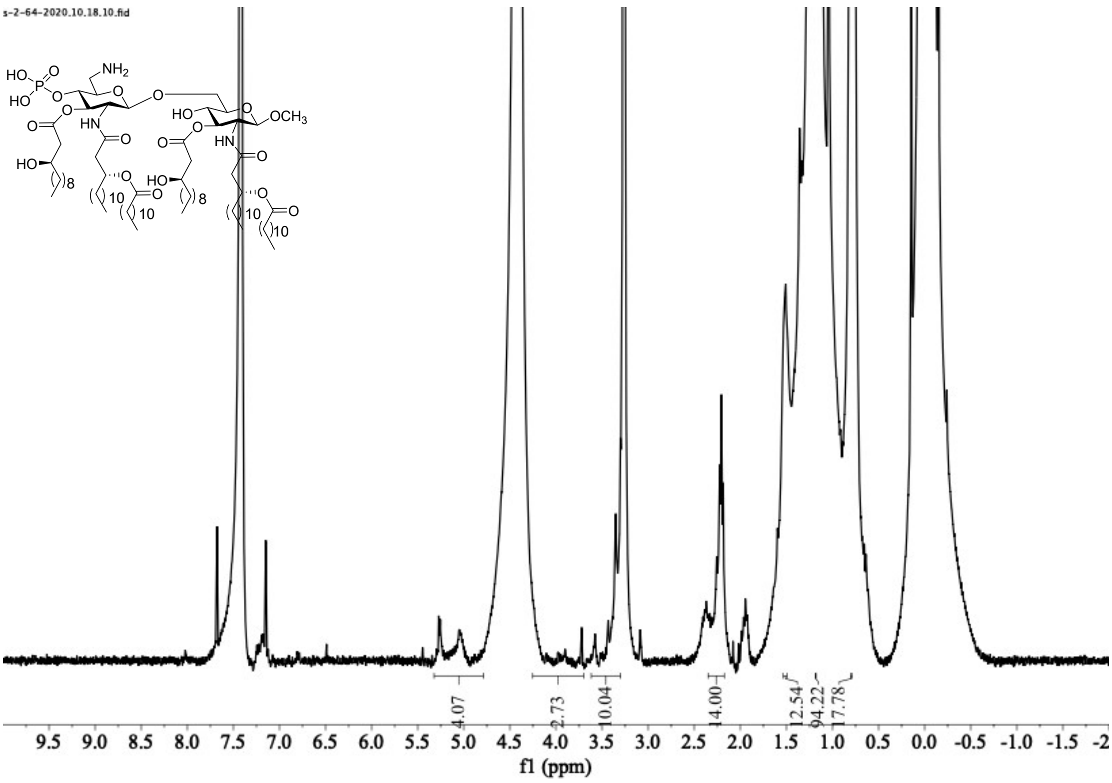


HRMS spectrum of compound **64**

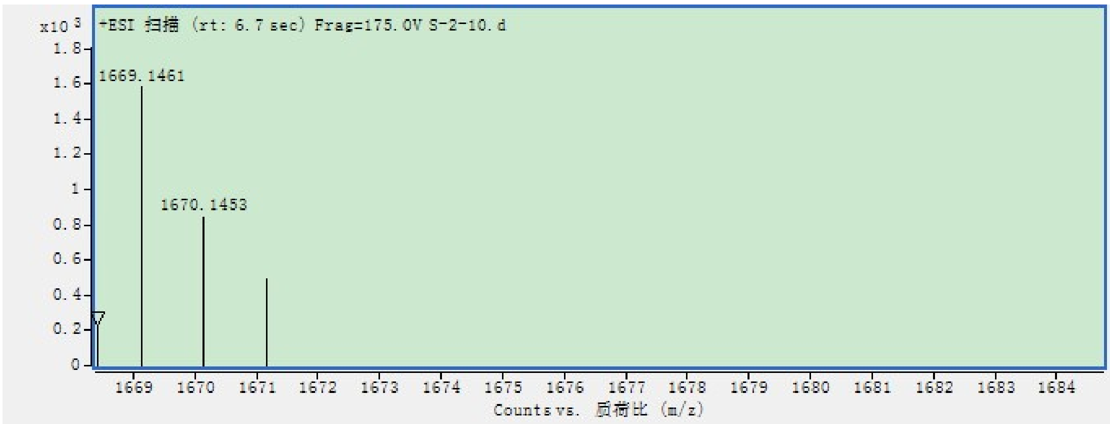
^{1}H NMR spectrum of compound **9** ($CD_3OD/CDCl_3$=1:3, 400 MHz)



HRMS spectrum of compound **9**



^{1}H NMR spectrum of compound **10** ($CD_3OD/CDCl_3$, 400 MHz)



HRMS spectrum of compound **10**