SUPPLEMENTARY INFORMATION

Photodegradation and Inhibition of Drug-Resistant Influenza Virus Neuraminidase Using Anthraquinone-Sialic Acid Hybrids

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Page Contents

S2 ….. General methods for chemical synthesis.

S2 ….. Synthesis of anthraquinone-sialic acid hybrid **1** (Scheme S1).

S4 ….. Synthesis of anthraquinone-sialic acid hybrid **2** (Scheme S2).

S8 ….. Synthesis of anthraquinone-sialic acid hybrid **3** (Scheme S3).

S13 ….. Reagents and apparatus for analytical and biochemical assays.

S13 ….. Photodegradation of neuraminidases.

S14 ….. Polyacrylamide gel electrophoresis and immunoblotting.

S14 ….. Enzyme inhibition assay.

S14 ….. EPR spectrometry.

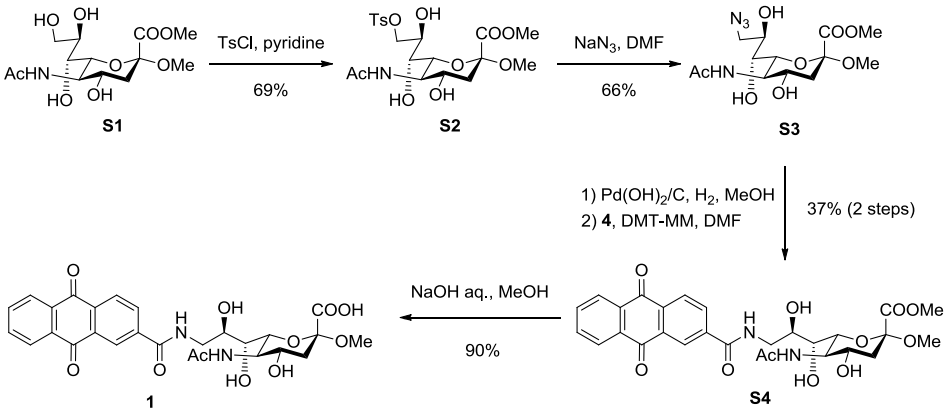
S15 ….. References

S16 ….. ^{1}H NMR and ^{13}C NMR spectrum charts.

General methods for chemical synthesis.

Melting points were determined on a micro hot-stage (Yanako MP-S3) and were uncorrected. Optical rotations were measured on a JASCO P-2200 plarimeter. ^{1}H-NMR spectra were recorded on a JEOL ECA-500 (500 MHz) spectrometer or JEOL Lambda (300 MHz) spectrometer using tetramethylsilane as internal standard. ^{13}C-NMR spectra were taken on a JEOL ECA-500 (125 MHz) spectrometer at room temperature. ESI-TOF Mass spectra were measured on a Waters LCT premier XE. The reactions were monitored by thin layer chromatography carried out on Merck TLC 60F-254 (0.25 mm) using UV light and *p*-anisaldehyde, ninhydrin or 10% ethanolic phosphomolybdic acid as developing agent. Column chromatography separations were performed using silica gel 60 N (spherical, neutral) (Kanto Chemical Co., Inc.). Reverse phase column chromatography separations were performed using Wakosil 40C18 (Wako). Gel filtration chromatography separations were performed using Sephadex LH-20 (GE Healthcare), respectively. Air and/or moisture sensitive reactions were carried out under an argon atmosphere using ovend-dried glassware. In general, organic solvents were purified and dried, and evaporation and concentration were carried out under reduced pressure below 40 ^{o}C.

Synthesis of anthraquinone-sialic acid hybrid 1 (Scheme S1).



Scheme S1. Synthesis of anthraquinone-sialic acid hybrid **1**.

Methyl [*O*-methyl (5-acetamido-3,5-dideoxy-9-*O*-(4-toluenesulfonyl)-D-*glycero*-α-D-*galacto*-2-nonulopyranosyl)]nonate (S2).

To a solution of **S1** (878 mg, 2.60 mmol) in dry pyridine (36.0 mL) was added *p*-TsCl (1.35 g, 7.08 mmol) under Ar atmosphere at room temperature. After being stirred for 5 h, the reaction mixture was diluted with MeOH (30 mL) and concentrated *in vacuo*. Purification of the residue by silica-gel column chromatography (160 g, $CHCl_3$/MeOH=5/1) gave **S2** (894 mg, 1.82 mmol, 69% yield). Data for **S2**: White form; R_f 0.45 (5/1 $CHCl_3$/MeOH); $[\alpha]^{25}_{D}$ +1.3 ^{o} (*c* 0.53, MeOH); ^{1}H-NMR (500 MHz, CD_3OD) δ 7.84-7.74 (2H, m), 7.46-7.439 (2H, m), 4.32 (1H, dd, *J* = 2.2, 10.0 Hz), 4.07 (1H, dd, *J* =

6.3, 10.0 Hz), 3.99 (1H, ddd, *J* = 2.2, 6.3, 8.6 Hz), 3.80 (3H, s), 3.70 (1H, dd, *J* = 10.0, 10.4 Hz), 3.64-3.58 (1H, m), 3.54 (1H, dd, *J* = 1.5, 10.4 Hz), 3.44 (1H, dd, *J* = 1.5, 8.6 Hz), 3.26 (3H, s), 2.61 (1H, dd, *J* = 4.3, 12.6 Hz), 2.44 (3H, s), 1.99 (3H, s), 1.67 (1H, dd, *J* = 12.5, 12.6 Hz); ^{13}C-NMR (125 MHz, CD_3OD) δ 173.9, 169.2, 145.1, 132.9, 129.7, 127.8, 99.1, 73.2, 72.3, 68.8, 68.6, 67.1, 52.5, 51.9, 50.8, 40.1, 21.4, 20.3; HRMS (ESI-TOF) *m/z* 514.1349 (514.1359 calcd for $C_{20}H_{29}NNaO_{11}S$, $[M+Na]^+$).

Methyl [*O*-methyl (5-acetamido-9-azido-3,5-dideoxy-D-*glycero*-α-D-*galacto*-2-nonulopyranosyl)]nonate (S3).

To a solution of **S2** (894 mg, 1.82 mmol) in dry DMF (40.0 mL) was added NaN_3 (624 mg, 9.60 mmol) under Ar atmosphere at room temperature. After being stirred for 15 h at 70 °C, the reaction mixture was concentrated *in vacuo*. Purification of the residue by silica-gel column chromatography (90 g, $CHCl_3$/MeOH=5/1) gave **S3** (432 mg, 1.19 mmol, 66% yield). Data for **S3**: White solid; R_f 0.38 (5/1 $CHCl_3$/MeOH); $[\alpha]^{25}_D$ −2.3 ° (*c* 0.46, MeOH); mp 172 °C; ^{1}H-NMR (500 MHz, CD_3OD) δ 3.99 (1H, ddd, *J* = 2.3, 6.3, 8.9 Hz), 3.84 (3H, s), 3.74 (1H, dd, *J* = 10.1, 10.3 Hz), 3.68-3.57 (2H, m), 3.54 (1H, dd, *J* = 2.3, 12.9 Hz), 3.47 (1H, dd, *J* = 1.7, 8.9 Hz), 3.37 (1H, dd, *J* = 6.3, 12.9 Hz), 3.34 (3H, s), 2.64 (1H, dd, *J* = 4.6, 12.9 Hz), 2.01 (3H, s), 1.70 (1H, dd, *J* = 12.3, 12.9 Hz); ^{13}C-NMR (125 MHz, CD_3OD) δ 173.9, 169.4, 99.0, 73.3, 70.2, 69.6, 67.2, 54.0, 52.5, 52.0, 50.7, 40.1, 21.4; HRMS (ESI-TOF) *m/z* 363.1515 (363.1516 calcd for $C_{13}H_{23}N_4O_8$, $[M+H]^+$).

Methyl [*O*-methyl (5-acetamido-9-(2-anthraquinonylamido)-3,5-dideoxy-D-*glycero*-α-D-*galacto*-2-nonulopyranosyl)]nonate (S4).

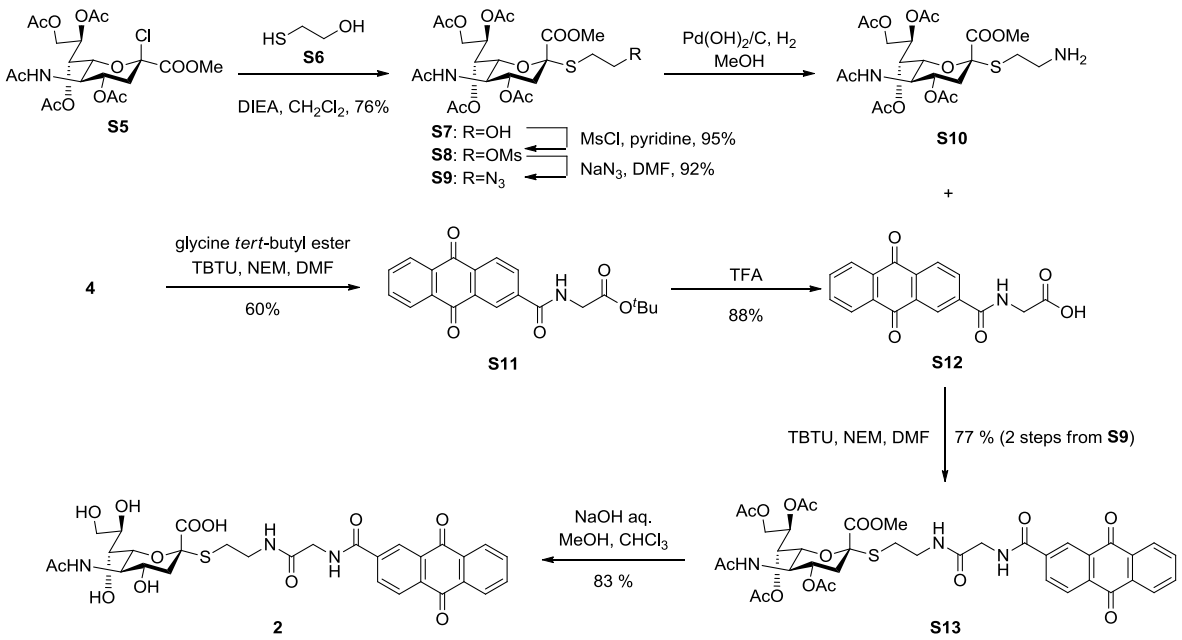
A suspension of **S3** (56.5 mg, 0.156 mmol) and $Pd(OH)_2$/C (40.0 mg) in MeOH (2.00 mL) was stirred under H_2 atmosphere (balloon) at room temperature for 2.5 h. The mixture was filtrated through filter paper, and the filtrate was concentrated *in vacuo* to afford the corresponding crude amino sialic acid derivative. To a solution of the crude amino sialic acid derivative in dry DMF (4.00 mL) were added anthrequinone-2-carboxylic acid (**4**) (42.2 mg, 0.167 mmol) and DMT-MM (122 mg, 0.441 mmol) under Ar atmosphere at room temperature. After being stirred for 1.5 h, the reaction mixture was poured into water (5 mL). The resulting mixture was extracted with $CHCl_3$ (5 mL × 3). The extracts were washed with brine, dried over anhydrous Na_2SO_4, and concentrated *in vacuo*. Purification of the residue by silica-gel column chromatography (20 g, $CHCl_3$/MeOH=5/1) gave **S4** (33.2 mg, 58.2 μmol, 37% yield in 2 steps). Data for **S4**: Yellow solid; R_f 0.27 (5/1 $CHCl_3$/MeOH); $[\alpha]^{25}_D$ +1.1 ° (*c* 0.14, MeOH); mp 132 °C; ^{1}H-NMR (500 MHz, CD_3OD) δ 8.61-8.59 (1H, m), 8.26-8.18 (4H, m), 7.85-7.82 (2H, m), 4.11 (1H, ddd, *J* = 3.2, 8.0, 8.6 Hz), 3.88 (1H, dd, *J* = 3.2, 13.7 Hz), 3.84 (3H, s), 3.81 (1H, dd, *J* = 10.0, 10.0 Hz), 3.72-3.64 (2H, m), 3.58 (1H, dd, *J* = 8.0, 13.7 Hz), 3.50 (1H, dd, *J* = 1.2, 8.6 Hz), 3.37 (3H, s), 2.65 (1H, dd, *J* = 4.6, 12.9 Hz), 2.01 (3H, s), 1.74 (1H, dd, *J* = 12.3, 12.9 Hz); ^{13}C-NMR (125 MHz, CD_3OD) δ 182.3, 182.2, 173.7, 169.4, 167.4, 139.7, 135.1, 134.3, 133.6, 133.5,

133.4, 132.5, 127.1, 126.8, 125.7, 99.1, 73.3, 70.7, 69.4, 67.2, 52.5, 51.9, 50.8, 43.7, 40.1, 21.4 ; HRMS (ESI-TOF) *m/z* 571.1931 (571.1928 calcd for $C_{28}H_{31}N_2O_{11}$, $[M+H]^+$).

***O*-Methyl (5-acetamido-9-(2-anthraquinonylamido)-3,5-dideoxy-D-*glycero*-α-D-*galacto*-2-nonulopyranosyl)nonic acid (1).**

To a solution of **S4** (31.4 mg, 55.0 μmol) in dry MeOH (2.00 mL) was added 10 wt% NaOH aq. (125 μL, 0.275 mmol) under Ar atmosphere at 0 °C. After being stirred for 4 h at room temperature, the reaction mixture was neutralized by addition of Amberlite IR-120 (H^+ type). The resulting mixture was filtered, and then the filtrate was concentrated *in vacuo*. Purification of the residue by reversed phase chromatography (3 g, H_2O/MeOH=100/0 → 50/50) gave **1** (27.5 mg, 49.4 μmol, 90% yield). Data for **1**: Yellow solid; R_f 0.33 (20/10/1/0.1 $CHCl_3$/MeOH/H_2O/AcOH); $[\alpha]^{25}_D$ −11.1 ° (*c* 0.23, MeOH); mp 177-180 °C; ^{1}H-NMR (500 MHz, D_2O) δ 7.52-7.47 (2H, m), 7.45-7.38 (4H, m), 7.37-7.32 (1H, m), 3.99 (1H, ddd, *J* = 3.2, 8.3, 8.6 Hz), 3.82-3.75 (2H, m), 3.70-3.63 (2H, m), 3.49 (1H, dd, *J* = 1.2, 8.6 Hz), 3.34 (1H, dd, *J* = 8.3, 14.0 Hz), 3.31 (3H, s), 2.64 (1H, dd, *J* = 4.6, 12.3 Hz), 1.95 (3H, s), 1.64 (1H, dd, *J* = 12.1, 12.3 Hz); ^{13}C-NMR (125 MHz, D_2O) δ 182.1, 181.9, 175.1, 172.0, 166.4, 137.8, 135.0, 133.4, 132.6, 131.6, 131.4, 130.9, 127.1, 126.7, 125.0, 99.8, 72.8, 70.0, 69.8, 67.8, 61.8, 51.7, 43.2, 39.5, 22.2; HRMS (ESI-TOF) *m/z* 555.1620 (555.1615 calcd for $C_{27}H_{27}N_2O_{11}$, $[M-H]^-$).

Synthesis of anthraquinone-sialic acid hybrid 2 (Scheme S2).



Scheme S2. Synthesis of anthraquinone-sialic acid hybrid **2**.

Methyl [2-hydroxyethyl (5-acetamido-4,7,8,9-tetra-*O*-acetyl-3,5-dideoxy-2-thio-D-*glycero*-α-D-*galacto*-2-nonulopyranosyl)]nonate (S7).

To a solution of **S5**[1] (219 mg, 0.429 mmol) in dry CH_2Cl_2 (4.50 mL) were added 2-mercaptoethanol (**S6**) (0.882 mL, 12.5 mmol) and DIEA (0.748 mL, 4.29 mmol) under Ar atmosphere at room temperature. After being stirred for 27 h, the reaction was quenched by addition of water (10 mL). The resulting mixture was extracted with $CHCl_3$ (5 mL×3). The extracts were washed with brine, dried over anhydrous Na_2SO_4, and concentrated *in vacuo*. Purification of the residue by silica-gel column chromatography (20 g, EtOAc) gave **S7** (179 mg, 0.325 mmol, 76% yield). Data for **7**: White foam; R_f 0.24 (EtOAc); $[\alpha]^{25}_D$ +10.8 ° (*c* 0.50, $CHCl_3$); ^{1}H-NMR (500 MHz, $CDCl_3$) δ 5.42-5.38 (1H, m), 5.31 (1H, dd, *J* = 2.0, 9.2 Hz), 5.24-5.17 (1H, m), 4.87 (1H, ddd, *J* = 4.6, 10.3, 12.1 Hz), 4.30 (1H, dd, *J* = 2.6, 12.6 Hz), 4.06 (1H, dd, *J* = 5.7, 12.6 Hz), 4.05 (1H, ddd, *J* = 10.3, 10.6, 10.9 Hz), 3.83 (1H, dd, *J* = 2.0, 10.9 Hz), 3.81 (3H, s), 3.78-3.70 (1H, m), 3.67-3.60 (1H, m), 2.89-2.75 (2H, m), 2.73 (1H, br-s), 2.72 (1H, dd, *J* = 4.6, 12.6 Hz), 2.20 (3H, s), 2.16 (3H, s), 2.04 (3H, s), 2.03 (3H, s), 2.01 (1H, dd, *J* =12.1, 12.6 Hz), 1.88 (3H, s); ^{13}C-NMR (125 MHz, $CDCl_3$) δ 170.8, 170.6, 170.5, 170.0, 168.7, 82.8, 74.1, 69.7, 68.6, 67.1, 62.3, 61.8, 53.0, 48.8, 37.9, 31.3, 22.9, 21.2, 20.7, 20.6 ; HRMS (ESI-TOF) *m/z* 552.1731 (552.1751 calcd for $C_{22}H_{34}NO_{13}S$, $[M+H]^+$).

Methyl [2 (*O*-methanesulfonyl)ethyl-(5-acetamido-4,7,8,9-tetra-*O*-acetyl-3,5-dideoxy-2-thio-D-*glycero*-α-D-*galacto*-2-nonulopyranosyl)]nonate (S8).

To a solution of **S7** (169 mg, 0.306 mmol) in dry pyridine (3.00 mL) was added MsCl (100 μL, 1.29 mmol) under Ar atmosphere at 0 °C. After being stirred for 2 h at room temperature, the reaction was quenched by addition of water (6 mL). The resulting mixture was extracted with $CHCl_3$ (5 mL×3). The extracts were washed with brine, dried over anhydrous Na_2SO_4, and concentrated *in vacuo*. Purification of the residue by silica-gel column chromatography (6 g, EtOAc) gave **S8** (182 mg, 0.289 mmol, 95% yield). Data for **S8**: White foam; R_f 0.33 (EtOAc); $[\alpha]^{25}_D$ +5.0 ° (*c* 0.49, $CHCl_3$); ^{1}H-NMR (500 MHz, $CDCl_3$) δ 5.39 (1H, d, *J* = 10.0 Hz), 5.35 (1H, ddd, *J* = 2.6, 5.3, 9.3 Hz), 5.30 (1H, dd, *J* = 2.0, 9.3 Hz), 4.89 (1H, ddd, *J* = 4.6, 10.6, 12.3 Hz), 4.37 (1H, td, *J* = 6.6, 10.6 Hz), 4.30 (1H, td, *J* = 6.6, 10.6 Hz), 4.27 (1H, dd, *J* = 2.6, 12.6 Hz), 4.06 (1H, dd, *J* = 5.3, 12.6 Hz), 4.03 (1H, ddd, *J* = 10.0, 10.6, 10.6 Hz), 3.83 (3H, s), 3.82 (1H, dd, *J* = 2.0, 10.6 Hz), 3.10 (3H, s), 3.03 (2H, dt, *J* = 6.6, 6.6 Hz), 2.74 (1H, dd, *J* = 4.6, 12.3 Hz), 2.17 (3H, s), 2.15 (3H, s), 2.04 (6H, s), 1.98 (1H, dd, *J* = 12.3, 12.3 Hz), 1.89 (3H, s); ^{13}C-NMR (125 MHz, $CDCl_3$) δ 170.9, 170.7, 170.3, 170.2, 170.1, 168.6, 82.8, 74.2, 69.4, 69.3, 67.9, 67.1, 62.4, 53.4, 49.4, 38.0, 37.6, 28.2, 23.2, 21.3, 20.9, 20.8; HRMS (ESI-TOF) *m/z* 630.1526 (630.1533 calcd for $C_{23}H_{36}NO_{15}S_2$, $[M+H]^+$).

Methyl [2-azidoethyl (5-acetamido-4,7,8,9-tetra-*O*-acetyl-3,5-dideoxy-2-thio-D-*glycero*-α-D-*galacto*-2-nonulopyranosyl)]nonate (S9).

To a solution of **S8** (140 mg, 0.223 mmol) in dry DMF (3.50 mL) was added NaN_3 (81.0 mg, 1.25 mmol) under Ar atmosphere at room temperature. After being stirred for 2 h at 80 ^oC, the reaction was quenched by addition of water (8 mL). The resulting mixture was extracted with $CHCl_3$ (5 mL × 3). The extracts were washed with brine, dried over anhydrous Na_2SO_4, and concentrated *in vacuo*. Purification of the residue by silica-gel column chromatography (12 g, EtOAc) gave **S9** (118 mg, 0.205 mmol, 92% yield). Data for **S9**: Yellow foam; R_f 0.49 (EtOAc); $[\alpha]^{25}_D$ +1.8 ^{o} (*c* 0.19, $CHCl_3$); ^{1}H-NMR (500 MHz, $CDCl_3$) δ 5.37 (1H, ddd, *J* = 2.3, 5.5, 9.2 Hz), 5.31 (1H, dd, *J* = 1.7, 9.2 Hz), 5.20 (1H, d, *J* = 10.1 Hz), 4.89 (1H, ddd, *J* = 4.6, 10.3, 12.9 Hz), 4.28 (1H, dd, *J* = 2.3, 12.6 Hz), 4.08 (1H, dd, *J* = 5.5, 12.6 Hz), 4.02 (1H, ddd, *J* = 10.1, 10.3, 10.3 Hz), 3.83 (1H, dd, *J* = 1.7, 10.3 Hz), 3.82 (3H, s), 3.51 (1H, td, *J* = 6.3, 12.6 Hz), 3.42 (1H, td, *J* = 6.9, 12.6 Hz), 2.94 (1H, td, *J* = 6.3, 14.1 Hz), 2.82 (1H, td, *J* = 6.9, 14.1 Hz), 2.74 (1H, dd, *J* = 4.6, 12.9 Hz), 2.18 (3H, s), 2.15 (3H, s), 2.04 (3H, s), 2.03 (3H, s), 2.00 (1H, dd, *J* = 12.9, 12.9 Hz), 1.89 (3H, s), 1.71 (3H, s); ^{13}C-NMR (125 MHz, $CDCl_3$) δ 171.0, 170.8, 170.3, 170.2, 170.1, 168.6, 83.0, 74.2, 69.5, 68.2, 67.2, 62.3, 53.2, 51.4, 49.5, 38.1, 29.0, 23.3, 21.3, 20.9, 20.8 ; HRMS (ESI-TOF) *m/z* 577.1818 (577.1816 calcd for $C_{22}H_{33}N_4O_{12}S$, $[M+H]^+$).

***tert*-Butyl 2-(anthraquinone-2-carboxamido) acetate (S11).**

To a solution of anthraquinone 2-carboxylic acid (**4**) (468 mg, 1.86 mmol) in dry DMF (37.0 mL) were added NEM (0.565 mL, 4.46 mmol) and TBTU (599 mg, 1.86 mmol) under Ar atmosphere at 0 ^oC. After being stirred for 5 min, glycine *tert*-butyl ester hydrochloride (512 mg, 3.91 mmol) was added to the reaction mixture. After being stirred for 17 h at room temperature, the reaction was quenched by addition of 1N HCl aq. (30 mL). The resulting mixture was extracted with EtOAc (20 mL × 3). The extracts were washed with brine, dried over anhydrous Na_2SO_4, and concentrated *in vacuo*. The residue was recrystallized from MeOH to give **S11** (407 mg, 1.11 mmol, 60 % yield). Data for **S11**: Yellow solid; R_f 0.56 (3/1 toluene/EtOAc); mp 193 ^oC; ^{1}H-NMR (500 MHz, $CDCl_3$) δ 8.66 (1H, d, *J* = 1.7 Hz), 8.39 (2H, d, *J* = 8.0 Hz), 8.35-8.31 (2H, m), 8.29 (1H, dd, *J* = 1.7, 8.0 Hz), 7.85-7.81 (2H, m), 6.92 (1H, t, *J* = 4.9 Hz), 4.21 (1H, d, *J* = 4.9 Hz), 1.53 (9H, s); ^{13}C-NMR (125 MHz, $CDCl_3$) δ 182.0, 181.9, 168.8, 165.6, 138.6, 134.7, 134.1, 133.0, 132.9, 132.7, 127.4, 127.0, 125.2, 82.3, 42.5, 27.8; HRMS (ESI-TOF) *m/z* 366.1333 (366.1341 calcd for $C_{21}H_{20}NO_5$, $[M+H]^+$).

2-(Anthraquinone-2-carboxamido) acetic acid (S12).

The anthraquinone derivative **S11** (110 mg, 0.301 mmol) was dissolved in TFA (2.00 mL) under Ar atmosphere at room temperature. After being stirred for 5 h, the reaction mixture was concentrated *in vacuo* to give **S12** (82.4 mg, 0.266 mmol, 88% yield). Data for **S12**: Yellow solid; R_f 0.43 (EtOAc); mp 272 ^oC; ^{1}H-NMR (500 MHz, DMSO-d_6) δ 12.72 (1H, br-s), 9.35 (1H, t, *J* =6.1 Hz), 8.67 (2H, d, *J* = 1.6 Hz), 8.35 (1H, dd, *J* = 1.6, 8.0 Hz), 8.30 (1H, d, *J* = 8.0 Hz), 8.24 (2H, m), 7.96 (2H, m), 4.00 (2H, d, *J* = 6.1 Hz); ^{13}C-NMR (125 MHz, DMSO-d_6) δ 182.7, 171.6, 165.6, 139.2, 135.3, 135.2, 133.7,

133.6, 133.4, 127.7, 127.4, 127.3, 126.1, 41.9; HRMS (ESI-TOF) *m/z* 308.0558 (308.0559 calcd for $C_{17}H_{10}NO_5$, $[M-H]^-$).

Methyl [2-(anthraquinone-2-carboxamido)ethyl (5-acetamido-4,7,8,9-tetra-*O*-acetyl-3,5-dideoxy-2-thio-D-*glycero*-α-D-*galacto*-2-nonulopyranosyl)]nonate (S13).

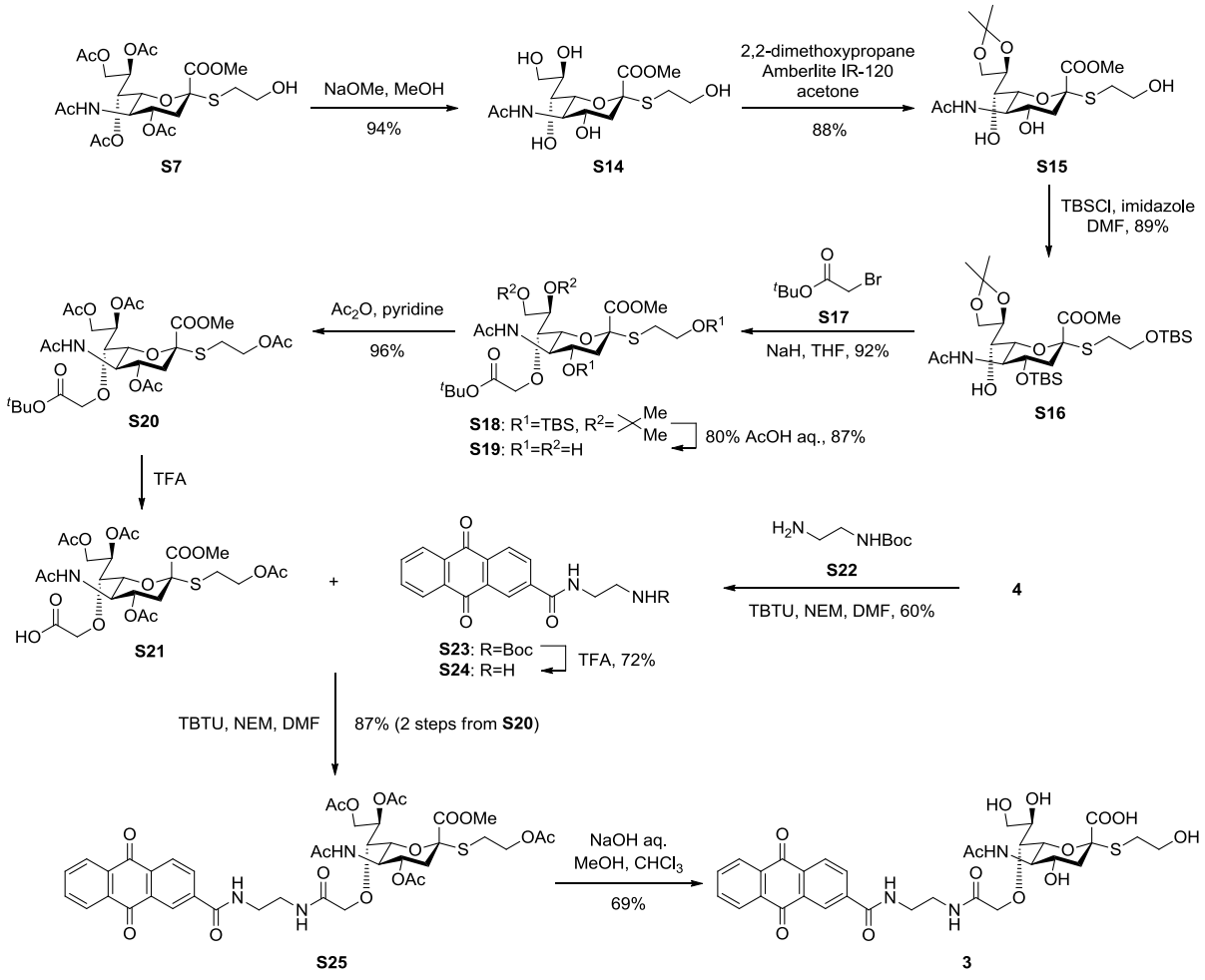
A suspension of **S9** (89.8 mg, 0.156 mmol) and $Pd(OH)_2$/C (40.0 mg) in MeOH (2.00 mL) was stirred under H_2 atmosphere (balloon) at room temperature for 0.5 h. The mixture was filtrated through filter paper, and the filtrate was concentrated *in vacuo* to give the crude **S10**. To a solution of **S12** (84.4 mg, 0.273 mmol) in dry DMF (5.00 mL) were added NEM (40.0 μL, 0.316 mmol) and TBTU (50.0 mg, 0.155 mmol) under Ar atmosphere at room temperature. After being stirred for 5 min, the crude **S10** diluted with DMF (4.00 mL) was added to the reaction mixture. The resulting mixture was stirring for 3.5 h at room temperature, and then the reaction was quenched by addition of 1 N HCl aq. (10 mL). The resulting mixture was extracted with $CHCl_3$ (10 mL×3). The extracts were washed with brine, dried over anhydrous Na_2SO_4, and concentrated *in vacuo*. Purification of the residue by silica-gel column chromatography (50 g, $CHCl_3$/acetone=1/1) gave **S13** (101 mg, 0.120 mmol, 77% yield in 2 steps). Data for **S13**: Yellow solid; R_f 0.49 (5/1 $CHCl_3$/MeOH); $[\alpha]^{25}_D$ +8.0 ^{o} (*c* 0.31, $CHCl_3$); mp 258 ^{o}C; ^{1}H-NMR (500 MHz, $CDCl_3$) δ 8.71 (1H, d, *J* = 1.7 Hz), 8.40 (1H, d, *J* = 8.0 Hz), 8.35-8.31 (3H, m), 7.85-7.82 (2H, m), 7.34 (1H, br-t, *J* = 4.9 Hz), 7.04 (1H, t, *J* = 6.0 Hz), 5.34 (1H, ddd, *J* = 3.5, 5.7, 9.5 Hz), 5.29 (1H, dd, *J* = 2.0, 9.5 Hz), 5.14 (1H, d, *J* = 10.0 Hz), 4.86 (1H, ddd, *J* = 4.9, 10.6, 12.6 Hz), 4.29 (1H, dd, *J* = 4.9, 17.1 Hz), 4.25 (1H, dd, *J* = 3.5, 12.4 Hz), 4.19 (1H, dd, *J* = 4.9, 17.1 Hz), 4.05 (1H, dd, *J* = 5.7, 12.4 Hz), 4.05 (1H, dt, *J* = 10.0, 10.6, 10.5 Hz), 3.79 (3H, s), 3.79 (1H, dd, *J* = 2.0, 10.6 Hz), 3.67-3.59 (1H, m), 3.42-3.35 (1H, m), 2.84 (1H, ddd, *J* = 5.0, 5.7, 14.2 Hz), 2.71 (1H, dd, *J* = 4.9, 12.6 Hz), 2.67 (1H, ddd, *J* = 5.2, 5.5, 14.2 Hz), 2.18 (3H, s), 2.15 (3H, s), 2.04 (3H, s), 2.03 (3H, s), 2.01 (1H, dd, *J* = 12.6, 12.6 Hz), 1.88 (3H, s); ^{13}C-NMR (125 MHz, $CDCl_3$) δ 182.6, 182.5, 171.2, 171.1, 171.0, 170.4, 170.3, 168.8, 168.3, 165.7, 139.0, 135.3, 134.5, 133.6, 133.5, 133.5, 133.1, 127.9, 127.5, 125.7, 83.0, 74.9, 67.6, 67.5, 62.8, 53.3, 49.4, 43.4, 40.5, 38.5, 27.9, 23.3, 21.4, 21.1, 21.0, 20.9; HRMS (ESI-TOF) *m/z* 842.2454 (842.2442 calcd for $C_{39}H_{44}N_3O_{16}S$, $[M+H]^+$).

2-(Anthraquinone-2-carboxamido)ethyl (5-acetamido-3,5-dideoxy-2-thio-D-*glycero*-α-D-*galacto*-2-nonulopyranosyl)nonic acid (2).

To a solution of **S13** (39.6 mg, 47.0 μmol) in a mixture of dry $CHCl_3$ (1.00 mL) and dry MeOH (3.00 mL) was added 10 wt% NaOH aq. (645 μL, 1.42 mmol) under Ar atmosphere at 0 ^{o}C. After being stirred for 3.5 h at room temperature, the reaction mixture was neutralized by addition of Amberlite IR-120 (H^+ type). The resulting mixture was filtered, and then the filtrate was concentrated *in vacuo*. Purification of the residue by reversed phase chromatography (5 g, H_2O/MeOH=100/0 → 50/50) and recrystallization from EtOAc gave **2** (25.7 mg, 39.0 μmol, 83% yield). Data for **2**: Yellow solid; R_f

0.20 (20/10/1 $CHCl_3$/MeOH/H_2O); $[\alpha]^{25}_D$ −15.6 ^{o} (*c* 0.18, MeOH); mp 178 ^{o}C; ^{1}H-NMR (500 MHz, DMSO-d_6/D_2O=9/1) δ 8.65 (1H, dd, *J* = 1.8, 8.3 Hz), 8.38-8.18 (4H, m), 7.93-7.89 (2H, m), 3.56-3.49 (3H, m), 3.35-3.25 (6H, m), 3.21 (1H, ddd, *J* = 2.0, 8.6, 8.9 Hz), 3.15 (1H, dd, *J* = 2.0, 8.9 Hz), 2.78-2.66 (3H, m), 1.83 (3H, s), 1.35 (1H, dd, *J* = 11.5, 11.5 Hz); ^{13}C-NMR (125 MHz, DMSO-d_6) δ 182.7, 182.6, 182.5, 173.0, 165.7, 139.3, 135.3, 135.0, 133.4, 133.4, 127.6, 127.4, 127.3, 126.3, 79.5, 75.7, 71.8, 69.1, 67.6, 63.4, 56.5, 52.9, 43.1, 28.9, 22.9, 18.8; HRMS (ESI-TOF) *m/z* 658.1735 (658.1707 calcd for $C_{30}H_{32}N_3O_{12}S$, $[M-H]^-$).

Synthesis of anthraquinone-sialic acid hybrid 3 (Scheme S3).



Scheme S3. Synthesis of anthraquinone-sialic acid hybrid **3**.

Methyl [2-hydroxyethyl (5-acetamido-3,5-dideoxy-2-thio-D-*glycero*-α-D-*galacto*-2-nonulopyranosyl)]nonate (S14).

To a solution of **S7** (238 mg, 0.431 mmol) in dry MeOH (8.00 mL) was added 0.20 M NaOMe in MeOH (0.450 mL, 90.0 μmol) under Ar atmosphere at room temperature. After being stirred for 6 h,

the reaction mixture was neutralized with Amberlite IR-120 (H^+ type). The resulting mixture was filtered, and then the filtrate was concentrated *in vacuo*. Purification of the residue by silica-gel column chromatography (20 g, $CHCl_3$/MeOH=4/1) gave **S14** (156 mg, 0.406 mmol, 94% yield). Data for **S14**: White foam; R_f 0.16 (4/1 $CHCl_3$/MeOH); $[\alpha]^{25}_D$ +26.5 ^{o} (*c* 0.59, MeOH); ^{1}H-NMR (300 MHz, CD_3OD) δ 3.84 (3H, s), 3.84-3.78 (3H, m), 3.71-3.57 (4H, m), 3.48 (1H, dd, *J* = 1.6, 8.8 Hz), 3.44 (1H, dd, *J* = 1.6, 10.2 Hz), 2.89 (1H, td, *J* = 6.3, 13.7 Hz), 2.78 (1H, td, *J* = 7.1, 13.7 Hz), 2.76 (1H, dd, *J* = 4.6, 12.9 Hz), 1.99 (3H, s), 1.79 (1H, dd, *J* = 12.7, 12.9 Hz); ^{13}C-NMR (125 MHz, CD_3OD) δ 174.0, 170.8, 83.2, 75.8, 71.3, 68.8, 67.6, 63.4, 61.0, 52.8, 52.4, 40.8, 31.6, 21.8; HRMS (ESI-TOF) *m/z* 384.1316 (384.1328 calcd for $C_{14}H_{26}NO_9S$, $[M+H]^+$).

Methyl [2-hydroxyethyl (5-acetamido-3,5-dideoxy-8,9-*O*-isopropyliden-2-thio-D-*glycero*-α-D-*galacto*-2-nonulopyranosyl)]nonate (S15).

To a solution of **S14** (69.3mg, 0.181 mmol) in dry acetone (4.00 mL) was added Amberlite IR-120 (H^+ type) (100 mg) followed by 2,2-dimethoxypropane (66.5 μL, 0.543 mmol) under Ar atmosphere at room temperature. After being stirred for 1 h, the reaction mixture was filtered to remove the Amberlite and the filtrate was concentrated *in vacuo*. Purification of the residue by silica-gel column chromatography (6 g, $CHCl_3$/MeOH=4/1) gave **S15** (67.2 mg, 0.159 mmol, 88% yield). Data for **S15**: White foam; R_f 0.53 (4/1 $CHCl_3$/MeOH); $[\alpha]^{25}_D$ +0.8 ^{o} (*c* 0.20, MeOH); ^{1}H-NMR (300 MHz, CD_3OD) δ 4.23 (1H, ddd, *J* = 5.9, 6.4, 7.1 Hz), 4.08 (1H, dd, *J* = 6.4, 8.3 Hz), 3.96 (1H, dd, *J* = 5.9, 8.3 Hz), 3.80 (3H, s, CO_2CH_3), 3.79 (1H, dd, *J* = 9.9, 10.5 Hz), 3.70-3.58 (3H, m), 3.48 (1H, dd, *J* = 1.2, 7.1 Hz), 3.44 (1H, dd, *J* = 1.2, 10.5 Hz), 2.93 (1H, td, *J* = 6.3, 13.5 Hz), 2.82 (1H, td, *J* = 6.8, 13.5 Hz), 2.73 (1H, dd, *J* = 4.7, 12.6 Hz), 1.97 (3H, s), 1.73 (1H, dd, *J* = 11.3, 12.6 Hz), 1.35 (3H, s), 1.34 (3H, s); ^{13}C-NMR (125 MHz, CD_3OD) δ 173.4, 169.7, 108.7, 83.4, 75.9, 75.4, 69.7, 67.5, 66.6, 61.1, 52.3, 51.7, 40.9, 31.7, 25.9, 24.4, 21.4; HRMS (ESI-TOF) *m/z* 424.1626 (424.1641 calcd for $C_{17}H_{30}NO_9S$, $[M+H]^+$).

Methyl [2-*O*-(*tert*-bulyldimethylsilyl)ethyl (5-acetamido-4-*O*-*tert*-bulyldimethylsilyl-3,5-dideoxy-8,9-*O*-isopropyliden-2-thio-D-*glycero*-α-D-*galacto*-2-nonulopyranosyl)]nonate (S16).

To a solution of **S15** (633 mg, 1.49 mmol) in dry DMF (18.8 mL) was added imidazole (509 mg, 7.48 mmol) followed by TBSCl (563 mg, 3.74 mmol) under Ar atmosphere at room temperature. After being stirred for 16 h, the reaction was quenched by addition of water (20 mL). The resulting mixture was extracted with $CHCl_3$ (15 mL×3). The extracts were washed with brine, dried over anhydrous Na_2SO_4, and concentrated *in vacuo*. Purification of the residue by silica-gel column chromatography (130 g, $CHCl_3$/MeOH=10/1) gave **S16** (869 mg, 1.33 mmol, 89% yield). Data for **S16**: Colorless syrup; R_f 0.85 (5/1 $CHCl_3$/MeOH), 0.33 (1/1 hexane/EtOAc); $[\alpha]^{25}_D$ −3.9 ^{o} (*c* 0.50, $CHCl_3$); ^{1}H-NMR (500 MHz, $CDCl_3$) δ 5.31 (1H, d, *J* = 8.1 Hz), 4.25 (1H, td, *J* = 6.3, 13.5 Hz), 4.12 (1H, br-d, *J* = 4.9

Hz), 4.08 (1H, dd, *J* = 6.3, 8.3 Hz), 3.99 (1H, dd, *J* = 6.3, 8.3 Hz), 3.79-3.73 (2H, m), 3.77 (3H, s), 3.70-3.65 (2H, m), 3.48 (1H, br-ddd, *J* = 0.9, 4.9, 13.5 Hz), 3.28 (1H, dd, *J* = 0.9, 10.6 Hz), 2.91 (1H, ddd, *J* = 6.0, 7.5, 13.0 Hz), 2.81 (1H, ddd, *J* = 6.6, 7.5, 13.0 Hz), 2.69 (1H, dd, *J* = 4.6, 12.9 Hz), 1.98 (3H, s), 1.81 (1H, dd, *J* = 10.6, 12.9 Hz), 1.36 (3H, s), 1.34 (3H, s), 0.85 (9H, s), 0.84 (9H, s), 0.08 (3H, s), 0.06 (3H, s), 0.03 (6H, s); ^{13}C-NMR (125 MHz, $CDCl_3$) δ 172.1, 169.8, 108.6, 83.0, 76.3, 74.9, 70.2, 68.9, 67.1, 62.8, 53.3, 52.4, 41.7, 31.7, 26.8, 25.8, 25.5, 23.1, 18.2, 17.7, -4.2, -4.8, -5.3; HRMS (ESI-TOF) *m/z* 652.3352 (652.3371 calcd for $C_{29}H_{58}NO_9SSi_2$, $[M+H]^+$).

Methyl [2-*O*-(*tert*-bulyldimethylsilyl)ethyl (5-acetamido-7-*O*-[(*tert*-butyl)acetate]-4-*O*-(*tert*-bulyldimethylsilyl)-3,5-dideoxy-8,9-*O*-isopropyliden-2-thio-D-*glycero*-α-D-*galacto*-2-nonulopyranosyl)]nonate (S18).

To a solution of **S16** (32.3 mg, 49.5 μmol) in dry THF (2.00 mL) was added 60% NaH (8.80 mg, 0.220 mmol) under Ar atmosphere at 0 °C. After being stirred for 5 min, *tert*-butyl bromoacetate (**S17**) (30.0 μL, 0.205 mmol) was added to the reaction mixture. After being stirred for 1 h at room temperature, the reaction was quenched by addition of water (5 mL) at 0 °C. The resulting mixture was extracted with $CHCl_3$ (5 mL × 3). The extracts were washed with brine, dried over anhydrous Na_2SO_4, and concentrated *in vacuo*. Purification of the residue by silica-gel column chromatography (5 g, hexane/EtOAc=2/1) gave **S18** (35.0 mg, 45.7 μmol, 92% yield). Data for **S18**: White foam; R_f 0.53 (1/1 hexane/EtOAc); $[\alpha]^{25}_D$ +13.0 ° (*c* 0.43, $CHCl_3$); ^{1}H-NMR (500 MHz, $CDCl_3$) δ 6.83 (1H, d, *J* = 6.6 Hz), 4.59 (1H, ddd, *J* = 4.6, 8.5, 11.2 Hz), 4.42 (1H, ABq, *J* = 17.5 Hz), 4.28 (1H, dd, *J* =7.2, 7.2 Hz), 4.18 (1H, ABq, *J* = 17.5 Hz), 4.11-4.02 (3H, m), 3.93 (1H, m), 3.75 (3H, s), 3.62 (2H, dd, *J* = 6.6, 6.9 Hz), 3.25 (1H, ddd, *J* = 6.6, 8.5, 8.5 Hz), 2.80-2.70 (2H, m), 2.57 (1H, dd, *J* = 4.6, 12.6 Hz), 1.82 (3H, s), 1.65 (1H, dd, *J* = 11.2, 12.6 Hz), 1.43 (9H, s), 1.41 (3H, s), 1.27 (3H, s), 0.82 (9H, s), 0.81 (9H, s), 0.00 (3H, s), −0.02 (6H, s), −0.03 (3H, s); ^{13}C-NMR (125 MHz, $CDCl_3$) δ 171.4, 170.5, 169.5, 107.6, 83.2, 82.0, 79.2, 76.1, 74.5, 68.6, 65.4, 64.6, 62.6, 56.2, 52.7, 42.5, 31.6, 28.1, 26.3, 25.9, 25.7, 24.2, 23.8, 18.3, 17.9, −4.80, −4.84, −5.27, −5.28; HRMS (ESI-TOF) *m/z* 766.4067 (766.4052 calcd for $C_{35}H_{68}NO_{11}SSi_2$, $[M+H]^+$).

Methyl [2-hydroxyethyl (5-acetamido-7-*O*-[(*tert*-butyl)acetate]-3,5-dideoxy-2-thio-D-*glycero*-α-D-*galacto*-2-nonulopyranosyl)]nonate (S19).

The sialic acid derivative **S18** (236 mg, 0.474 mmol) was dissolved in 80 vol% aqueous AcOH (3.00 mL) under Ar atmosphere at room temperature. After being stirred for 3 days, the reaction mixture was concentrated *in vacuo*. Purification of the residue by silica-gel column chromatography (30 g, $CHCl_3$/MeOH=4/1) gave **S19** (205 mg, 0.412 mmol, 87% yield). Data for **S19**: White foam; R_f 0.34 (4/1 $CHCl_3$/MeOH); $[\alpha]^{25}_D$ +38.9 ° (*c* 0.24, $CHCl_3$); ^{1}H-NMR (500 MHz, CD_3OD) δ 4.28 (1H, ABq, *J* = 16.0 Hz), 4.11 (1H, ABq, *J* = 16.0 Hz), 3.90 (1H, dd, *J* = 10.3, 10.3 Hz), 3.90-3.87 (1H, m), 3.83

(1H, dd, *J* = 2.9, 11.8 Hz), 3.82 (3H, s), 3.71 (1H, dd, *J* = 4.6, 11.8 Hz), 3.69-3.62 (3H, m), 3.54 (1H, ddd, *J* = 4.6, 10.3, 12.0 Hz), 3.51 (1H, dd, *J* = 1.0, 8.1 Hz), 2.90 (1H, td, *J* = 6.3, 13.8 Hz), 2.79 (1H, td, *J* = 6.9, 13.8 Hz), 2.70 (1H, dd, *J* = 4.6, 12.6 Hz), 1.97 (3H, s), 1.83 (1H, dd, *J* = 12.0, 12.6 Hz), 1.48 (9H, s); ^{13}C-NMR (125 MHz, CD_3OD) δ 172.4, 170.4, 83.1, 81.6, 78.4, 75.0, 71.0, 70.2, 68.7, 62.8, 61.1, 52.2, 52.1, 40.6, 31.5, 27.1, 21.7; HRMS (ESI-TOF) *m/z* 498.1995 (498.2009 calcd for $C_{20}H_{36}NO_{11}S$, $[M+H]^+$).

Methyl [2-hydroxyethyl (5-acetamido-4,7,8,9-tetra-*O*-acetyl-7-*O*-[(*tert*-butyl)acetate]-3,5-dideoxy-2-thio-D-*glycero*-α-D-*galacto*-2-nonulopyranosyl)]nonate (S20).

To a solution of **S19** (99.9 mg, 0.201 mmol) in dry pyridine (4.00 mL) was added dry acetic anhydride (2.00 mL) under Ar atmosphere at room temperature. After being stirred for 14 h, the reaction was quenched by addition of water (10 mL). The resulting mixture was extracted with $CHCl_3$ (8 mL × 3). The extracts were washed with brine, dried over anhydrous Na_2SO_4, and concentrated *in vacuo*. Purification of the residue by silica-gel column chromatography (25 g, EtOAc) gave **S20** (128 mg, 0.193 mmol, 96% yield). Data for **S20**: White foam; R_f 0.48 (EtOAc); $[\alpha]^{25}_D$ +8.3 ^{o} (*c* 0.38, $CHCl_3$); ^{1}H-NMR (500 MHz, $CDCl_3$) δ 5.87 (1H, d, *J* = 8.6 Hz), 5.30 (1H, ddd, *J* = 2.3, 5.5, 6.9 Hz), 5.14 (1H, ddd, *J* = 4.9, 10.6, 12.6 Hz), 4.62 (1H, dd, *J* = 2.3, 12.5 Hz), 4.25 (1H, dd, *J* = 5.5, 12.5 Hz), 4.20-4.13 (1H, m), 4.18 (1H, ABq, *J* = 16.3 Hz), 4.12-4.02 (2H, m), 4.06 (1H, ABq, *J* = 16.3 Hz), 3.86 (1H, dd, *J* = 1.5, 12.6 Hz), 3.79 (3H, s), 3.68 (1H, dd, *J* = 1.5, 6.9 Hz), 2.97-2.87 (2H, m), 2.71 (1H, dd, *J* = 4.9, 12.6 Hz), 2.12 (3H, s), 2.06 (3H, s), 2.05 (3H, s), 2.04 (3H, s), 1.93 (3H, s), 1.93 (1H, dd, *J* =12.6, 12.6 Hz), 1.49 (9H, s); ^{13}C-NMR (125 MHz, $CDCl_3$) δ 170.8, 170.7, 170.5, 170.4, 170.0, 169.6, 168.8, 82.6, 82.2, 74.5, 70.5, 70.3, 69.1, 63.3, 62.8, 53.1, 50.7, 37.8, 28.1, 27.8, 23.6, 21.2, 21.0, 20.9; HRMS (ESI-TOF) *m/z* 666.2426 (666.2432 calcd for $C_{28}H_{44}NO_{15}S$, $[M+H]^+$).

***tert*-Butyl [2-(anthraquinone-2-carboxamido)ethyl] carbamate (S23).**

To a solution of **4** (242 mg, 0.961 mmol) in dry DMF (10.0 mL) were added NEM (750 μL, 5.93 mmol) and TBTU (376 mg, 1.17 mmol) under Ar atmosphere at 0 ^{o}C. After being stirred for 5 min, the solution of *N*-(*tert*-butoxycarbonyl)-1,2-diaminoethane (**S22**) (231 mg, 1.44 mmol) in DMF (2.00 mL) was added to the reaction mixture. After being stirred for 16 h at room temperature, the reaction mixture was quenched by addition of 1 N HCl aq. (10 mL). The resulting mixture was extracted with $CHCl_3$ (10 mL × 3). The extracts were washed with brine, dried over anhydrous Na_2SO_4, and concentrated *in vacuo*. The residue was recrystallized from EtOAc to give **S23** (229 mg, 0.582 mmol, 60 % yield). Data for **S23**: Yellow solid; R_f 0.86 (5/1 $CHCl_3$/MeOH); mp 195 ^{o}C; ^{1}H-NMR (500 MHz, DMSO-d_6) δ 8.94 (1H, t, *J* = 5.7 Hz), 8.61 (1H, s), 8.30 (1H, d, *J* = 7.7 Hz), 8.25-8.15 (3H, m), 7.94-7.90 (2H, m), 6.98 (1H, t, *J* = 5.7 Hz), 3.37 (2H, dt, *J* = 5.7, 6.3 Hz), 3.19 (2H, dt, *J* = 5.7, 6.3 Hz), 1.40 (9H, s); ^{13}C-NMR (125 MHz, DMSO-d_6) δ 182.6, 165.3, 156.3, 139.9, 135.1, 135.0, 133.5, 133.5,

133.4, 127.5, 127.4, 127.3, 126.1, 78.2, 40.0, 28.8; HRMS (ESI-TOF) *m/z* 395.1599 (395.1607 calcd for $C_{22}H_{23}N_2O_5$, $[M+H]^+$).

***N*-(2-Aminoethyl)-anthraquinone-2-carboxamide (S24).**

The anthraquinone derivative **S23** (91.6 mg, 0.232 mmol) was dissolved in TFA (2.00 mL) under Ar atmosphere at room temperature. After being stirred for 2 h, the reaction mixture was concentrated *in vacuo*. The residue was dissolved in a mixture of MeOH (3.00 mL) and 1N HCl aq. (6.00 mL), and then stirred for 1 h at room temperature. The resulting mixture was concentrated *in vacuo* to give **S24** (55.2 mg, 0.167 mmol, 72% yield). Data for **S24**: Yellow solid; R_f 0.10 (3/1 $CHCl_3$/MeOH); mp 229 ^oC; ^1H-NMR (500 MHz, DMSO-d_6) δ 9.13 (1H, t, J = 5.7 Hz), 8.70 (1H, d, J = 1.8 Hz), 8.39 (1H, dd, J = 1.8, 8.1 Hz), 8.32 (1H, d, J = 8.1 Hz), 8.28-8.23 (2H, m), 8.00-7.95 (4H, m), 3.59 (2H, dt, J = 5.7, 6.0 Hz), 3.05 (2H, br-dt, J = 5.8, 6.0 Hz); ^{13}C-NMR (125 MHz, DMSO-d_6) δ 182.6, 165.8, 139.5, 135.2, 135.1, 133.6, 133.5, 127.5, 127.4, 127.3, 126.3, 38.9, 37.9; HRMS (ESI-TOF) *m/z* 295.1059 (295.1083 calcd for $C_{17}H_{15}N_2O_3$, $[M+H]^+$).

Methyl (2-hydroxyethyl [5-acetamido-7-*O*-(*N*-(2-acetaminoethyl)-anthraquinone-2-carboxamide)-4,7,8,9-tetra-*O*-acetyl-3,5-dideoxy-2-thio-D-*glycero*-α-D-*galacto*-2-nonulopyranosyl]) nonate (S25).

The sialic acid derivative **S20** (74.3 mg, 0.112 mmol) was dissolved in TFA (2.00 mL) under Ar atmosphere and stirred for 2 h at room temperature. The reaction mixture was concentrated *in vacuo* to give crude **S21**. The crude **S21** was diluted with dry DMF (3.00 mL), and to the solution were added NEM (77.2 μL, 0.610 mmol) and TBTU (102 mg, 0.316 mmol) under Ar atmosphere at room temperature. After being stirred for 5 min, the solution of the anthraquinone derivative **S24** (35.2 mg, 0.106 mmol) was added to the reaction mixture. After being stirred for 2.5 h, the reaction mixture was quenched by addition of water (5 mL). The resulting mixture was extracted with $CHCl_3$ (3 mL × 3). The extracts were washed with brine, dried over anhydrous Na_2SO_4, and concentrated *in vacuo*. Purification of the residue by silica-gel column chromatography (30 g, $CHCl_3$/acetone=1/1) gave **S25** (81.9 mg, 92.4 μmol, 87% yield in 2 steps from **S20**). Data for **S25**: Yellow solid; R_f 0.92 (4/1 $CHCl_3$/MeOH); $[\alpha]^{25}_D$ +5.5 ^{o} (*c* 0.39, $CHCl_3$); mp 100 ^oC; ^1H-NMR (500 MHz, $CDCl_3$) δ 8.72 (1H, d, J = 1.2 Hz), 8.38-8.28 (5H, m), 7.85-7.80 (2H, m), 7.68 (1H, dd, J = 5.7, 6.0 Hz), 5.77 (1H, d, J = 9.7 Hz), 5.36 (1H, ddd, J = 2.3, 5.5, 7.7 Hz), 4.86 (1H, ddd, J = 4.6, 10.6, 12.6 Hz), 4.62 (1H, dd, J = 2.3, 12.3 Hz), 4.30 (1H, ABq, J = 14.7 Hz), 4.24 (1H, ABq, J = 14.7 Hz), 4.32-4.19 (3H, m), 4.14 (1H, dd, J = 5.5, 12.3 Hz), 3.86-3.78 (2H, m), 3.79 (3H, s), 3.78-3.72 (1H, m), 3.69 (1H, dd, J = 1.7, 10.6 Hz), 3.66-3.59 (1H, m), 2.96 (1H, td, J = 6.3, 14.3 Hz), 2.84 (1H, td, J = 6.9, 14.3 Hz), 2.71 (1H, dd, J = 4.6, 12.6 Hz), 2.12 (3H, s), 2.06 (6H, s), 2.04 (3H, s), 1.99 (1H, dd, J = 12.6, 12.6 Hz), 1.92 (3H, s); ^{13}C-NMR (125 MHz, $CDCl_3$) δ 182.6, 182.5, 171.2, 171.1, 171.0, 170.7, 170.3, 170.1, 168.6, 166.0,

139.9, 135.0, 134.4, 133.6, 133.5, 133.2, 127.7, 127.4, 127.3, 126.1, 82.9, 75.9, 75.4, 71.1, 69.6, 69.5, 63.5, 62.8, 53.3, 50.2, 41.6, 39.0, 37.9, 28.1, 23.4, 21.2, 21.0, 20.9, 20.8; HRMS (ESI-TOF) *m/z* 886.2709 (886.2704 calcd for $C_{41}H_{48}N_3O_{17}S$, $[M+H]^+$).

2-Hydroxyethyl (5-acetamido-7-*O*-[*N*-(2-acetaminoethyl)-anthraquinone-2-carboxamide]-4,7,8,9-tetra-*O*-acetyl-3,5-dideoxy-2-thio-D-*glycero*-α-D-*galacto*-2-nonulopyranosyl)nonic acid (3). To a solution of **S25** (74.1 mg, 83.6 μmol) in a mixture of dry $CHCl_3$ (1.00 mL) and dry MeOH (5.00 mL) was added 10 wt% NaOHaq (2.00 mL、4.40 mmol) under Ar atmosphere at 0 °C. After being stirred for 2 h at room temperature, the reaction mixture was neutralized by addition of Amberlite IR-120 (H^+ type). The resulting mixture was filtered, and then the filtrate was concentrated *in vacuo*. Purification of the residue by reversed phase chromatography (5 g, H_2O/MeOH=100/0 → 70/30) and recrystallization from EtOAc gave **3** (40.6 mg, 57.7 μmol, 69% yield). Data for **3**: Yellow solid; R_f 0.10 (2/1 $CHCl_3$/MeOH); $[\alpha]^{25}_D$ +25.8 ° (*c* 0.22, MeOH); mp 205 °C; ^{1}H-NMR (500 MHz, DMSO-d_6/D_2O=9/1) δ 8.61 (1H, d, *J* = 1.4 Hz), 8.32 (1H, dd, *J* = 1.7, 8.0 Hz), 8.28 (1H, d, *J* = 8.0 Hz), 8.26-8.21 (2H, m), 7.98-7.95 (2H, m), 4.04 (1H, ABq, *J* = 14.6 Hz), 3.95 (1H, ABq, *J* = 14.6 Hz), 3.87-3.82 (1H, m), 3.68 (1H, dd, *J* = 9.5, 10.3 Hz), 3.63-3.38 (11H, m), 2.83-2.75 (1H, m), 2.70-2.63 (2H, m), 1.84 (3H, s), 1.43 (1H, dd, *J* = 11.5, 11.5 Hz); ^{13}C-NMR (125 MHz, DMSO-d_6) δ 182.8, 182.7, 171.6, 171.0, 170.6, 165.8, 139.8, 135.3, 135.0, 133.5, 133.5, 133.4, 127.7, 127.4, 127.3, 126.2, 85.7, 79.5, 77.3, 74.9, 70.4, 70.0, 69.6, 62.7, 61.5, 56.5, 52.3, 42.6, 38.2, 32.2, 23.4; HRMS (ESI-TOF) *m/z* 702.1964 (702.1969 calcd for $C_{32}H_{36}N_3O_{13}S$, $[M-H]^-$).

Reagents and apparatus for analytical and biochemical assays.

Recombinant influenza virus H1N1 (A/California/04/2009) neuraminidases (wild type (non-drug (oseltamivir)-resistant) and H274Y subtype (drug (oseltamivir)-resistant)) were purchased from Sino Biological Inc. The substrate for enzyme inhibition assay, 2'-(4-methylumbelliferyl)-α-D-*N*-acetylneuraminic acid, sodium salt hydrate, was purchased from Toronto Research Chemicals Inc. B-100A (UVP Inc., 365 nm, 100 W) was used for photo-irradiation in the UV visible region. EPR spectrum experiments were carried out with a Bruker Biospin EMX EPR.

Photodegradation of Neuraminidases.

Neuraminidase degradation experiments were performed with each neuraminidase (125 mU) in a volume of 85.0 μL in 50 mM Tris buffer (containing 5 mM $CaCl_2$ and 200 mM NaCl, pH 7.5) at 25 °C for 15min. or 60 min. under irradiation with a UV lamp (UVP Inc., 365 nm, 100 W) placed 10 cm from the sample.

Polyacrylamide gel Electrophoresis and immunoblotting.[2]

Electrophoresis buffer consisted of SDS (5%, wt/vol), glycerol (27%, vol/vol), DTT (0.5%, wt/vol) and bromophenol blue (0.007%, wt/vol); 5.0 μL of buffer was added to each 10.0 μL of sample. Gels (10% SDS) were run by applying 50 mA for 2 h. The separated proteins were transferred into transfer buffer (the mixture of tris (3 g) and glycine (14.4 g) in MeOH (200mL) was diluted with distilled water adjusted to total amount of 1000 mL) at 200 mA for 2 h to blot onto a Amersham Hybond ECL Nitrocellulose Membrane (GE Healthcare). Nonspecific binding sites were blocked for 30 min by immersing the membrane in a blocking solution (tris-buffered saline with Tween 20 (TBST): 10 mM Tris-HCl, (pH 7.6) containing 150 mM NaCl, 0.1% vol/vol Tween 20, and 3% wt/vol nonfat dry milk). After a short wash in TBST, the membrane was incubated in a 1:100 dilution of primary antibody (mouse monoclonal antibody to H1N1 neuraminidase) in TBST with 3% wt/vol nonfat dry milk for 15 h at 4 ^{o}C. After washing with TBST (30 min, 5 times), the membrane was incubated in a 1:1000 of horseradish peroxidase-conjugated secondary antibody anti-mouse IgG (GE Healthcare) in TBST with 3% wt/vol nonfat dry milk for 3 h at room temperature. After washing with TBST (30 min, 5 times), the immunocomplexes were detected by using ECL reagent, Immobilon Western (Millipore, Billerica, MA). Exposure to RX-U films (Fuji Film) was carried out for 1 to 5 min.

Enzyme inhibition assay.[3.4]

5.00 μL of enzyme solution (25 U/mL in 50 mM Tris buffer (containing 5 mM $CaCl_2$ and 200 mM NaCl, pH 7.5)) and 80.0 μL of each concentration of compound in 50 mM Tris buffer (containing 5 mM $CaCl_2$ and 200 mM NaCl, pH 7.5) were added to each 0.5 mL micro test tube (Eppendorf Co., Ltd.). Following pre-incubation at 25 ^{o}C for 15 min., 5.00 μL of the substrate solution (3.88 mM in the same buffer) was then added to the test tube, resulting in final compound concentrations that ranged from 10.0 nM to 630 μM. Following further incubation at 25 ^{o}C for 10 min, the enzyme reaction was terminated by the addition of 10 μL of 10wt% NaOH aq. and each sample was moved to a 96-well plate (black polystyrene, flat bottom, non-sterile, Costar). In the case of photo-irradiation, neuraminidase was pre-incubated for 15 or 60 minutes under irradiation with a UV lamp (UVP Inc., 365 nm, 100 W) placed at 10 cm from the sample. 4-Methylumbelliferone was immediately quantified by fluorometrically by a microplate reader SAFIRE (TECAN Inc.). The excitation wavelength was 365 nm and the emission wavelength was 450 nm. For the determination of enzyme activity, nonlinear regression analysis with Prism® version 5 (Graphpad Software, Inc.) was used.

EPR spectrometry.[5]

EPR spectrum experiments were carried out with a Bruker Biospin EMX EPR and recorded under the following conditions: temperature 296 K, microwave frequency 9.394 GHz, microwave power 16 mW, field modulation 0.1 mT at 100 kHz, scan time 2 min. DMPO was used as a spin-trapping agent. To a

1.00 mM compound (20.0 μL in 50 mM Tris buffer (containing 5 mM $CaCl_2$ and 200 mM NaCl, pH 7.5)), 5.00 mM DETAPAC (40.0 μL in same buffer), DMPO (11.1 μL in same buffer) and the buffer (128.9 μL) were added and under an aerobic condition. The mixed solution was collected in a flat cell, irradiated with UV lamp (UVP Inc., 365 nm, 100 W) at a distance of 40 cm, and subjected immediately to EPR measurement.

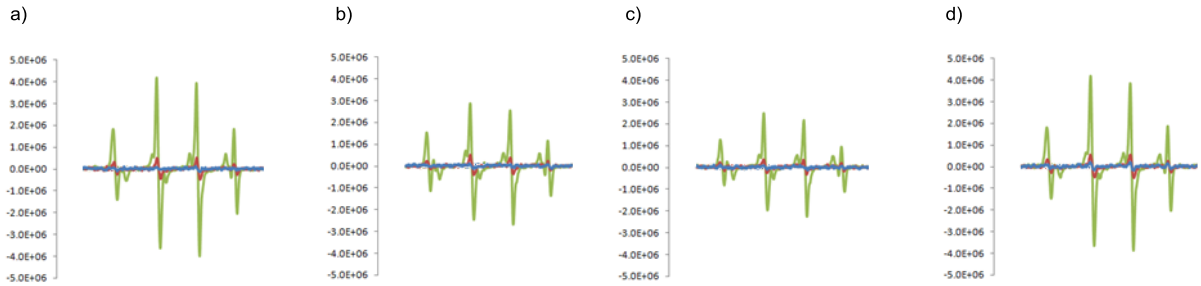


Fig. S1. EPR spectra obtained during photo-irradiation of **1**-**4** in the presence of DMPO. Each compound (100 μM) was incubated with DMPO (500 mM) in Tris buffer (pH 7.0, 50 mM) containing diethylenetriamine pentaacetic acid (1 mM) under irradiation with a UV lamp (365 nm, 100 W) at 25 °C. Spectra (a–d) represent **1**, **2**, **3**, and **4**, respectively. Blue, red, and green lines show EPR spectra after 0 s, after 120 s without UV, and after 120 s with UV, respectively.

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4 H. J. Jeong, Y. B. Ryu, S. -J. Park, J. H. Kim, H. -J. Kwon, J. H. Kim, K. H. Park, M. -C. Rho and W. S. Lee, *Bioorg. Med. Chem.*, 2009, **17**, 6816.

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^{1}H NMR and ^{13}C NMR spectrum charts.

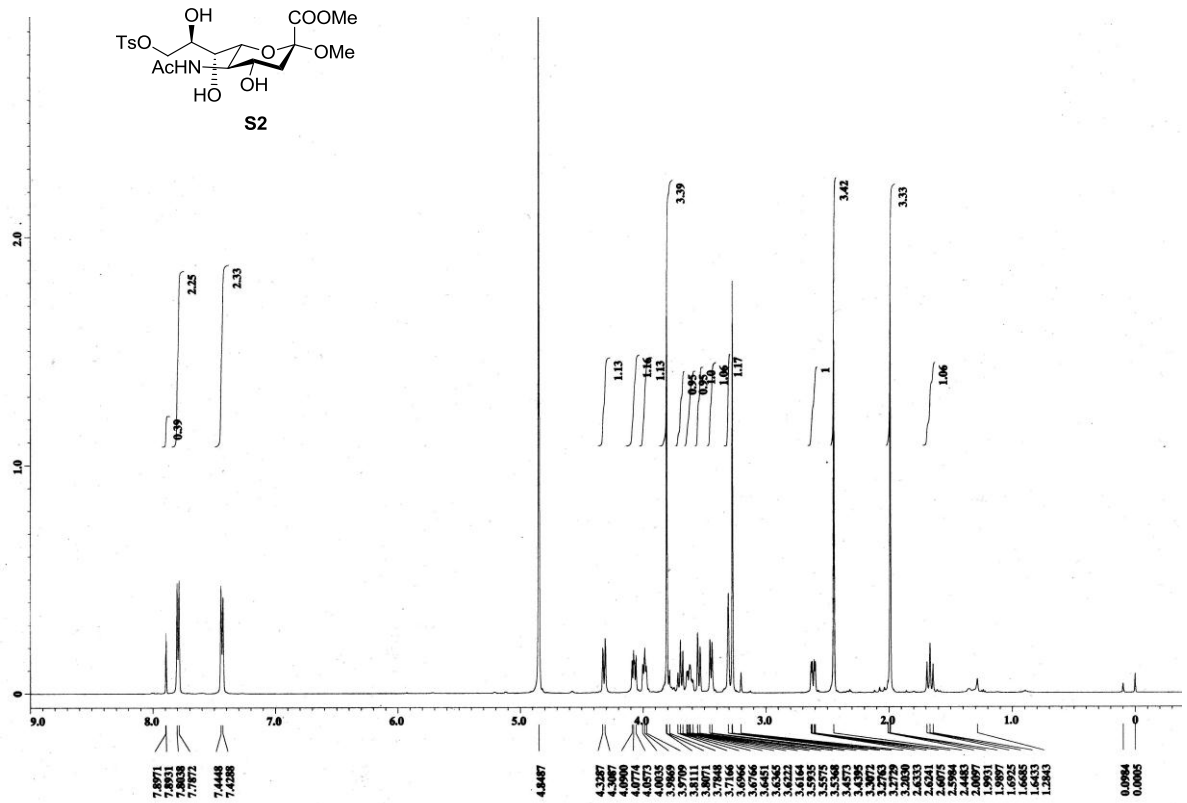

Fig. S2. ^{1}H-NMR spectrum of compound **S2**

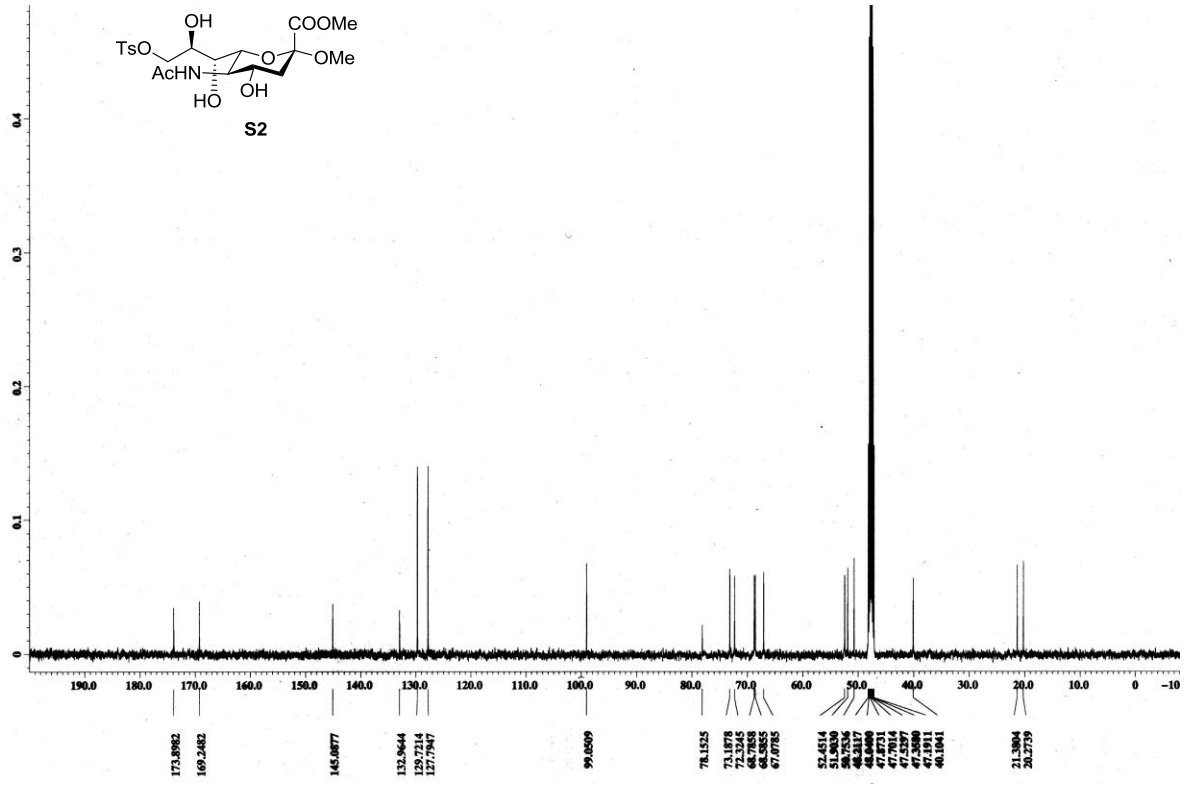

Fig. S3. ^{13}C -NMR spectrum of compound **S2**

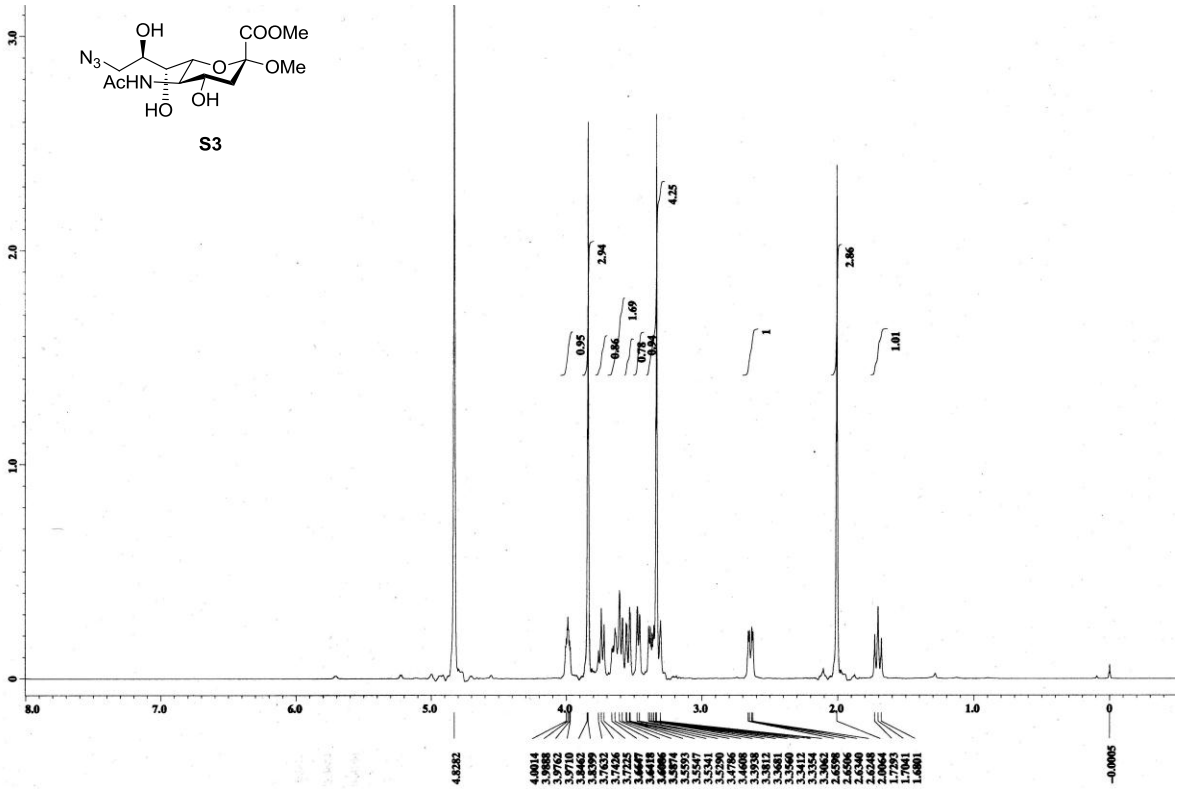

Fig. S4. ^{1}H-NMR spectrum of compound **S3**

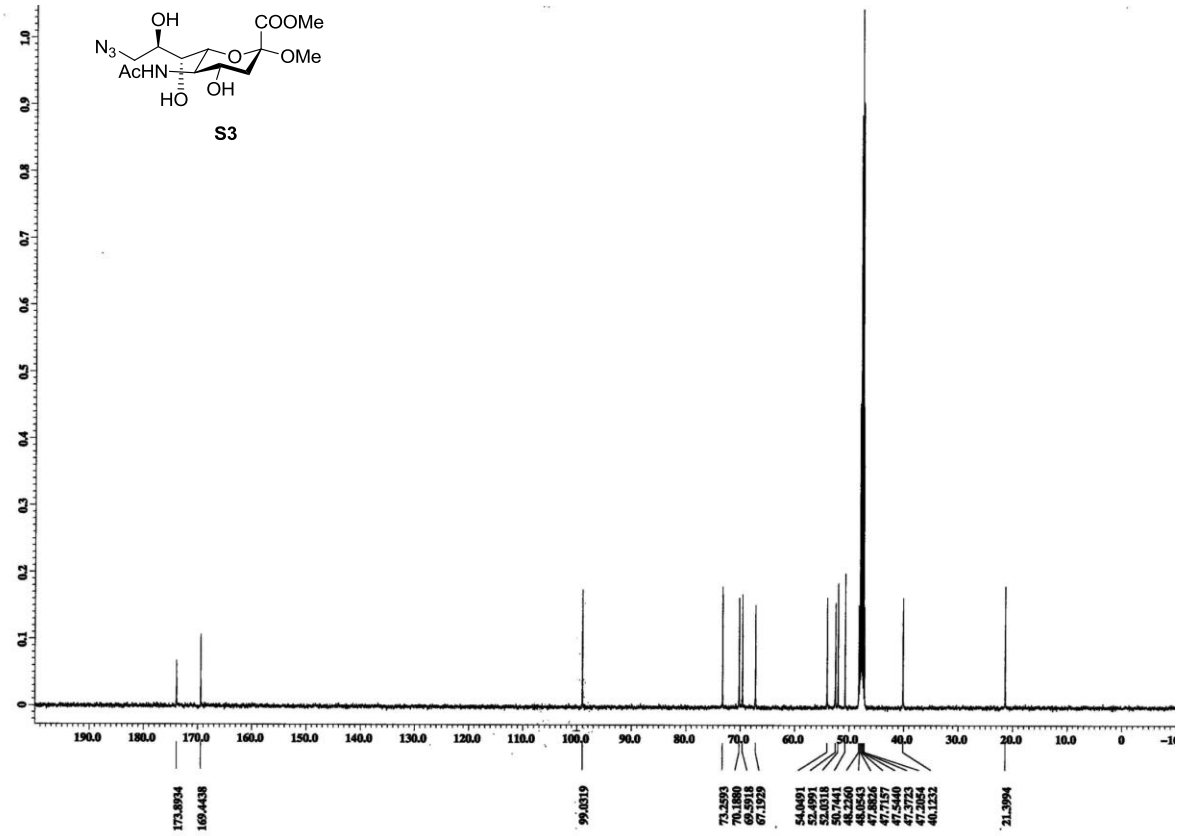

Fig. S5 ^{13}C -NMR spectrum of compound **S3**

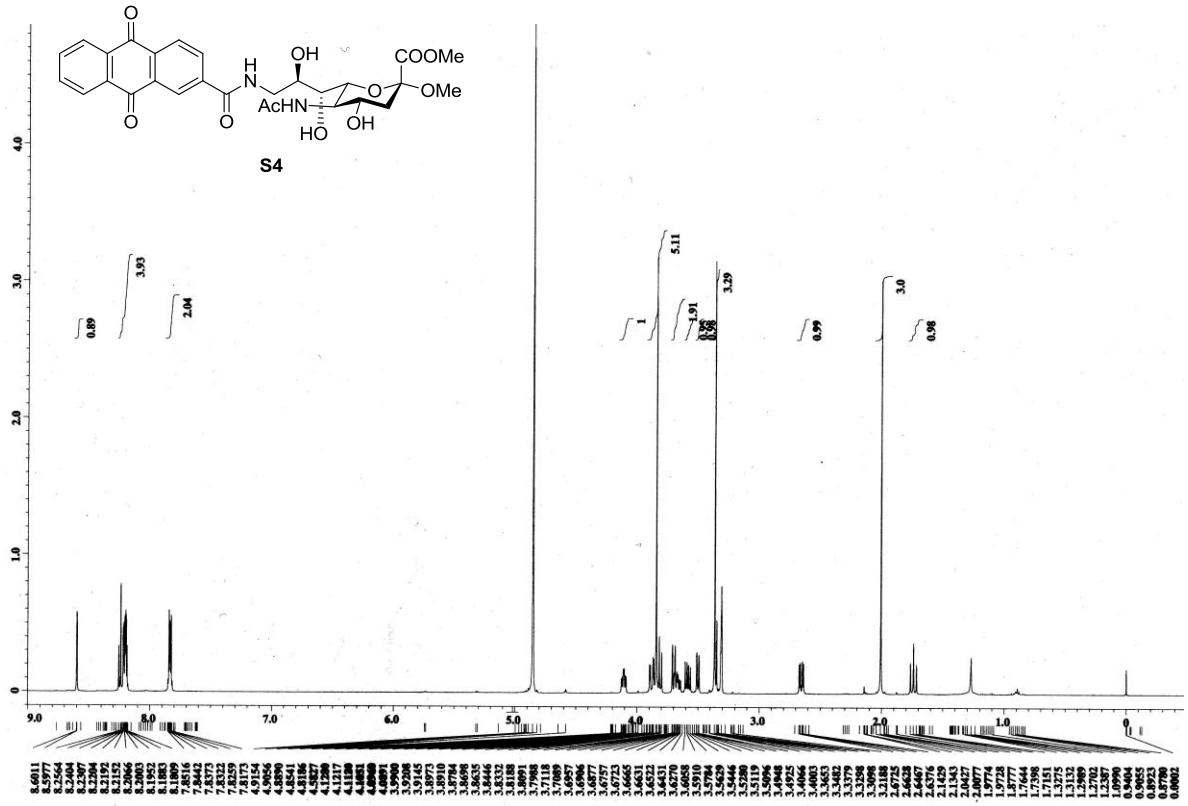

Fig. S6. ^{1}H-NMR spectrum of compound **S4**

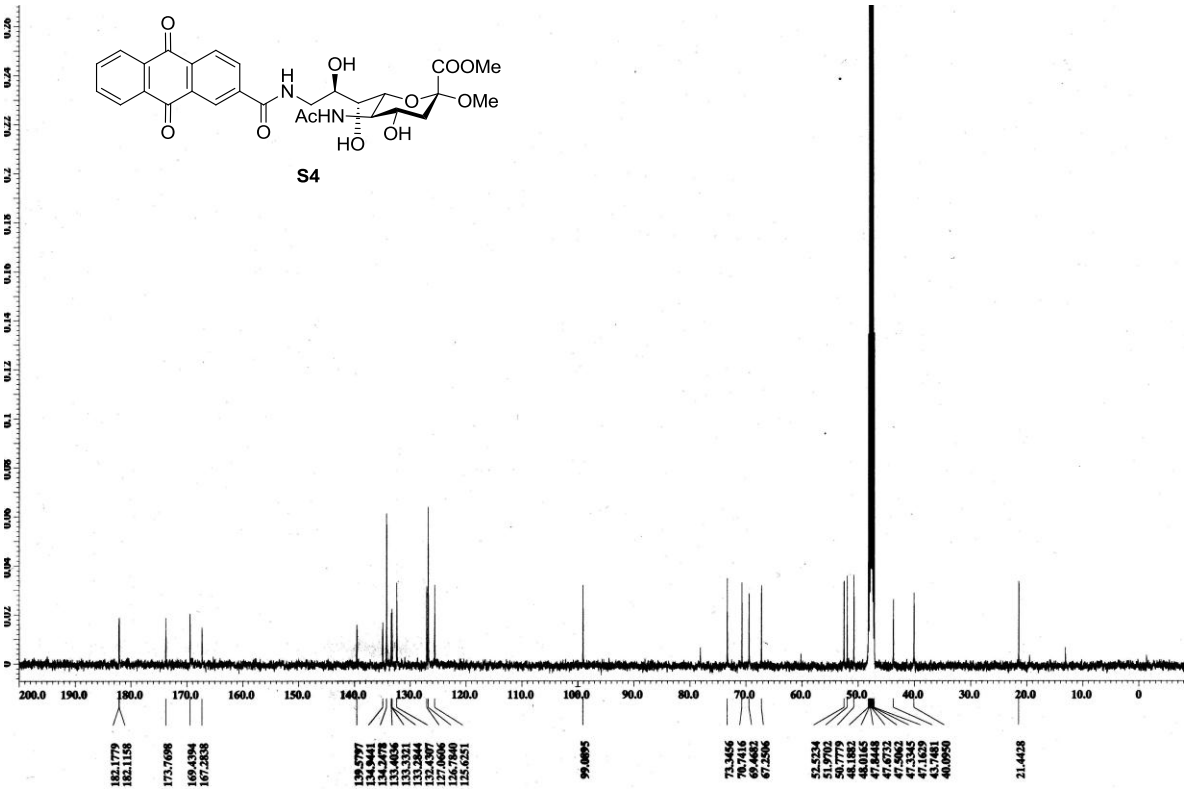

Fig. S7. ^{13}C -NMR spectrum of compound **S4**

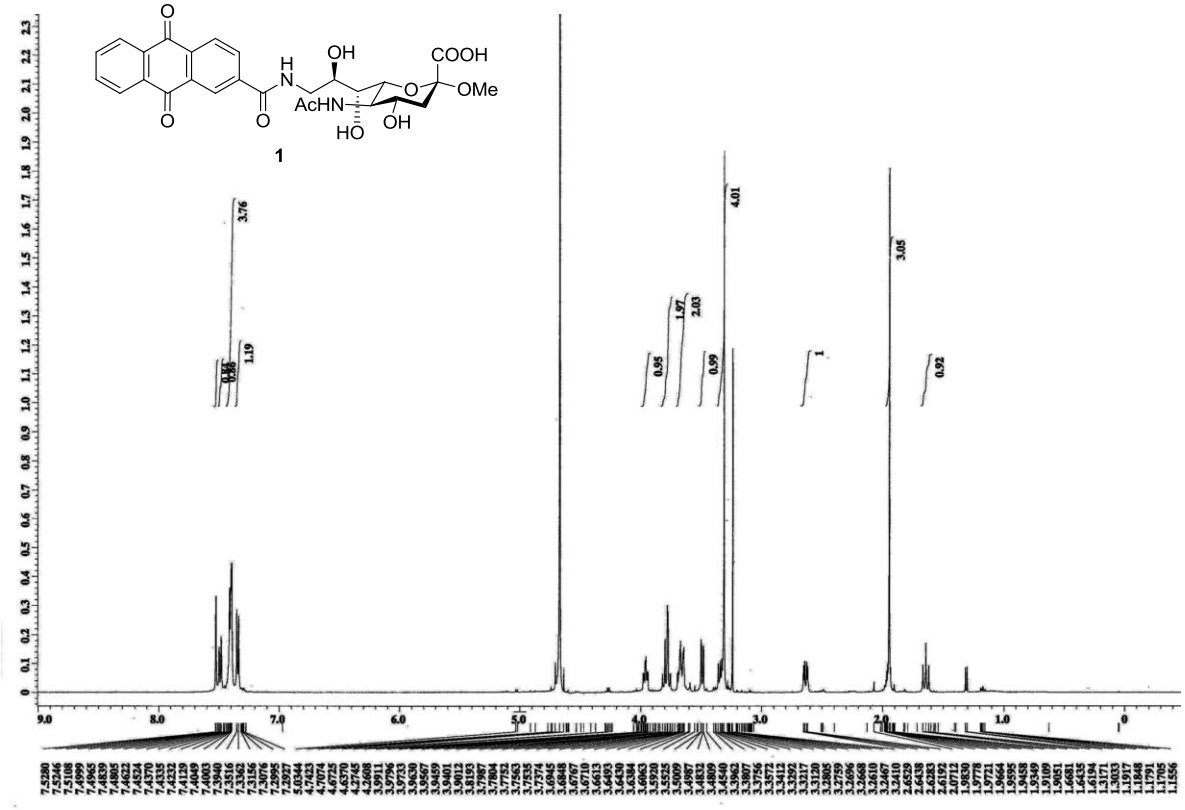

Fig. S8. ^{1}H-NMR spectrum of compound **1**

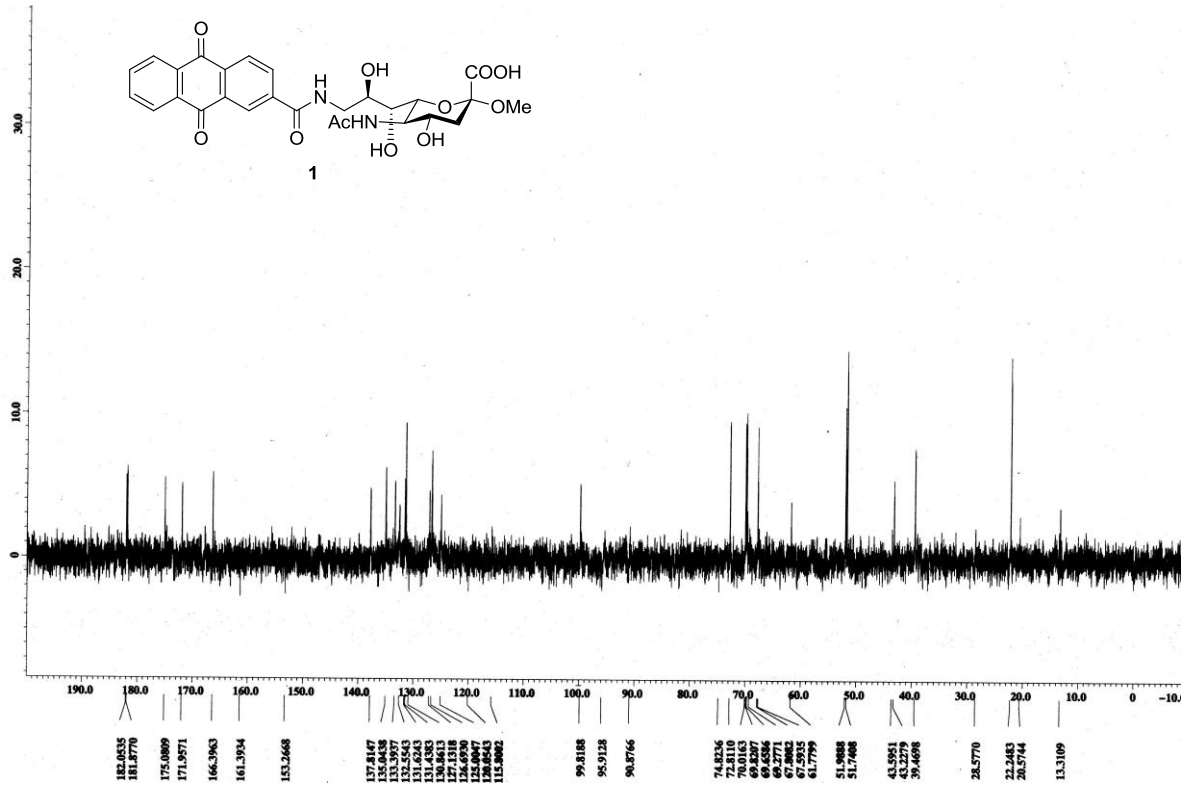

Fig. S9. ^{13}C -NMR spectrum of compound **1**

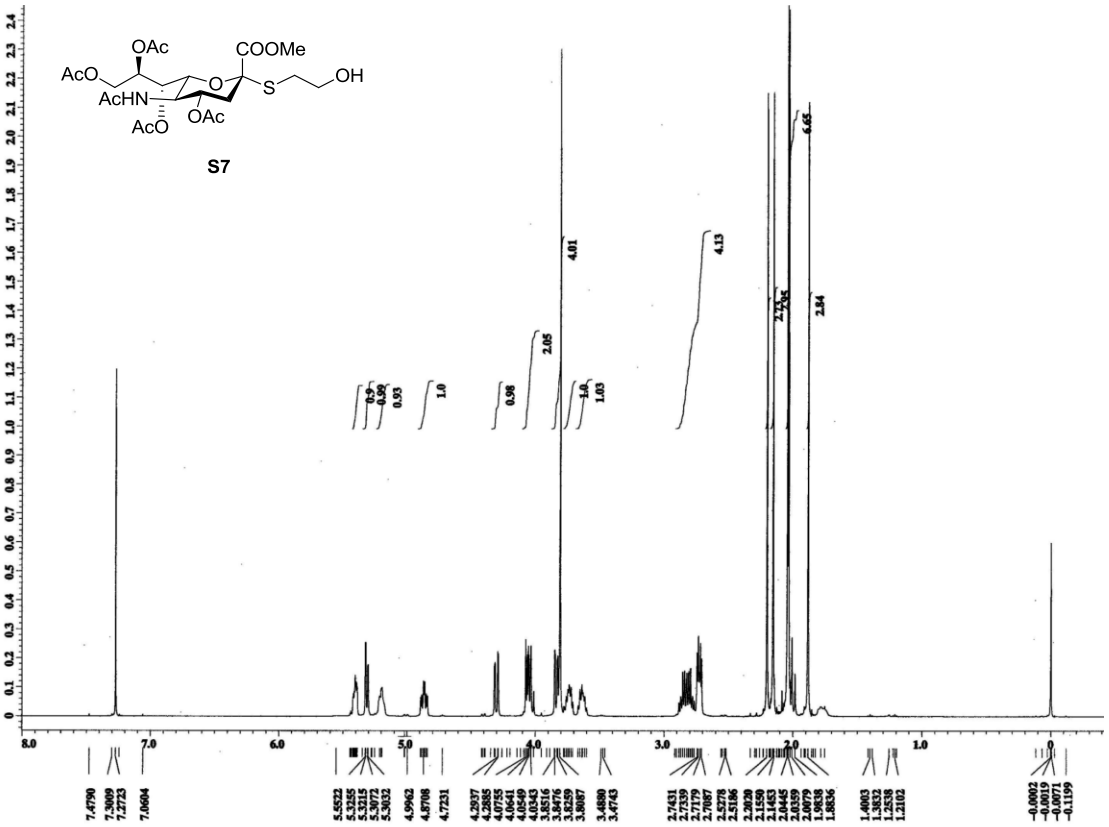

Fig. S10. ^{1}H-NMR spectrum of compound **S7**

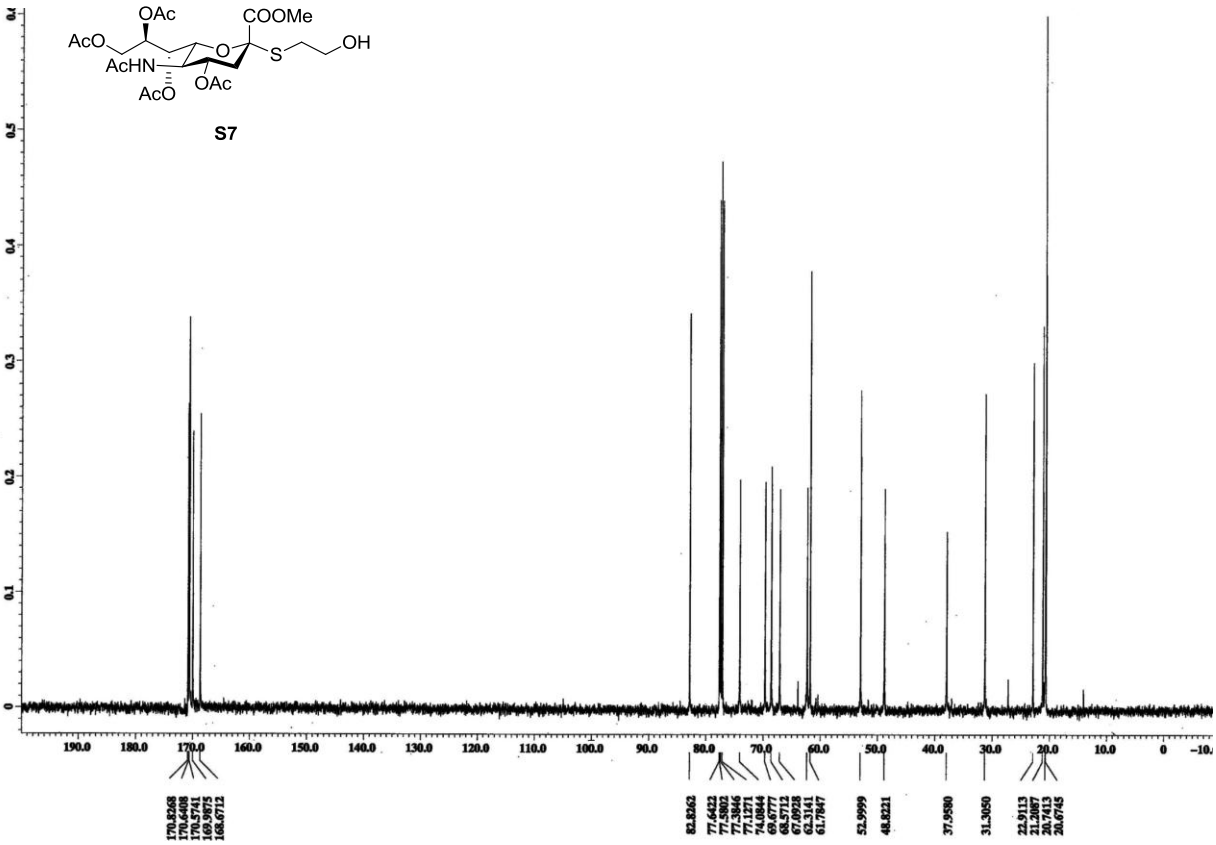

Fig. S11 ^{13}C -NMR spectrum of compound **S7**

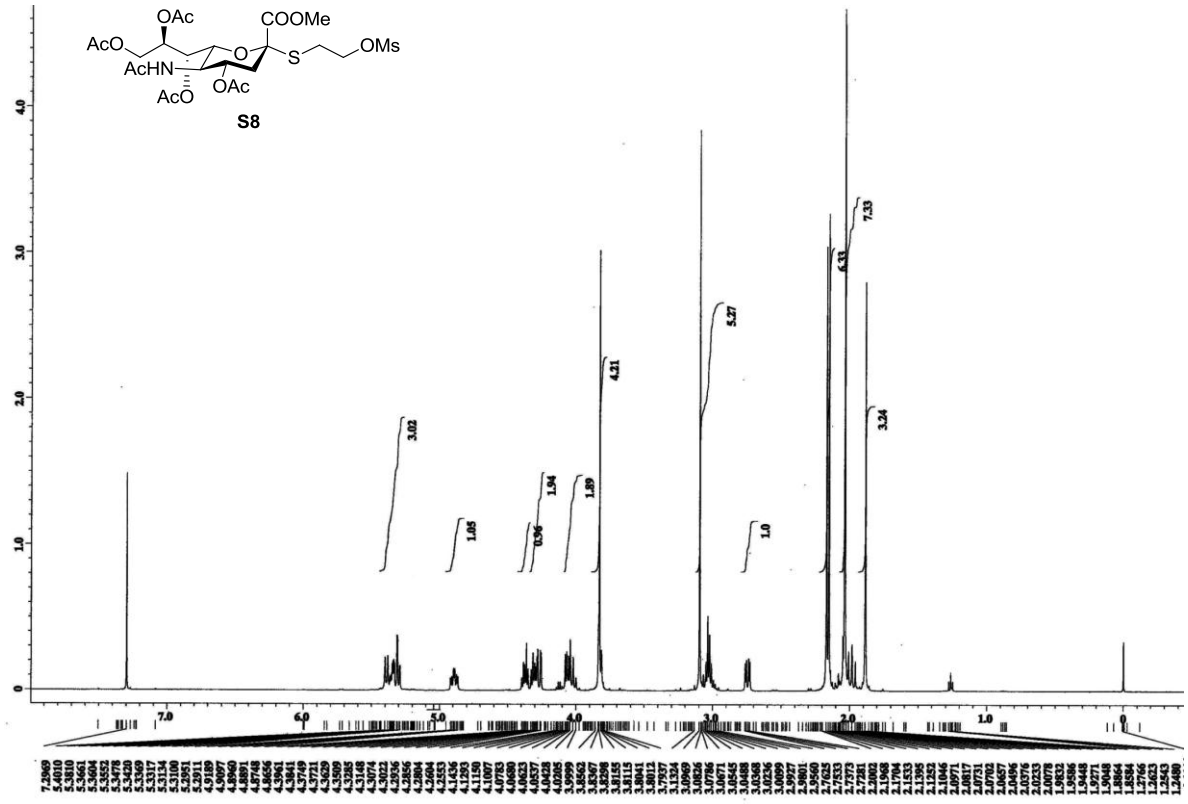

Fig. S12. ^{1}H-NMR spectrum of compound **S8**

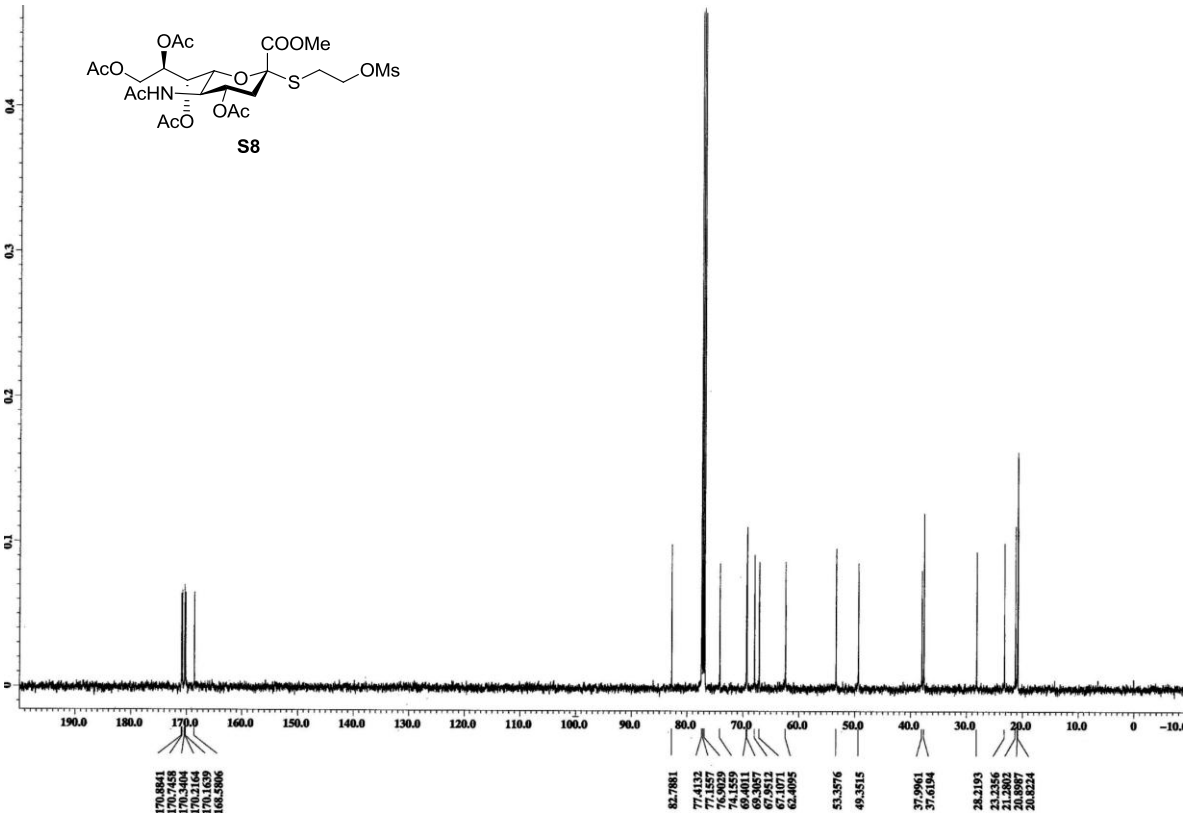

Fig. S13. ^{13}C -NMR spectrum of compound **S8**

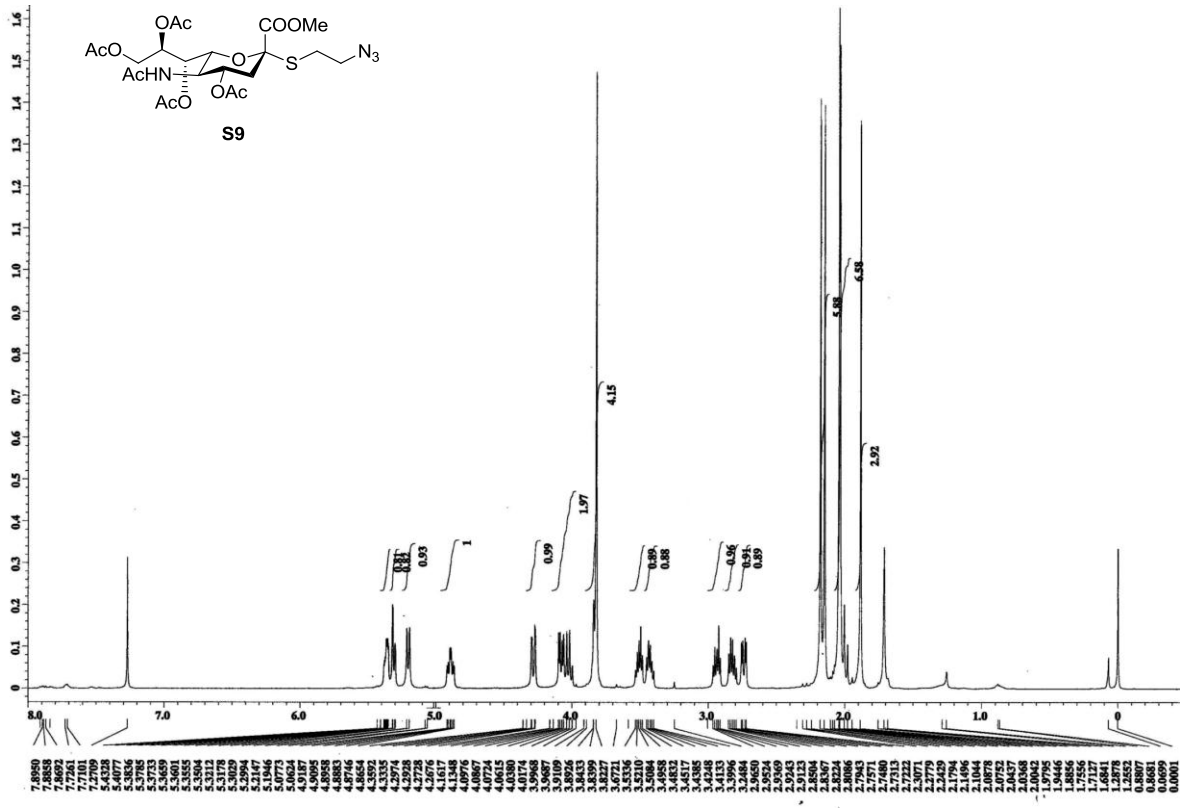

Fig. S14. ^{1}H-NMR spectrum of compound **S9**

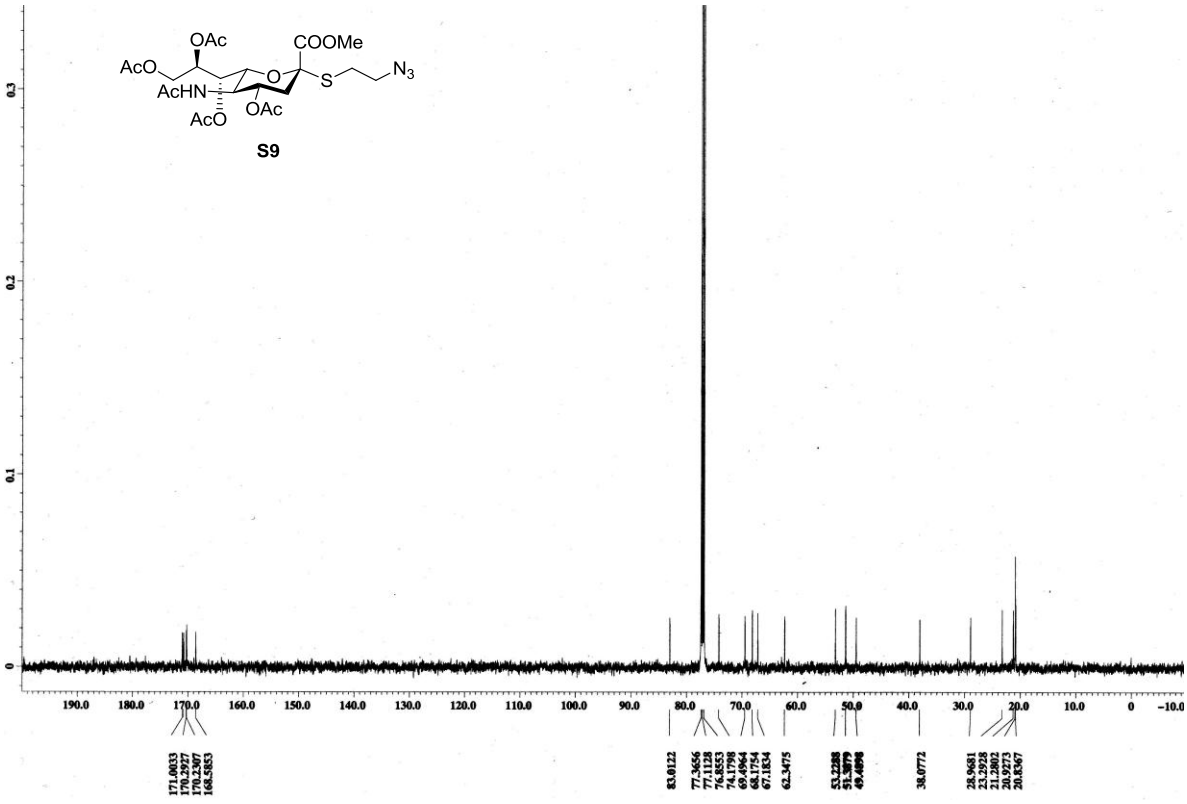

Fig. S15. ^{13}C -NMR spectrum of compound **S9**

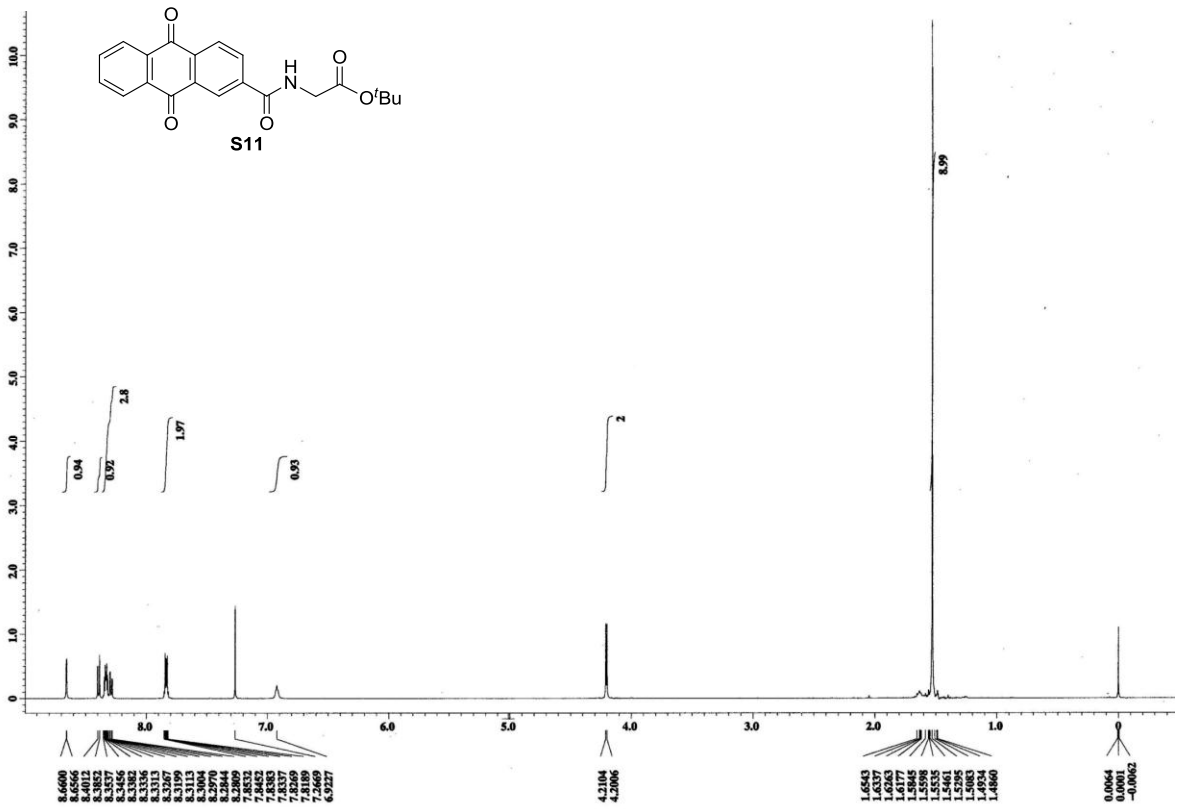

Fig. S16. ^{1}H-NMR spectrum of compound **S11**

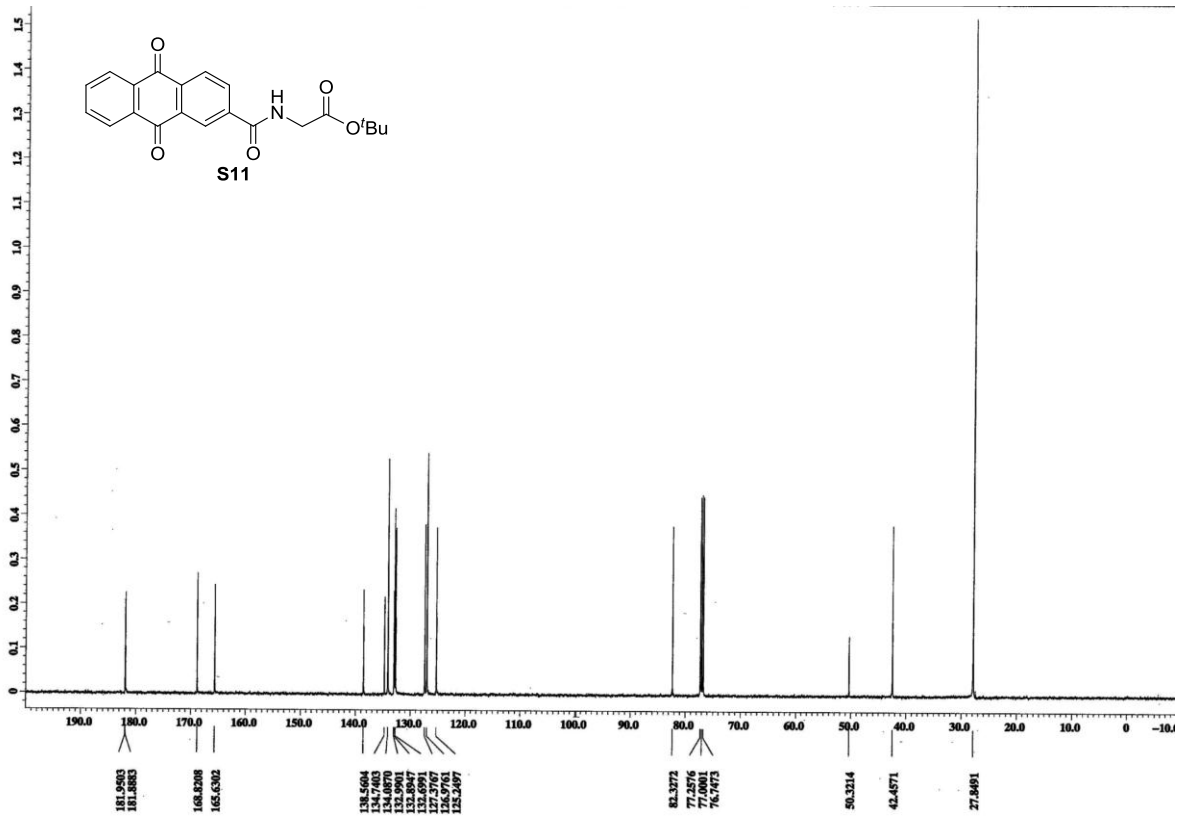

Fig. S17. ^{13}C -NMR spectrum of compound **S11**

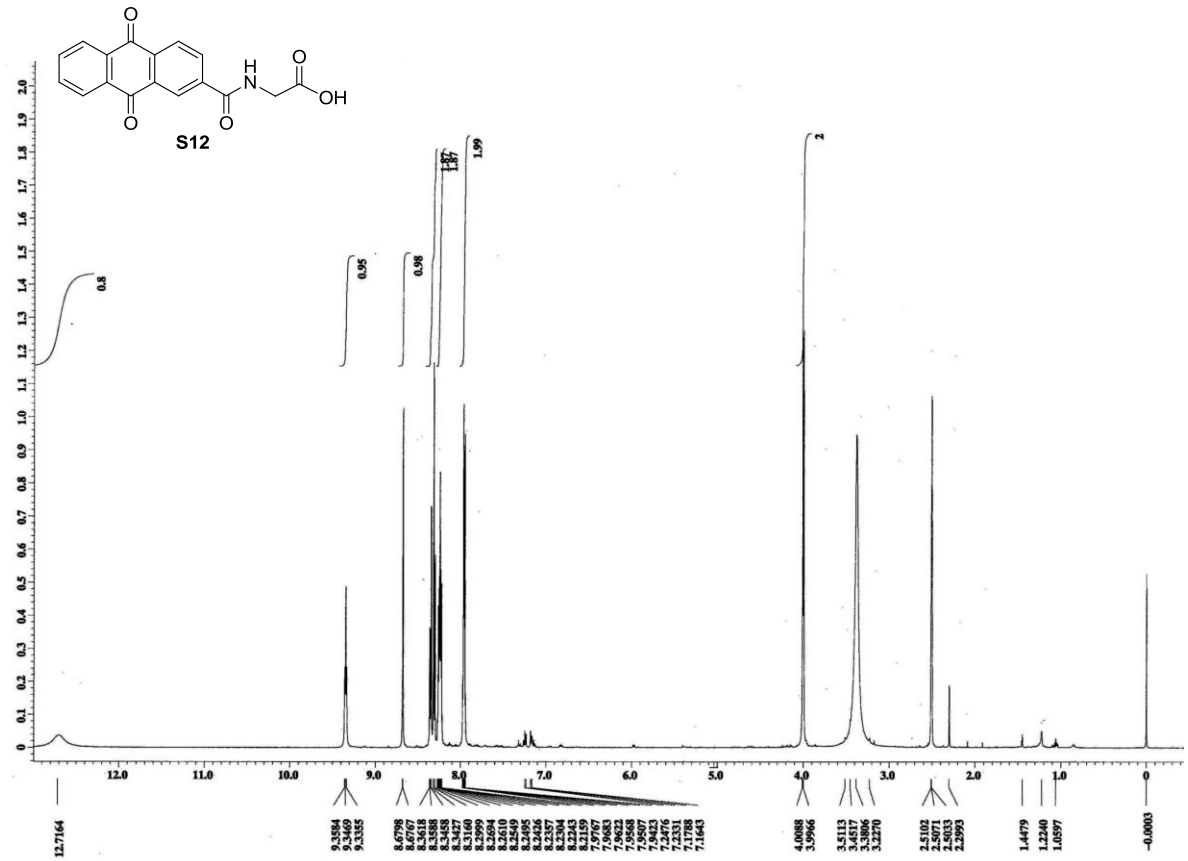

Fig. S18. ^{1}H-NMR spectrum of compound **S12**

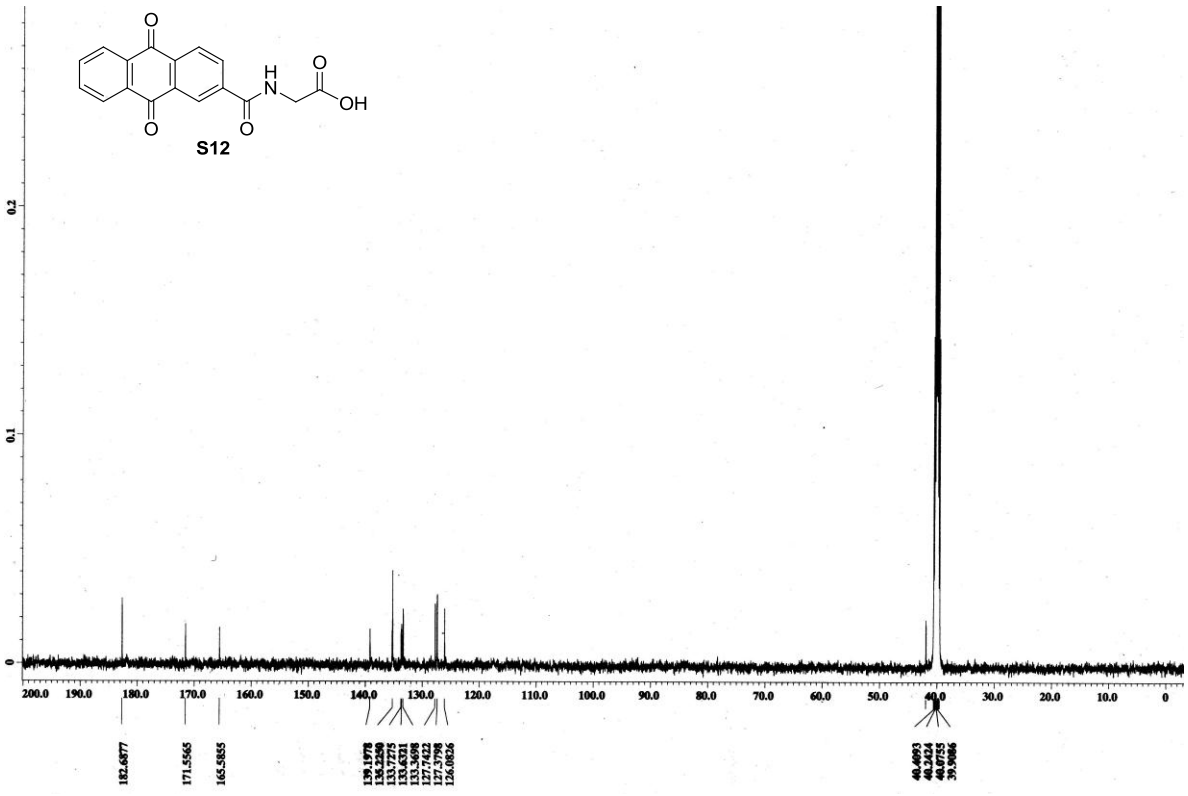

Fig. S19. ^{13}C -NMR spectrum of compound **S12**

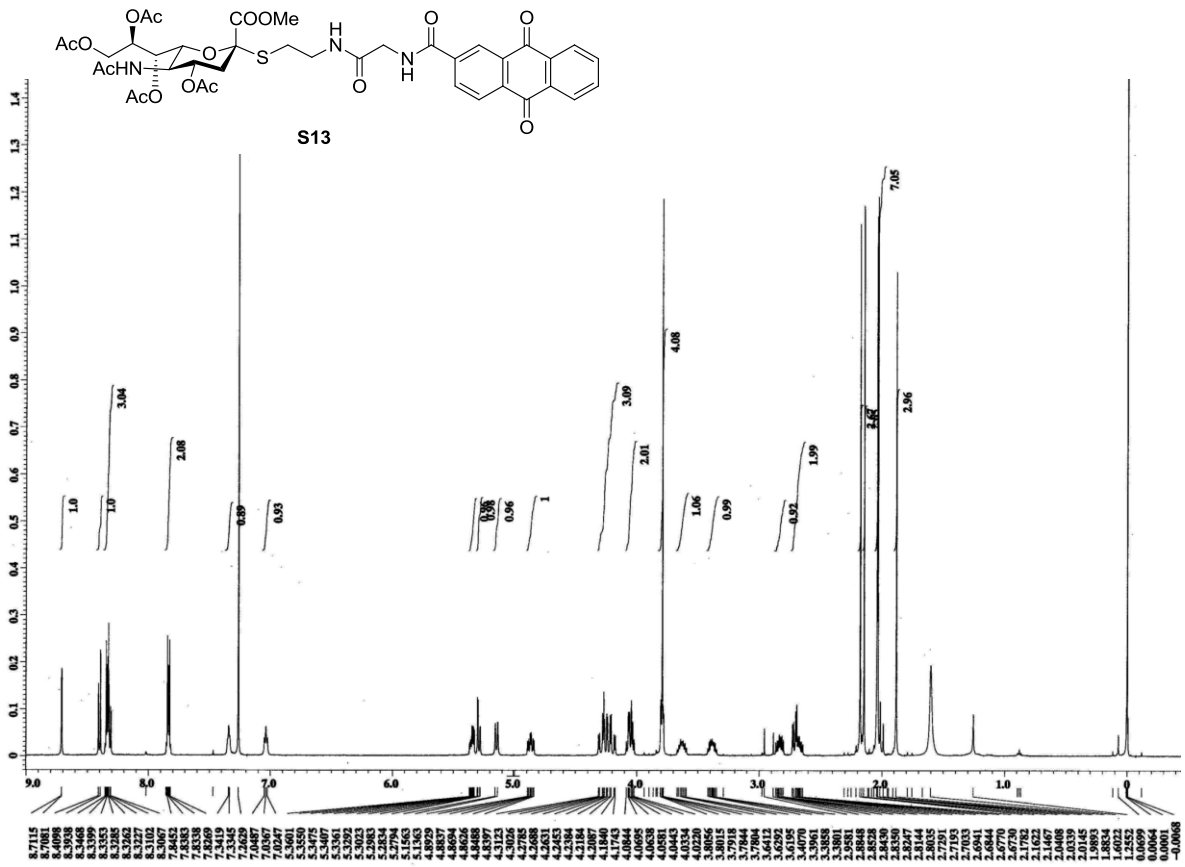

Fig. S20. ^{1}H-NMR spectrum of compound **S13**

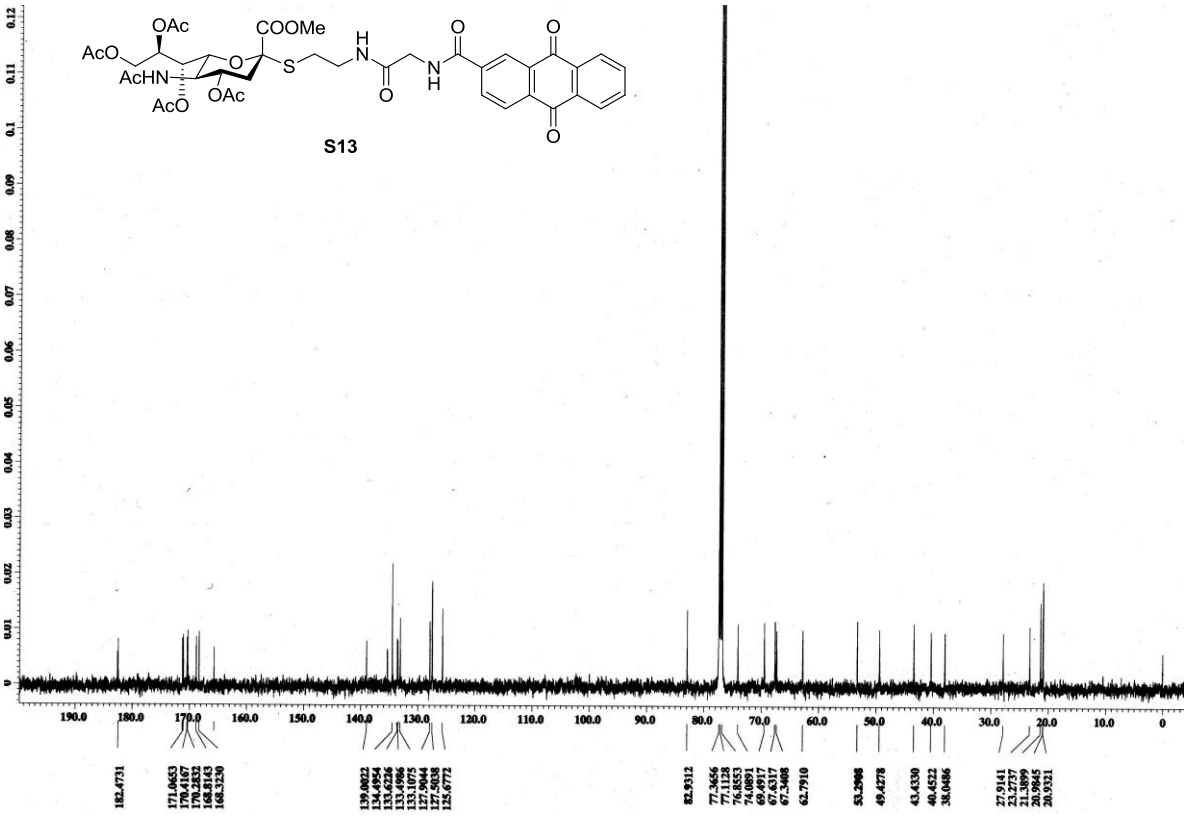

Fig. S21. ^{13}C -NMR spectrum of compound **S13**

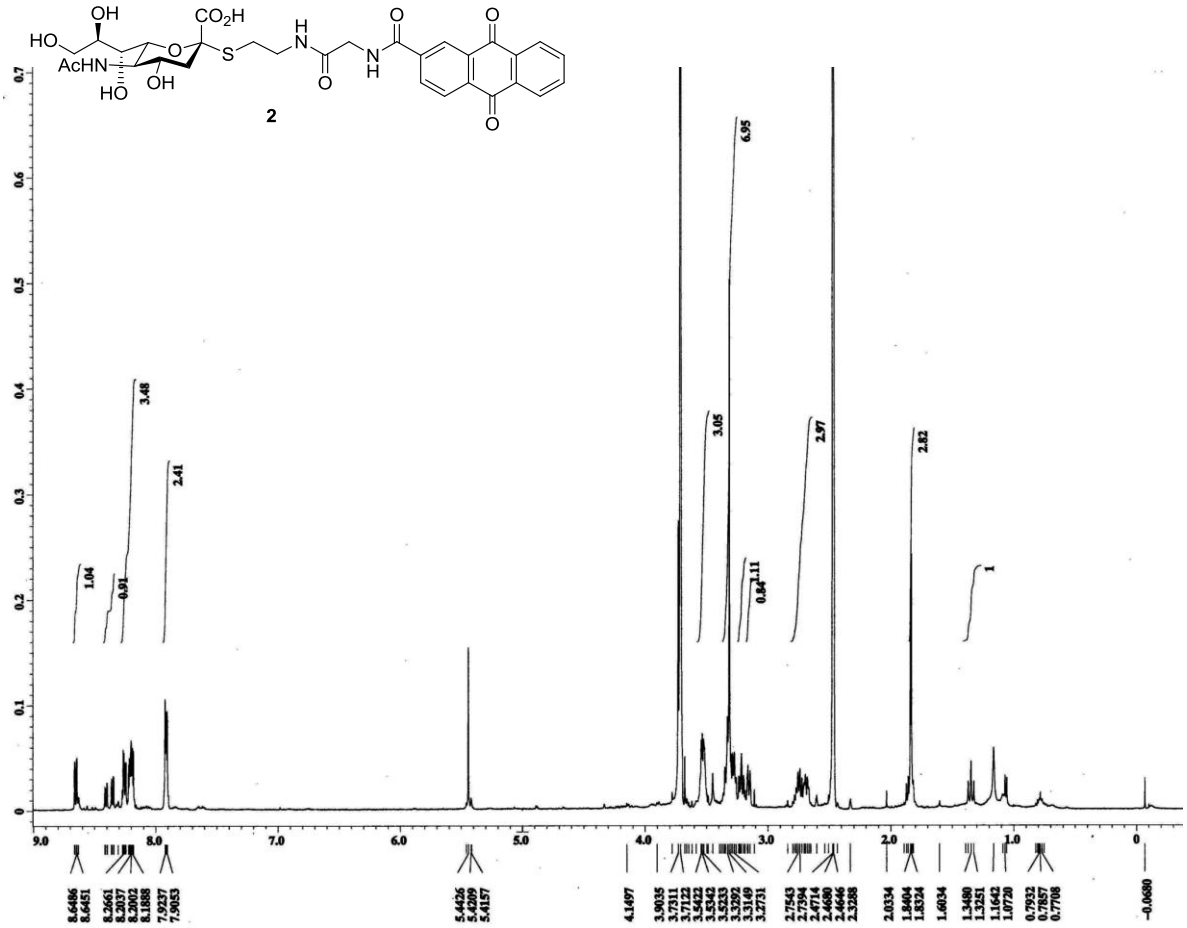

Fig. S22. ^{1}H-NMR spectrum of compound **2**

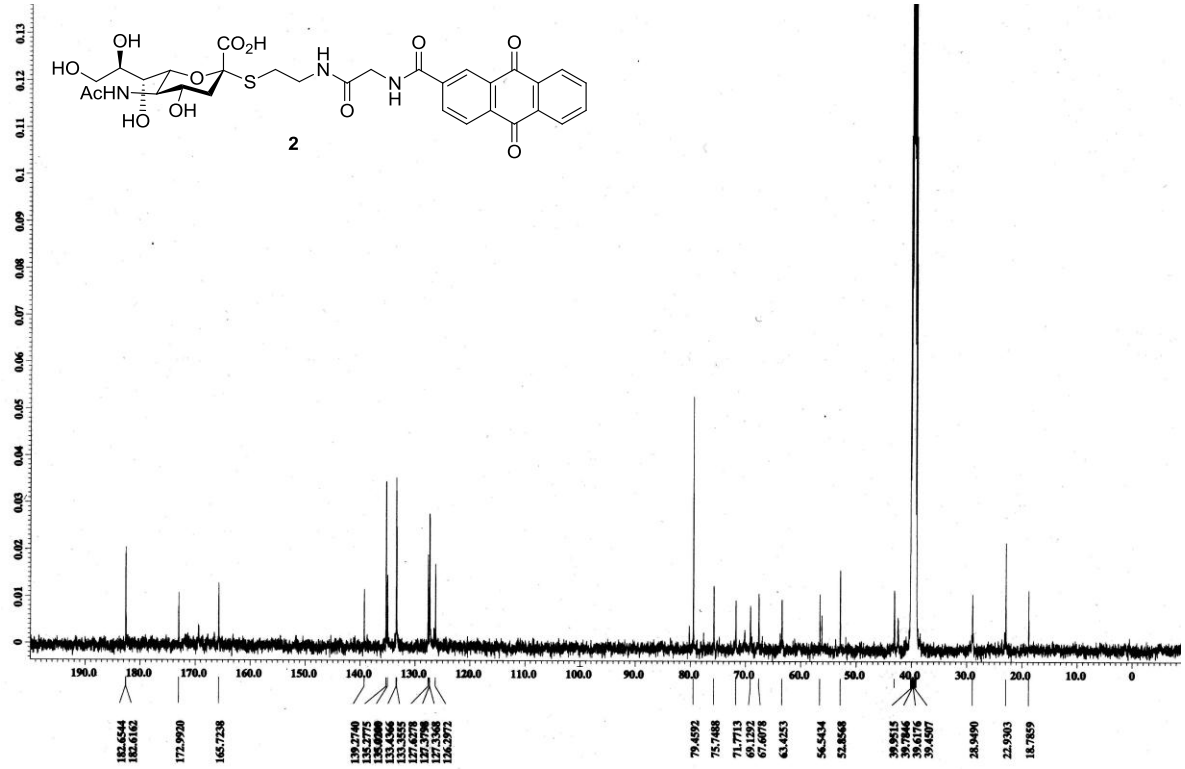

Fig. S23. ^{13}C -NMR spectrum of compound **2**

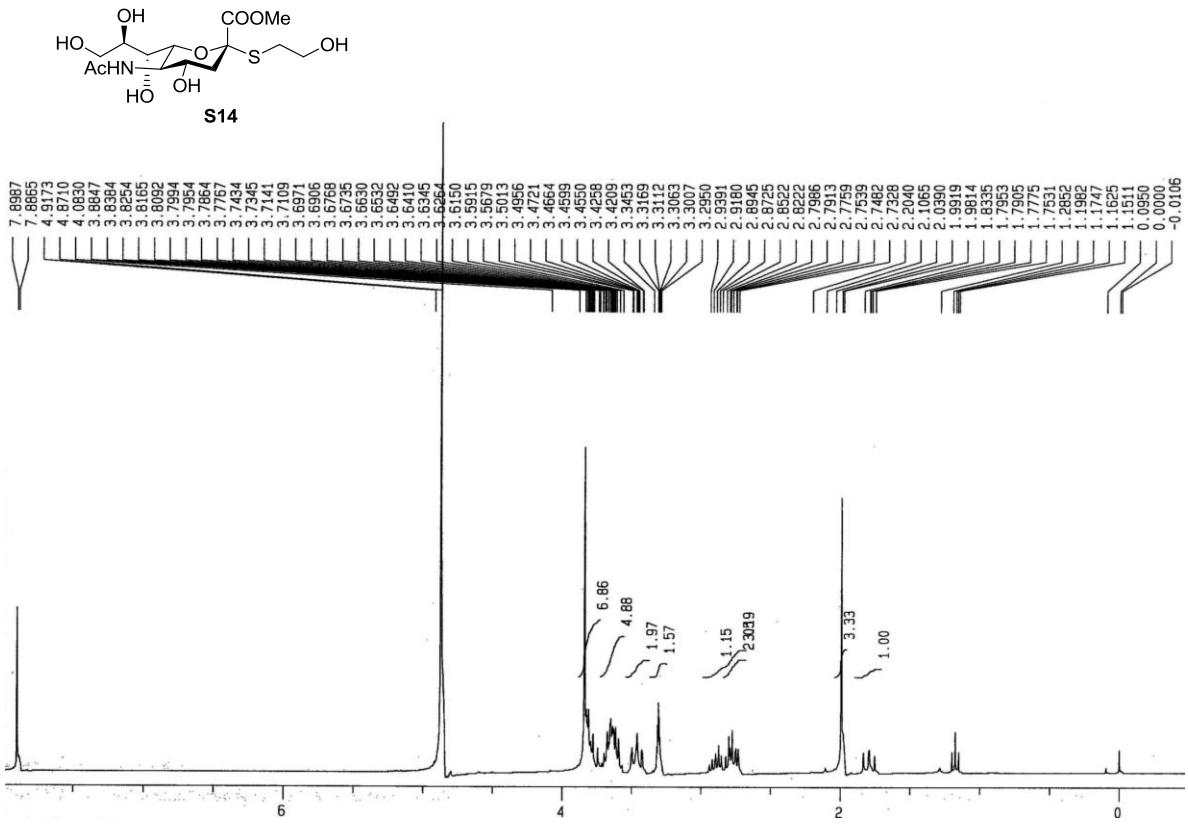

Fig. S26. ^{1}H-NMR spectrum of compound **S14**

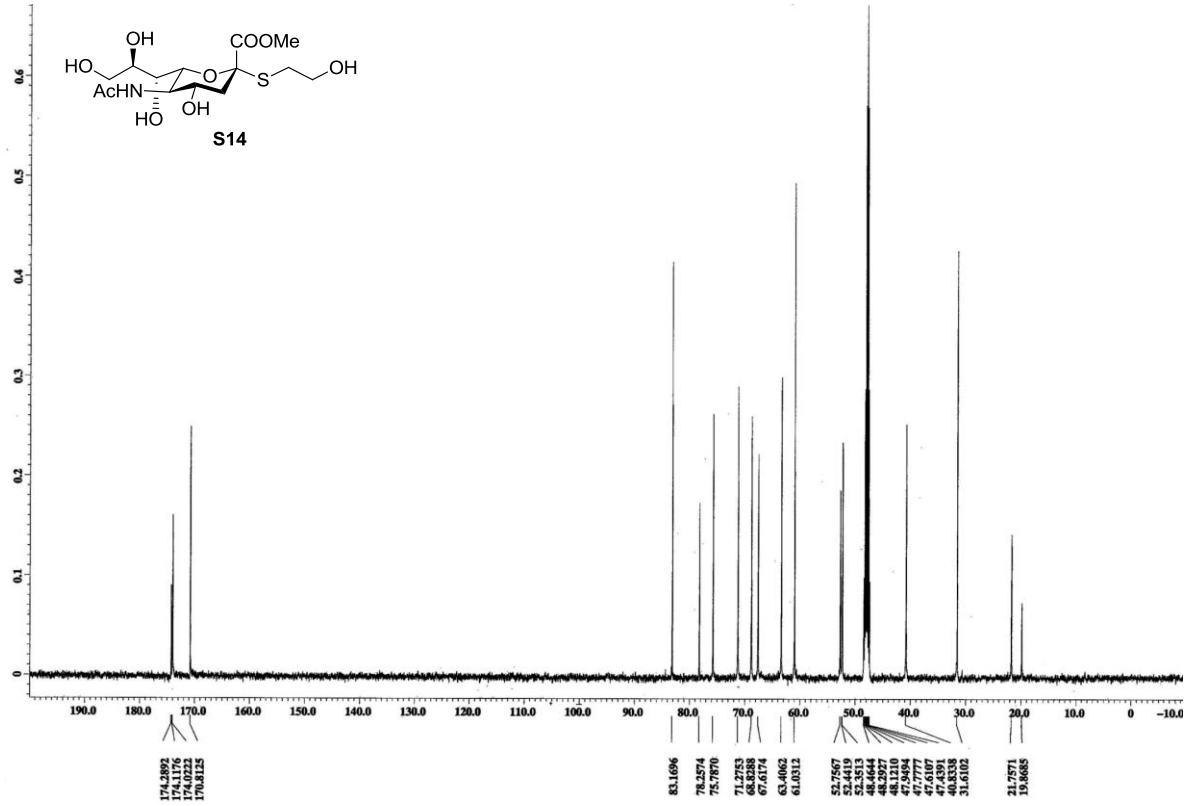

Fig. S27. ^{13}C -NMR spectrum of compound **S14**

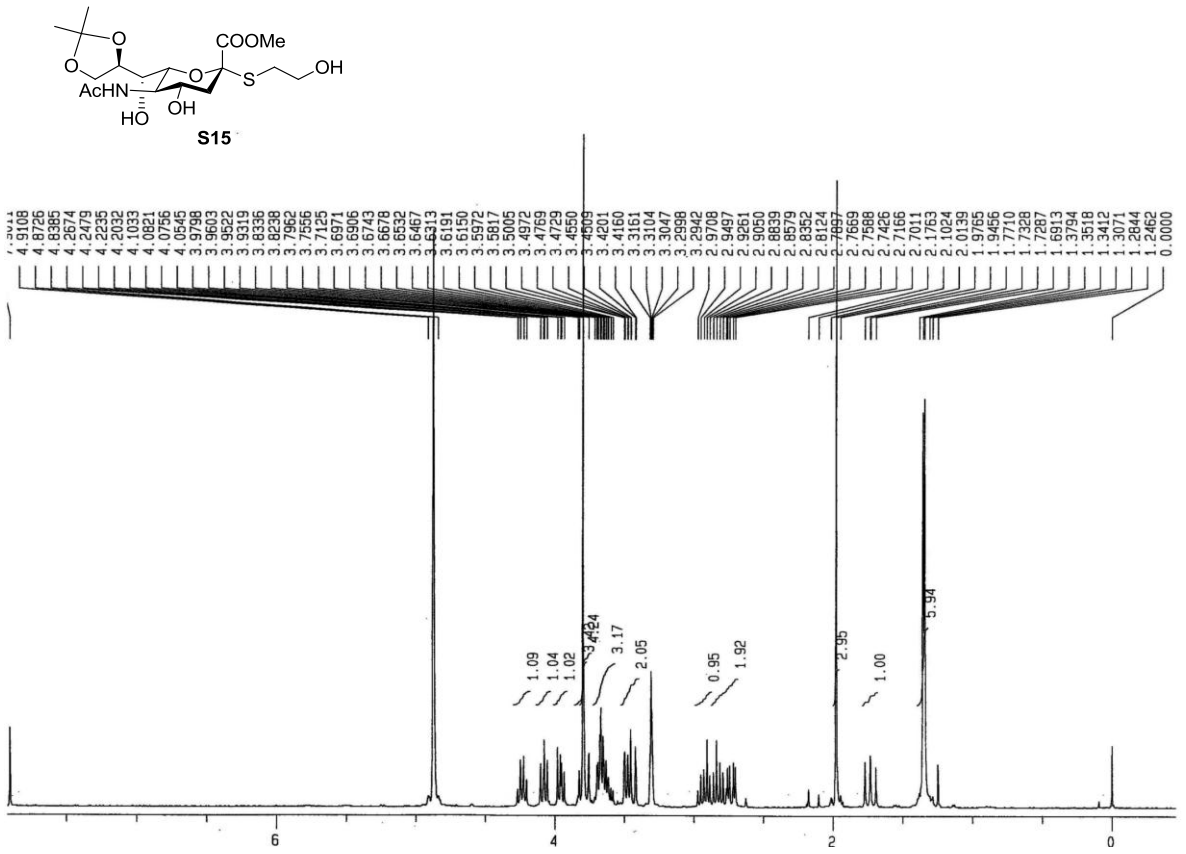

Fig. S28. ^{1}H-NMR spectrum of compound **S15**

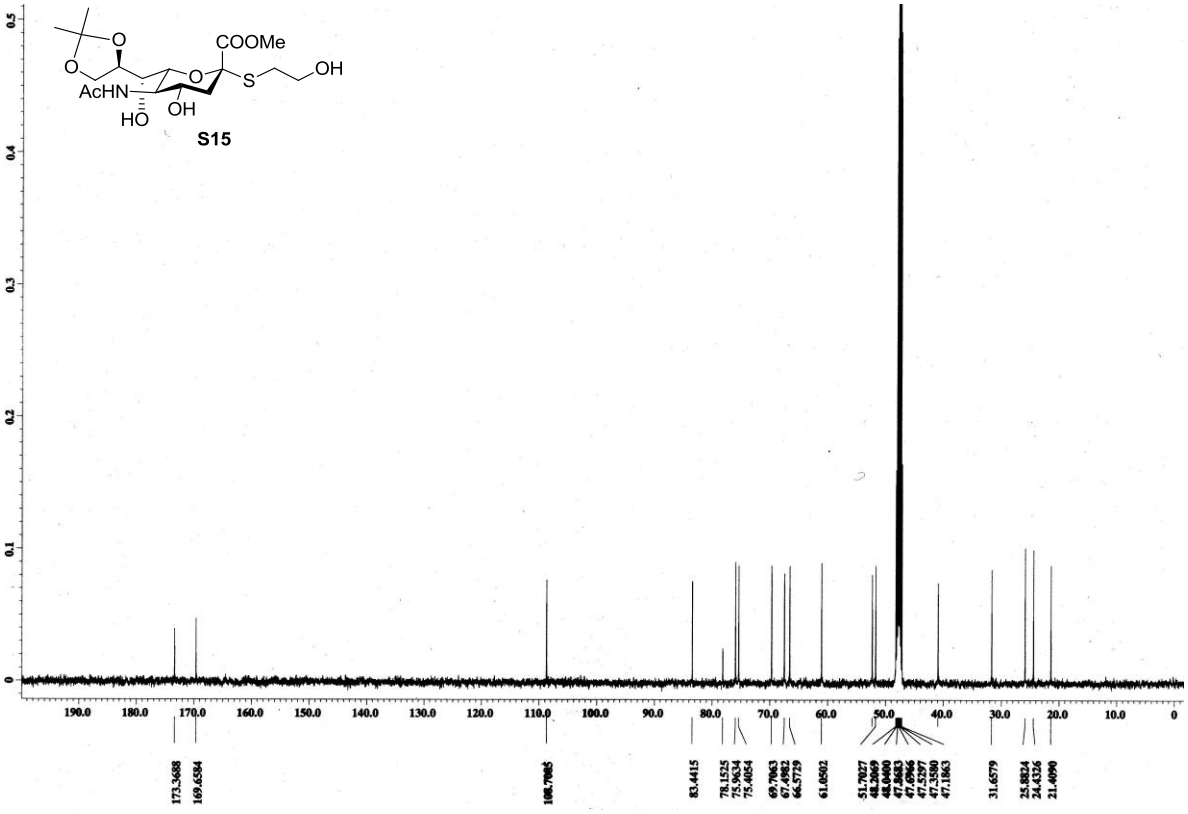

Fig. S29. ^{13}C -NMR spectrum of compound **S15**

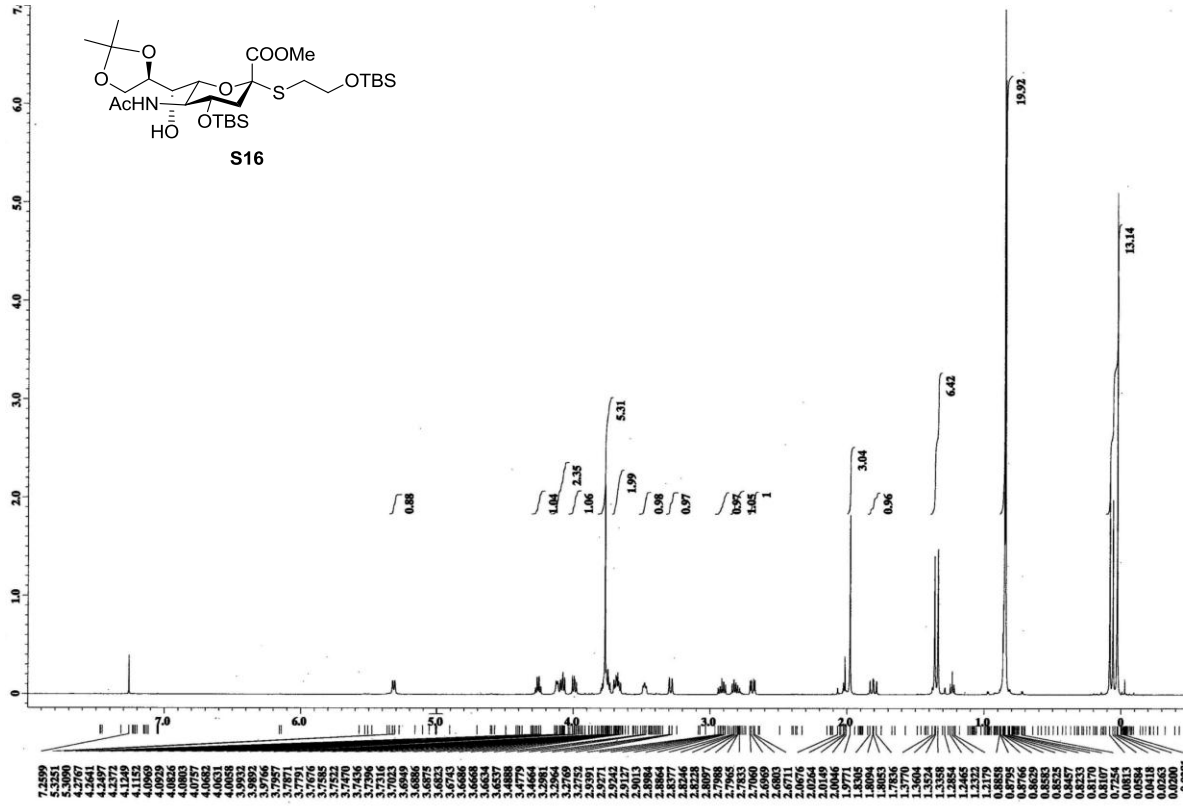

Fig. S30. ^{1}H-NMR spectrum of compound **S16**

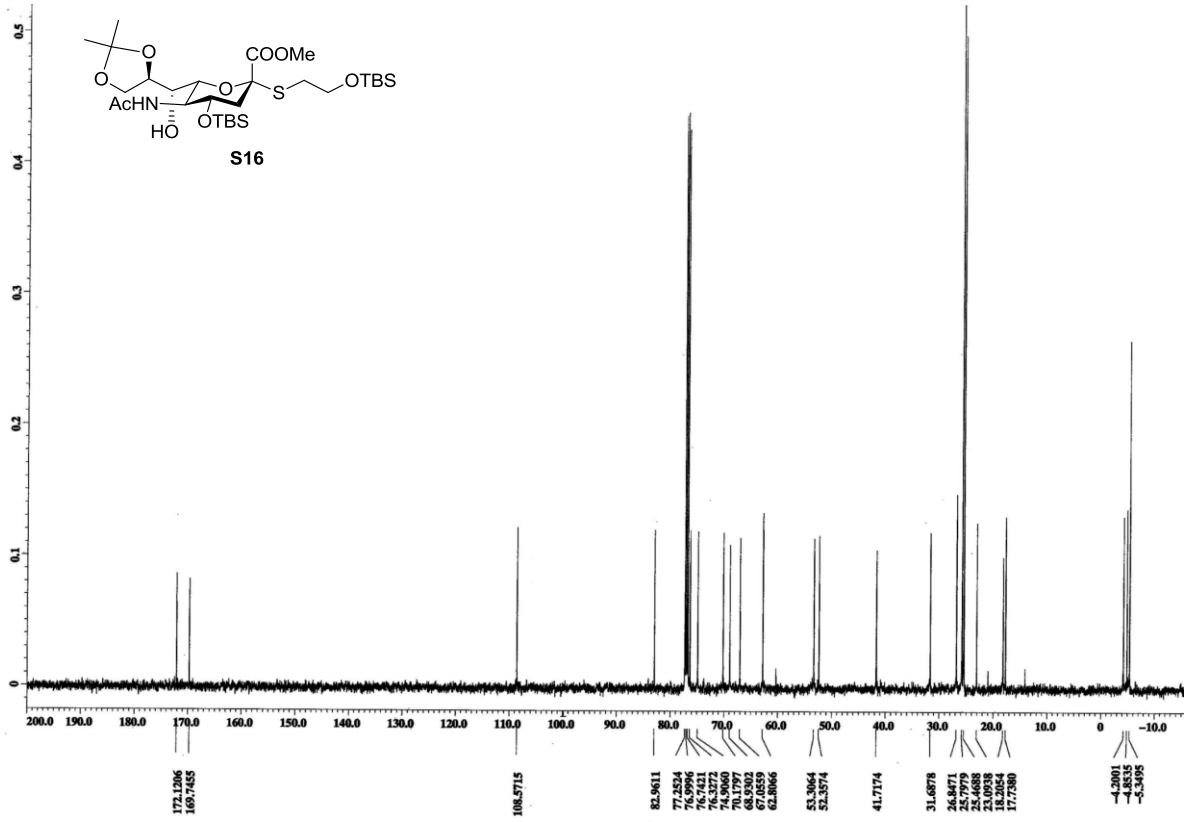

Fig. S31. ^{13}C -NMR spectrum of compound **S16**

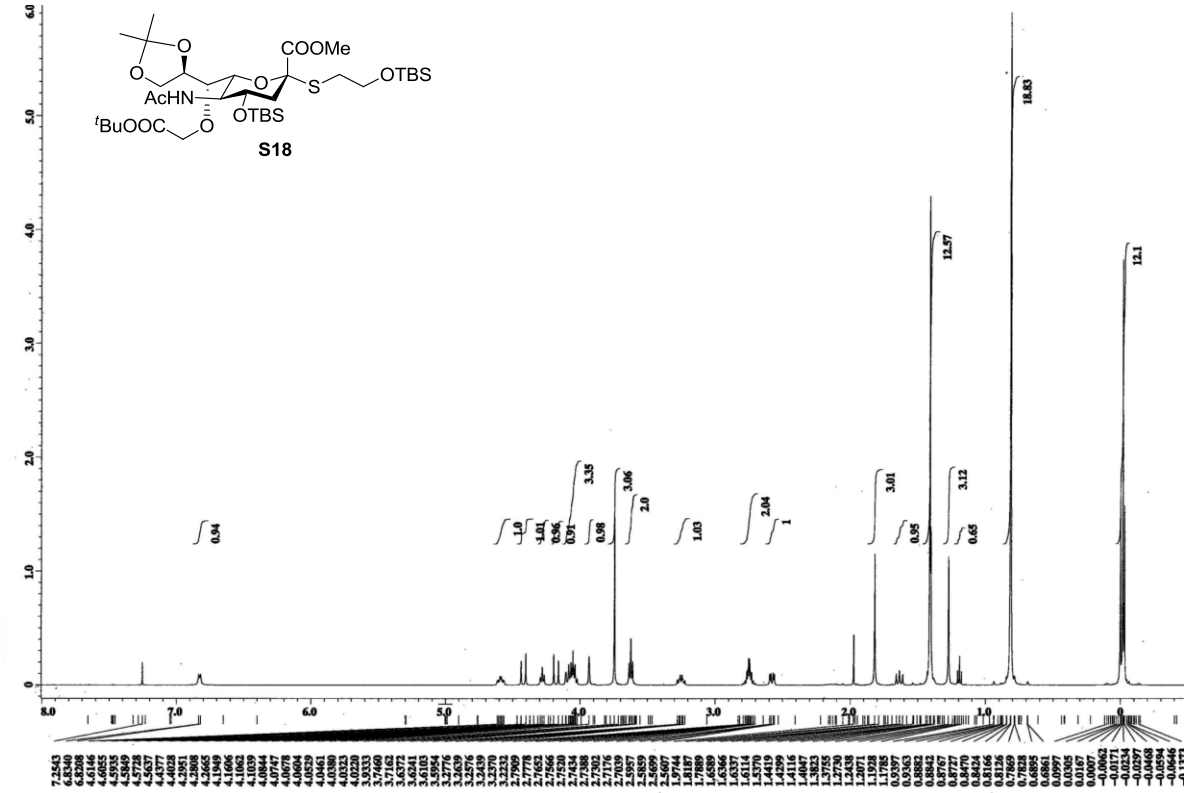

Fig. S32. ^{1}H-NMR spectrum of compound **S18**

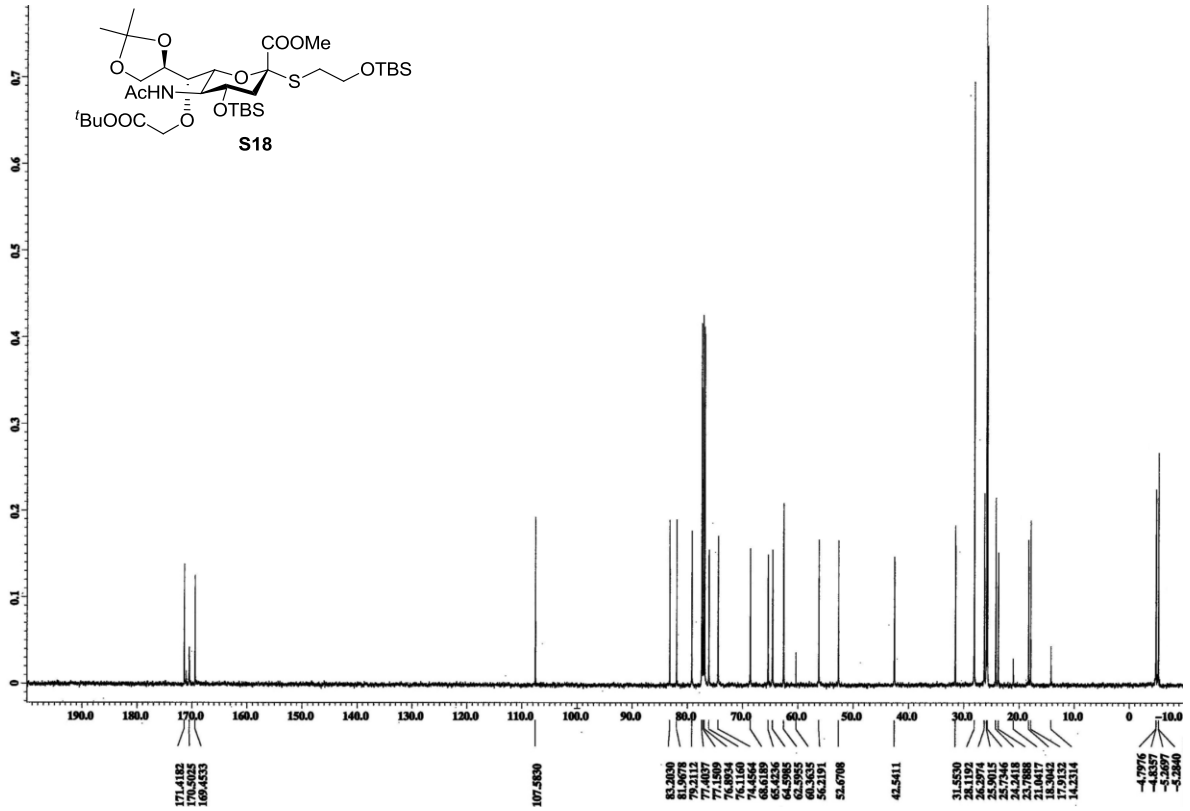

Fig. S33. ^{13}C -NMR spectrum of compound **S18**

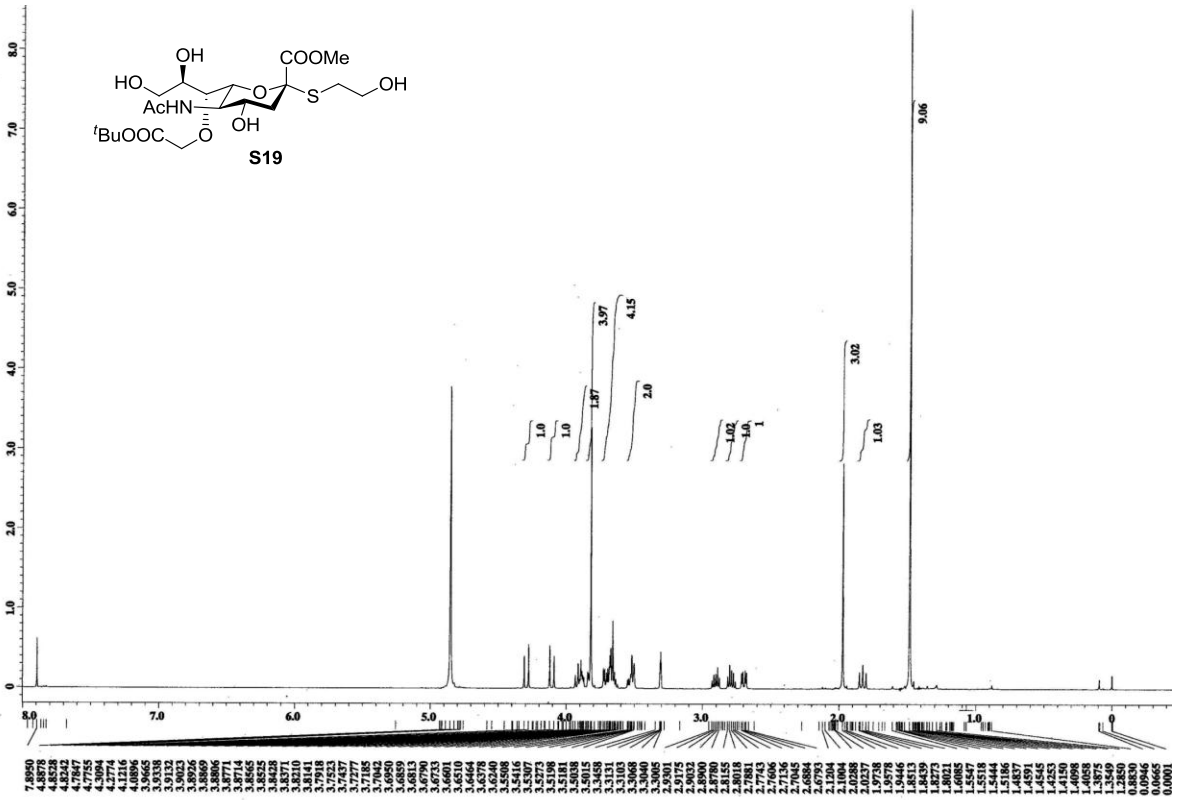

Fig. S34. ^{1}H-NMR spectrum of compound **S19**

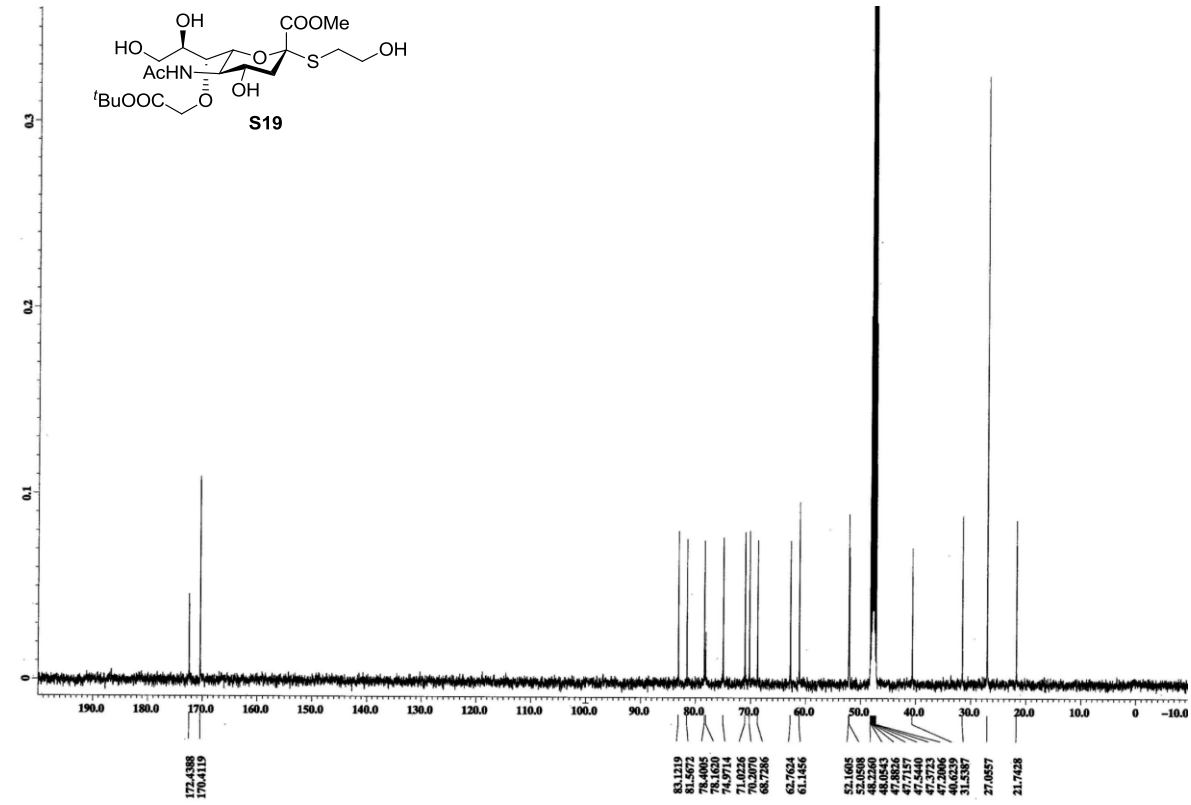

Fig. S35. ^{13}C -NMR spectrum of compound **S19**

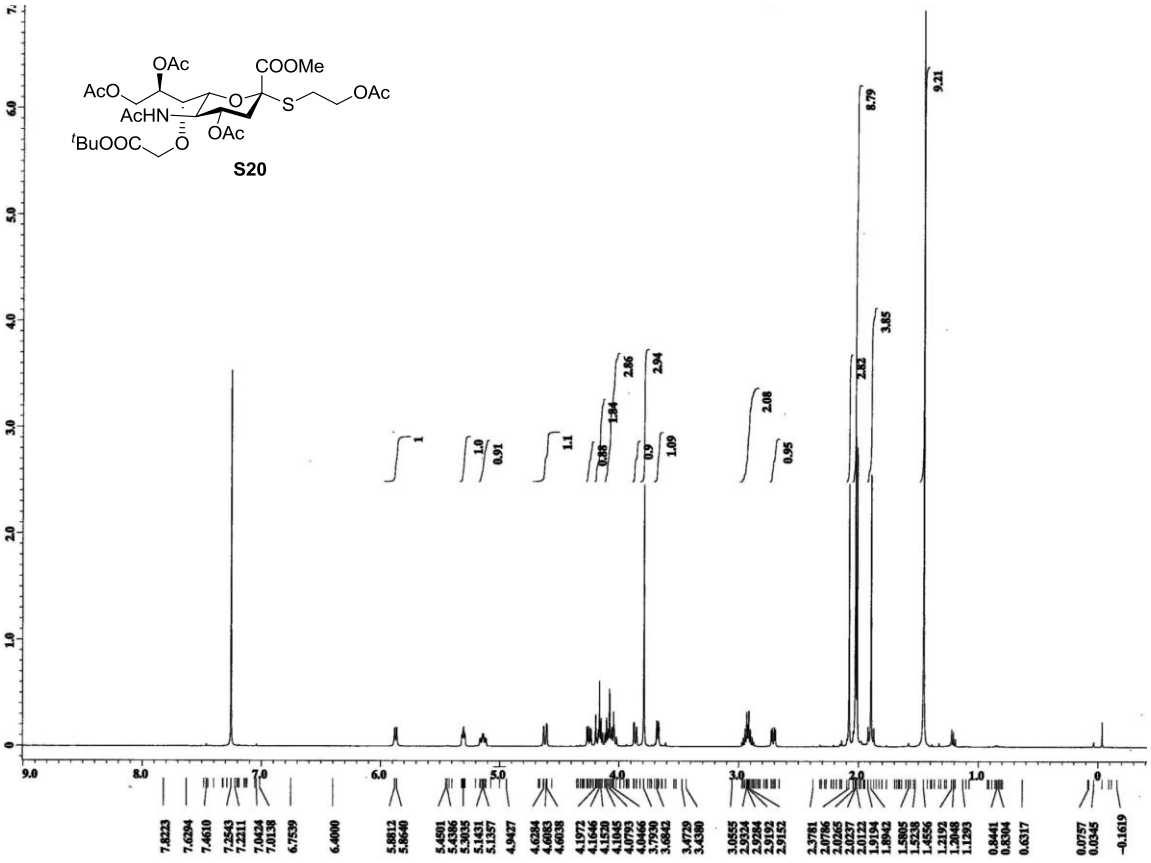

Fig. S36. ^{1}H-NMR spectrum of compound **S20**

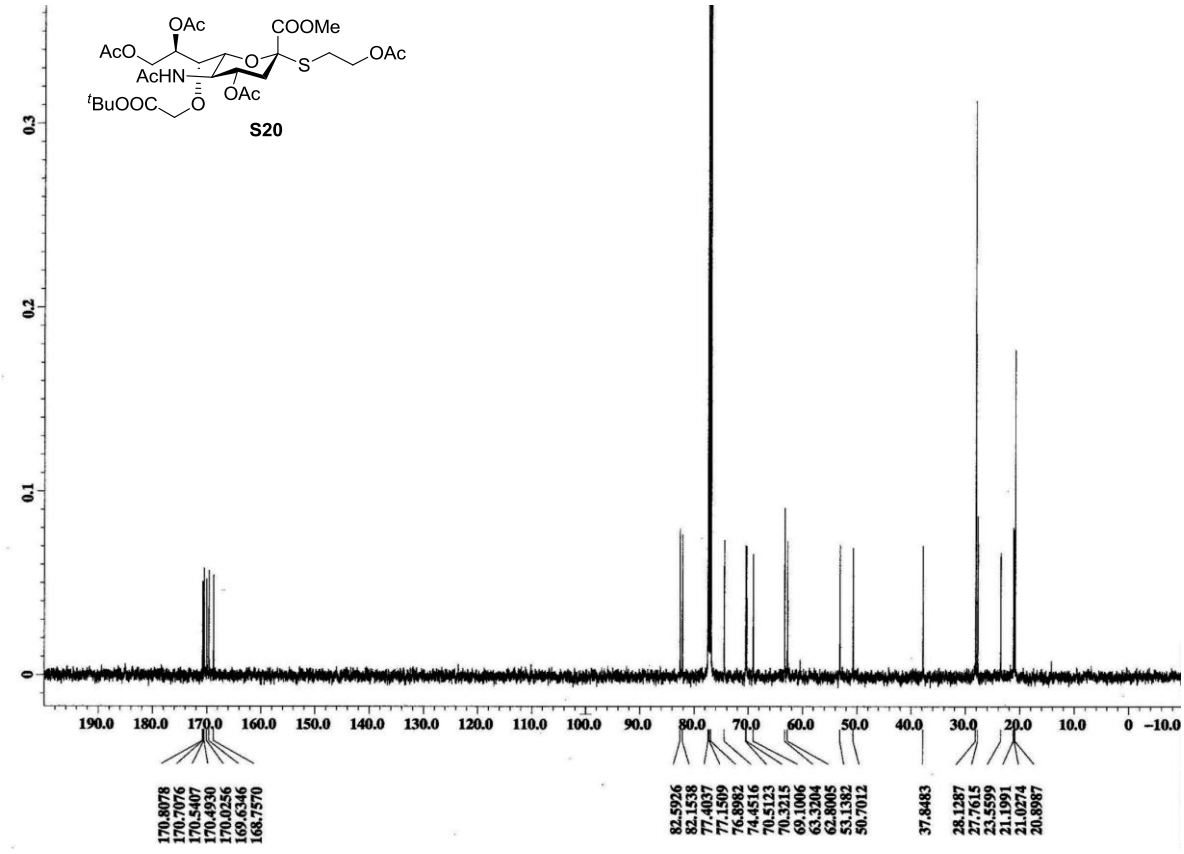

Fig. S37. ^{13}C -NMR spectrum of compound **S20**

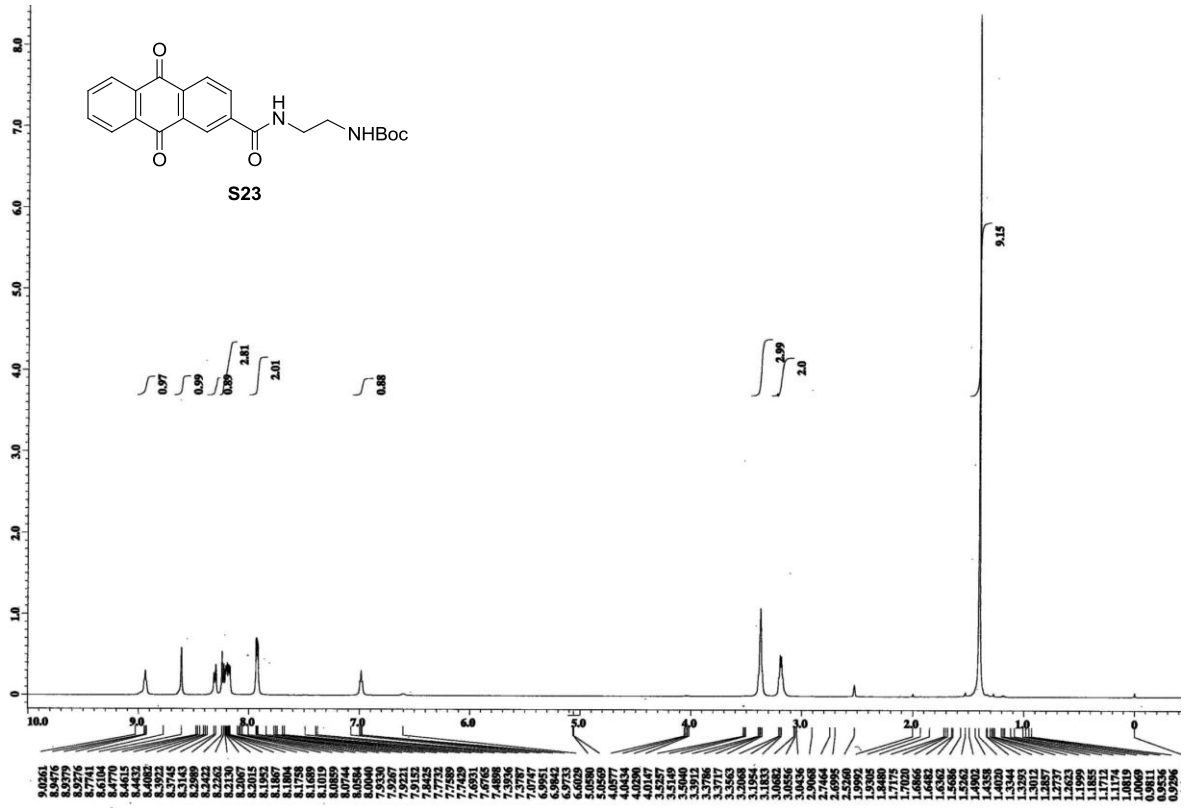

Fig. S38. ^{1}H-NMR spectrum of compound ***S23***

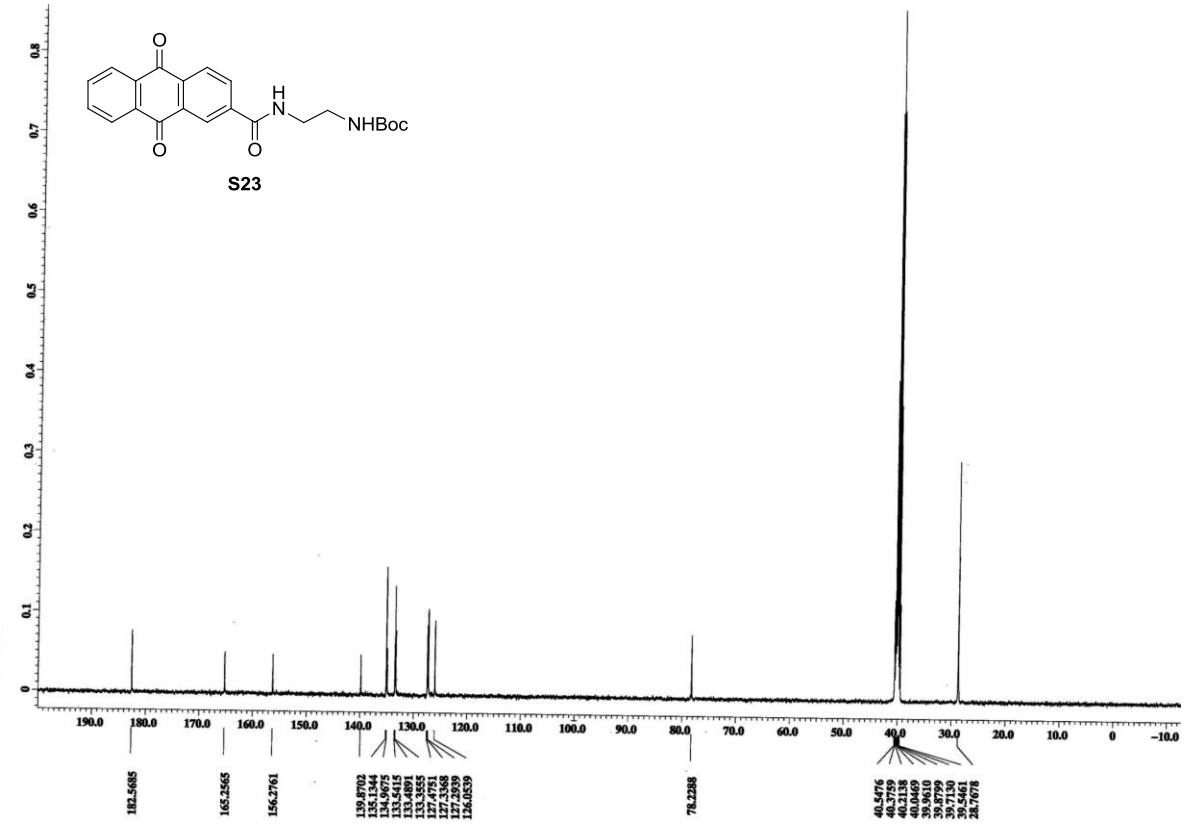

Fig. S39. ^{13}C -NMR spectrum of compound ***S23***

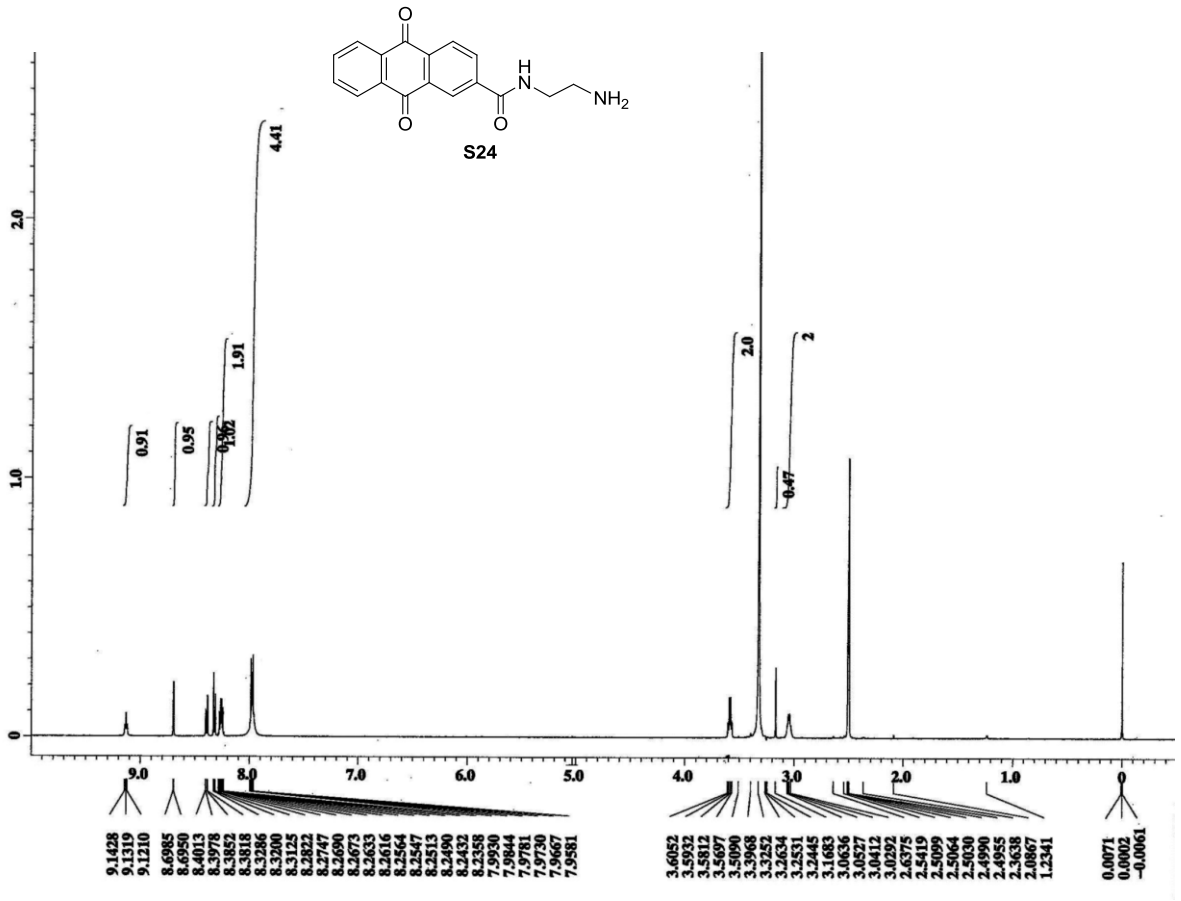

Fig. S40. ^{1}H-NMR spectrum of compound **S24**

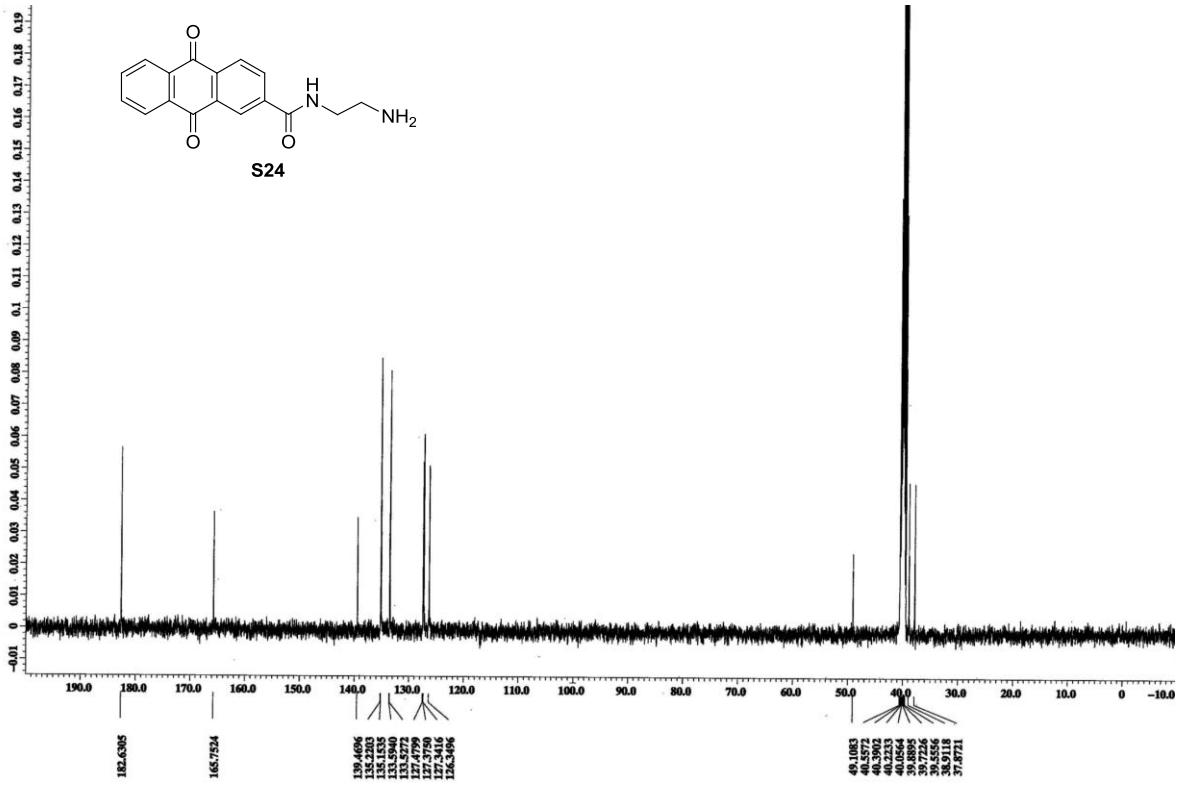

Fig. S41. ^{13}C -NMR spectrum of compound **S24**

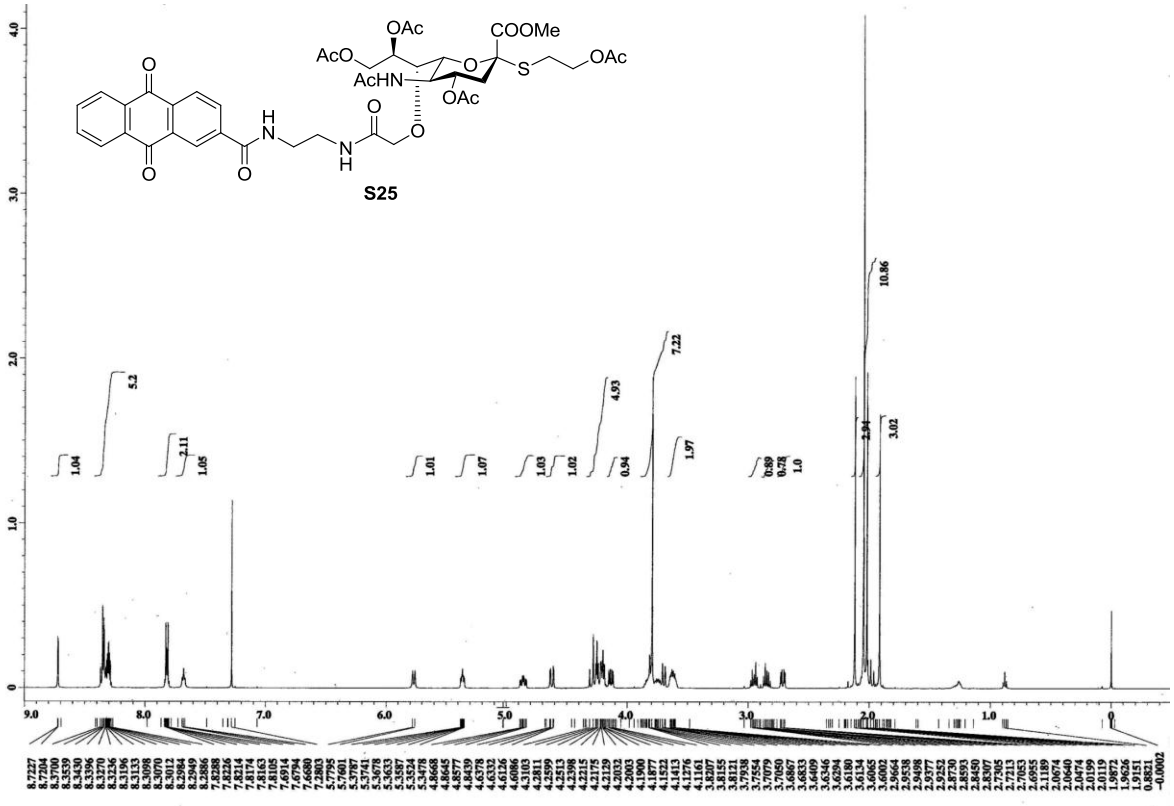

Fig. S42. ^{1}H-NMR spectrum of compound **S25**

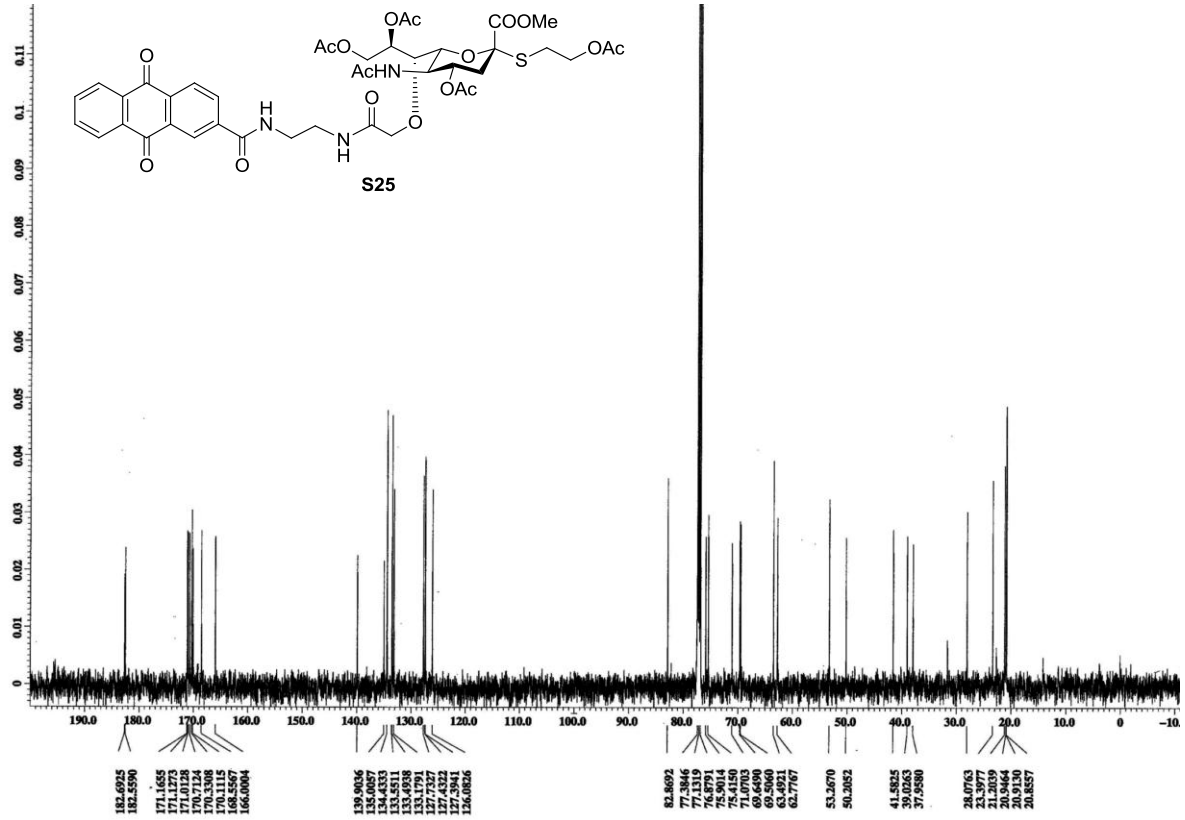

Fig. S43. ^{13}C -NMR spectrum of compound **S25**

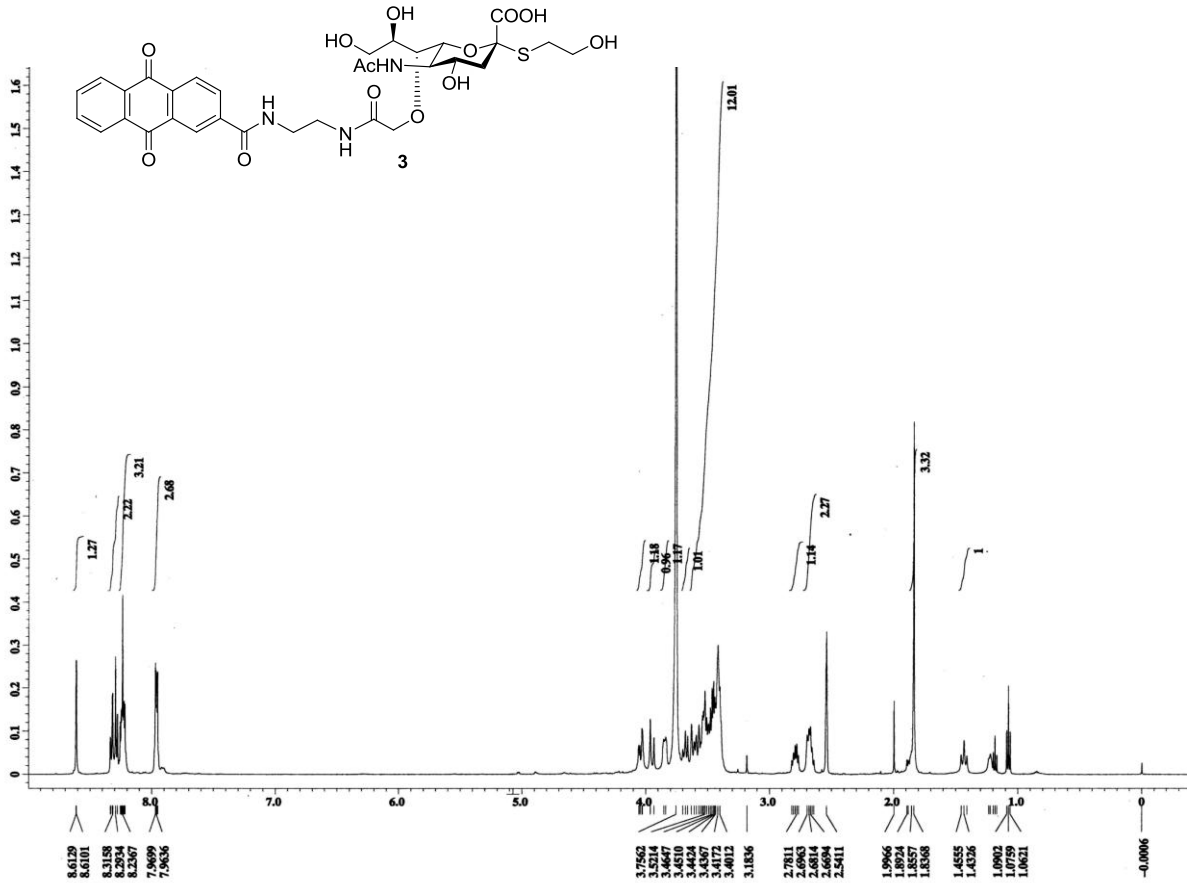

Fig. S44. ^{1}H-NMR spectrum of compound **3**

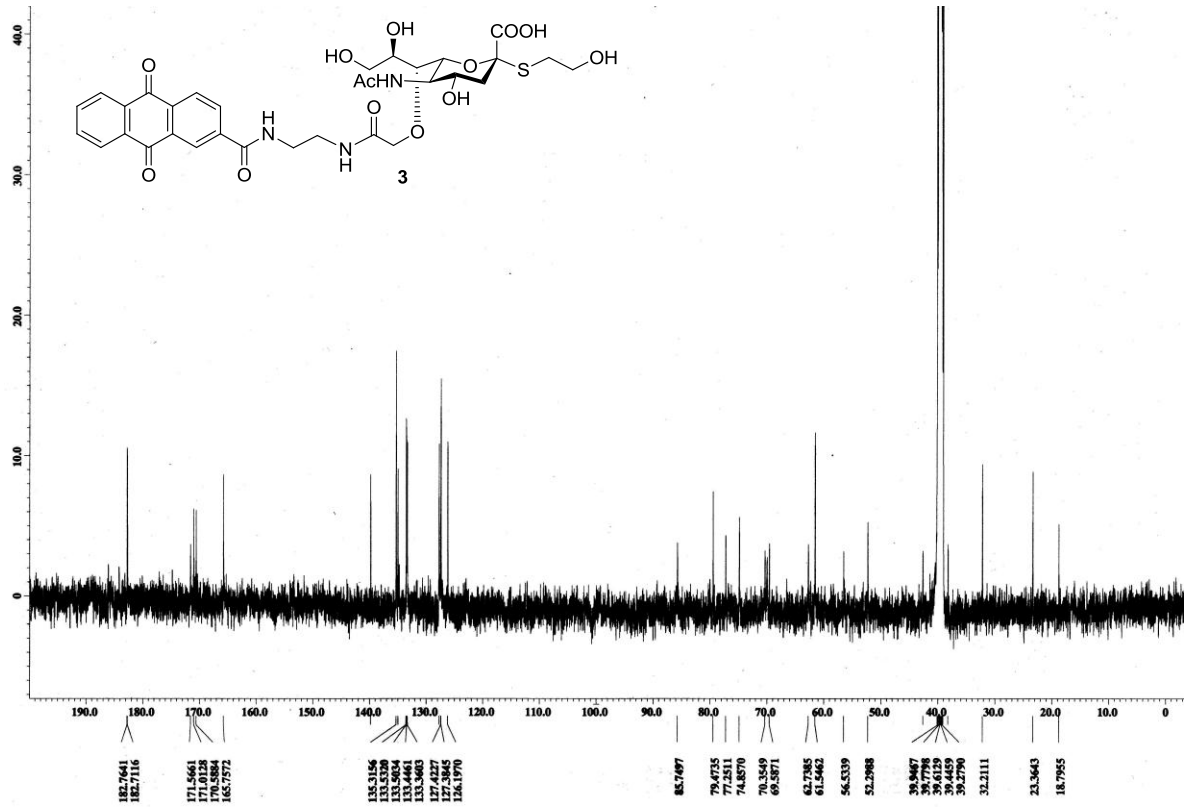

Fig. S45. ^{13}C -NMR spectrum of compound **3**