Supporting information

Synthesis, optimization, and evaluation of glycosylated naphthalimide derivatives as efficient and selective insect β-N-acetylhexosaminidase OfHex1 inhibitors

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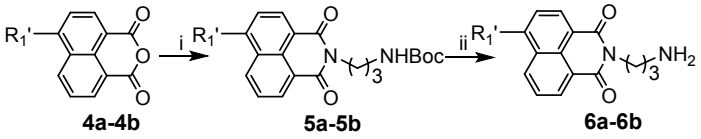


6a: R_1'=Br; **6b**: R_1'=Cl

Scheme S1. Synthesis of naphthalimide derivatives **6a-6b**. (i) *tert*-butyl (3-aminopropyl) carbamate, EtOH; (ii) DCM, CF_3COOH.

4-Substituted-1,8-naphthalic anhydride **4a-4b** (30 mmol, 1 eq) and *tert*-butyl (3-aminopropyl) carbamate (33 mmol, 1.1 eq) were mixed in EtOH (200 mL). The mixture was heated to reflux for 4 h, until TLC (petroleum ether/EtOAc, 5:1 v/v) indicated that the reaction was complete. The mixture was cooled to room temperature and the precipitate was then filtered, dried, and recrystallized from ethanol to obtain **5a-5b**.

tert-Butyl (3-(6-bromo-1,3-dioxo-1*H*-benzo[*de*]isoquinolin-2(3*H*)-yl)propyl)carbamate (**5a**): light yellow solid; (9.5 g, 73.1%) yield; ^{1}H NMR (300 MHz, $CDCl_3$) δ 8.67 (dd, *J* = 7.3, 1.2 Hz, 1H, ArH), 8.55 (dd, *J* = 8.5, 1.2 Hz, 1H, ArH), 8.41 (d, *J* = 7.8 Hz, 1H, ArH), 8.05 (d, 1H, *J* = 7.8 Hz, ArH), 7.85 (dd, *J* = 8.5, 7.3 Hz, 1H, ArH), 5.21 (br s, 1H, NH), 4.27 (t, *J* = 6.3 Hz, 2H, CH_2), 3.15 – 3.12 (m, 2H, CH_2), 1.91 (m, 2H, CH_2), 1.44 (s, 9H, 3 CH_3).

tert-Butyl (3-(6-chloro-1,3-dioxo-1*H*-benzo[*de*]isoquinolin-2(3*H*)-yl)propyl)carbamate (**5b**): light yellow solid; (9.6 g, 82.5%) yield; ^{1}H NMR (300 MHz, $CDCl_3$) δ 8.66 (d, *J* = 7.3 Hz, 1H, ArH), 8.57 (dd, *J* = 8.5, 0.8 Hz, 1H, ArH), 8.40 (d, *J* = 7.9 Hz, 1H, ArH), 8.01 (d, *J* = 7.8 Hz, 1H, ArH), 7.85 (dd, *J* = 8.4, 7.4 Hz, 1H, ArH), 5.17 (br s, 1H, NH), 4.25 (t, *J* = 6.3 Hz, 2H, CH_2), 3.16 – 3.11 (m, 2H, CH_2), 1.92 (m, 2H, CH_2), 1.45 (s, 9H, 3 CH_3).

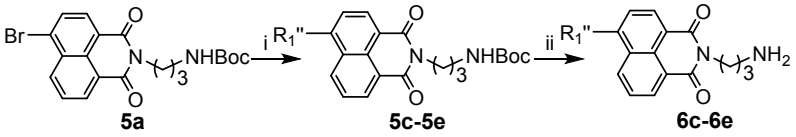
5a-5b (10 mmol) was added into a solution of trifluoroacetic acid (10 mL) in DCM (40 ml), and the mixture was stirred for 10 h at room temperature, until TLC (petroleum ether/EtOAc, 5:1 v/v) indicated that the reaction was complete. The reaction mixture was poured into NaOH solution (2 M, 100 mL), following phase separation, the water layer was extracted with another DCM (3 × 50 mL). The organic phases were combined, dried over Na_2SO_4, and concentrated to yield **6a-6b**.

(3-Aminopropyl)-6-bromo-1*H*-benzo[*de*]isoquinoline-1,3(2*H*)-dione (**6a**): light yellow solid; (2.6 g, 79.1%) yield; ^{1}H NMR (300 MHz, DMSO-d_6) δ 8.52 –8.48 (m, 2H, ArH), 8.23 (d, *J* = 8.3

Hz, 1H, ArH), 8.16 (dd, J = 8.1, 7.6 Hz, 1H, ArH), 7.99 (d, J = 8.5 Hz, 1H, ArH), 4.07 (t, J = 6.8 Hz, 2H, CH_2), 2.61 (t, J = 6.8 Hz, 2H, CH_2), 2.03–1.93 (m, 2H, CH_2).

3-(3-Aminopropyl)-6-chloro-1*H*-benzo[*de*]isoquinoline-1,3(2*H*)-dione (**6b**): light yellow solid; (2.3 g, 80.9%) yield; ^{1}H NMR (300 MHz, DMSO-d_6) δ 8.41 – 8.30 (m, 2H, ArH), 8.14 (d, J = 7.9 Hz, 1H, ArH), 7.89 – 7.70 (m, 2H, ArH), 4.00 (t, J = 6.8 Hz, 2H, CH_2), 2.65 (t, J = 6.8 Hz, 2H, CH_2), 1.99–1.81 (m, 2H, CH_2).

1.2 Synthesis of naphthalimide derivatives 6c-6e[1,2]



6c: R_1''=OCH_3; **6d**: R_1''=$N(CH_3)_2$; **6e**: R_1''=piperidyl

Scheme S2. Synthesis of naphthalimide derivatives **6c-6e**. (i) MeOH, KOH for **5c**; dimethylamine, 2-methoxyethanol for **5d**; piperidine, 2-methoxyethanol for **5e**; (ii) DCM, CF_3COOH.

Compound **5a** (7.1 g, 20 mmol) was added into a solution of KOH (1.7 g, 30 mmol) in MeOH (100 mL) and 2-methoxyethanol (20 mL). The mixture was then refluxed for 5 h, until TLC (petroleum ether/EtOAc, 4:1 v/v) indicated that the reaction was complete. After the reaction mixture was concentrated *in vacuo*, the resulting residue was further purified by silica gel column chromatography (petroleum ether/EtOAc, 10:1 v/v), and **5c** was obtained as a light yellow solid. (6.4 g, 83.1%) yield; ^{1}H NMR (300 MHz, $CDCl_3$) δ 8.54 (dd, J = 8.3, 1.1 Hz, 1H, ArH), 8.43 (d, J = 8.0 Hz, 1H, ArH), 8.40 (d, J = 8.2, 1H, ArH), 7.81 (dd, J = 8.1, 7.0 Hz, 1H, ArH), 7.33 (d, J = 8.4 Hz, 1H, ArH), 5.10 (br s, 1H, NH), 4.23 (t, J = 6.3 Hz, 2H, CH_2), 4.11(s, 3H, OCH_3), 3.19 – 3.10 (m, 2H, CH_2), 1.93 (m, 2H, CH_2), 1.41 (s, 9H, 3 CH_3).

Compound **5a** (7.1 g, 20 mmol) was dissolved in 2-methoxyethanol (80 mL), then 40% dimethylamine aqueous solution (10 mL) was added. The mixture was refluxed for 5 h under N_2, until TLC (petroleum ether/EtOAc, 4:1 v/v) indicated that the reaction was complete. After the reaction mixture was concentrated *in vacuo*, **5d** was prepared by recrystallized from EtOH as a yellow solid. (6.5 g, 82.1%) yield; ^{1}H NMR (300 MHz, $CDCl_3$) δ 8.57 (dd, J = 7.4, 1.1 Hz, 1H, ArH), 8.46 (d, J = 8.1 Hz, 1H, ArH), 8.44(dd, J = 8.4, 1.2 Hz, 1H, ArH), 7.67 (dd, J = 8.6, 7.4 Hz,

1H, ArH), 7.12 (d, J = 8.1, 1H, ArH), 5.17 (br s, 1H, NH), 4.27 (t, J = 6.1 Hz, 2H, CH_2), 3.23 – 3.10 (m, 2H, CH_2), 3.12 (s, 6H, 2 NCH_3), 1.97 – 1.86 (m, 2H, CH_2), 1.44 (s, 9H, 3 CH_3).

Compound **5a** (7.1 g, 20 mmol) was dissolved in 2-methoxyethanol (80 mL), then piperidine (8 mL) was added. The reaction mixture was refluxed for 5h under N_2, until TLC (petroleum ether/EtOAc, 5:1 v/v) indicated that the reaction was complete. After the reaction mixture was concentrated *in vacuo*, compound **5e** was yielded by recrystallized from EtOH as a yellow solid. (6.0 g, 68.8%) yield; ^{1}H NMR (300 MHz, $CDCl_3$) δ 8.55 (dd, J = 7.3, 1.1 Hz, 1H, ArH), 8.47 (d, J = 8.0 Hz, 1H, ArH), 8.36 (dd, J = 8.3, 1.1 Hz, 1H, ArH), 7.63 (dd, J = 8.3, 7.1 Hz, 1H, ArH), 7.12 (d, J = 8.2 Hz, 1H, ArH), 5.17 (br s, 1H, NH), 4.30 (t, J = 5.6 Hz, 2H, CH_2), 3.29 – 3.10 (m, 6H, 3 CH_2), 1.97 – 1.80 (m, 6H, 3 CH_2), 1.78 – 1.66 (m, 2H, CH_2), 1.36 (s, 9H, 3 CH_3).

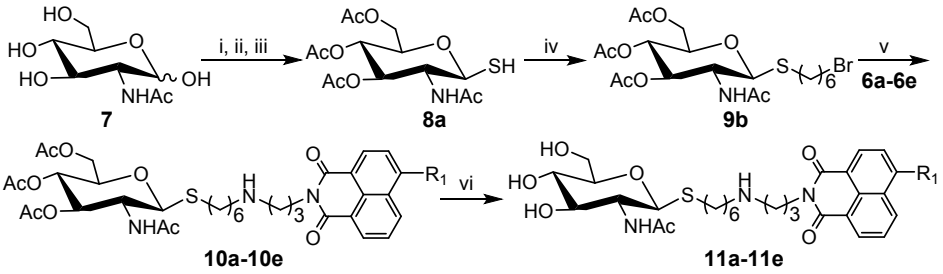
The preparation process from **5c-5e** to **6c-6e** was the same as that used for compounds **6a-6b**.

2-(3-Aminopropyl)-6-methoxy-1*H*-benzo[*de*]isoquinoline-1,3(2*H*)-dione (**6c**): light yellow solid; (83.6%) yield; ^{1}H NMR (300 MHz, DMSO-d_6) δ 8.41 (dd, J = 7.8, 3.2 Hz, 2H, ArH), 8.35 (d, J = 8.3 Hz, 1H, ArH), 7.74 (dd, J = 8.1, 7.6 Hz, 1H, ArH), 7.24 (d, J = 8.5 Hz, 1H, ArH), 4.19 – 4.00 (m, 5H, OCH_3, CH_2), 2.82 (dd, J = 9.0, 6.8 Hz, 2H, CH_2), 2.04 – 1.94 (m, 2H, CH_2).

2-(3-Aminopropyl)-6-(dimethylamino)-1*H*-benzo[*de*]isoquinoline-1,3(2*H*)-dione (**6d**): yellow solid; (82.6%) yield; ^{1}H NMR (300 MHz, $CDCl_3$) δ 8.57 (d, J = 8.2 Hz, 1H, ArH), 8.49 – 8.41 (m, 2H, ArH), 7.70 (dd, J = 8.2, 7.5 Hz, 1H, ArH), 7.13 (d, J = 8.2 Hz, 1H, ArH), 4.30 (t, J = 6.9 Hz, 2H, CH_2), 2.79 – 2.73 (m, 2H, CH_2), 2.34 (s, 6H, 2 CH_3), 1.99 – 1.85 (m, 2H, CH_2).

2-(3-Aminopropyl)-6-(piperidin-1-yl)-1*H*-benzo[*de*]isoquinoline-1,3(2*H*)-dione (**6e**): yellow solid; (80.7%) yield; ^{1}H NMR (300 MHz, $CDCl_3$) δ 8.55 (dd, J = 7.3, 1.1 Hz, 1H, ArH), 8.46 (d, J = 8.1 Hz, 1H, ArH), 8.37 (dd, J = 8.4, 1.1 Hz, 1H, ArH), 7.65 (dd, J = 8.4, 7.4 Hz, 1H, ArH), 7.16 (d, J = 8.2 Hz, 1H, ArH), 4.31 (t, J = 5.6 Hz, 2H, CH_2), 3.27 – 3.14 (m, 4H, 2 CH_2), 2.82 – 2.73 (m, 2H, CH_2), 2.08 – 1.81 (m, 6H, 3 CH_2), 1.79 – 1.61 (m, 2H, CH_2).

1.3 Synthesis of thioglycosyl-naphthalimide derivatives 11a-11e



11a: R_1=Br; **11b**: R_1=Cl; **11c**: R_1=OCH_3; **11d**: R_1=$N(CH_3)_2$; **11e**: R_1=piperidyl

Scheme S3. Synthesis of glycosylated naphthalimide derivatives **11a-11e**. (i) AcCl; (ii) thiourea, acetone; (iii) $Na_2S_2O_5$, DCM, H_2O; (iv) 1,6-dibromohexane, K_2CO_3, acetone, H_2O; (v) **6a-6e**, K_2CO_3, CH_3CN; (vi) NH_3, MeOH.

Compound **8a** and **9b** were synthesized from N-acetyl-D-glucosamine as described previously.[3]

N-Acetyl-D-glucosamine (20 g, 90.5 mmol) was added into acetyl chloride (80 mL, 373.6 mmol) and stirred for 48 h at room temperature, until TLC (EtOAc) indicated that the reaction was completed. The reaction mixture was poured into ice water (500 mL) and DCM (300 mL) was then added. Following phase separation, the organic layer was washed with saturated $NaHCO_3$ aqueous solution (2×100 mL), water (2×100 mL), dried over Na_2SO_4, filtered, and concentrated *in vacuo* to obtain 2-acetamido-3,4,6-tri-O-acetyl-2-deoxy-α-D-glucopyranosyl chloride, which was used without further purification.

2-acetamido-3,4,6-tri-O-acetyl-2-deoxy-α-D-glucopyranosyl chloride (10 g, 28.3 mmol) and thiourea (3.9 g, 51.2 mmol) were mixed in acetone (120 mL). The mixture was heated to reflux for 4 h until a white precipitate was observed. The solid precipitate was then filtered and washed with acetone (2×20 mL). As a result, 2-acetamido-3,4,6-tri-O-acetyl-β-D-glucopyranosyl- 1-isothiouronium chloride was obtained. (10.5g, 86.9%) yield; $[\alpha]_D^{25}$ -25.1 (c=1.0, H_2O); ^{1}H NMR (300 MHz, DMSO-d_6) δ ppm 9.45(s, 2H, NH_2), 9.19(s, 2H, NH_2), 8.46 (d, J = 9.3 Hz, 1H, NH), 5.65 (d, J = 9.7 Hz, 1H, H-1), 5.14 (t, J = 9.8 Hz, 1H, H-3), 4.94 (t, J = 9.7 Hz, 1H, H-4), 4.17–4.27 (m, 2H, H-5/H-6a), 3.92–4.13 (m, 2H, H-2/ H-6b), 1.91, 1.97, 2.03 (3s, 9H, 3 OAc), 1.79 (s, 3H, NAc).

A mixture of 2-acetamido-3,4,6-tri-O-acetyl-β-D-glucopyranosyl-1-isothiouronium chloride (5 g, 11.3 mmol) and sodium metabisulfite (4.3 g, 22.6 mmol) in DCM (60 mL) and H_2O (40 mL) was heated to reflux for 3 h, until TLC (EtOAc) indicated that the reaction was completed. Prior to phase separation, the reaction mixture was cooled down to room temperature. After the aqueous

layer underwent another round of extraction with DCM (60mL), the resulting organic layers (from both rounds) were combined and washed with H_2O (50 mL), and further dried over N15bSO_4. The resulting white solid was harvested by filtration, concentration, and recrystallized from acetate/petrol; and the final 2-acetamido-3,4,6-tri-O-acetyl-2-deoxy-1-thio-β- D-glucopyranose (**8a**) was obtained. (3.7 g, 90.2 %) yield; $[\alpha]_D^{25}$ -15.1 (c=1.0,$CHCl_3$); ^{1}H NMR (300 MHz, $CDCl_3$) δ 5.78 (d, *J* = 9.5 Hz, 1H, NH), 5.20 – 5.03 (m, 2H, H-3, H-4), 4.60 (d, *J* = 9.9 Hz, 1H, H-1), 4.25 (dd, *J* = 12.4, 4.8 Hz, 1H, H-6b), 4.19 – 4.05 (m, 2H, H-6a, H-2), 3.70 (ddd, *J* = 9.8, 4.7, 2.2 Hz, 1H, H-5), 2.57 (s, 1H, SH), 2.10 (s, 3H, OAc), 2.05 (s, 3H, OAc), 2.03 (s, 3H, OAc), 1.99 (s, 3H, NAc).

A solution of thiol **8a** (4.0 g, 11.0 mmol) in acetone (100 mL) and H_2O (50 mL) was mixed with solid potassium carbonate (1.8 g, 13.2 mmol), then 1,6-dibromohexane (21.4 g, 88 mmol) was added. The mixture was stirred for 10 h at room temperature until TLC (petroleum ether/EtOAc, 3:1 v/v) indicated that the reaction was complete. After the solution was concentrated *in vacuo*, the residue was diluted with DCM (150 mL), washed with H_2O (200 mL), brine (200 mL), dried over Na_2SO_4, and concentrated. Finally, the residue was purified by flash column chromatography to obtain **9b**.

6-Bromohexyl 2-acetamido-3,4,6-tri-O-acetyl-2-deoxy-1-thio-β-D-glucopyranoside (**9b**): white solid; (4.0g, 77.5 %) yield; $[\alpha]_D^{25}$ -92.5 (c=0.6,$CHCl_3$); ^{1}H NMR (300 MHz, DMSO-d_6) δ 7.96 (d, *J* = 9.4 Hz, 1H, NH), 5.07 (t, *J* = 9.8 Hz, 1H, H-3), 4.83 (t, *J* = 9.7 Hz, 1H, H-4), 4.67 (d, *J* = 10.4 Hz, 1H, H-1), 4.14 (dd, *J* = 12.3, 5.1 Hz, 1H, H-6b), 4.01 (dd, *J* = 12.2, 2.2 Hz, 1H, H-6a), 3.91–3.76 (m, 2H, H-2, H-5), 3.51 (t, *J* = 6.7 Hz, 2H, CH_2Br), 2.69–2.52 (m, 2H, SCH_2), 2.00, 1.96, 1.91 (3 s, 9H, 3 OAc), 1.76 (s, 3H, NAc), 1.85–1.72 (m, 2H, CH_2), 1.61–1.47 (m, 2H, CH_2), 1.43–1.27 (m, 4H, 2 CH_2).

Following compound **9b** (1.6 g, 3 mmol) and **6a-6e** (4.5 mmol, 1.5 eq) were dissolved in acetonitrile (70 ml), K_2CO_3 (0.5 g, 3.6 mmol) was added. The solution was refluxed for 4 h under N_2, and the completion of the reaction was confirmed by TLC (EtOAc/MeOH, 6:1 v/v) analysis. The mixture was concentrated *in vacuo*, and the resulting residue was further purified by silica gel column chromatography using EtOAc/CH_3OH (12:1, v/v) to yield **10a-10e**.

2-[3-[6-[(2-Acetamido-3,4,6-tri-*O*-acetyl-β-D-glucopyranosyl) thio] hexylamino] propyl] -6-bromo-1*H*-benzo[*de*]isoquinoline-1,3(2*H*)-dione (**10a**): light yellow oil; (1.5 g, 64.3 %) yield; $[\alpha]_D^{25}$ -89.2 (c=1.0, DMSO); ^{1}H NMR (300 MHz, DMSO-d_6) δ 8.40 – 8.32 (m, 1H, ArH), 8.26 (d, *J* = 8.5 Hz, 1H, ArH), 8.10 (d, *J* = 7.9 Hz, 1H, ArH), 8.04 – 7.94 (m, 2H, NHAc, ArH), 7.85 – 7.76

(m, 1H, ArH), 5.10 (t, *J* = 9.7 Hz, 1H, H-3), 4.85 (t, *J* = 9.7 Hz, 1H, H-4), 4.70 (d, *J* = 10.4 Hz, 1H, H-1), 4.16 (dd, *J* = 12.3, 5.1 Hz, 1H, H-6b), 4.08 – 3.96 (m, 3H, CH_2NC=O, H-6a), 3.94 – 3.78 (m, 2H, H-2, H-5), 2.70 – 2.57 (m, 2H, CH_2), 2.55 – 2.50 (m, 2H, SCH_2), 2.45 (t, *J* = 6.7 Hz, 2H, CH_2), 2.00, 1.98, 1.93 (3 s, 9H, 3 OAc), 1.78 (s, 3H, NAc), 1.77 – 1.68 (m, 2H, CH_2), 1.59 – 1.45 (m, 2H, CH_2), 1.40 – 1.29 (m, 2H, CH_2), 1.28 – 1.14 (m, 4H, 2 CH_2); ^{13}C NMR (75 MHz, DMSO-d_6) δ 170.04, 169.71, 169.36, 169.17, 162.74, 162.68, 132.38, 131.39, 131.17, 130.76, 129.56, 129.08, 128.55, 127.98, 122.52, 121.73, 83.57, 74.75, 73.84, 68.79, 62.22, 52.36, 49.18, 47.05, 38.38, 29.36, 28.27, 27.74, 26.44, 22.74, 20.56, 20.49, 20.43; HRMS (ESI) calcd for $C_{35}H_{45}BrN_3O_{10}S$ ($M+H^+$) 778.2009, found 778.2031.

2-[3-[6-[(2-Acetamido-3,4,6-tri-*O*-acetyl-β-D-glucopyranosyl) thio] hexylamino] propyl] -6-chloro-1*H*-benzo[*de*]isoquinoline-1,3(2*H*)-dione (**10b**): light yellow oil; (1.6 g, 72.7 %) yield; $[\alpha]_D^{25}$ -82.6 (c=1.0, DMSO); ^{1}H NMR (300 MHz, DMSO-d_6) δ 8.50 (d, *J* = 8.0 Hz, 2H, ArH), 8.34 (d, *J* = 7.9 Hz, 1H, ArH), 8.05 (d, *J* = 9.4 Hz, 1H, NHAc), 8.01 – 7.88 (m, 2H, ArH), 5.10 (t, *J* = 9.7 Hz, 1H, H-3), 4.85 (t, *J* = 9.7 Hz, 1H, H-4), 4.73 (d, *J* = 10.4 Hz, 1H, H-1), 4.16 (dd, *J* = 12.4, 5.1 Hz, 1H, H-6b), 4.12 – 3.98 (m, 3H, CH_2NC═O, H-6a), 3.93 – 3.80 (m, 2H, H-2, H-5), 3.15 – 2.94 (m, 2H, CH_2), 2.92 – 2.79 (m, 2H, CH_2), 2.75 – 2.54 (m, 2H, SCH_2), 2.10 – 2.00 (m, 5H, CH_2, OAc), 1.99 (s, 3H, OAc), 1.93 (s, 3H, OAc), 1.78 (s, 3H, NAc), 1.67 – 1.43 (m, 4H, 2 CH_2), 1.41 – 1.24 (m, 4H, 2 CH_2); ^{13}C NMR (75 MHz, DMSO-d_6) δ 170.09, 169.69, 169.40, 169.19, 163.23, 162.95, 137.58, 131.61, 130.89, 130.09, 128.65, 128.41, 127.74, 122.75, 121.45, 83.50, 74.70, 73.83, 68.75, 62.18, 52.30, 46.92, 44.99, 37.43, 29.18, 29.08, 27.71, 25.69, 25.61, 24.74, 22.77, 20.64, 20.53, 20.46; HRMS (ESI) calcd for $C_{35}H_{45}ClN_3O_{10}S$ ($M+H^+$) 734.2514, found 734.2497.

2-[3-[6-[(2-Acetamido-3,4,6-tri-*O*-acetyl-β-D-glucopyranosyl) thio] hexylamino] propyl] -6-methoxy-1*H*-benzo[*de*]isoquinoline-1,3(2*H*)-dione (**10c**): light yellow oil; (1.5 g, 68.2 %) yield; $[\alpha]_D^{25}$ -93.4 (c=1.0, DMSO); ^{1}H NMR (300 MHz, $CDCl_3$) δ 8.56 – 8.42 (m, 3H, ArH), 7.75 – 7.60 (m, 1H, ArH), 7.11 (d, *J* = 9.5 Hz, 1H, NHAc), 7.04 (d, *J* = 7.1 Hz, 1H, ArH), 5.29 (t, *J* = 9.7 Hz, 1H, H-3), 5.07 (t, *J* = 9.7 Hz, 1H, H-4), 4.83 (d, *J* = 10.4 Hz, 1H, H-1), 4.31 – 4.19 (m, 3H, H-6b, CH_2NC=O), 4.16 – 4.04 (m, 5H, OCH_3, H-6a, H-2), 3.82 – 3.72 (m, 1H, H-5), 3.11 – 2.93 (m, 4H, 2 CH_2), 2.82 – 2.57 (m, 2H, SCH_2), 2.43 – 2.27 (m, 2H, CH_2), 2.06 (s, 3H, OAc), 2.00, 1.99 (2 s, 6H, 2 OAc), 1.98 (s, 3H, NAc), 1.94 – 1.80 (m, 2H, CH_2), 1.72 – 1.56 (m, 2H, CH_2), 1.54 – 1.37 (m, 4H, 2 CH_2); ^{13}C NMR (75 MHz, $CDCl_3$) δ 170.36, 170.31, 170.26, 169.07, 164.51, 163.98, 160.94, 133.69, 131.52, 128.89, 125.66, 123.04, 121.26, 113.80, 105.13, 83.91, 75.18, 73.69, 68.46,

62.11, 56.02, 52.85, 47.72, 45.23, 36.80, 29.50, 28.58, 27.32, 25.61, 25.53, 24.85, 22.93, 20.42, 20.36, 20.26; HRMS (ESI) calcd for $C_{36}H_{48}N_3O_{11}S$ ($M+H^+$) 730.3010, found 730.3016.

2-[3-[6-[(2-Acetamido-3,4,6-tri-*O*-acetyl-β-D-glucopyranosyl) thio] hexylamino] propyl] -6-dimethylamino-1*H*-benzo[*de*]isoquinoline-1,3(2*H*)-dione (**10d**): yellow oil; (1.4 g, 63.6 %) yield; $[\alpha]_D^{25}$ -85.5 (c=1.0, DMSO); ^{1}H NMR (300 MHz, $CDCl_3$) δ 8.57 (dd, *J* = 7.3, 1.1 Hz, 1H, ArH), 8.50 – 8.42 (m, 2H, ArH), 7.67 (dd, *J* = 8.4, 7.4 Hz, 1H, ArH), 7.12 (d, *J* = 8.3 Hz, 1H, ArH), 5.94 (d, *J* = 9.4 Hz, 1H, NHAc), 5.21 (t, *J* = 9.7 Hz, 1H, H-3), 5.09 (t, *J* = 9.6 Hz, 1H, H-4), 4.64 (d, *J* = 10.4 Hz, 1H, H-1), 4.31 – 4.19 (m, 3H, H-6b, CH_2NC=O), 4.17 – 4.08 (m, 2H, H-6a, H-2), 3.76 – 3.65 (m, 1H, H-5), 3.12 (s, 6H, 2 NCH_3), 2.78 – 2.60 (m, 6H, 3 CH_2), 2.60 – 2.47 (m, 2H, CH_2), 2.08, 2.03, 2.02 (3 s, 9H, 3 OAc), 1.97 (s, 3H, NAc), 1.69 – 1.52 (m, 4H, 2 CH_2), 1.47 – 1.33 (m, 4H, 2 CH_2); ^{13}C NMR (75 MHz, DMSO-d_6) δ 170.08, 169.73, 169.39, 169.17, 163.81, 163.16, 156.64, 132.34, 131.56, 130.61, 129.70, 125.05, 124.32, 122.43, 113.45, 113.06, 83.55, 74.71, 73.83, 68.75, 62.19, 52.32, 48.90, 46.78, 44.49, 37.77, 29.32, 28.94, 28.19, 27.60, 26.33, 22.75, 20.59, 20.52, 20.45; HRMS (ESI) calcd for $C_{37}H_{51}N_4O_{10}S$ ($M+H^+$) 743.3326, found 743.3320.

2-[3-[6-[(2-Acetamido-3,4,6-tri-*O*-acetyl-β-D-glucopyranosyl) thio] hexylamino] propyl] -6-(piperidin-1-yl)-1*H*-benzo[*de*]isoquinoline-1,3(2*H*)-dione (**10e**): yellow oil; (1.4 g, 60.9 %) yield; $[\alpha]_D^{25}$ -80.8 (c=1.0, DMSO); ^{1}H NMR (300 MHz, DMSO-d_6) δ 8.34 (d, *J* = 7.2 Hz, 1H, ArH), 8.30 – 8.20 (m, 2H, ArH), 7.98 (d, *J* = 9.4 Hz, 1H, NHAc), 7.76 – 7.63 (m, 1H, ArH), 7.16 (d, *J* = 8.2 Hz, 1H, ArH), 5.07 (t, *J* = 9.7 Hz, 1H, H-3), 4.82 (t, *J* = 9.7 Hz, 1H, H-4), 4.67 (d, *J* = 10.4 Hz, 1H, H-1), 4.13 (dd, *J* = 12.3, 5.1 Hz, 1H, H-6b), 4.05 – 3.93 (m, 3H, CH_2NC=O, H-6a), 3.91 – 3.75 (m, 2H, H-2, H-5), 3.17 – 3.02 (m, 4H, 2 CH_2), 2.66 – 2.49 (m, 4H, CH_2, SCH_2), 2.48 – 2.38 (m, 2H, CH_2), 1.98 (s, 3H, OAc), 1.95 (s, 3H, OAc), 1.90 (s, 3H, OAc), 1.83 – 1.67 (m, 9H, NAc, 3 CH_2), 1.66 – 1.54 (m, 2H, CH_2), 1.53 – 1.40 (m, 2H, CH_2), 1.39 – 1.29 (m, 2H, CH_2), 1.28 – 1.17 (m, 4H, 2 CH_2); ^{13}C NMR (75 MHz, DMSO-d_6) δ 170.05, 169.71, 169.37, 169.15, 163.65, 163.11, 156.69, 132.23, 130.54, 130.49, 129.18, 125.75, 125.47, 122.54, 115.09, 114.86, 83.57, 74.73, 73.84, 68.77, 62.20, 54.04, 52.34, 49.03, 46.88, 37.87, 29.34, 29.19, 28.24, 27.78, 26.40, 25.82, 23.96, 22.73, 20.56, 20.49, 20.43; HRMS (ESI) calcd for $C_{40}H_{55}N_4O_{10}S$ ($M+H^+$) 783.3639, found 783.3649.

A solution of **10a-10e** (1.0 mmol) was suspended in anhydrous MeOH (10 mL), and saturated solution of NH_3 in MeOH (10 mL) was then added. The reaction was stirred for 50 h at room temperature, until TLC (EtOAc/MeOH/H_2O, 8:1:1 v/v/v) indicated that the reaction was complete. The mixture was concentrated *in vacuo* and recrystallized from MeOH/ether to obtain **11a-11e**.

2-[3-[6-[(2-Acetamido-β-D-glucopyranosyl)thio]hexylamino] propyl]-6- bromo-1*H*-benzo[*de*] isoquinoline-1,3(2*H*)-dione (**11a**): light yellow solid; (0.6 g, 90.9 %) yield; $[\alpha]_D^{25}$ -40.1 (c=0.5, DMSO); ^{1}H NMR (300 MHz, DMSO-d_6) δ 8.58 – 8.34 (m, 2H, ArH), 8.30 – 8.08 (m, 2H, ArH), 7.93 (dd, *J* = 8.4, 7.5 Hz, 1H, ArH), 7.72 (d, *J* = 9.3 Hz, 1H, NHAc), 4.34 (d, *J* = 10.3 Hz, 1H, H-1), 4.10 – 3.99 (m, 2H, H-3, H-4), 3.70 (d, *J* = 11.6 Hz, 1H, H-6b), 3.53 (dd, *J* = 19.6, 9.7 Hz, 1H, H-2), 3.48 – 3.40 (m, 1H, H-6a), 3.34 – 3.22 (m, 1H, H-5), 3.16 – 3.05 (m, 2H, CH_2Ar), 2.66 – 2.52 (m, 4H, 2 CH_2), 2.44 (t, *J* = 6.7 Hz, 2H, CH_2), 1.85 – 1.68 (m, 5H, NAc, CH_2), 1.57 – 1.41 (m, 2H, CH_2), 1.37 – 1.16 (m, 6H, 3 CH_2); ^{13}C NMR (75 MHz, DMSO-d_6) δ 169.17, 163.44, 163.16, 137.73, 131.79, 131.08, 130.28, 128.84, 128.66, 127.92, 123.01, 121.71, 84.39, 81.45, 75.82, 70.79, 61.47, 54.80, 49.48, 47.34, 38.44, 37.68, 29.74, 29.29, 28.56, 28.18, 26.68, 23.32; HRMS (ESI) calcd for $C_{29}H_{39}BrN_3O_7S$ ($M+H^+$) 652.1692, found 652.1673.

2-[3-[6-[(2-Acetamido-β-D-glucopyranosyl)thio] hexylamino]propyl]-6- chloro-1*H*-benzo[*de*] isoquinoline-1,3(2*H*)-dione (**11b**): light yellow solid; (0.55 g, 90.2 %) yield; $[\alpha]_D^{25}$ -49.4 (c=0.5, DMSO); ^{1}H NMR (300 MHz, DMSO-d_6) δ 8.61 – 8.48 (m, 2H, ArH), 8.39 (d, *J* = 7.9 Hz, 1H, ArH), 8.05 – 7.94 (m, 2H, ArH), 7.75 (d, *J* = 9.3 Hz, 1H, NHAc), 5.02 (br s, 2H, 2 OH), 4.33 (d, *J* = 10.2 Hz, 1H, H-1), 4.09 (t, *J* = 6.7 Hz, 2H, H-3, H-4), 3.68 (d, *J* = 11.6 Hz, 1H, H-6b), 3.58 – 3.42 (m, 2H, H-2, H-6a), 3.33 – 3.25 (m, 1H, H-5), 3.09 (m, 2H, CH_2NC=O), 2.96 – 2.85 (m, 2H, CH_2), 2.84 – 2.70 (m, 2H, CH_2), 2.59 (t, *J* = 6.1 Hz, 2H, CH_2), 2.08 – 1.91 (m, 2H, CH_2), 1.80 (s, 3H, NAc), 1.58 – 1.42 (m, 4H, 2 CH_2), 1.34 – 1.24 (m, 4H, 2 CH_2); ^{13}C NMR (75 MHz, DMSO-d_6) δ 169.05, 163.32, 163.04, 137.61, 131.67, 130.96, 130.16, 128.72, 128.54, 127.80, 122.89, 121.59, 84.22, 81.30, 75.60, 70.69, 61.35, 54.64, 47.24, 45.28, 37.56, 29.01, 28.92, 27.91, 26.18, 25.75, 25.16, 23.18; HRMS (ESI) calcd for $C_{29}H_{39}ClN_3O_7S$ ($M+H^+$) 608.2197, found 608.2216.

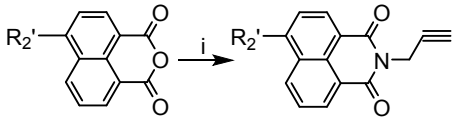
2-[3-[6-[(2-Acetamido-β-D-glucopyranosyl) thio] hexylamino] propyl]-6-methoxy-1*H*-benzo [*de*]isoquinoline-1,3(2*H*)-dione (**11c**): light yellow solid; (0.55 g, 91.7 %) yield; $[\alpha]_D^{25}$ -61.1 (c=0.5, DMSO); ^{1}H NMR (300 MHz, DMSO-d_6) δ 8.48 – 8.30 (m, 3H, ArH), 7.74 (m, 2H, ArH, NHAc), 7.24 (d, *J* = 8.4 Hz, 1H, ArH), 5.03 (br s, 2H, 2 OH), 4.35 (d, *J* = 10.3 Hz, 1H, H-1), 4.11 (s, 3H, OCH_3), 4.05 (t, *J* = 7.1 Hz, 2H, H-3, H-4), 3.70 (d, *J* = 11.6 Hz, 1H, H-6b), 3.62 – 3.44 (m, 2H, H-2, H-6b), 3.33 – 3.26 (m, 1H, H-5), 3.15 – 3.07 (m, 2H, CH_2Ar), 2.67 – 2.52 (m, 4H, 2 CH_2), 2.45 (t, *J* = 6.7 Hz, 2H, CH_2), 1.82 (s, 3H, NAc), 1.78 – 1.70 (m, 2H, CH_2), 1.59 – 1.41 (m, 2H, CH_2), 1.39 – 1.18 (m, 6H, 3 CH_2); ^{13}C NMR (75 MHz, DMSO-d_6) δ 169.04, 163.65, 163.01, 160.33, 133.24, 130.99, 128.53, 128.20, 126.33, 122.75, 121.90, 114.27, 106.24, 84.26, 81.31, 75.69, 70.68,

61.35, 56.68, 54.69, 49.35, 47.19, 38.09, 29.61, 29.18, 28.43, 28.12, 26.55, 23.17; HRMS (ESI) calcd for $C_{30}H_{42}N_3O_8S$ ($M+H^+$) 604.2693, found 604.2695.

2-[3-[6-[(2-Acetamido-β-D-glucopyranosyl) thio] hexylamino] propyl]-6- dimethylamino-1*H*-benzo[*de*]isoquinoline-1,3(2*H*)-dione (**11d**): yellow solid; (0.56 g, 90.3 %) yield; $[\alpha]_D^{25}$ -52.5 (c=0.5, DMSO); ^{1}H NMR (300 MHz, DMSO-d_6) δ 8.52 – 8.39 (m, 2H, ArH), 8.31 (d, J = 8.3 Hz, 1H, ArH), 7.79 – 7.67 (m, 2H, ArH, NHAc), 7.18 (d, J = 8.4 Hz, 1H, ArH), 4.34 (d, J = 10.3 Hz, 1H, H-1), 4.06 (t, J = 7.1 Hz, 2H, H-3, H-4), 3.70 (d, J = 11.5 Hz, 1H, H-6b), 3.59 – 3.43 (m, 2H, H-2, H-6a), 3.33 – 3.26 (m, 1H, H-5), 3.14 – 3.10 (m, 2H, CH_2Ar), 3.09 (s, 6H, 2 NCH_3), 2.65 – 2.56 (m, 2H, CH_2), 2.54 (d, J = 6.5 Hz, 2H, CH_2), 2.45 (t, J = 6.8 Hz, 2H, CH_2), 1.82 (s, 3H, NAc), 1.79 – 1.70 (m, 2H, CH_2), 1.57 – 1.43 (m, 2H, CH_2), 1.42 – 1.32 (m, 2H, CH_2), 1.31 – 1.20 (m, 4H, 2 CH_2); ^{13}C NMR (75 MHz, DMSO-d_6) δ 169.04, 163.77, 163.13, 156.62, 132.34, 131.54, 130.61, 129.68, 125.05, 124.32, 122.42, 113.44, 113.07, 84.26, 81.31, 75.69, 70.68, 61.35, 54.68, 49.32, 47.14, 44.49, 39.95, 37.95, 29.57, 29.17, 28.42, 28.12, 26.54, 23.17; HRMS (ESI) calcd for $C_{31}H_{45}N_4O_7S$ ($M+H^+$) 617.3009, found 617.3018.

2-[3-[6-[(2-Acetamido-β-D-glucopyranosyl) thio] hexylamino] propyl]-6- (piperidin-1-yl)-1*H*-benzo[*de*]isoquinoline-1,3(2*H*)-dione (**11e**): yellow solid; (0.59 g, 89.4 %) yield; $[\alpha]_D^{25}$ -58.9 (c=0.5, DMSO); ^{1}H NMR (300 MHz, DMSO-d_6) δ 8.55 – 8.27 (m, 3H, ArH), 7.84 – 7.59 (m, 2H, ArH, NHAc), 7.27 (d, J = 8.2 Hz, 1H, ArH), 5.00 (s, 2H, 2 OH), 4.34 (d, J = 10.3 Hz, 1H, H-1), 4.07 (t, J = 6.9 Hz, 2H, H-3, H-4), 3.69 (d, J = 11.5 Hz, 1H, H-6b), 3.60 – 3.41 (m, 2H, H-2, H-6a), 3.33 – 3.23 (m, 1H, H-5), 3.22 – 3.19 (m, 2H, CH_2), 3.18 – 3.14 (m, 2H, CH_2), 3.13 – 3.06 (m, 2H, CH_2), 2.65 – 2.52 (m, 6H, 3 CH_2), 1.89 – 1.71 (m, 9H, NAc, 3 CH_2), 1.72 – 1.58 (m, 2H, CH_2), 1.57 – 1.44 (m, 2H, CH_2), 1.44 – 1.33 (m, 2H, CH_2), 1.33 – 1.20 (m, 4H, 2 CH_2); ^{13}C NMR (75 MHz, DMSO-d_6) δ 169.01, 163.76, 163.22, 156.79, 132.34, 130.65, 129.27, 125.88, 125.54, 122.62, 115.13, 114.99, 84.26, 81.32, 75.67, 70.68, 61.35, 54.67, 54.08, 48.93, 48.72, 46.80, 37.84, 29.13, 28.94, 28.33, 27.59, 26.39, 25.83, 23.97, 23.18; HRMS (ESI) calcd for $C_{34}H_{49}N_4O_7S$ ($M+H^+$) 657.3322, found 657.3316.

1.4 Synthesis of naphthalimide derivatives 12a-12b



12a: R_2'=Br; **12b**: R_2'=Cl

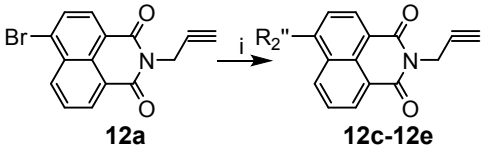
Scheme S4. Synthesis of naphthalimide derivatives **12a-12b**. (i) 2-propynylamine, EtOH.

3-Propynylamine (33 mmol, 1.1 eq) was added to a suspension of 1,8-naphthalic anhydride **4a-4b** (30 mmol, 1 eq) in EtOH (200 mL). The mixture was refluxed for about 6 h until the completion was detected by TLC (petroleum ether/EtOAc, 5:1 v/v). Then the mixture was cooled to room temperature and the precipitate was then filtered, dried, and recrystallized from ethanol to obtain **12a-12b**.

6-Bromo-2-(prop-2-yn-1-yl)-1*H*-benzo[*de*]isoquinoline-1,3(2*H*)-dione (**12a**)[4]: light yellow solid; (8.2 g, 87.0 %) yield; ^{1}H NMR (300 MHz, DMSO-d_6) δ 8.55 (dd, J = 7.3, 1.0 Hz, 1H, ArH), 8.49 (dd, J = 8.5, 1.0 Hz, 1H, ArH), 8.31 (d, J = 7.9 Hz, 1H, ArH), 8.18 (d, J = 7.9 Hz, 1H, ArH), 7.97 (dd, J = 8.5, 7.3 Hz, 1H, ArH), 4.77 (d, J = 2.5 Hz, 2H, CH_2), 3.20 (t, J = 2.4 Hz, 1H, ≡CH).

6-Chloro-2-(prop-2-yn-1-yl)-1*H*-benzo[*de*]isoquinoline-1,3(2*H*)-dione (**12b**)[5]: light yellow solid; (7.2 g, 88.9 %) yield; ^{1}H NMR (300 MHz, DMSO-d_6) δ 8.60 – 8.48 (m, 2H, ArH), 8.37 (d, J = 7.9 Hz, 1H, ArH), 8.05 – 7.90 (m, 2H, ArH), 4.76 (d, J = 2.4 Hz, 2H, CH_2), 3.19 (t, J = 2.4 Hz, 1H, ≡CH).

1.5 Synthesis of naphthalimide derivatives 12c-12e



12c: R_2''=OCH_3; **12d**: R_2''=$N(CH_3)_2$; **12e**: R_2''=piperidyl

Scheme S5. Synthesis of naphthalimide derivatives **12c-12e**. (i) MeOH, KOH for **12c**; dimethylamine, 2-methoxyethanol for **12d**; piperidine, 2-methoxyethanol for **12e**.

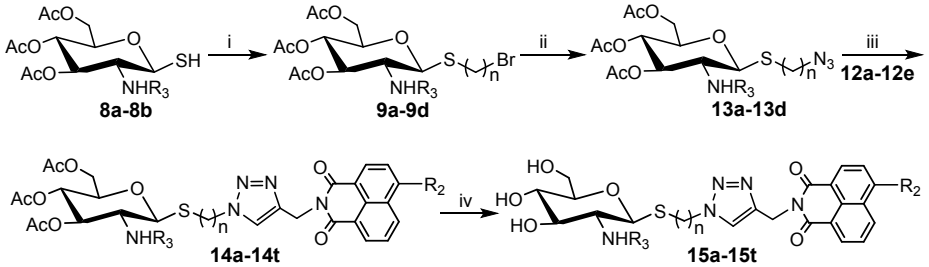
Compound **12a** (6.3 g, 20 mmol) was added into a solution of KOH (1.7 g, 30 mmol) in MeOH (100 mL) and 2-methoxyethanol (20 mL). The mixture was then refluxed for 5 h, until TLC (petroleum ether/ EtOAc, 6:1 v/v) indicated the completion of the reaction. After the mixture was

concentrated *in vacuo*, the resulting residue was further purified by silica gel column chromatography (petroleum ether/ EtOAc, 8:1 v/v), and **12c** was obtained as a light yellow solid. (4.1 g, 77.3%) yield; ^{1}H NMR (300 MHz, $CDCl_3$) δ 8.67 – 8.51 (m, 3H, ArH), 7.70 (dd, *J* = 8.4, 7.3 Hz, 1H, ArH), 7.04 (d, *J* = 8.3 Hz, 1H, ArH), 4.95 (d, *J* = 2.5 Hz, 2H, CH_2), 4.13 (s, 3H, OCH_3), 2.19 (t, *J* = 2.5 Hz, 1H, ≡CH). ^{13}C NMR (75 MHz, $CDCl_3$) δ 162.71, 162.06, 160.11, 132.88, 130.90, 128.42, 128.03, 124.96, 122.56, 121.05, 113.69, 104.26, 77.87, 69.25, 55.25, 28.26; HRMS (ESI) calcd for $C_{16}H_{12}NO_3$ ($M+H^+$) 266.0817, found 266.0802.

Compound **12a** (6.3 g, 20 mmol) was dissolved in 2-methoxyethanol (80 mL), then 40% dimethylamine aqueous solution (10 mL) was added. The mixture was refluxed for 5 h under N_2, until TLC (petroleum ether/EtOAc, 6:1 v/v) indicated the completion of the reaction. After the mixture was concentrated *in vacuo*, **12d**[6] was prepared by recrystallized from EtOH as a yellow solid. (4.4 g, 79.0 %) yield; ^{1}H NMR (300 MHz, $CDCl_3$) δ 8.60 (dd, *J* = 7.3, 1.2 Hz, 1H, ArH), 8.50 (d, *J* = 8.2 Hz, 1H, ArH), 8.45 (dd, *J* = 8.5, 1.2 Hz, 1H, ArH), 7.66 (dd, *J* = 8.5, 7.3 Hz, 1H, ArH), 7.11 (d, *J* = 8.3 Hz, 1H, ArH), 4.95 (d, *J* = 2.5 Hz, 2H, CH_2), 3.12 (s, 6H, 2 NCH_3), 2.17 (t, *J* = 2.5 Hz, 1H, ≡CH).

Compound **12a** (6.3 g, 20 mmol) was dissolved in 2-methoxyethanol (80 mL), then piperidine (10 mL) was added. The reaction mixture was refluxed for 5h under N_2, until TLC (petroleum ether/EtOAc, 6:1 v/v) indicated that the reaction was complete. After the reaction mixture was concentrated *in vacuo*, compound **12e**[7] was yielded by recrystallized from EtOH as a yellow solid. (4.9 g, 76.6%) yield; ^{1}H NMR (300 MHz, DMSO-d_6) δ 8.45 (dd, *J* = 7.3, 1.0 Hz, 1H, ArH), 8.39 – 8.33 (m, 2H, ArH), 7.78 (dd, *J* = 8.4, 7.3 Hz, 1H, ArH), 7.26 (d, *J* = 8.2 Hz, 1H, ArH), 4.75 (d, *J* = 2.4 Hz, 2H, ≡CCH_2), 3.21 – 3.14 (m, 4H, 2 CH_2), 3.13 (t, *J* = 2.4 Hz, 1H, ≡CH), 1.84 – 1.76 (m, 4H, 2 CH_2), 1.69 – 1.60 (m, 2H, CH_2).

1.6 Synthesis of thioglycosyl-naphthalimide derivatives 15a-15t



R_2= Br, Cl, OCH_3, $N(CH_3)_2$, piperidyl; R_3= Ac, Cbz; n= 5, 6

15a: R_2=Br, R_3=Ac, n=5; **15b**: R_2=Br, R_3=Ac, n=6; **15c**: R_2=Br, R_3=Cbz, n=5; **15d**: R_2=Br, R_3=Cbz, n=6;

15e: R_2=Cl, R_3=Ac, n=5; **15f**: R_2=Cl, R_3=Ac, n=6; **15g**: R_2=Cl, R_3=Cbz, n=5; **15h**: R_2=Cl, R_3=Cbz, n=6;
15i: R_2=OCH_3, R_3=Ac, n=5; **15j**: R_2=OCH_3, R_3=Ac, n=6; **15k**: R_2=OCH_3, R_3=Cbz, n=5;
15l: R_2=OCH_3, R_3=Cbz, n=6; **15m**: R_2=$N(CH_3)_2$, R_3=Ac, n=5; **15n**: R_2=$N(CH_3)_2$, R_3=Ac, n=6;
15o: R_2=$N(CH_3)_2$, R_3=Cbz, n=5; **15p**: R_2=$N(CH_3)_2$, R_3=Cbz, n=6; **15q**: R_2=piperidyl, R_3=Ac, n=5;
15r: R_2=piperidyl, R_3=Ac, n=6; **15s**: R_2=piperidyl, R_3=Cbz, n=5; **15t**: R_2=piperidyl, R_3=Cbz, n=6

Scheme S6. Synthesis of glycosylated naphthalimide derivatives **15a-15t**. (i) a, ω-dibromoalkane, K_2CO_3, acetone, H_2O; (ii) NaN_3, K_2CO_3, acetone, H_2O; (iii) **12a-12e**, $CuSO_4$, sodium ascorbate, THF, H_2O; (iv) NH_3, MeOH.

2-Acetamido-3,4,6-tri-O-acetyl-2-deoxy-1-thio-β-D-glucopyranose (**8a**) was synthesized from N-acetyl-D-glucosamine as described previously.[3, 8] White solid; (65.2 % over three steps) yield; $[\alpha]_D^{25}$ -15.1 (c=1.0,$CHCl_3$); ^{1}H NMR (300 MHz, $CDCl_3$) δ 5.78 (d, *J* = 9.5 Hz, 1H, NH), 5.20 – 5.03 (m, 2H, H-3, H-4), 4.60 (d, *J* = 9.9 Hz, 1H, H-1), 4.25 (dd, *J* = 12.4, 4.8 Hz, 1H, H-6b), 4.19 – 4.05 (m, 2H, H-6a, H-2), 3.70 (ddd, *J* = 9.8, 4.7, 2.2 Hz, 1H, H-5), 2.57 (s, 1H, SH), 2.10 (s, 3H, OAc), 2.05 (s, 3H, OAc), 2.03 (s, 3H, OAc), 1.99 (s, 3H, NAc)

2-[[(Phenylmethoxy)carbonyl]amino]-3,4,6-tri-O-acetyl-2-deoxy-1-thio-β-D-glucopyranose (**8b**) was synthesized from D-Glucosamine hydrochloride as described previously.[9] White solid; (41.8 % over four steps) yield; $[\alpha]_D^{25}$ +11.4 (c=1.0,$CHCl_3$); ^{1}H NMR (300 MHz, $CDCl_3$) δ 7.41 – 7.29 (m, 5H, ArH), 5.25 – 5.03 (m, 5H, H-3, $PhCH_2$, H-4, H-1), 4.61 (t, *J* = 9.5 Hz, 1H, NH), 4.24 (dd, *J* = 12.4, 4.9 Hz, 1H, H-6b), 4.11 (dd, *J* = 12.4, 1.8 Hz, 1H, H-6a), 3.83 – 3.62 (m, 2H, H-2, H-5), 2.49 (d, *J* = 9.2 Hz, 1H, SH), 2.09 (s, 3H, OAc), 2.01 (s, 3H, OAc), 1.92 (s, 3H, OAc).

A solution of thiol **8a-8b** (11.0 mmol, 1.0 eq) in acetone (100 mL) and H_2O (50 mL) was mixed with solid potassium carbonate (13.2 mmol, 1.2 eq), then α, ω- dibromoalkane (88 mmol, 8.0 eq) was added. The mixture was stirred for 10 h at room temperature until TLC (petroleum ether/EtOAc, 3:1 v/v) indicated that the reaction was complete. After the solution was concentrated *in vacuo*, the residue was diluted with DCM (150 mL), washed with H_2O (200 mL), brine (200 mL), dried over Na_2SO_4, and concentrated. Finally, the residue was purified by flash column chromatography to obtain **9a-9d**.

5-Bromopentyl 2-acetamido-3,4,6-tri-O-acetyl-2-deoxy-1-thio-β-D-glucopyranoside (**9a**)[3]: white solid; (4.1g, 73.2 %) yield; $[\alpha]_D^{25}$ -63.2 (c=0.5, $CHCl_3$); ^{1}H NMR (300 MHz, $CDCl_3$) δ 6.26 (d, *J* = 9.3 Hz, 1H, NH), 5.23 (t, *J* = 9.8 Hz, 1H, H-3), 5.08 (t, *J* = 9.7 Hz, 1H, H-4), 4.67 (d, *J* = 10.4 Hz, 1H, H-1), 4.25 (dd, J = 12.3, 5.0 Hz, 1H, H-6b), 4.18–4.02 (m, 2H, H-6a, H-2), 3.75 (ddd, *J* = 9.9, 4.9, 2.3 Hz, 1H, H-5), 3.42 (t, *J* = 6.7 Hz, 2H, CH_2Br), 2.83–2.61 (m, 2H, SCH_2), 2.09, 2.04,

2.03 (3 s, 9H, 3 OAc), 1.97 (s, 3H, NAc), 1.87 (m, 2H, CH_2), 1.71–1.60 (m, 2H, CH_2), 1.60–1.46 (m, 2H, CH_2).

5-Bromopentyl 2-[[(phenylmethoxy) carbonyl] amino]- 3,4,6-tri-O- acetyl-2-deoxy-1-thio- β-D-glucopyranoside (**9c**): white solid; (5.3g, 80.3 %) yield; $[\alpha]_D^{25}$ -47.1 (c=0.5, $CHCl_3$); ^{1}H NMR (300 MHz, $CDCl_3$) δ 7.40 – 7.28 (m, 5H, ArH), 5.26 – 5.00 (m, 5H, H-3, $PhCH_2$, H-4, H-1), 4.60 (d, *J* = 10.0 Hz, 1H, NH), 4.24 (dd, *J* = 12.3, 5.0 Hz, 1H, H-6b), 4.12 (dd, *J* = 12.4, 2.1 Hz, 1H, H-6a), 3.86 – 3.62 (m, 2H, H-2, H-5), 3.38 (t, *J* = 6.8 Hz, 2H, CH_2Br), 2.80 – 2.59 (m, 2H, SCH_2), 2.07 (s, 3H, OAc), 2.01 (s, 3H, OAc), 1.92 (s, 3H, OAc), 1.90 – 1.78 (m, 2H, CH_2), 1.70 – 1.42 (m, 4H, 2 CH_2); ^{13}C NMR (75 MHz, $CDCl_3$) δ 170.70, 170.62, 169.39, 155.73, 136.35, 128.48, 128.14, 127.96, 84.68, 75.87, 73.61, 68.65, 66.98, 62.39, 55.12, 33.46, 32.21, 29.74, 28.75, 27.27, 20.75, 20.59, 20.52; HRMS (ESI) calcd for $C_{25}H_{35}BrNO_9S$ ($M+H^+$) 604.1216, found 604.1211.

6-Bromohexyl 2-[[(phenylmethoxy) carbonyl] amino]- 3,4,6-tri-O- acetyl-2-deoxy-1-thio- β-D-glucopyranoside (**9d**): white solid; (5.2g, 76.5 %) yield; $[\alpha]_D^{25}$ -49.9 (c=0.5, $CHCl_3$); ^{1}H NMR (300 MHz, $CDCl_3$) δ 7.46 – 7.29 (m, 5H, ArH), 5.29 – 4.96 (m, 5H, H-3, $PhCH_2$, H-4, H-1), 4.60 (d, *J* = 10.0 Hz, 1H, NH), 4.24 (dd, *J* = 12.3, 5.0 Hz, 1H, H-6b), 4.12 (dd, *J* = 12.3, 2.2 Hz, 1H, H-6a), 3.86 – 3.62 (m, 2H, H-2, H-5), 3.39 (t, *J* = 6.7 Hz, 2H, CH_2Br), 2.69 (s, 2H, SCH_2), 2.07 (s, 3H, OAc), 2.01 (s, 3H, OAc), 1.92 (s, 3H, OAc), 1.89 – 1.74 (m, 2H, CH_2), 1.69 – 1.52 (m, 2H, CH_2), 1.52 – 1.29 (m, 4H, 2 CH_2); ^{13}C NMR (75 MHz, $CDCl_3$) δ 170.35, 170.28, 169.06, 155.40, 136.02, 128.12, 127.76, 127.58, 84.34, 75.45, 73.28, 68.33, 66.57, 62.06, 54.74, 33.39, 32.19, 29.54, 29.01, 27.48, 27.28, 20.39, 20.24, 20.17; HRMS (ESI) calcd for $C_{26}H_{37}BrNO_9S$ ($M+H^+$) 618.1372, found 618.1376.

Compounds **9a-9b** (2 mmol, 1 eq) were dissolved in acetone/H_2O (2:1, 45 mL), then NaN_3 (0.65 g, 10 mmol) was added. The reaction mixture was refluxed for 20 h, and TLC analysis (petroleum ether/ EtOAc, 4:1) was performed to identify the completion of the reaction. The mixture was extracted with DCM (3×80 mL). Then the organic extracts were combined, dried over Na_2SO_4, filtered, and concentrated *in vacuo*. The residue was purified by flash column chromatography to acquire **13a-13d**.

5-Azidopentyl 2-acetamido-3,4,6-tri-O-acetyl-2-deoxy-1-thio-β-D-glucopyranoside (**13a**)[10]: white solid; (0.80 g, 84.2 %) yield; $[\alpha]_D^{25}$ -58.4 (c=0.5, $CHCl_3$); ^{1}H NMR (300 MHz, $CDCl_3$) δ 6.15 (d, J = 9.4 Hz, 1H, NH), 5.17 (t, J = 9.8 Hz, 1H, H-3), 5.02 (t, J = 9.7 Hz, 1H, H-4), 4.60 (d, J = 10.4 Hz, 1H, H-1), 4.19 (dd, J = 12.3, 5.0 Hz, 1H, H-6b), 4.13–3.96 (m, 2H, H-6a, H-2), 3.69 (ddd, J =

9.9, 4.9, 2.4 Hz, 1H, H-5), 3.22 (t, J = 6.7 Hz, 2H, CH_2N_3), 2.75–2.56 (m, 2H, SCH_2), 2.03, 1.98, 1.97 (3 s, 9H, 3 OAc), 1.90 (s, 3H, NAc), 1.65–1.50 (m, 4H, 2 CH_2), 1.48–1.38 (m, 2H, CH_2).

6-Azidohexyl 2-acetamido-3,4,6-tri-O-acetyl-2-deoxy-1-thio-β-D-glucopyranoside (**13b**)[10]: white solid; (0.82 g, 83.7 %) yield; $[\alpha]_D^{25}$ -55.8(c=0.5, $CHCl_3$); ^{1}H NMR (300 MHz, DMSO- d_6) δ 7.97 (d, J = 9.4 Hz, 1H, NH), 5.07 (t, J = 9.8 Hz, 1H, H-3), 4.83 (t, J = 9.7 Hz, 1H, H-4), 4.67 (d, J = 10.4 Hz, 1H, H-1), 4.14 (dd, J = 12.3, 5.0 Hz, 1H, H-6b), 4.01 (dd, J = 12.2, 1.8 Hz, 1H, H-6a), 3.91–3.78 (m, 2H, H-2, H-5), 3.31 (t, J = 6.6 Hz, 2H, CH_2N_3), 2.74–2.52 (m, 2H, SCH_2), 2.00, 1.97, 1.90 (3 s, 9H, 3 OAc), 1.76 (s, 3H, NAc), 1.60–1.45 (m, 4H, 2 CH_2), 1.39–1.27 (m, 4H, 2 CH_2).

5-Azidopentyl 2-[[(phenylmethoxy) carbonyl] amino]- 3,4,6-tri-O- acetyl-2-deoxy-1-thio- β-D-glucopyranoside (**13c**): white solid; (0.89 g, 80.9 %) yield; $[\alpha]_D^{25}$ -41.7 (c=0.5, $CHCl_3$); ^{1}H NMR (300 MHz, $CDCl_3$) δ 7.42 – 7.28 (m, 5H, ArH), 5.28 – 4.99 (m, 5H, H-3, $PhCH_2$, H-4, H-1), 4.59 (d, *J* = 9.8 Hz, 1H, NH), 4.24 (dd, *J* = 12.3, 5.0 Hz, 1H, H-6b), 4.12 (dd, *J* = 12.3, 2.2 Hz, 1H, H-6a), 3.86 – 3.61 (m, 2H, H-2, H-5), 3.25 (t, *J* = 6.7 Hz, 2H, CH_2N_3), 2.78 – 2.57 (m, 2H, SCH_2), 2.07 (s, 3H, OAc), 2.01 (s, 3H, OAc), 1.92 (s, 3H, OAc), 1.70 – 1.52 (m, 4H, 2 CH_2), 1.51 – 1.39 (m, 2H, CH_2); ^{13}C NMR (75 MHz, $CDCl_3$) δ 170.35, 170.25, 169.04, 155.37, 136.00, 128.12, 127.78, 127.60, 84.35, 75.53, 73.25, 68.29, 66.61, 62.03, 54.77, 50.89, 29.40, 28.74, 28.02, 25.47, 20.36, 20.22, 20.15; HRMS (ESI) calcd for $C_{25}H_{35}N_4O_9S$ ($M+H^+$) 567.2125, found 567.2113.

6-Azidohexyl 2-[[(phenylmethoxy) carbonyl] amino]- 3,4,6-tri-O- acetyl-2-deoxy-1-thio- β-D-glucopyranoside (**13d**): white solid; (0.90 g, 77.6 %) yield; $[\alpha]_D^{25}$ -62.4 (c=0.5, $CHCl_3$); ^{1}H NMR (300 MHz, $CDCl_3$) δ 7.41 – 7.28 (m, 5H, ArH), 5.27 – 4.98 (m, 5H, H-3, $PhCH_2$, H-4, H-1), 4.59 (d, *J* = 9.9 Hz, 1H, NH), 4.24 (dd, *J* = 12.3, 5.0 Hz, 1H, H-6b), 4.12 (dd, *J* = 12.1, 2.2 Hz, 1H, H-6a), 3.86 – 3.62 (m, 2H, H-2, H-5), 3.25 (t, *J* = 6.8 Hz, 2H, CH_2N_3), 2.78 – 2.59 (m, 2H, SCH_2), 2.07 (s, 3H, OAc), 2.01 (s, 3H, OAc), 1.92 (s, 3H, OAc), 1.69 – 1.50 (m, 4H, 2 CH_2), 1.46 – 1.29 (m, 4H, 2 CH_2); ^{13}C NMR (75 MHz, $CDCl_3$) δ 170.35, 170.28, 169.06, 155.43, 136.04, 128.11, 127.75, 127.56, 84.31, 75.43, 73.29, 68.34, 66.55, 62.06, 54.73, 50.95, 29.50, 29.04, 28.32, 27.87, 25.87, 20.35, 20.22, 20.15; HRMS (ESI) calcd for $C_{26}H_{37}N_4O_9S$ ($M+H^+$) 581.2281, found 581.2293.

A mixture of the azides **13a-13d** (1.5 mmol, 1eq) and alkyne **12a-12e** (1.5 mmol, 1eq) was suspended in THF/H_2O (1:1, 30 mL). A solution of copper sulfate (0.3mmol，0.2 eq) and sodium ascorbate (0.45mmol，0.3 eq) in H_2O (3 mL) was then added. The reaction mixture was stirred at rt for 4 h, until TLC (EtOAc) indicated that the reaction was complete. The mixture was concentrated *in vacuo*, the residue was diluted with DCM (150 mL), and washed with H_2O (200

mL), brine (200 mL), dried over Na_2SO_4, filtered and concentrated. The residue was purified by flash column chromatography to obtain **14a-14t**.

6-Bromo-2-[[1-[5-[(2-acetamido-3,4,6-tri-O-acetyl-β-D-glucopyranosyl)thio]pentyl]-1*H*-1,2,3-triazol-4-yl]methyl]-1*H*-benzo[*de*]isoquinoline-1,3(2*H*)-dione (**14a**): light yellow solid; (0.89 g, 75.4 %) yield; $[\alpha]_D^{25}$ -72.3 (c=0.5, DMSO); ^{1}H NMR (300 MHz, DMSO-d_6) δ 8.47 – 8.40 (m, 1H, ArH), 8.35 (d, *J* = 8.6 Hz, 1H, ArH), 8.18 (d, *J* = 7.9 Hz, 1H, ArH), 8.08 – 8.00 (m, 2H, ArH), 7.93 (d, *J* = 9.4 Hz, 1H, NH), 7.89 – 7.81 (m, 1H, ArH), 5.24 (s, 2H, $ArCH_2Ar$), 5.05 (t, *J* = 9.7 Hz, 1H, H-3), 4.82 (t, *J* = 9.7 Hz, 1H, H-4), 4.64 (d, *J* = 10.4 Hz, 1H, H-1), 4.26 (t, *J* = 7.1 Hz, 2H, CH_2), 4.11 (dd, *J* = 12.3, 5.1 Hz, 1H, H-6b), 3.98 (dd, *J* = 11.6, 2.3 Hz, 1H, H-6a), 3.89 – 3.77 (m, 2H, H-2, H-5), 2.63 – 2.50 (m, 2H, SCH_2), 1.96 (s, 3H, OAc), 1.95 (s, 3H, OAc), 1.90 (s, 3H, OAc), 1.74 (s, 5H, NAc, CH_2), 1.58 – 1.46 (m, 2H, CH_2), 1.33 – 1.19 (m, 2H, CH_2); ^{13}C NMR (75 MHz, DMSO-d_6) δ 170.07, 169.74, 169.38, 169.19, 162.60, 162.55, 142.76, 132.77, 131.77, 131.37, 131.12, 129.77, 129.41, 128.78, 128.23, 123.36, 122.57, 121.79, 83.51, 74.73, 73.83, 68.72, 62.13, 52.29, 49.31, 35.46, 29.30, 29.14, 28.68, 25.13, 22.74, 20.56, 20.52, 20.45; HRMS (ESI) calcd for $C_{34}H_{39}BrN_5O_{10}S$ ($M+H^+$) 788.1601, found 788.1604.

6-Bromo-2-[[1-[6-[(2-acetamido-3,4,6-tri-O-acetyl-β-D-glucopyranosyl)thio]hexyl]-1*H*-1,2,3-triazol-4-yl]methyl]-1*H*-benzo[*de*]isoquinoline-1,3(2*H*)-dione (**14b**): light yellow solid; (0.93 g, 77.5 %) yield; $[\alpha]_D^{25}$ -68.1 (c=0.5, DMSO); ^{1}H NMR (300 MHz, DMSO-d_6) δ 8.41 (ddd, *J* = 9.6, 7.9, 1.0 Hz, 2H, ArH), 8.20 (d, *J* = 7.9 Hz, 1H, ArH), 8.07 (d, *J* = 7.9 Hz, 1H, ArH), 8.02 (s, 1H, ArH), 7.95 (d, *J* = 9.5 Hz, 1H, NH), 7.87 (dd, *J* = 8.5, 7.3 Hz, 1H, ArH), 5.24 (s, 2H, $ArCH_2Ar$), 5.05 (t, *J* = 9.8 Hz, 1H, H-3), 4.81 (t, *J* = 9.7 Hz, 1H, H-4), 4.64 (d, *J* = 10.4 Hz, 1H, H-1), 4.25 (t, *J* = 7.1 Hz, 2H, CH_2), 4.12 (dd, *J* = 12.3, 5.1 Hz, 1H, H-6b), 3.98 (dd, *J* = 12.2, 2.1 Hz, 1H, H-6a), 3.89 – 3.75 (m, 2H, H-2, H-5), 2.65 – 2.49 (m, 2H, SCH_2), 1.96, 1.95 (2 s, 6H, 2 OAc), 1.90 (s, 3H, OAc), 1.80 – 1.66 (m, 5H, OAc, CH_2), 1.54 – 1.40 (m, 2H, CH_2), 1.35 – 1.11 (m, 4H, 2 CH_2); ^{13}C NMR (75 MHz, DMSO-d_6) δ 170.07, 169.74, 169.38, 169.17, 162.64, 162.58, 142.79, 132.79, 131.79, 131.40, 131.15, 129.81, 129.42, 128.82, 128.29, 123.31, 122.63, 121.84, 83.55, 74.71, 73.83, 68.74, 62.15, 52.32, 49.37, 35.48, 29.66, 29.27, 29.16, 27.60, 25.51, 22.74, 20.58, 20.53, 20.45; HRMS (ESI) calcd for $C_{35}H_{41}BrN_5O_{10}S$ ($M+H^+$) 802.1758, found 802.1755.

6-Bromo-2-[[1-[5-[[2-[[(phenylmethoxy)carbonyl]amino]-3,4,6-tri-O-acetyl-β-D-glucopyrano syl]thio]pentyl]-1*H*-1,2,3-triazol-4-yl]methyl]-1*H*-benzo[*de*]isoquinoline-1,3(2*H*)-dione (**14c**): light yellow solid; (1.1 g, 83.3 %) yield; $[\alpha]_D^{25}$ -82.5 (c=0.5, DMSO); ^{1}H NMR (300

MHz, DMSO-d_6) δ 8.44 (dd, J = 7.3, 1.0 Hz, 1H, ArH), 8.36 (dd, J = 8.5, 1.0 Hz, 1H, ArH), 8.19 (d, J = 7.9 Hz, 1H, ArH), 8.10 – 8.00 (m, 2H, ArH), 7.85 (dd, J = 8.5, 7.4 Hz, 1H, ArH), 7.46 (d, J = 9.6 Hz, 1H, NH), 7.35 – 7.20 (m, 5H, ArH), 5.25 (s, 2H, $ArCH_2Ar$), 5.12 – 4.92 (m, 3H, $PhCH_2$, H-3), 4.83 (t, J = 9.7 Hz, 1H, H-4), 4.63 (d, J = 10.3 Hz, 1H, H-1), 4.25 (t, J = 7.1 Hz, 2H, CH_2), 4.11 (dd, J = 12.4, 5.0 Hz, 1H, H-6b), 4.02 – 3.94 (m, 1H, H-6a), 3.83 – 3.70 (m, 1H, H-5), 3.56 (q, J = 10.0 Hz, 1H, H-2), 2.67 – 2.50 (m, 2H, SCH_2), 1.95 (s, 6H, 2 OAc), 1.83 (s, 3H, OAc), 1.79 – 1.67 (m, 2H, CH_2), 1.59 – 1.45 (m, 2H, CH_2), 1.37 – 1.19 (m, 2H, CH_2); ^{13}C NMR (75 MHz, DMSO-d_6) δ 170.08, 169.64, 169.38, 162.63, 162.57, 155.86, 142.78, 137.27, 132.79, 131.78, 131.38, 131.13, 129.79, 129.42, 128.79, 128.36, 128.26, 127.79, 127.43, 123.36, 122.60, 121.81, 83.74, 74.80, 73.89, 68.70, 65.40, 62.10, 54.53, 49.29, 35.47, 29.30, 29.18, 28.70, 25.10, 20.57, 20.51, 20.39; HRMS (ESI) calcd for $C_{40}H_{43}BrN_5O_{11}S$ ($M+H^+$) 880.1863, found 880.1861.

6-Bromo-2-[[1-[6-[[2-[[(phenylmethoxy)carbonyl]amino]-3,4,6-tri-O-acetyl-β-D-glucopyranosyl] thio] hexyl]-1*H*-1,2,3-triazol-4-yl]methyl]-1*H*-benzo[*de*]isoquinoline-1,3(2*H*)-dione (**14d**): light yellow solid; (1.2 g, 89.6 %) yield; $[\alpha]_D^{25}$ -81.1 (c=0.5, DMSO); ^{1}H NMR (300 MHz, DMSO-d_6) δ 8.54 – 8.39 (m, 2H, ArH), 8.25 (d, J = 7.9 Hz, 1H, ArH), 8.12 (d, J = 7.9 Hz, 1H, ArH), 8.05 (s, 1H, ArH), 7.91 (dd, J = 8.4, 7.4 Hz, 1H, ArH), 7.48 (d, J = 9.6 Hz, 1H, NH), 7.40 – 7.22 (m, 5H, ArH), 5.28 (s, 2H, $ArCH_2Ar$), 5.16 – 4.96 (m, 3H, $PhCH_2$, H-3), 4.86 (t, J = 9.7 Hz, 1H, H-4), 4.66 (d, J = 10.3 Hz, 1H, H-1), 4.28 (t, J = 7.1 Hz, 2H, CH_2), 4.15 (dd, J = 12.3, 5.0 Hz, 1H, H-6b), 4.01 (dd, J = 12.0, 1.7 Hz, 1H, H-6a), 3.86 – 3.72 (m, 1H, H-5), 3.58 (q, J = 10.0 Hz, 1H, H-2), 2.68 – 2.52 (m, 2H, SCH_2), 1.99 (s, 3H, OAc), 1.98 (s, 3H, OAc), 1.86 (s, 3H, OAc), 1.82 – 1.67 (m, 2H, CH_2), 1.59 – 1.42 (m, 2H, CH_2), 1.40 – 1.26 (m, 2H, CH_2), 1.25 – 1.10 (m, 2H, CH_2); ^{13}C NMR (75 MHz, DMSO-d_6) δ 170.08, 169.64, 169.39, 162.66, 162.61, 155.86, 142.79, 137.27, 132.81, 131.81, 131.42, 131.16, 129.84, 129.43, 128.83, 128.35, 127.78, 127.41, 123.33, 122.65, 121.87, 83.76, 74.78, 73.88, 68.72, 65.38, 62.12, 54.55, 49.38, 35.49, 29.66, 29.31, 29.13, 27.58, 25.52, 20.59, 20.52, 20.39; HRMS (ESI) calcd for $C_{41}H_{45}BrN_5O_{11}S$ ($M+H^+$) 894.2020, found 894.2022.

6-Chloro-2-[[1-[5-[(2-acetamido-3,4,6-tri-O-acetyl-β-D-glucopyranosyl)thio]pentyl]-1*H*-1,2,3- triazol-4-yl]methyl]-1*H*-benzo[*de*]isoquinoline-1,3(2*H*)-dione (**14e**): light yellow solid; (0.88 g, 80.0 %) yield; $[\alpha]_D^{25}$ -71.9 (c=0.5, DMSO); ^{1}H NMR (300 MHz, DMSO-d_6) δ 8.47 – 8.33 (m, 2H, ArH), 8.26 (d, J = 7.9 Hz, 1H, ArH), 8.07 – 7.90 (m, 2H, ArH, NH), 7.89 – 7.79 (m, 2H, ArH), 5.23 (s, 2H, $ArCH_2Ar$), 5.05 (t, J = 9.7 Hz, 1H, H-3), 4.82 (t, J = 9.7 Hz, 1H, H-4), 4.65 (d, J = 10.4 Hz, 1H, H-1), 4.26 (t, J = 7.1 Hz, 2H, CH_2), 4.11 (dd, J = 12.3, 5.1 Hz, 1H, H-6b), 3.98 (dd, J = 12.1,

2.1 Hz, 1H, H-6a), 3.90 – 3.73 (m, 2H, H-2, H-5), 2.69 – 2.49 (m, 2H, SCH_2), 1.96, 1.95 (2 s, 6H, 2 OAc), 1.90 (s, 3H, OAc), 1.82 – 1.68 (m, 5H, NAc, CH_2), 1.61 – 1.45 (m, 2H, CH_2), 1.34 – 1.17 (m, 2H, CH_2); ^{13}C NMR (75 MHz, DMSO-d_6) δ 170.06, 169.74, 169.37, 169.18, 162.68, 162.39, 137.73, 131.75, 131.01, 130.16, 128.58, 128.41, 128.31, 127.70, 123.38, 122.54, 121.23, 83.52, 74.74, 73.83, 68.74, 62.14, 52.30, 49.31, 35.44, 29.30, 29.14, 28.68, 25.12, 22.73, 20.55, 20.51, 20.44; HRMS (ESI) calcd for $C_{34}H_{39}ClN_5O_{10}S$ ($M+H^+$) 744.2106, found 744.2101.

6-Chloro-2-[[1-[6-[(2-acetamido-3,4,6-tri-O-acetyl-β-D-glucopyranosyl)thio]hexyl]-1*H*-1,2,3- triazol-4-yl]methyl]-1*H*-benzo[*de*]isoquinoline-1,3(2*H*)-dione (**14f**): light yellow solid; (0.92 g, 70.8 %) yield; $[\alpha]_D^{25}$ -67.2 (c=0.5, DMSO); ^{1}H NMR (300 MHz, DMSO-d_6) δ 8.61 – 8.53 (m, 2H, ArH), 8.41 (d, J = 7.9 Hz, 1H, ArH), 8.06 – 7.90 (m, 4H, ArH, NH), 5.27 (s, 2H, $ArCH_2Ar$), 5.04 (t, J = 9.8 Hz, 1H, H-3), 4.81 (t, J = 9.7 Hz, 1H, H-4), 4.64 (d, J = 10.4 Hz, 1H, H-1), 4.25 (t, J = 7.1 Hz, 2H, CH_2), 4.11 (dd, J = 12.2, 5.1 Hz, 1H, H-6b), 3.98 (dd, J = 12.4, 2.1 Hz, 1H, H-6a), 3.89 – 3.74 (m, 2H, H-2, H-5), 2.65 – 2.50 (m, 2H, SCH_2), 1.96 (s, 3H, OAc), 1.95 (s, 3H, OAc), 1.90 (s, 3H, OAc), 1.79 – 1.65 (m, 5H, NAc, CH_2), 1.55 – 1.39 (m, 2H, CH_2), 1.37 – 1.10 (m, 4H, 2 CH_2); ^{13}C NMR (75 MHz, DMSO-d_6) δ 170.07, 169.73, 169.38, 169.16, 162.88, 162.59, 142.85, 137.81, 131.91, 131.19, 130.36, 128.79, 128.66, 128.62, 127.88, 123.24, 122.83, 121.53, 83.55, 74.71, 73.83, 68.74, 62.15, 52.32, 49.37, 35.53, 29.64, 29.27, 29.16, 27.60, 25.50, 22.74, 20.59, 20.53, 20.45; HRMS (ESI) calcd for $C_{35}H_{41}ClN_5O_{10}S$ ($M+H^+$) 758.2263, found 758.2272.

6-Chloro-2-[[1-[5-[[2-[[(phenylmethoxy)carbonyl]amino]-3,4,6-tri-O-acetyl-β-D-glucopyrano syl]thio]pentyl]-1*H*-1,2,3-triazol-4-yl]methyl]-1*H*-benzo[*de*]isoquinoline-1,3(2*H*)-dione (**14g**): light yellow solid; (1.1 g, 88.0 %) yield; $[\alpha]_D^{25}$ -77.3 (c=0.5, DMSO); ^{1}H NMR (300 MHz, DMSO-d_6) δ 8.54 – 8.41 (m, 2H, ArH), 8.32 (d, J = 7.9 Hz, 1H, ArH), 8.03 (s, 1H, ArH), 7.95 – 7.84 (m, 2H, ArH), 7.45 (d, J = 9.6 Hz, 1H, NH), 7.36 – 7.18 (m, 5H, ArH), 5.25 (s, 2H, $ArCH_2Ar$), 5.11 – 4.93 (m, 3H, H-3, $PhCH_2$), 4.83 (t, J = 9.7 Hz, 1H, H-4), 4.63 (d, J = 10.3 Hz, 1H, H-1), 4.25 (t, J = 7.1 Hz, 2H, CH_2), 4.11 (dd, J = 12.4, 5.1 Hz, 1H, H-6b), 3.98 (d, J = 12.3 Hz, 1H, H-6a), 3.81 – 3.71 (m, 1H, H-5), 3.56 (q, J = 10.0 Hz, 1H, H-2), 2.67 – 2.50 (m, 2H, SCH_2), 1.96, 1.95 (2 s, 6H, 2 OAc), 1.83 (s, 3H, OAc), 1.78 – 1.67 (m, 2H, CH_2, CH_2), 1.61 – 1.43 (m, 2H, CH_2, CH_2), 1.33 – 1.19 (m, 2H, CH_2, CH_2); ^{13}C NMR (75 MHz, DMSO-d_6) δ 170.08, 169.63, 169.38, 162.76, 162.47, 155.86, 142.81, 137.77, 137.27, 131.81, 131.08, 130.24, 128.65, 128.50, 128.37, 127.79, 127.43, 123.34, 122.64, 121.34, 83.74, 74.80, 73.89, 68.71, 65.40, 62.11, 54.53, 49.29,

35.47, 29.30, 29.18, 28.70, 25.10, 20.56, 20.51, 20.38; HRMS (ESI) calcd for $C_{40}H_{43}ClN_5O_{11}S$ ($M+H^+$) 836.2368, found 836.2360.

6-Chloro-2-[[1-[6-[[2-[[(phenylmethoxy)carbonyl]amino]-3,4,6-tri-O-acetyl-β-D-glucopy ranosyl] thio] hexyl]-1*H*-1,2,3-triazol-4-yl]methyl]-1*H*-benzo[*de*]isoquinoline-1,3(2*H*)-dione (**14h**): light yellow solid; (1.1 g, 85.9 %) yield; $[\alpha]_D^{25}$ -84.5 (c=0.5, DMSO); ^{1}H NMR (300 MHz, DMSO-d_6) δ 8.52 (m, 2H, ArH), 8.37 (d, J = 7.9 Hz, 1H, ArH), 8.05 (s, 1H, ArH), 8.00 – 7.88 (m, 2H, ArH), 7.47 (d, J = 9.7 Hz, 1H, NH), 7.37 – 7.24 (m, 5H, ArH), 5.28 (s, 2H, $ArCH_2Ar$), 5.15 – 4.94 (m, 3H, $PhCH_2$, H-3), 4.85 (t, J = 9.7 Hz, 1H, H-4), 4.65 (d, J = 10.4 Hz, 1H, H-1), 4.27 (t, J = 7.1 Hz, 2H, CH_2), 4.14 (dd, J = 12.4, 5.1 Hz, 1H, H-6b), 4.00 (dd, J = 12.1, 1.8 Hz, 1H, H-6a), 3.84 – 3.71 (m, 1H, H-5), 3.58 (q, J = 10.0 Hz, 1H, H-2), 2.69 – 2.52 (m, 2H, SCH_2), 1.99 (s, 3H, OAc), 1.97 (s, 3H, OAc), 1.86 (s, 3H, OAc), 1.81 – 1.68 (m, 2H, CH_2), 1.59 – 1.42 (m, 2H, CH_2), 1.37 – 1.25 (m, 2H, CH_2), 1.24 – 1.11 (m, 2H, CH_2); ^{13}C NMR (75 MHz, DMSO-d_6) δ 170.09, 169.63, 169.38, 162.79, 162.51, 155.86, 142.82, 137.77, 137.28, 131.84, 131.11, 130.27, 128.69, 128.54, 128.47, 128.36, 127.79, 127.41, 123.30, 122.69, 121.39, 83.76, 74.77, 73.87, 68.71, 65.38, 62.12, 54.55, 49.37, 35.49, 29.65, 29.31, 29.13, 27.58, 25.52, 20.59, 20.52, 20.39; HRMS (ESI) calcd for $C_{41}H_{45}ClN_5O_{11}S$ ($M+H^+$) 850.2525, found 850.2537.

6-Methoxy-2-[[1-[5-[(2-acetamido-3,4,6-tri-O-acetyl-β-D-glucopyranosyl)thio]pentyl]-1*H*-1,2,3- triazol-4-yl]methyl]-1*H*-benzo[*de*]isoquinoline-1,3(2*H*)-dione (**14i**): light yellow solid; (0.81 g, 73.6 %) yield; $[\alpha]_D^{25}$ -86.0 (c=0.5, DMSO); ^{1}H NMR (300 MHz, DMSO-d_6) δ 8.51 – 8.34 (m, 3H, ArH), 8.02 (s, 1H, ArH), 7.97 (d, J = 9.4 Hz, 1H, NH), 7.81 – 7.71 (m, 1H, ArH), 7.25 (d, J = 8.5 Hz, 1H, ArH), 5.27 (s, 2H, $ArCH_2Ar$), 5.10 – 5.02 (t, J = 9.7 Hz, 1H, H-3), 4.84 (t, J = 9.7 Hz, 1H, H-4), 4.67 (d, J = 10.4 Hz, 1H, H-1), 4.28 (t, J = 7.1 Hz, 2H, CH_2), 4.16 (dd, J = 7.6, 4.5 Hz, 1H, H-6b), 4.11 (s, 3H, OCH_3), 4.03 – 3.95 (m, 1H, H-6a), 3.89 – 3.82 (m, 2H, H-2, H-5), 2.69 – 2.56 (m, 2H, SCH_2), 1.98 (s, 3H, OAc), 1.98 (s, 3H, OAc), 1.93 (s, 3H, OAc), 1.79 – 1.73 (m, 5H, NAc, CH_2), 1.57 – 1.49 (m, 2H, CH_2), 1.34 – 1.21 (m, 2H, CH_2); ^{13}C NMR (75 MHz, DMSO-d_6) δ 170.12, 170.08, 169.74, 169.38, 169.19, 163.40, 162.70, 160.53, 143.18, 133.51, 131.24, 128.66, 128.48, 126.42, 123.22, 122.83, 121.84, 114.16, 106.32, 83.51, 74.71, 73.82, 68.70, 62.12, 56.73, 52.28, 49.27, 35.20, 29.30, 29.14, 28.67, 25.12, 22.72, 20.55, 20.51, 20.44; HRMS (ESI) calcd for $C_{35}H_{42}N_5O_{11}S$ ($M+H^+$) 740.2602, found 740.2606.

6-Methoxy-2-[[1-[6-[(2-acetamido-3,4,6-tri-O-acetyl-β-D-glucopyranosyl)thio]hexyl]-1*H*-1,2,3- triazol-4-yl]methyl]-1*H*-benzo[*de*]isoquinoline-1,3(2*H*)-dione (**14j**): light yellow solid; (0.82 g,

72.6 %) yield; $[\alpha]_D^{25}$ -74.9 (c=0.5, DMSO); ^{1}H NMR (300 MHz, DMSO-d_6) δ 8.53 – 8.34 (m, 3H, ArH), 8.10 – 7.93 (m, 2H, ArH, NH), 7.76 (dd, *J* = 8.3, 7.5 Hz, 1H, ArH), 7.26 (d, *J* = 8.5 Hz, 1H, ArH), 5.27 (s, 2H, $ArCH_2Ar$), 5.08 (t, *J* = 9.7 Hz, 1H, H-3), 4.84 (t, *J* = 9.7 Hz, 1H, H-4), 4.67 (d, *J* = 10.4 Hz, 1H, H-1), 4.27 (t, *J* = 7.1 Hz, 2H, CH_2), 4.21 – 4.08 (m, 4H, H-6a, OCH_3), 4.00 (dd, *J* = 12.2, 2.0 Hz, 1H, H-6a), 3.92 – 3.78 (m, 2H, H-2, H-5), 2.66 – 2.52 (m, 2H, CH_2), 1.99 (s, 3H, OAc), 1.98 (s, 3H, OAc), 1.93 (s, 3H, OAc), 1.83 – 1.68 (m, 5H, NAc, CH_2), 1.59 – 1.41 (m, 2H, CH_2), 1.36 – 1.16 (m, 4H, 2 CH_2); ^{13}C NMR (75 MHz, DMSO-d_6) δ 170.09, 169.74, 169.39, 169.18, 163.41, 162.72, 160.54, 143.18, 133.51, 131.25, 128.68, 128.48, 126.43, 123.19, 122.84, 121.86, 114.18, 106.34, 83.55, 74.70, 73.83, 68.72, 62.14, 56.74, 52.31, 49.34, 35.21, 29.67, 29.28, 29.16, 27.60, 25.51, 22.73, 20.58, 20.52, 20.44; HRMS (ESI) calcd for $C_{36}H_{44}N_5O_{11}S$ ($M+H^+$) 754.2758, found 754.2753.

6-Methoxy-2-[[1-[5-[[2-[[(phenylmethoxy)carbonyl]amino]-3,4,6-tri-O-acetyl-β-D-glucopyranosyl]thio]pentyl]-1*H*-1,2,3-triazol-4-yl]methyl]-1*H*-benzo[*de*]isoquinoline-1,3(2*H*)-dione (**14k**): light yellow solid; (1.0 g, 80.1 %) yield; $[\alpha]_D^{25}$ -80.3 (c=0.5, DMSO); ^{1}H NMR (300 MHz, DMSO-d_6) δ 8.26 (m, 3H, ArH), 7.99 (s, 1H, ArH), 7.65 – 7.55 (m, 1H, ArH), 7.47 (d, *J* = 9.6 Hz, 1H, NH), 7.38 – 7.18 (m, 5H, ArH), 7.06 (d, *J* = 8.5 Hz, 1H, ArH), 5.22 (s, 2H, $ArCH_2Ar$), 5.14 – 4.92 (m, 3H, $PhCH_2$, H-3), 4.85 (t, *J* = 9.7 Hz, 1H, H-4), 4.65 (d, *J* = 10.4 Hz, 1H, H-1), 4.25 (t, *J* = 7.0 Hz, 2H, CH_2), 4.12 (dd, *J* = 12.3, 4.9 Hz, 1H, H-6b), 4.02 (s, 3H, OCH_3), 4.00 – 3.92 (m, 1H, H-6a), 3.82 – 3.70 (m, 1H, H-5), 3.59 (q, *J* = 10.0 Hz, 1H, H-2), 2.68 – 2.50 (m, 2H, SCH_2), 1.95 (s, 3H, OAc), 1.95 (s, 3H, OAc), 1.84 (s, 3H, OAc), 1.80 – 1.66 (m, 2H, CH_2), 1.58 – 1.41 (m, 2H, CH_2), 1.36 – 1.18 (m, 2H, CH_2); ^{13}C NMR (75 MHz, DMSO-d_6) δ 170.08, 169.65, 169.39, 163.28, 162.57, 160.35, 155.89, 143.19, 137.27, 133.29, 131.04, 128.44, 128.35, 128.28, 127.78, 127.43, 126.15, 123.30, 122.62, 121.62, 113.97, 106.06, 83.77, 74.82, 73.92, 68.73, 65.43, 62.11, 56.59, 54.56, 49.27, 35.12, 29.32, 29.20, 28.70, 25.11, 20.53, 20.48, 20.37; HRMS (ESI) calcd for $C_{41}H_{46}N_5O_{12}S$ ($M+H^+$) 832.2864, found 832.2867.

6-Methoxy-2-[[1-[6-[[2-[[(phenylmethoxy)carbonyl]amino]-3,4,6-tri-O-acetyl-β-D-glucopyranosyl]thio] hexyl]-1*H*-1,2,3-triazol-4-yl]methyl]-1*H*-benzo[*de*]isoquinoline-1,3(2*H*)-dione (**14l**): light yellow solid; (1.1 g, 86.6 %) yield; $[\alpha]_D^{25}$ -85.4 (c=0.5, DMSO); ^{1}H NMR (300 MHz, DMSO-d_6) δ 8.37 – 8.18 (m, 3H, ArH), 7.99 (s, 1H, ArH), 7.62 (dd, *J* = 8.3, 7.5 Hz, 1H, ArH), 7.47 (d, *J* = 9.7 Hz, 1H, NH), 7.37 – 7.19 (m, 5H, ArH), 7.10 (d, *J* = 8.5 Hz, 1H, ArH), 5.23 (s, 2H, $ArCH_2Ar$), 5.14 – 4.93 (m, 3H, H-3, $PhCH_2$), 4.85 (t, *J* = 9.7 Hz, 1H, H-4), 4.65 (d, *J* = 10.3 Hz, 1H, H-1), 4.25 (t,

J = 7.1 Hz, 2H, CH_2), 4.13 (dd, *J* = 12.4, 4.9 Hz, 1H, H-6b), 4.03 (s, 3H, OCH_3), 3.98 (m, 1H, H-6a), 3.81 – 3.72 (m, 1H, H-5), 3.58 (q, *J* = 10.0 Hz, 1H, H-2), 2.69 – 2.49 (m, 2H, SCH_2), 1.96 (2 s, 6H, 2 OAc), 1.84 (s, 3H, OAc), 1.79 – 1.64 (m, 2H, CH_2), 1.57 – 1.39 (m, 2H, CH_2), 1.35 – 1.14 (m, 4H, 2 CH_2); ^{13}C NMR (75 MHz, DMSO-d_6) δ 170.07, 169.64, 169.39, 163.30, 162.59, 160.38, 155.88, 143.18, 137.27, 133.32, 131.07, 128.49, 128.34, 127.77, 127.41, 126.19, 123.27, 122.66, 121.67, 114.02, 106.11, 83.79, 74.80, 73.91, 68.75, 65.40, 62.13, 56.61, 54.59, 49.36, 35.13, 29.68, 29.33, 29.14, 27.59, 25.54, 20.55, 20.49, 20.37; HRMS (ESI) calcd for $C_{42}H_{47}N_5NaO_{12}S$ ($M+Na^+$) 868.2840, found 868.2844.

6-(Dimethylamino)-2-[[1-[5-[(2-acetamido-3,4,6-tri-O-acetyl-β-D-glucopyranosyl)thio]pentyl]-1*H*-1,2,3-triazol-4-yl]methyl]-1*H*-benzo[*de*]isoquinoline-1,3(2*H*)-dione (**14m**): yellow syrup; (0.91 g, 80.5 %) yield; $[\alpha]_D^{25}$ -67.7 (c=0.5, DMSO); ^{1}H NMR (300 MHz, DMSO-d_6) δ 8.47 – 8.34 (m, 2H, ArH), 8.24 (d, *J* = 8.3 Hz, 1H, ArH), 8.00 – 7.92 (m, 2H, ArH, NH), 7.73 – 7.61 (m, 1H, ArH), 7.11 (d, *J* = 8.4 Hz, 1H, ArH), 5.23 (s, 2H, $ArCH_2Ar$), 5.06 (t, *J* = 9.7 Hz, 1H, H-3), 4.82 (t, *J* = 9.7 Hz, 1H, H-4), 4.65 (d, *J* = 10.4 Hz, 1H, H-1), 4.24 (t, *J* = 7.1 Hz, 2H, CH_2), 4.12 (dd, *J* = 12.3, 5.1 Hz, 1H, H-6b), 3.98 (dd, *J* = 9.7, 2.6 Hz, 1H, H-6a), 3.91 – 3.76 (m, 2H, H-2, H-5), 3.04 (s, 6H, 2 NCH_3), 2.67 – 2.49 (m, 2H, SCH_2), 1.96 (s, 3H, OAc), 1.95 (s, 3H, OAc), 1.90 (s, 3H, OAc), 1.80 – 1.65 (m, 5H, NAc, CH_2), 1.58 – 1.44 (m, 2H, CH_2), 1.32 – 1.19 (m, 2H, CH_2); ^{13}C NMR (75 MHz, DMSO-d_6) δ 170.07, 169.74, 169.38, 169.20, 163.45, 162.73, 156.73, 143.33, 132.48, 131.74, 130.75, 129.77, 124.97, 124.23, 123.13, 122.26, 113.16, 112.95, 83.52, 74.73, 73.83, 68.71, 62.12, 52.29, 49.25, 44.45, 35.13, 29.31, 29.15, 28.68, 25.12, 22.73, 20.55, 20.51, 20.44; HRMS (ESI) calcd for $C_{36}H_{45}N_6O_{10}S$ ($M+H^+$) 753.2918, found 753.2913.

6-(Dimethylamino)-2-[[1-[6-[(2-acetamido-3,4,6-tri-O-acetyl-β-D-glucopyranosyl)thio]hexyl]-1*H*-1,2,3-triazol-4-yl]methyl]-1*H*-benzo[*de*]isoquinoline-1,3(2*H*)-dione (**14n**): yellow syrup; (0.95 g, 82.6 %) yield; $[\alpha]_D^{25}$ -78.9 (c=0.5, DMSO); ^{1}H NMR (300 MHz, DMSO-d_6) δ 8.53 – 8.41 (m, 2H, ArH), 8.32 (d, *J* = 8.3 Hz, 1H, ArH), 8.03 – 7.94 (m, 2H, ArH, NH), 7.74 (dd, *J* = 8.4, 7.4 Hz, 1H, ArH), 7.18 (d, *J* = 8.4 Hz, 1H, ArH), 5.27 (s, 2H, $ArCH_2Ar$), 5.08 (t, *J* = 9.8 Hz, 1H, H-3), 4.85 (t, *J* = 9.7 Hz, 1H, H-4), 4.67 (d, *J* = 10.4 Hz, 1H, H-1), 4.26 (t, *J* = 7.1 Hz, 2H, CH_2), 4.15 (dd, *J* = 12.3, 5.3 Hz, 1H, H-6b), 4.04 (d, *J* = 12.1 Hz, 1H, H-6a), 3.92 – 3.81 (m, 2H, H-2, H-5), 3.09 (s, 6H, 2 NCH_3), 2.69 – 2.53 (m, 2H, SCH_2), 1.99 (s, 3H, OAc), 1.98 (s, 3H, OAc), 1.93 (s, 3H, OAc), 1.79 – 1.68 (m, 5H, NAc, CH_2), 1.57 – 1.42 (m, 2H, CH_2), 1.37 – 1.26 (m, 2H, CH_2), 1.24 – 1.17 (m, 2H, CH_2); ^{13}C NMR (75 MHz, DMSO-d_6) δ 170.08, 169.74, 169.39, 169.17, 163.50,

162.78, 156.80, 143.33, 132.53, 131.80, 130.81, 129.83, 125.05, 124.30, 123.08, 122.33, 113.22, 113.03, 83.55, 74.70, 73.83, 68.72, 62.14, 52.31, 49.32, 44.48, 35.15, 29.67, 29.29, 29.16, 27.60, 25.51, 22.74, 20.58, 20.52, 20.45; HRMS (ESI) calcd for $C_{37}H_{47}N_6O_{10}S$ ($M+H^+$) 767.3074, found 767.3071.

6-(Dimethylamino)-2-[[1-[5-[[2-[[(phenylmethoxy)carbonyl]amino]-3,4,6-tri-O-acetyl-β-D-glucopyranosyl]thio]pentyl]-1*H*-1,2,3-triazol-4-yl]methyl]-1*H*-benzo[*de*]isoquinoline-1,3(2*H*)-dione (**14o**): yellow syrup; (1.12 g, 88.1 %) yield; $[\alpha]_D^{25}$ -69.1 (c=0.5, DMSO); ^{1}H NMR (300 MHz, DMSO-d_6) δ 8.48 – 8.33 (m, 2H, ArH), 8.25 (d, *J* = 8.3 Hz, 1H, ArH), 7.96 (s, 1H, ArH), 7.66 (dd, *J* = 8.4, 7.4 Hz, 1H, ArH), 7.47 (d, *J* = 9.6 Hz, 1H, NH), 7.36 – 7.19 (m, 5H, ArH), 7.10 (d, *J* = 8.4 Hz, 1H, ArH), 5.24 (s, 2H, $ArCH_2Ar$), 5.15 – 4.93 (m, 3H, $PhCH_2$, H-3), 4.84 (t, *J* = 9.7 Hz, 1H, H-4), 4.64 (d, *J* = 10.3 Hz, 1H, H-1), 4.23 (t, *J* = 7.1 Hz, 2H, CH_2), 4.12 (dd, *J* = 12.4, 5.0 Hz, 1H, H-6b), 3.98 (d, *J* = 12.1 Hz, 1H, H-6a), 3.82 – 3.67 (m, 1H, H-5), 3.57 (q, *J* = 10.0 Hz, 1H, H-2), 3.04 (s, 6H, 2 NCH_3), 2.71 – 2.49 (m, 2H, SCH_2), 1.95, 1.94 (2 s, 6H, 2 OAc), 1.83 (s, 3H, OAc), 1.79 – 1.64 (m, 2H, CH_2), 1.61 – 1.44 (m, 2H, CH_2), 1.33 – 1.17 (m, 2H, CH_2); ^{13}C NMR (75 MHz, DMSO-d_6) δ 170.08, 169.64, 169.38, 163.47, 162.74, 156.73, 155.88, 143.35, 137.28, 132.49, 131.73, 130.75, 129.78, 128.37, 127.79, 127.43, 124.96, 124.25, 123.13, 122.27, 113.18, 112.95, 83.76, 74.81, 73.91, 68.73, 65.42, 62.11, 54.56, 49.25, 44.45, 35.13, 29.31, 29.20, 28.70, 25.11, 20.55, 20.50, 20.38; HRMS (ESI) calcd for $C_{42}H_{48}N_6NaO_{11}S$ ($M+Na^+$) 867.2999, found 867.2991.

6-(Dimethylamino)-2-[[1-[6-[[2-[[(phenylmethoxy)carbonyl]amino]-3,4,6-tri-O-acetyl-β-D-glucopyranosyl] thio] hexyl] -1*H*-1,2,3-triazol-4-yl] methyl] -1*H*- benzo[*de*]isoquinoline-1,3(2*H*)-dione (**14p**): yellow syrup; (1.14 g, 89.1 %) yield; $[\alpha]_D^{25}$ -62.8 (c=0.5, DMSO); ^{1}H NMR (300 MHz, DMSO-d_6) δ 8.58 – 8.41 (m, 2H, ArH), 8.32 (d, *J* = 8.3 Hz, 1H, ArH), 7.98 (s, 1H, ArH), 7.73 (dd, *J* = 8.4, 7.4 Hz, 1H, ArH), 7.48 (d, *J* = 9.6 Hz, 1H, NH), 7.39 – 7.23 (m, 5H, ArH), 7.18 (d, *J* = 8.4 Hz, 1H, ArH), 5.28 (s, 2H, $ArCH_2Ar$), 5.17 – 4.96 (m, 3H, H-3, PCH_2), 4.85 (t, *J* = 9.7 Hz, 1H, H-4), 4.66 (d, *J* = 10.4 Hz, 1H, H-1), 4.26 (t, *J* = 7.1 Hz, 2H, CH_2), 4.15 (dd, *J* = 12.3, 5.0 Hz, 1H, H-6b), 4.01 (dd, *J* = 11.5, 2.4 Hz, 1H, H-6a), 3.88 – 3.75 (m, 1H, H-5), 3.58 (q, *J* = 10.0 Hz, 1H, H-2), 3.09 (s, 6H, 2 NCH_3), 2.73 – 2.52 (m, 2H, SCH_2), 1.99 (s, 3H, OAc), 1.98 (s, 3H, OAc), 1.86 (s, 3H, OAc), 1.80 – 1.67 (m, 2H, CH_2), 1.57 – 1.43 (m, 2H, CH_2), 1.38 – 1.25 (m, 2H, CH_2), 1.24 – 1.15 (m, 2H, CH_2); ^{13}C NMR (75 MHz, DMSO-d_6) δ 170.09, 169.63, 169.39, 163.51, 162.79, 156.80, 155.87, 143.33, 137.28, 132.54, 131.80, 130.81, 129.83, 128.37, 127.79, 127.41, 125.04, 124.31, 123.10, 122.34, 113.24, 113.03, 83.77, 74.78, 73.89, 68.72, 65.38, 62.11, 54.57, 49.33,

44.48, 35.15, 29.67, 29.33, 29.14, 27.58, 25.53, 20.59, 20.51, 20.39; HRMS (ESI) calcd for $C_{43}H_{51}N_6O_{11}S$ ($M+H^+$) 859.3337, found 859.3338.

6-(Piperidin-1-yl)-2-[[1-[5-[(2-acetamido-3,4,6-tri-O-acetyl-β-D-glucopyranosyl)thio]pentyl]-1*H*-1,2,3-triazol-4-yl]methyl]-1*H*-benzo[*de*]isoquinoline-1,3(2*H*)-dione (**14q**): yellow syrup; (0.95 g, 79.8 %) yield; $[\alpha]_D^{25}$ -86.6 (c=0.5, DMSO); ^{1}H NMR (300 MHz, DMSO-d_6) δ 8.46 – 8.25 (m, 3H, ArH), 8.02 – 7.88 (m, 2H, ArH), 7.80 – 7.70 (m, 1H, ArH, NH), 7.24 (d, *J* = 8.2 Hz, 1H, ArH), 5.25 (s, 2H, $ArCH_2Ar$), 5.05 (t, *J* = 9.8 Hz, 1H, H-3), 4.82 (t, *J* = 9.7 Hz, 1H, H-4), 4.65 (d, *J* = 10.3 Hz, 1H, H-1), 4.25 (t, *J* = 7.1 Hz, 2H, CH_2), 4.12 (dd, *J* = 12.2, 5.0 Hz, 1H, H-6b), 3.97 (d, *J* = 11.7 Hz, 1H, H-6a), 3.89 – 3.76 (m, 2H, H-2, H-5), 3.21 – 3.07 (m, 4H, 2 CH_2), 2.68 – 2.50 (m, 2H, SCH_2), 1.96 (s, 3H, OAc), 1.95 (s, 3H, OAc), 1.90 (s, 3H, OAc), 1.86 – 1.76 (m, 6H, 3 CH_2), 1.73 (s, 3H, NAc), 1.69 – 1.60 (m, 2H, CH_2), 1.55 – 1.44 (m, 2H, CH_2), 1.37 – 1.19 (m, 2H, CH_2); ^{13}C NMR (75 MHz, DMSO-d_6) δ 170.07, 169.73, 169.37, 169.20, 163.43, 162.84, 156.97, 143.26, 132.52, 130.84, 129.37, 125.87, 125.55, 123.10, 122.52, 114.98, 114.94, 83.51, 74.73, 73.84, 68.74, 62.13, 54.07, 52.31, 49.26, 35.19, 29.29, 29.14, 28.68, 25.82, 25.12, 23.95, 22.72, 20.62, 20.55, 20.51, 20.43; HRMS (ESI) calcd for $C_{39}H_{49}N_6O_{10}S$ ($M+H^+$) 793.3231, found 793.3238.

6-(Piperidin-1-yl)-2-[[1-[6-[(2-acetamido-3,4,6-tri-O-acetyl-β-D-glucopyranosyl)thio]hexyl]-1*H*-1,2,3-triazol-4-yl]methyl]-1*H*-benzo[*de*]isoquinoline-1,3(2*H*)-dione (**14r**): yellow syrup; (0.95 g, 78.5 %) yield; $[\alpha]_D^{25}$ -77.1 (c=0.5, DMSO); ^{1}H NMR (300 MHz, DMSO-d_6) δ 8.50 – 8.28 (m, 3H, ArH), 8.03 – 7.91 (m, 2H, ArH, NH), 7.76 (dd, *J* = 8.4, 7.4 Hz, 1H, ArH), 7.26 (d, *J* = 8.2 Hz, 1H, ArH), 5.25 (s, 2H, $ArCH_2Ar$), 5.06 (t, *J* = 9.7 Hz, 1H, H-3), 4.82 (t, *J* = 9.7 Hz, 1H, H-4), 4.65 (d, *J* = 10.4 Hz, 1H, H-1), 4.24 (t, *J* = 7.1 Hz, 2H, CH_2), 4.13 (dd, *J* = 12.3, 5.1 Hz, 1H, H-6b), 3.97 (dd, *J* = 11.6, 2.5 Hz, 1H, H-6a), 3.90 – 3.77 (m, 2H, H-2, H-5), 3.24 – 3.05 (m, 4H, CH_2), 2.63 – 2.50 (m, 2H, SCH_2), 1.96 (2 s, 6H, 2 OAc), 1.90 (s, 3H, OAc), 1.86 – 1.76 (m, 4H, 2 CH_2), 1.76 – 1.67 (m, 5H, NAc, CH_2), 1.66 – 1.56 (m, 2H, CH_2), 1.54 – 1.40 (m, 2H, CH_2), 1.33 – 1.22 (m, 2H, CH_2), 1.22 – 1.13 (m, 2H, CH_2); ^{13}C NMR (75 MHz, DMSO-d_6) δ 170.08, 169.73, 169.38, 169.16, 163.44, 162.86, 156.98, 143.26, 132.53, 130.85, 129.39, 125.90, 125.57, 123.08, 122.54, 114.97, 83.55, 74.70, 73.83, 68.73, 62.14, 54.08, 52.31, 49.32, 35.20, 29.66, 29.28, 29.16, 27.60, 25.82, 25.51, 23.96, 22.73, 21.14, 20.57, 20.52, 20.44; HRMS (ESI) calcd for $C_{40}H_{51}N_6O_{10}S$ ($M+H^+$) 807.3387, found 807.3388.

6-(Piperidin-1-yl)-2-[[1-[5-[[2-[[(phenylmethoxy)carbonyl]amino]-3,4,6-tri-O-acetyl-β-D-glucopyranosyl]thio]pentyl]-1*H*-1,2,3-triazol-4-yl]methyl]-1*H*-benzo[*de*]isoquinoline-1,3(2*H*)-dione

(**14s**): yellow syrup; (1.13 g, 85.0 %) yield; $[\alpha]_D^{25}$ -74.2 (c=0.5, DMSO); ^{1}H NMR (300 MHz, DMSO-d_6) δ 8.37 (d, *J* = 7.2 Hz, 1H, ArH), 8.33 – 8.24 (m, 2H, ArH), 7.97 (s, 1H, ArH), 7.76 – 7.64 (m, 1H, ArH), 7.46 (d, *J* = 9.6 Hz, 1H, NH), 7.36 – 7.22 (m, 5H, ArH), 7.18 (d, *J* = 8.2 Hz, 1H, ArH), 5.24 (s, 2H, $ArCH_2Ar$), 5.03 (t, *J* = 12.1 Hz, 3H, $PhCH_2$, H-3), 4.84 (t, *J* = 9.7 Hz, 1H, H-4), 4.64 (d, *J* = 10.3 Hz, 1H, H-1), 4.23 (t, *J* = 7.1 Hz, 2H, CH_2), 4.12 (dd, *J* = 12.4, 5.0 Hz, 1H, H-6b), 3.98 (d, *J* = 10.5 Hz, 1H, H-6a), 3.82 – 3.70 (m, 1H, H-5), 3.57 (q, *J* = 10.0 Hz, 1H, H-2), 3.21 – 3.02 (m, 4H, 2 CH_2), 2.71 – 2.49 (m, 2H, SCH_2), 1.95 (s, 3H, OAc), 1.95 (s, 3H, OAc), 1.83 (s, 3H, OAc), 1.81 – 1.67 (m, 6H, 3 CH_2), 1.66 – 1.56 (m, 2H, CH_2), 1.55 – 1.45 (m, 2H, CH_2), 1.33 – 1.68 (m, 2H, CH_2); ^{13}C NMR (75 MHz, DMSO-d_6) δ 170.08, 169.64, 169.38, 163.39, 162.79, 156.91, 155.87, 143.26, 137.28, 132.47, 130.77, 129.30, 128.36, 127.79, 127.43, 125.80, 125.49, 123.14, 122.45, 114.89, 83.75, 74.80, 73.90, 68.71, 65.41, 62.10, 54.54, 54.04, 49.25, 35.17, 29.31, 29.18, 28.70, 25.81, 25.10, 23.95, 20.55, 20.50, 20.37; HRMS (ESI) calcd for $C_{45}H_{53}N_6O_{11}S$ ($M+H^+$) 885.3493, found 885.3497.

6-(Piperidin-1-yl)-2-[[1-[6-[[2-[[(phenylmethoxy)carbonyl]amino]-3,4,6-tri-O-acetyl-β-D-glu copyranosyl] thio] hexyl] -1*H*-1,2,3-triazol-4-yl] methyl] -1*H*- benzo[*de*]isoquinoline-1,3(2*H*)-dione (**14t**): yellow syrup; (1.14 g, 84.4 %) yield; $[\alpha]_D^{25}$ -73.5 (c=0.5, DMSO); ^{1}H NMR (300 MHz, DMSO-d_6) δ 8.37 (d, *J* = 7.2 Hz, 1H, ArH), 8.33 – 8.24 (m, 2H, ArH), 7.97 (s, 1H, ArH), 7.77 – 7.64 (m, 1H, ArH), 7.46 (d, *J* = 9.6 Hz, 1H, NH), 7.36 – 7.22 (m, 5H, ArH), 7.18 (d, *J* = 8.2 Hz, 1H, ArH), 5.24 (s, 2H, $ArCH_2Ar$), 5.16 – 4.92 (m, 3H, H-3, $PhCH_2$), 4.84 (t, *J* = 9.7 Hz, 1H, H-4), 4.64 (d, *J* = 10.3 Hz, 1H, H-1), 4.22 (t, *J* = 7.1 Hz, 2H, CH_2), 4.13 (dd, *J* = 12.4, 5.0 Hz, 1H, H-6b), 4.00 (d, *J* = 10.5 Hz, 1H, H-6a), 3.83 – 3.70 (m, 1H, H-5), 3.57 (q, *J* = 10.0 Hz, 1H, H-2), 3.18 – 3.04 (m, 4H, 2 CH_2), 2.68 – 2.48 (m, 2H, SCH_2), 1.96 (s, 6H, 2 OAc), 1.83 (s, 3H, OAc), 1.81 – 1.66 (m, 6H, 3 CH_2), 1.65 – 1.53 (m, 2H, CH_2), 1.52 – 1.39 (m, 2H, CH_2), 1.35 – 1.22 (m, 2H, CH_2), 1.22 – 1.13 (m, 2H, CH_2); ^{13}C NMR (75 MHz, DMSO-d_6) δ 170.40, 170.07, 169.63, 169.38, 163.40, 162.80, 156.91, 155.87, 143.26, 137.28, 132.47, 130.77, 129.32, 128.35, 127.78, 127.41, 125.80, 125.50, 123.12, 122.47, 114.91, 83.78, 74.80, 73.90, 68.74, 65.39, 62.13, 54.58, 54.05, 49.34, 35.17, 29.67, 29.33, 29.14, 27.59, 25.81, 25.53, 23.95, 20.57, 20.50, 20.38; HRMS (ESI) calcd for $C_{46}H_{55}N_6O_{11}S$ ($M+H^+$) 899.3650, found 899.3648.

A solution of **14a-14t** (1 mmol) in anhydrous MeOH (15 mL) was mixed with saturated MeOH-NH_3 solution (10 mL). The mixture was stirred for 50 h at room temperature, until TLC

(EtOAc/MeOH/H_2O, 8:1:1 v/v/v) was performed to identify the completion of the reaction. The solution was concentrated *in vacuo* and recrystallized from MeOH/ether to yield **15a-15t**.

6-Bromo-2-[[1-[5-[(2-acetamido-β-D-glucopyranosyl)thio]pentyl]-1*H*-1,2,3-triazol-4-yl]methyl]-1*H*-benzo[*de*]isoquinoline-1,3(2*H*)-dione (**15a**): yellow solid; (0.55 g, 83.3 %) yield; $[\alpha]_D^{25}$ -33.6 (c=0.2, DMSO); ^{1}H NMR (300 MHz, DMSO-d_6) δ 8.50 – 8.32 (m, 2H, ArH), 8.24 – 8.13 (m, 1H, ArH), 8.11 – 7.97 (m, 2H, ArH), 7.88 (dd, *J* = 8.4, 7.4 Hz, 1H, ArH), 7.69 (d, *J* = 9.3 Hz, 1H, NH), 5.24 (s, 2H, $ArCH_2Ar$), 4.65 (br s, 3H, 3 OH), 4.33 – 4.18 (m, 3H, H-3, H-4, H-1), 3.65 (d, *J* = 11.6 Hz, 1H, H-6b), 3.56 – 3.36 (m, 2H, H-2, H-6a), 3.30 – 3.20 (m, 1H, H-5), 3.11 – 3.00 (m, 2H, CH_2), 2.62 – 2.50 (m, 2H, SCH_2), 1.85 – 1.66 (m, 5H, NAc, CH_2), 1.56 – 1.41 (m, 2H, CH_2), 1.31 – 1.17 (m, 2H, CH_2); ^{13}C NMR (75 MHz, DMSO-d_6) δ 169.05, 162.66, 162.61, 142.77, 132.81, 131.81, 131.42, 131.17, 129.83, 129.42, 128.84, 128.32, 123.33, 122.64, 121.85, 84.26, 81.29, 75.68, 70.67, 61.35, 54.64, 49.31, 35.49, 29.36, 29.01, 28.53, 25.28, 23.16; HRMS (ESI) calcd for $C_{28}H_{33}BrN_5O_7S$ ($M+H^+$) 662.1284, found 662.1297.

6-Bromo-2-[[1-[6-[(2-acetamido-β-D-glucopyranosyl)thio]hexyl]-1*H*-1,2,3-triazol-4-yl]methyl]-1*H*-benzo[*de*]isoquinoline-1,3(2*H*)-dione (**15b**): yellow solid; (0.58 g, 85.3 %) yield; $[\alpha]_D^{25}$ -37.2 (c=0.2, DMSO); ^{1}H NMR (300 MHz, DMSO-d_6) δ 8.39 (dd, *J* = 7.3, 1.0 Hz, 1H, ArH), 8.32 (dd, *J* = 8.5, 1.0 Hz, 1H, ArH), 8.15 (d, *J* = 7.9 Hz, 1H, ArH), 8.05 – 7.96 (m, 2H, ArH), 7.82 (dd, *J* = 8.5, 7.4 Hz, 1H, ArH), 7.66 (d, *J* = 9.3 Hz, 1H, NH), 5.20 (s, 2H, $ArCH_2Ar$), 4.42 (br s, 3H, 3 OH), 4.28 – 4.16 (m, 3H, H-3, H-4, H-1), 3.62 (d, *J* = 11.5 Hz, 1H, H-6b), 3.52 – 3.33 (m, 2H, H-2, H-6a), 3.27 – 3.17 (m, 1H, H-5), 3.06 – 2.98 (m, 2H, CH_2), 2.57 – 2.46 (m, 2H, SCH_2), 1.78 – 1.61 (m, 5H, NAc, CH_2), 1.50 – 1.32 (m, 2H, CH_2), 1.29 – 1.05 (m, 4H, 2 CH_2); ^{13}C NMR (75 MHz, DMSO-d_6) δ 169.07, 162.63, 162.57, 142.78, 132.78, 131.78, 131.39, 131.14, 129.79, 129.42, 128.80, 128.26, 123.32, 122.59, 121.80, 84.23, 81.28, 75.67, 70.68, 61.36, 54.67, 49.39, 35.48, 29.66, 29.06, 28.97, 27.73, 25.55, 23.16; HRMS (ESI) calcd for $C_{29}H_{35}BrN_5O_7S$ ($M+H^+$) 676.1441, found 676.1435.

6-Bromo-2-[[1-[5-[[2-[[(phenylmethoxy)carbonyl]amino]-β-D-glucopyranosyl]thio]pentyl]-1*H*-1,2,3-triazol-4-yl]methyl]-1*H*-benzo[*de*]isoquinoline-1,3(2*H*)-dione (**15c**): yellow solid; (0.64 g, 848 %) yield; $[\alpha]_D^{25}$ -29.1 (c=0.2, DMSO); ^{1}H NMR (300 MHz, DMSO-d_6) δ 8.48 – 8.40 (m, 1H, ArH), 8.34 (dd, *J* = 8.5, 0.8 Hz, 1H, ArH), 8.19 (d, *J* = 7.9 Hz, 1H, ArH), 8.10 – 8.01 (m, 2H, ArH), 7.85 (dd, *J* = 8.4, 7.4 Hz, 1H, ArH), 7.41 – 7.26 (m, 5H, ArH), 7.23 (d, *J* = 9.1 Hz, 1H, NH), 5.28 (s, 2H, $ArCH_2Ar$), 5.12 – 4.98 (m, 2H, H-3, H-4), 4.88 (br s, 3H, 3 OH), 4.40 – 4.21 (m, 3H, H-1,

$PhCH_2$), 3.70 (d, *J* = 11.0 Hz, 1H, H-6b), 3.51 – 3.40 (m, 1H, H-6a), 3.37 – 3.23 (m, 2H, H-2, H-5), 3.17 – 3.02 (m, 2H, CH_2), 2.66 – 2.58 (m, 2H, SCH_2), 1.80 – 1.71 (m, 2H, CH_2), 1.61 – 1.46 (m, 2H, CH_2), 1.38 – 1.17 (m, 2H, CH_2); ^{13}C NMR (75 MHz, DMSO-d_6) δ 169.70, 162.57, 162.52, 156.14, 142.76, 137.39, 132.72, 131.73, 131.32, 131.08, 129.70, 129.41, 128.72, 128.31, 128.16, 127.70, 127.60, 123.39, 122.49, 121.70, 84.51, 81.32, 75.52, 70.71, 65.18, 61.32, 56.74, 49.30, 35.45, 29.37, 29.02, 28.55, 25.25; HRMS (ESI) calcd for $C_{34}H_{37}BrN_5O_8S$ ($M+H^+$) 754.1546, found 754.1539.

6-Bromo-2-[[1-[6-[[2-[[(phenylmethoxy) carbonyl] amino] -β-D-glucopyranosyl] thio] hexyl]-1*H*-1,2,3-triazol-4-yl]methyl]-1*H*-benzo[*de*]isoquinoline-1,3(2*H*)-dione (**15d**): yellow solid; (0.66 g, 85.8 %) yield; $[\alpha]_D^{25}$ -33.0 (c=0.2, DMSO); ^{1}H NMR (300 MHz, DMSO-d_6) δ 8.55 – 8.40 (m, 2H, ArH), 8.24 (d, *J* = 7.9 Hz, 1H, ArH), 8.18 – 8.03 (m, 2H, ArH), 7.98 – 7.86 (m, 1H, ArH), 7.50 – 7.15 (m, 6H, ArH, NH), 5.28 (s, 2H, $ArCH_2Ar$), 5.11 – 4.93 (m, 2H, H-3, H-4), 4.40 – 4.19 (m, 3H, H-1, $PhCH_2$), 3.69 (d, *J* = 10.9 Hz, 1H, H-6b), 3.53 – 3.39 (m, 1H, H-6a), 3.36 – 3.23 (m, 2H, H-2, H-5), 3.17 – 3.02 (m, 2H, CH_2), 2.64 – 2.56 (m, 2H, SCH_2), 1.80 – 1.68 (m, 2H, CH_2), 1.55 – 1.39 (m, 2H, CH_2), 1.39 – 1.13 (m, 4H, $2CH_2$); ^{13}C NMR (75 MHz, DMSO-d_6) δ 162.67, 162.62, 156.12, 142.79, 137.41, 132.82, 131.81, 131.42, 131.17, 129.84, 129.43, 128.84, 128.30, 127.69, 127.58, 123.32, 122.64, 121.86, 84.44, 81.32, 75.50, 70.72, 65.14, 61.32, 56.77, 49.39, 35.49, 29.66, 29.06, 28.95, 27.71, 25.57; HRMS (ESI) calcd for $C_{35}H_{38}BrN_5NaO_8S$ ($M+Na^+$) 790.1522, found 790.1531.

6-Chloro-2-[[1-[5-[(2-acetamido-β-D-glucopyranosyl)thio]pentyl]-1*H*-1,2,3-triazol-4-yl]methyl]-1*H*-benzo[*de*]isoquinoline-1,3(2*H*)-dione (**15e**): light yellow solid; (0.52 g, 84.1 %) yield; $[\alpha]_D^{25}$ -44.3 (c=0.2, DMSO); ^{1}H NMR (300 MHz, DMSO-d_6) δ 8.49 – 8.39 (m, 2H, ArH), 8.28 (d, *J* = 7.9 Hz, 1H, ArH), 8.03 (s, 1H, ArH), 7.91 – 7.83 (m, 2H, ArH), 7.70 (d, *J* = 9.3 Hz, 1H, NH), 5.24 (s, 2H, $ArCH_2Ar$), 4.47 (br s, 3H, 3 OH), 4.33 – 4.20 (m, 3H, H-3, H-4, H-1), 3.65 (d, *J* = 11.5 Hz, 1H, H-6b), 3.49 (dd, *J* = 19.6, 9.8 Hz, 1H, H-2), 3.41 (dd, *J* = 11.2, 4.3 Hz, 1H, H-6a), 3.30 – 3.20 (m, 1H, H-5), 3.10 – 3.03 (m, 2H, CH_2), 2.58 – 2.51 (m, 2H, SCH_2), 1.77 (s, 3H, NAc), 1.75 – 1.68 (m, 2H, CH_2), 1.57 – 1.42 (m, 2H, CH_2), 1.33 – 1.17 (m, 2H, CH_2); ^{13}C NMR (75 MHz, DMSO-d_6) δ 169.07, 162.72, 162.44, 142.77, 137.75, 131.79, 131.06, 130.20, 128.62, 128.44, 128.36, 127.74, 123.34, 122.57, 121.27, 84.28, 81.30, 75.66, 70.67, 61.35, 54.63, 49.31, 35.46, 29.36, 29.02, 28.53, 25.28, 23.15; HRMS (ESI) calcd for $C_{28}H_{33}ClN_5O_7S$ ($M+H^+$) 618.1789, found 618.1799.

6-Chloro-2-[[1-[6-[(2-acetamido-β-D-glucopyranosyl)thio]hexyl]-1*H*-1,2,3-triazol-4-yl]methyl]-1*H*-benzo[*de*]isoquinoline-1,3(2*H*)-dione (**15f**): light yellow solid; (0.52 g, 82.3 %) yield; $[\alpha]_D^{25}$ -35.7 (c=0.2, DMSO); ^{1}H NMR (300 MHz, DMSO-d_6) δ 8.57 – 8.44 (m, 2H, ArH), 8.34 (d, *J* = 7.9 Hz, 1H, ArH), 8.03 (s, 1H, ArH), 7.98 – 7.87 (m, 2H, ArH), 7.70 (d, *J* = 9.3 Hz, 1H, NH), 5.25 (s, 2H, $ArCH_2Ar$), 5.01 (br s, 2H, 2 OH), 4.50 (br s, 1H, OH), 4.34 – 4.18 (m, 3H, H-3, H-4, H-1), 3.65 (d, *J* = 11.6 Hz, 1H, H-6b), 3.56 – 3.45 (m, 1H, H-2), 3.37 – 3.33 (m, 1H, H-6a), 3.29 – 3.20 (m, 1H, H-5), 3.11 – 3.01 (m, 2H, CH_2), 2.62 – 2.51 (m, 2H, SCH_2), 1.80 – 1.67 (m, 5H, NAc, CH_2), 1.55 – 1.36 (m, 2H, CH_2), 1.34 – 1.24 (m, 2H, CH_2), 1.23 – 1.10 (m, 2H, CH_2); ^{13}C NMR (75 MHz, DMSO-d_6) δ 169.03, 162.79, 162.51, 142.81, 137.77, 131.85, 131.12, 130.28, 128.71, 128.53, 128.47, 127.81, 123.29, 122.67, 121.37, 84.24, 81.28, 75.64, 70.66, 61.32, 54.63, 49.37, 35.50, 29.65, 29.06, 28.97, 27.73, 25.54, 23.17; HRMS (ESI) calcd for $C_{29}H_{35}ClN_5O_7S$ ($M+H^+$) 632.1946, found 632.1936.

6-Chloro-2-[[1-[5-[[2-[[(phenylmethoxy)carbonyl]amino]-β-D-glucopyranosyl]thio]pentyl]-1*H*-1,2,3-triazol-4-yl]methyl]-1*H*-benzo[*de*]isoquinoline-1,3(2*H*)-dione (**15g**): light yellow solid; (0.63 g, 88.6 %) yield; $[\alpha]_D^{25}$ -22.8 (c=0.2, DMSO); ^{1}H NMR (300 MHz, DMSO-d_6) δ 8.55 – 8.43 (m, 2H, ArH), 8.33 (d, *J* = 7.9 Hz, 1H, ArH), 8.02 (s, 1H, ArH), 7.97 – 7.86 (m, 2H, ArH), 7.42 – 7.22 (m, 5H, ArH), 7.17 (d, *J* = 8.9 Hz, 1H, NH), 5.26 (s, 2H, $ArCH_2Ar$), 5.09 – 4.93 (m, 2H, H3, H-4), 4.63 (br s, 3H, 3 OH), 4.33 – 4.15 (m, 3H, H-1, $PhCH_2$), 3.65 (d, *J* = 11.1 Hz, 1H, H-6b), 3.47 – 3.34 (m, 1H, H-6a), 3.30 – 3.19 (m, 2H, H-2, H-5), 3.13 – 2.99 (m, 2H, CH_2), 2.62 – 2.53 (m, 2H, SCH_2), 1.76 – 1.66 (m, 2H, CH_2), 1.60 – 1.40 (m, 2H, CH_2), 1.34 – 1.18 (m, 2H, CH_2); ^{13}C NMR (75 MHz, DMSO-d_6) δ 162.79, 162.51, 156.13, 142.80, 137.78, 137.41, 131.83, 131.11, 130.26, 128.67, 128.53, 128.46, 128.32, 127.79, 127.71, 127.61, 123.31, 122.67, 121.37, 84.51, 81.33, 75.51, 70.73, 65.16, 61.32, 56.74, 49.29, 35.49, 29.36, 28.56, 25.25, 22.57; HRMS (ESI) calcd for $C_{34}H_{37}ClN_5O_8S$ ($M+H^+$) 710.2051, found 710.2056.

6-Chloro-2-[[1-[6-[[2-[[(phenylmethoxy) carbonyl] amino] -β-D-glucopyranosyl] thio] hexyl]-1*H*-1,2,3-triazol-4-yl]methyl]-1*H*-benzo[*de*]isoquinoline-1,3(2*H*)-dione (**15h**): light yellow solid; (0.62 g, 85.6 %) yield; $[\alpha]_D^{25}$ -30.7 (c=0.2, DMSO); ^{1}H NMR (300 MHz, DMSO-d_6) δ 8.50 (dd, *J* = 7.9, 3.8 Hz, 2H, ArH), 8.35 (d, *J* = 7.9 Hz, 1H, ArH), 8.05 (s, 1H, ArH), 7.99 – 7.86 (m, 2H, ArH), 7.43 – 7.24 (m, 5H, ArH), 7.20 (d, *J* = 8.3 Hz, 1H, NH), 5.28 (s, 2H, $ArCH_2Ar$), 5.16 – 4.91 (m, 4H, H-3, H-4, $PhCH_2$), 4.51 (t, *J* = 5.5 Hz, 1H, OH), 4.41 – 4.20 (m, 3H, 2 OH, H-1), 3.69 (dd, *J* = 11.1, 5.5 Hz, 1H, H-6b), 3.53 – 3.38 (m, 1H, H-6a), 3.33 – 3.20 (m, 2H, H-2, H-5), 3.17 –

2.93 (m, 2H, CH_2), 2.74 – 2.54 (m, 2H, SCH_2), 1.86 – 1.65 (m, 2H, CH_2), 1.57 – 1.38 (m, 2H, CH_2), 1.37 – 1.09 (m, 4H, 2 CH_2); ^{13}C NMR (75 MHz, DMSO-d_6) δ 162.77, 162.48, 156.12, 142.80, 137.76, 137.42, 131.82, 131.09, 130.24, 128.66, 128.49, 128.42, 128.30, 127.77, 127.70, 127.58, 123.32, 122.63, 121.33, 84.44, 81.33, 75.51, 70.72, 65.13, 61.33, 56.77, 49.38, 35.48, 29.66, 29.05, 28.95, 27.72, 25.57; HRMS (ESI) calcd for $C_{35}H_{39}ClN_5O_8S$ ($M+H^+$) 724.2208, found 724.2201.

6-Methoxy-2-[[1-[5-[(2-acetamido-β-D-glucopyranosyl)thio]pentyl]-1*H*-1,2,3-triazol-4-yl] methyl]-1*H*-benzo[*de*]isoquinoline-1,3(2*H*)-dione (**15i**): light yellow solid; (0.55 g, 89.6 %) yield; $[\alpha]_D^{25}$ -48.9 (c=0.2, DMSO); ^{1}H NMR (300 MHz, DMSO-d_6) δ 8.46 – 8.30 (m, 3H, ArH), 8.03 (s, 1H, ArH), 7.77 – 7.67 (m, 2H, ArH, NH), 7.20 (d, *J* = 8.5 Hz, 1H, ArH), 5.26 (s, 2H, $ArCH_2Ar$), 4.35 – 4.26 (m, 3H, H-3, H-4, H-1), 4.09 (s, 3H, OCH_3), 3.69 (d, *J* = 11.6 Hz, 1H, H-6b), 3.60 – 3.40 (m, 2H, H-2, H-6a), 3.34 – 3.23 (m, 1H, H-5), 3.15 – 3.05 (m, 2H, CH_2), 2.69 – 2.55 (m, 2H, SCH_2), 1.86 – 1.69 (m, 5H, NAc, CH_2), 1.61 – 1.45 (m, 2H, CH_2), 1.35 – 1.17 (m, 2H, CH_2); ^{13}C NMR (75 MHz, DMSO-d_6) δ 169.09, 163.36, 162.66, 160.46, 143.15, 133.45, 131.18, 128.57, 128.41, 126.34, 123.25, 122.74, 121.73, 114.06, 106.26, 84.26, 81.28, 75.68, 70.65, 61.34, 56.70, 54.63, 49.28, 35.18, 29.37, 29.02, 28.52, 25.28, 23.16; HRMS (ESI) calcd for $C_{29}H_{36}N_5O_8S$ ($M+H^+$) 614.2285, found 614.2282.

6-Methoxy-2-[[1-[6-[(2-acetamido-β-D-glucopyranosyl)thio]hexyl]-1*H*-1,2,3-triazol-4-yl] methyl]-1*H*-benzo[*de*]isoquinoline-1,3(2*H*)-dione (**15j**): light yellow solid; (0.52 g, 82.8 %) yield; $[\alpha]_D^{25}$ -43.1 (c=0.2, DMSO); ^{1}H NMR (300 MHz, DMSO-d_6) δ 8.39 (dd, *J* = 17.7, 8.1 Hz, 3H, ArH), 8.03 (s, 1H, ArH), 7.87 – 7.65 (m, 2H, ArH, NH), 7.22 (d, *J* = 8.4 Hz, 1H, ArH), 5.26 (s, 2H, $ArCH_2Ar$), 4.38 (br s, 3H, 3 OH), 4.34 – 4.24 (m, 3H, H-3, H-4, H-1), 4.10 (s, 3H, OCH_3), 3.69 (d, *J* = 11.6 Hz, 1H, H-6b), 3.60 – 3.39 (m, 2H, H-2, H-6a), 3.36 – 3.21 (m, 1H, H-5), 3.15 – 3.04 (m, 2H, CH_2), 2.64 – 2.55 (m, 2H, SCH_2), 1.83 – 1.70 (m, 5H, NAc, CH_2), 1.57 – 1.39 (m, 2H, CH_2), 1.35 – 1.11 (m, 4H, 2 CH_2); ^{13}C NMR (75 MHz, DMSO-d_6) δ 169.06, 163.38, 162.68, 160.49, 143.17, 133.47, 131.20, 128.61, 128.44, 126.38, 123.21, 122.77, 121.78, 114.10, 106.29, 84.24, 81.30, 75.67, 70.67, 61.35, 56.72, 54.66, 49.35, 35.19, 29.67, 29.06, 28.97, 27.74, 25.56, 23.16; HRMS (ESI) calcd for $C_{30}H_{38}N_5O_8S$ ($M+H^+$) 628.2441, found 628.2438.

6-Methoxy-2-[[1-[5-[[2-[[(phenylmethoxy)carbonyl]amino]-β-D-glucopyranosyl]thio]pent yl]-1*H*-1,2,3-triazol-4-yl]methyl]-1*H*-benzo[*de*]isoquinoline-1,3(2*H*)-dione (**15k**): light yellow solid; (0.61 g, 86.4 %) yield; $[\alpha]_D^{25}$ -39.2 (c=0.2, DMSO); ^{1}H NMR (300 MHz, DMSO-d_6) δ 8.54 – 8.33 (m, 3H, ArH), 8.01 (s, 1H, ArH), 7.76 (t, *J* = 7.8 Hz, 1H, ArH), 7.44 – 7.26 (m, 6H, ArH), 7.20 (d,

J = 8.7 Hz, 1H, NH), 5.27 (s, 2H, $ArCH_2Ar$), 5.16 – 4.91 (m, 2H, H-3, H-4), 4.41 – 4.20 (m, 6H, 3 OH, H-1, $PhCH_2$), 4.11 (s, 3H, OCH_3), 3.68 (d, *J* = 11.3 Hz, 1H, H-6b), 3.44 (d, *J* = 11.5 Hz, 1H, H-6a), 3.33 – 3.22 (m, 2H, H-2, H-5), 3.14 – 2.99 (m, 2H, CH_2), 2.68 – 2.54 (m, 2H, SCH_2), 1.81 – 1.68 (m, 2H, CH_2), 1.61 – 1.44 (m, 2H, CH_2), 1.35 – 1.18 (m, 2H, CH_2); ^{13}C NMR (75 MHz, DMSO-d_6) δ 163.42, 162.73, 160.54, 156.13, 143.17, 137.42, 133.53, 131.26, 128.68, 128.49, 128.33, 127.72, 127.63, 126.43, 123.21, 122.84, 121.85, 114.17, 106.35, 84.51, 81.34, 75.51, 70.71, 65.17, 61.31, 56.74, 49.26, 35.21, 29.37, 29.01, 28.55, 25.26; HRMS (ESI) calcd for $C_{35}H_{40}N_5O_9S$ ($M+H^+$) 706.2547, found 706.2549.

6-Methoxy-2-[[1-[6-[[2-[[(phenylmethoxy)carbonyl]amino]-β-D-glucopyranosyl]thio]hexyl] -1*H*-1,2,3-triazol-4-yl]methyl]-1*H*-benzo[*de*]isoquinoline-1,3(2*H*)-dione (**15l**): light yellow solid; (0.60 g, 83.3 %) yield; $[\alpha]_D^{25}$ -38.4 (c=0.2, DMSO); ^1H NMR (300 MHz, DMSO-d_6) δ 8.57 – 8.38 (m, 3H, ArH), 8.01 (s, 1H, ArH), 7.79 (dd, *J* = 8.3, 7.4 Hz, 1H, ArH), 7.37 – 7.25 (m, 6H, ArH), 7.19 (d, *J* = 9.0 Hz, 1H, NH), 5.27 (s, 2H, $ArCH_2Ar$), 5.09 – 4.94 (m, 2H, H-3, H-4), 4.37 – 4.20 (m, 3H, H-1, $PhCH_2$), 4.12 (s, 3H, OCH_3), 3.67 (d, *J* = 11.1 Hz, 1H, H-6b), 3.43 (d, *J* = 11.6, 1H, H-6a), 3.32 – 3.21 (m, 2H, H-2, H-5), 3.14 – 2.99 (m, 2H, CH_2), 2.63 – 2.53 (m, 2H, SCH_2), 1.79 – 1.66 (m, 2H, CH_2), 1.55 – 1.38 (m, 2H, CH_2), 1.37 – 1.12 (m, 4H, 2 CH_2); ^{13}C NMR (75 MHz, DMSO-d_6) δ 163.45, 162.77, 160.58, 156.11, 143.17, 137.43, 133.58, 131.31, 128.74, 128.54, 128.32, 127.71, 127.59, 126.50, 123.18, 122.90, 121.92, 114.24, 106.41, 84.44, 81.33, 75.51, 70.71, 65.13, 61.31, 56.78, 49.35, 35.23, 29.67, 29.06, 28.95, 27.72, 25.58; HRMS (ESI) calcd for $C_{36}H_{42}N_5O_9S$ ($M+H^+$) 720.2703, found 720.2709.

6-(Dimethylamino)-2-[[1-[5-[(2-acetamido-β-D-glucopyranosyl)thio]pentyl]-1*H*-1,2,3-triazol-4-yl]methyl]-1*H*-benzo[*de*]isoquinoline-1,3(2*H*)-dione (**15m**): yellow solid; (0.51 g, 81.4 %) yield; $[\alpha]_D^{25}$ -47.2 (c=0.2, DMSO); ^1H NMR (300 MHz, DMSO-d_6) δ 8.53 – 8.40 (m, 2H, ArH), 8.31 (d, *J* = 8.3 Hz, 1H, ArH), 8.00 (s, 1H, ArH), 7.79 – 7.65 (m, 2H, ArH, NH), 7.18 (d, *J* = 8.4 Hz, 1H, ArH), 5.27 (s, 2H, $ArCH_2Ar$), 5.03 (d, *J* = 4.8 Hz, 1H, OH), 4.98 (d, *J* = 5.4 Hz, 1H, OH), 4.52 (t, *J* = 5.8 Hz, 1H, OH), 4.37 – 4.21 (m, 3H, H-3, H-4, H-1), 3.68 (dd, *J* = 11.5, 5.8 Hz, 1H, H-6b), 3.52 (dd, *J* = 19.6, 9.8 Hz, 1H, H-2), 3.46 – 3.38 (m, 1H, H-6a), 3.33 – 3.21 (m, 1H, H-5), 3.17 – 3.03 (m, 8H, 2 NCH_3, CH_2), 2.64 – 2.53 (m, 2H, SCH_2), 1.80 (s, 3H, NAc), 1.79 – 1.70 (m, 2H, CH_2), 1.61 – 1.41 (m, 2H, CH_2), 1.35 – 1.14 (m, 2H, CH_2); ^{13}C NMR (75 MHz, DMSO-d_6) δ 169.04, 163.50, 162.78, 156.80, 143.31, 132.55, 131.82, 130.82, 129.83, 125.06, 124.28, 123.12, 122.31,

113.18, 113.03, 84.26, 81.30, 75.69, 70.65, 61.33, 54.62, 49.26, 44.49, 35.16, 29.38, 29.02, 28.52, 25.28, 23.17; HRMS (ESI) calcd for $C_{30}H_{39}N_6O_7S$ ($M+H^+$) 627.2601, found 627.2594.

6-(Dimethylamino)-2-[[1-[6-[(2-acetamido-β-D-glucopyranosyl)thio]hexyl]-1*H*-1,2,3-triazol-4-yl]methyl]-1*H*-benzo[*de*]isoquinoline-1,3(2*H*)-dione (**15n**): yellow solid; (0.51 g, 79.6 %) yield; $[\alpha]_D^{25}$ -36.9 (c=0.2, DMSO); ^{1}H NMR (300 MHz, DMSO-d_6) δ 8.58 – 8.41 (m, 2H, ArH), 8.32 (d, *J* = 8.3 Hz, 1H, ArH), 7.99 (s, 1H, ArH), 7.77 – 7.70 (m, 2H, ArH, NH), 7.19 (d, *J* = 8.4 Hz, 1H, ArH), 5.27 (s, 2H, $ArCH_2Ar$), 5.04 (s, 2H, 2 OH), 4.56 (s, 1H, OH), 4.37 – 4.20 (m, 3H, H-3, H-4, H-1), 3.69 (dd, *J* = 11.3, 4.0 Hz, 1H, H-6b), 3.59 – 3.50 (m, 1H, H-2), 3.47 – 3.40 (m, 1H, H-6a), 3.30 – 3.23 (m, 1H, H-5), 3.13 – 3.05 (m, 8H, 2 NCH_3, CH_2), 2.64 – 2.55 (m, 2H, SCH_2), 1.79 (s, 3H, NAc), 1.78 – 1.68 (m, 2H, CH_2), 1.52 – 1.42 (m, 2H, CH_2), 1.35 – 1.27 (m, 2H, CH_2), 1.25 – 1.17 (m, 2H, CH_2); ^{13}C NMR (75 MHz, DMSO-d_6) δ 169.04, 163.51, 162.80, 156.81, 143.32, 132.56, 131.83, 130.83, 129.83, 125.07, 124.28, 123.09, 122.32, 113.18, 113.04, 84.22, 81.28, 75.66, 70.66, 61.33, 54.65, 49.33, 44.50, 35.16, 29.67, 29.06, 28.97, 27.73, 25.55, 23.17; HRMS (ESI) calcd for $C_{31}H_{41}N_6O_7S$ ($M+H^+$) 641.2757, found 641.2760.

6-(Dimethylamino)-2-[[1-[5-[[2-[[(phenylmethoxy)carbonyl]amino]-β-D-glucopyranosyl] thio] pentyl]-1*H*-1,2,3-triazol-4-yl]methyl]-1*H*-benzo[*de*]isoquinoline-1,3(2*H*)-dione (**15o**): yellow solid; (0.56 g, 77.9 %) yield; $[\alpha]_D^{25}$ -43.8 (c=0.2, DMSO); ^{1}H NMR (300 MHz, DMSO-d_6) δ 8.52 – 8.38 (m, 2H, ArH), 8.30 (d, *J* = 8.3 Hz, 1H, ArH), 7.99 (s, 1H, ArH), 7.72 (dd, *J* = 8.4, 7.5 Hz, 1H, ArH), 7.40 – 7.25 (m, 5H, ArH), 7.21 (d, *J* = 9.1 Hz, 1H, NH), 7.16 (d, *J* = 8.4 Hz, 1H, ArH), 5.27 (s, 2H, $ArCH_2Ar$), 5.15 – 4.92 (m, 4H, H-3, H-4, H-1, OH), 4.53 (s, 1H, OH), 4.34 (d, *J* = 9.8 Hz, 1H, OH), 4.26 (t, *J* = 7.2 Hz, 2H, $PhCH_2$), 3.69 (d, *J* = 11.3 Hz, 1H, H-6b), 3.45 (d, *J* = 11.6 Hz, 1H, H-6a), 3.34 – 3.21 (m, 2H, H-2, H-5), 3.16 – 3.10 (m, 2H, CH_2), 3.08 (s, 6H, 2 CH_3), 2.69 – 2.53 (m, 2H, SCH_2), 1.84 – 1.67 (m, 2H, CH_2), 1.64 – 1.44 (m, 2H, CH_2), 1.38 – 1.14 (m, 2H, CH_2); ^{13}C NMR (75 MHz, DMSO-d_6) δ 163.49, 162.77, 156.77, 156.13, 143.32, 137.42, 132.53, 131.79, 130.80, 129.81, 128.34, 127.73, 127.63, 125.02, 124.26, 123.12, 122.29, 113.18, 113.00, 84.52, 81.33, 75.54, 70.71, 65.18, 61.33, 56.75, 49.25, 44.48, 35.15, 29.38, 29.03, 28.56, 25.27; HRMS (ESI) calcd for $C_{36}H_{43}N_6O_8S$ ($M+H^+$) 719.2863, found 719.2867.

6-(Dimethylamino)-2-[[1-[6-[[2-[[(phenylmethoxy)carbonyl]amino]-β-D-glucopyranosyl] thio] hexyl] -1*H*-1,2,3-triazol-4-yl] methyl] -1*H*- benzo[*de*]isoquinoline-1,3(2*H*)-dione (**15p**): yellow solid; (0.62 g, 84.6 %) yield; $[\alpha]_D^{25}$ -40.5 (c=0.2, DMSO); ^{1}H NMR (300 MHz, DMSO-d_6) δ 8.54 – 8.37 (m, 2H, ArH), 8.30 (d, *J* = 8.3 Hz, 1H, ArH), 7.99 (s, 1H, ArH), 7.72 (dd, *J* = 8.4, 7.5

Hz, 1H, ArH), 7.31 (dd, *J* = 12.1, 4.3 Hz, 5H, ArH), 7.22 (d, *J* = 9.1 Hz, 1H, NH), 7.16 (d, *J* = 8.4 Hz, 1H, ArH), 5.28 (s, 2H, $ArCH_2Ar$), 5.17 – 4.90 (m, 4H, H-3, H-4, H-1, OH), 4.55 (s, 1H, OH), 4.35 (d, *J* = 9.8 Hz, 1H, OH), 4.26 (t, *J* = 7.1 Hz, 2H, $PhCH_2$), 3.70 (d, *J* = 12.0 Hz, 1H, H-6b), 3.56 – 3.45 (m, 1H, H-6a), 3.32 – 3.22 (m, 2H, H-2, H-5), 3.18 – 3.01 (m, 8H, 2 NCH_3, CH_2), 2.65 – 2.57 (m, 2H, SCH_2), 1.79 – 1.66 (m, 2H, CH_2), 1.53 – 1.41 (m, 2H, CH_2), 1.35 – 1.25 (m, 2H, CH_2), 1.24 – 1.10 (m, 2H, CH_2); ^{13}C NMR (75 MHz, DMSO-d_6) δ 169.68, 163.49, 162.77, 156.77, 156.13, 143.32, 137.42, 132.52, 131.78, 130.79, 129.80, 128.31, 127.70, 127.58, 125.01, 124.25, 123.11, 122.28, 113.17, 112.99, 84.45, 81.32, 75.52, 70.73, 65.14, 61.34, 56.78, 49.34, 44.47, 35.14, 29.68, 29.08, 28.95, 27.71, 25.58; HRMS (ESI) calcd for $C_{37}H_{45}N_6O_8S$ ($M+H^+$) 733.3020, found 733.3011.

6-(Piperidin-1-yl)-2-[[1-[5-[(2-acetamido-β-D-glucopyranosyl)thio]pentyl]-1*H*-1,2,3-triazol-4-yl]methyl]-1*H*-benzo[*de*]isoquinoline-1,3(2*H*)-dione (**15q**): yellow solid; (0.52 g, 77.8 %) yield; $[\alpha]_D^{25}$ -48.5 (c=0.2, DMSO); ^{1}H NMR (300 MHz, DMSO-d_6) δ 8.45 – 8.34 (m, 1H, ArH), 8.34 – 8.22 (m, 2H, ArH), 7.98 (s, 1H, ArH), 7.75 – 7.68 (m, 2H, ArH, NH), 7.20 (d, *J* = 8.2 Hz, 1H, ArH), 5.23 (s, 2H, $ArCH_2Ar$), 5.05 (s, 1H, OH), 4.33 – 4.16 (m, 3H, H-3, H-4, H-1), 3.65 (d, *J* = 11.5 Hz, 1H, H-6b), 3.56 – 3.45 (m, 1H, H-2), 3.43 – 3.37 (m, 1H, H-6a), 3.32 – 3.21 (m, 1H, H-5), 3.18 – 3.09 (m, 4H, 2 CH_2), 3.09 – 3.04 (m, 2H, CH_2), 2.62 – 2.53 (m, 2H, SCH_2), 1.79 – 1.73 (m, 9H, 3 CH_2, NAc), 1.66 – 1.55 (m, 2H, CH_2), 1.55 – 1.42 (m, 2H, CH_2), 1.30 – 1.14 (m, 2H, CH_2); ^{13}C NMR (75 MHz, DMSO-d_6) δ 169.67, 169.08, 163.41, 162.81, 156.93, 143.23, 132.50, 130.81, 129.32, 125.85, 125.49, 123.13, 122.45, 114.95, 114.88, 84.27, 81.28, 75.67, 70.66, 61.33, 54.62, 54.05, 49.27, 35.18, 29.37, 28.52, 25.81, 25.57, 25.27, 23.15, 22.56; HRMS (ESI) calcd for $C_{33}H_{43}N_6O_7S$ ($M+H^+$) 667.2914, found 667.2919.

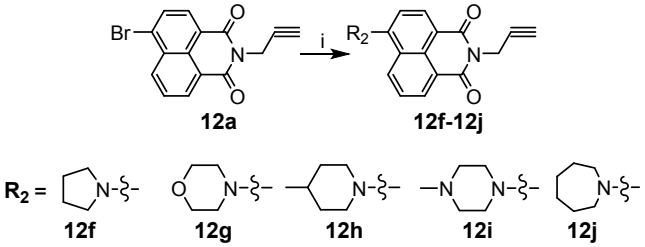
6-(Piperidin-1-yl)-2-[[1-[6-[(2-acetamido-β-D-glucopyranosyl)thio]hexyl]-1*H*-1,2,3-triazol-4-yl]methyl]-1*H*-benzo[*de*]isoquinoline-1,3(2*H*)-dione (**15r**): yellow solid; (0.54 g, 79.3 %) yield; $[\alpha]_D^{25}$ -49.3 (c=0.2, DMSO); ^{1}H NMR (300 MHz, DMSO-d_6) δ 8.41 (dd, *J* = 7.3, 0.9 Hz, 1H, ArH), 8.37 – 8.27 (m, 2H, ArH), 7.97 (s, 1H, ArH), 7.74 – 7.66 (m, 2H, ArH, NH), 7.24 (d, *J* = 8.2 Hz, 1H, ArH), 5.24 (s, 2H, $ArCH_2Ar$), 5.01 (s, 2H, 2 OH), 4.53 (s, 1H, OH), 4.33 – 4.20 (m, 3H, H-3, H-4, H-1), 3.66 (dd, *J* = 11.6, 4.1 Hz, 2H, H-6b), 3.52 – 3.47 (m, 1H, H-2), 3.42 – 3.38 (m, 1H, H-6a), 3.27 – 3.22 (m, 1H, H-5), 3.20 – 3.10 (m, 4H, 2 CH_2), 3.09 – 3.05 (m, 2H, CH_2), 2.61 – 2.54 (m, 2H, SCH_2), 1.76 – 1.69 (m, 9H, NAc, 3 CH_2), 1.66 – 1.56 (m, 2H, CH_2), 1.49 – 1.41 (m, 2H, CH_2), 1.31 – 1.25 (m, 2H, CH_2), 1.21 – 1.10 (m, 2H, CH_2); ^{13}C NMR (75 MHz, DMSO-d_6) δ 169.68, 169.07, 163.45, 162.86, 156.98, 143.24, 132.54, 130.85, 129.37, 125.90, 125.54, 123.09, 122.51,

115.00, 114.93, 84.23, 81.28, 75.66, 70.66, 61.33, 54.65, 54.07, 49.34, 35.20, 29.66, 29.13, 28.97, 27.73, 25.81, 25.56, 23.15, 22.56; HRMS (ESI) calcd for $C_{34}H_{45}N_6O_7S$ ($M+H^+$) 681.3070, found 681.3070.

6-(Piperidin-1-yl)-2-[[1-[5-[[2-[[(phenylmethoxy)carbonyl]amino]-β-D-glucopyranosyl]thio] pentyl]-1*H*-1,2,3-triazol-4-yl]methyl]-1*H*-benzo[*de*]isoquinoline-1,3(2*H*)-dione (**15s**): yellow solid; (0.61 g, 80.4 %) yield; $[\alpha]_D^{25}$ -43.6 (c=0.2, DMSO); ^{1}H NMR (300 MHz, DMSO-d_6) δ 8.53 – 8.33 (m, 3H, ArH), 7.99 (s, 1H, ArH), 7.80 (dd, *J* = 8.4, 7.4 Hz, 1H, ArH), 7.42 – 7.24 (m, 6H, ArH), 7.19 (d, *J* = 8.9 Hz, 1H, NH), 5.28 (s, 2H, $ArCH_2Ar$), 5.10 – 4.93 (m, 4H, H-3, H-4, H-1, OH), 4.51 (s, 1H, OH), 4.31 (d, *J* = 5.1 Hz, 1H, OH), 4.25 (t, *J* = 7.2 Hz, 2H, $PhCH_2$), 3.67 (dd, *J* = 11.4, 4.5 Hz, 1H, H-6b), 3.46 – 3.37 (m, 1H, H-6a), 3.32 – 3.23 (m, 2H, H-2, H-5), 3.23 – 3.14 (m, 4H, 2 CH_2), 3.12 – 3.01 (m, 2H, CH_2), 2.63 – 2.55 (m, 2H, SCH_2), 1.86 – 1.72 (m, 8H, 3 CH_2), 1.71 – 1.61 (m, 2H, CH_2), 1.58 – 1.42 (m, 2H, CH_2), 1.35 – 1.18 (m, 2H, CH_2); ^{13}C NMR (75 MHz, DMSO-d_6) δ 169.61, 163.47, 162.88, 157.01, 156.12, 143.25, 137.42, 132.57, 130.89, 129.41, 128.34, 127.73, 127.63, 125.94, 125.58, 123.10, 122.56, 115.05, 114.98, 84.49, 81.33, 75.51, 70.69, 65.16, 61.30, 56.73, 54.08, 49.24, 35.22, 29.37, 28.54, 25.82, 25.56, 25.26, 23.96; HRMS (ESI) calcd for $C_{39}H_{47}N_6O_8S$ ($M+H^+$) 759.3176, found 759.3169.

6-(Piperidin-1-yl)-2-[[1-[6-[[2-[[(phenylmethoxy)carbonyl]amino]-β-D-glu copyranosyl]thio] hexyl] -1*H*-1,2,3-triazol-4-yl] methyl] -1*H*- benzo[*de*]isoquinoline-1,3(2*H*)-dione (**15t**): yellow solid; (0.61 g, 77.3 %) yield; $[\alpha]_D^{25}$ -41.4 (c=0.2, DMSO); ^{1}H NMR (300 MHz, DMSO-d_6) δ 8.41 (d, *J* = 7.2 Hz, 1H, ArH), 8.33 (dd, *J* = 8.3, 2.3 Hz, 2H, ArH), 8.01 (s, 1H, ArH), 7.82 – 7.70 (m, 1H, ArH), 7.43 – 7.25 (m, 5H, ArH), 7.25 – 7.14 (m, 2H, ArH, NH), 5.28 (s, 2H, $ArCH_2Ar$), 5.20 – 4.87 (m, 3H, H-3, H-4, H-1), 4.35 (d, *J* = 5.7 Hz, 1H, OH), 4.26 (t, *J* = 7.1 Hz, 2H, $PhCH_2$), 3.71 (d, *J* = 11.3 Hz, 1H, H-6b), 3.47 (d, *J* = 11.6, 1H, H-6a), 3.36 – 3.24 (m, 2H, H-2, H-5), 3.22 – 3.01 (m, 6H, 3 CH_2), 2.66 – 2.57 (m, 2H, SCH_2), 1.85 – 1.71 (m, 6H, 3 CH_2), 1.69 – 1.56 (m, 2H, CH_2), 1.54 – 1.39 (m, 2H, CH_2), 1.39 – 1.25 (m, 2H, CH_2), 1.25 – 1.10 (m, 2H, CH_2); ^{13}C NMR (75 MHz, DMSO) δ 163.41, 162.81, 156.92, 156.13, 143.24, 137.42, 132.49, 130.79, 129.31, 128.31, 127.70, 127.58, 125.83, 125.48, 123.13, 122.45, 114.93, 114.88, 84.46, 81.33, 75.52, 70.74, 65.14, 61.34, 56.78, 54.05, 49.35, 35.18, 29.68, 29.07, 28.95, 27.72, 25.81, 25.58, 23.95; HRMS (ESI) calcd for $C_{40}H_{49}N_6O_8S$ ($M+H^+$) 773.3333, found 772.3345.

1.7 Synthesis of naphthalimide derivatives 12f-12j



Scheme S7. Synthesis of naphthalimide derivatives **12f-12j**. (i) pyrrolidine, 2-methoxyethanol for **12f**; morpholine, 2-methoxyethanol for **12g**; 4-methylpiperidine, 2-methoxyethanol for **12h**; 1-methylpiperazine, 2-methoxyethanol for **12i**; azepane, 2-methoxyethanol for **12j**.

Compounds **12f-12j** were synthesized from compound **12a** using the procedure described for the synthesis of compound **12e**.

2-(Prop-2-yn-1-yl)-6-(pyrrolidin-1-yl)-1*H*-benzo[*de*]isoquinoline-1,3(2*H*)-dione(**12f**): yellow solid; (82.5 %) yield; ^{1}H NMR (300 MHz, $CDCl_3$) δ 8.67 – 8.56 (m, 2H, ArH), 8.44 (d, *J* = 8.7 Hz, 1H, ArH), 7.53 (dd, *J* = 8.5, 7.5 Hz, 1H, ArH), 6.80 (d, *J* = 8.7 Hz, 1H, ArH), 4.96 (d, *J* = 2.5 Hz, 2H, ≡CCH_2), 3.88 – 3.73 (m, 4H, 2 CH_2), 2.16 (t, *J* = 2.5 Hz, 1H, ≡CH), 2.13 – 2.07 (m, 4H, 2 CH_2); HRMS (ESI) calcd for $C_{19}H_{17}N_2O_2$ ($M+H^+$) 305.1290, found 305.1283.

6-Morpholino-2-(prop-2-yn-1-yl)-1*H*-benzo[*de*]isoquinoline-1,3(2*H*)-dione (**12g**)[11]: yellow solid; (83.2 %) yield; ^{1}H NMR (300 MHz, $CDCl_3$) δ 8.63 (dd, *J* = 7.3, 1.2 Hz, 1H, ArH), 8.58 (d, *J* = 8.1 Hz, 1H, ArH), 8.44 (dd, *J* = 8.5, 1.2 Hz, 1H, ArH), 7.72 (dd, *J* = 8.4, 7.3 Hz, 1H, ArH), 7.24 (d, *J* = 8.1 Hz, 1H, ArH), 4.95 (d, *J* = 2.5 Hz, 2H, ≡CCH_2), 4.11 – 3.95 (m, 4H, CH_2), 3.32 – 3.21 (m, 4H, CH_2), 2.18 (t, *J* = 2.5 Hz, 1H, ≡CH).

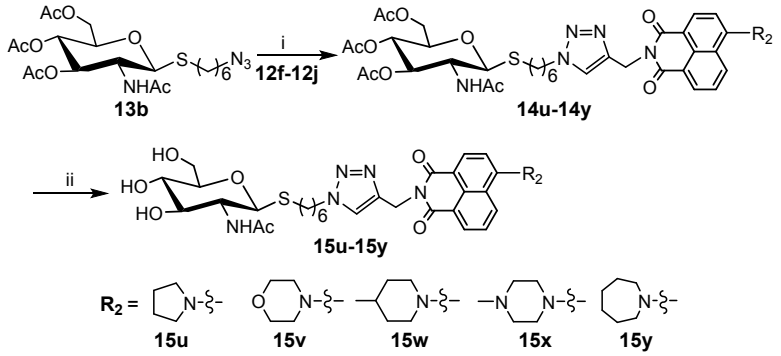
6-(4-Methylpiperidin-1-yl)-2-(prop-2-yn-1-yl)-1*H*-benzo[*de*]isoquinoline-1,3(2*H*)-dione (**12h**)[7]: yellow solid; (80.8 %) yield; ^{1}H NMR (300 MHz, $CDCl_3$) δ 8.61 (dd, *J* = 7.3, 1.0 Hz, 1H, ArH), 8.53 (d, *J* = 8.1 Hz, 1H, ArH), 8.39 (dd, *J* = 8.4, 1.1 Hz, 1H, ArH), 7.68 (dd, *J* = 8.4, 7.4 Hz, 1H, ArH), 7.18 (d, *J* = 8.2 Hz, 1H, ArH), 4.95 (d, *J* = 2.4 Hz, 2H, ≡CCH_2), 3.59 (d, *J* = 12.5 Hz, 2H, CH_2), 2.92 (t, *J* = 11.8 Hz, 2H, CH_2), 2.17 (t, *J* = 2.4 Hz, 1H, ≡CH), 1.87 (d, *J* = 9.9 Hz, 2H, CH_2), 1.66 – 1.48 (m, 3H, CH, CH_2), 1.09 (d, *J* = 5.9 Hz, 3H, CH_3).

6-(4-Methylpiperazin-1-yl)-2-(prop-2-yn-1-yl)-1*H*-benzo[*de*]isoquinoline-1,3(2*H*)-dione (**12i**)[12]: yellow solid; (74.5 %) yield; ^{1}H NMR (300 MHz, $CDCl_3$) δ 8.67 – 8.52 (m, 2H, ArH), 8.43 (dd, *J* = 8.5, 1.1 Hz, 1H, ArH), 7.70 (dd, *J* = 8.4, 7.4 Hz, 1H, ArH), 7.23 (d, *J* = 8.1 Hz, 1H, ArH),

4.95 (d, J = 2.5 Hz, 2H, ≡CCH_2), 3.39 – 3.24 (m, 4H, 2 CH_2), 2.84 – 2.68 (m, 4H, 2 CH_2), 2.45 (s, 3H, CH_3), 2.18 (t, J = 2.4 Hz, 1H, ≡CH).

6-(Azepan-1-yl)-2-(prop-2-yn-1-yl)-1*H*-benzo[*de*]isoquinoline-1,3(2*H*)-dione (**12j**)[12]: yellow solid; (81.1 %) yield; ^{1}H NMR (300 MHz, $CDCl_3$) δ 8.58 (dd, J = 7.3, 1.1 Hz, 1H, ArH), 8.50 – 8.40 (m, 2H, ArH), 7.61 (dd, J = 8.5, 7.3 Hz, 1H, ArH), 7.14 (d, J = 8.4 Hz, 1H, ArH), 4.95 (d, J = 2.5 Hz, 2H, ≡CCH_2), 3.68 – 3.53 (m, 4H, 2 CH_2), 2.17 (t, J = 2.5 Hz, 1H, ≡CH), 2.08 – 1.88 (m, 4H, 2 CH_2), 1.86 – 1.70 (m, 4H, 2 CH_2); HRMS (ESI) calcd for $C_{21}H_{22}N_2O_2$ ($M+H^+$) 333.1603, found 333.1612.

1.8 Synthesis of thioglycosyl-naphthalimide derivatives 15u-15y



Scheme S8. Synthesis of glycosylated naphthalimide derivatives **15u-15y**. (i) **12f-12j**, $CuSO_4$, sodium ascorbate, THF, H_2O; (iv) NH_3, MeOH.

Compounds **14u-14y** were synthesized from compound **13b** (1.5 mmol) using the procedure described for the synthesis of compounds **14a-14t** (from **13a-13d**).

6-(Pyrrolidin-1-yl)-2-[[1-[6-[(2-acetamido-3,4,6-tri-O-acetyl-β-D-glucopyranosyl)thio]hexyl]-1*H*-1,2,3-triazol-4-yl]methyl]-1*H*-benzo[*de*]isoquinoline-1,3(2*H*)-dione (**14u**): yellow syrup; (0.95g, 80.3 %) yield; $[\alpha]_D^{25}$ -64.9 (c=0.5, DMSO); ^{1}H NMR (300 MHz, DMSO-d_6) δ 8.58 (d, J = 8.6 Hz, 1H, ArH), 8.32 (d, J = 7.2 Hz, 1H, ArH), 8.09 (d, J = 8.7 Hz, 1H, ArH), 8.02 – 7.90 (m, 2H, ArH, NH), 7.54 – 7.43 (m, 1H, ArH), 6.69 (d, J = 8.9 Hz, 1H, ArH), 5.21 (s, 2H, $ArCH_2Ar$), 5.06 (t, J = 9.8 Hz, 1H, H-3), 4.82 (t, J = 9.7 Hz, 1H, H-4), 4.65 (d, J = 10.4 Hz, 1H, H-1), 4.23 (t, J = 7.0 Hz, 2H, CH_2), 4.12 (dd, J = 12.3, 5.0 Hz, 1H, H-6b), 3.98 (dd, J = 9.6, 2.5 Hz, 1H, H-6a), 3.89 – 3.75 (m, 2H, H-2, H-5), 3.73 – 3.58 (m, 4H, 2 CH_2), 2.65 – 2.49 (m, 2H, SCH_2), 1.97 (s, 3H, OAc), 1.97 – 1.93 (m, 7H, OAc, 2 CH_2), 1.90 (s, 3H, OAc), 1.82 – 1.65 (m, 5H, NAc, CH_2), 1.54 – 1.39 (m, 2H, CH_2), 1.36 – 1.22 (m, 2H, CH_2), 1.21 – 1.13 (m, 2H, CH_2); ^{13}C NMR (75 MHz, DMSO-

d_6) δ 170.08, 169.74, 169.39, 169.18, 163.62, 162.52, 152.20, 143.52, 133.00, 132.72, 130.67, 123.15, 123.09, 121.72, 121.46, 108.64, 108.42, 83.57, 74.72, 73.84, 68.74, 62.15, 59.85, 52.92, 52.34, 49.31, 34.97, 29.70, 29.30, 29.17, 27.61, 25.65, 25.53, 22.73, 20.57, 20.51, 20.44; HRMS (ESI) calcd for $C_{39}H_{49}N_6O_{10}S$ ($M+H^+$) 793.3231, found 793.3223.

6-Morpholino-2-[[1-[6-[(2-acetamido-3,4,6-tri-O-acetyl-β-D-glucopyranosyl)thio]hexyl]-1*H*-1,2, 3-triazol-4-yl]methyl]-1*H*-benzo[*de*]isoquinoline-1,3(2*H*)-dione (**14v**): yellow syrup; (1.0 g, 82.7 %) yield; $[\alpha]_D^{25}$ -54.5 (c=0.5, DMSO); ^{1}H NMR (300 MHz, DMSO-d_6) δ 8.51 – 8.33 (m, 3H, ArH), 8.05 – 7.94 (m, 2H, ArH, NH), 7.78 (t, *J* = 7.9 Hz, 1H, ArH), 7.32 (d, *J* = 8.2 Hz, 1H, ArH), 5.27 (s, 2H, $ArCH_2Ar$), 5.08 (t, *J* = 9.8 Hz, 1H, H-3), 4.85 (t, *J* = 9.7 Hz, 1H, H-4), 4.68 (d, *J* = 10.4 Hz, 1H, H-1), 4.27 (t, *J* = 7.1 Hz, 2H, CH_2), 4.15 (dd, *J* = 12.3, 5.2 Hz, 1H, H-6b), 4.03 – 3.97 (m, 1H, H-6b), 3.96 – 3.89 (m, 4H, 2 OCH_2), 3.88 – 3.79 (m, 2H, H-2, H-5), 3.28 – 3.16 (m, 4H, 2 CH_2), 2.69 – 2.53 (m, 2H, SCH_2), 1.99 (s, 3H, OAc), 1.99 (s, 3H, OAc), 1.93 (s, 3H, OAc), 1.81 – 1.70 (m, 5H, NAc, CH_2), 1.58 – 1.44 (m, 2H, CH_2), 1.36 – 1.27 (m, 2H, CH_2), 1.25 – 1.18 (m, 2H, CH_2); ^{13}C NMR (75 MHz, DMSO-d_6) δ 170.08, 169.74, 169.38, 169.17, 163.38, 162.82, 155.69, 143.20, 132.43, 130.91, 130.78, 129.29, 126.17, 125.38, 123.10, 122.58, 115.81, 115.14, 83.56, 74.71, 73.83, 68.74, 66.31, 62.15, 53.15, 52.32, 49.34, 35.24, 29.66, 29.28, 29.16, 27.60, 25.51, 22.73, 20.57, 20.52, 20.44; HRMS (ESI) calcd for $C_{39}H_{49}N_6O_{11}S$ ($M+H^+$) 809.3180, found 809.3175.

6-(4-Methylpiperidin-1-yl)-2-[[1-[6-[(2-acetamido-3,4,6-tri-O-acetyl-β-D-glucopyranosyl) thio]hexyl]-1*H*-1,2,3-triazol-4-yl]methyl]-1*H*-benzo[*de*]isoquinoline-1,3(2*H*)-dione (**14w**): yellow syrup; (1.02 g, 83.5 %) yield; $[\alpha]_D^{25}$ -68.3 (c=0.5, DMSO); ^{1}H NMR (300 MHz, DMSO-d_6) δ 8.47 – 8.40 (m, 1H, ArH), 8.34 (dd, *J* = 7.9, 3.5 Hz, 2H, ArH), 8.05 – 7.92 (m, 2H, ArH, NH), 7.81 – 7.71 (m, 1H, ArH), 7.25 (d, *J* = 8.2 Hz, 1H, ArH), 5.27 (s, 2H, $ArCH_2Ar$), 5.09 (t, *J* = 9.7 Hz, 1H, H-3), 4.85 (t, *J* = 9.7 Hz, 1H, H-4), 4.68 (d, *J* = 10.4 Hz, 1H, H-1), 4.26 (t, *J* = 7.1 Hz, 2H, CH_2), 4.16 (dd, *J* = 12.3, 5.1 Hz, 1H, H-6b), 4.02 (dd, *J* = 11.7, 2.4 Hz, 1H, H-6a), 3.92 – 3.79 (m, 2H, H-2, H-5), 3.50 (d, *J* = 11.0 Hz, 2H, CH_2), 2.87 (t, *J* = 10.9 Hz, 2H, CH_2), 2.70 – 2.53 (m, 2H, SCH_2), 2.00 (s, 3H, OAc), 1.99 (s, 3H, OAc), 1.94 (s, 3H, OAc), 1.85 – 1.68 (m, 7H, NAc, 2 CH_2), 1.61 – 1.42 (m, 5H, 2 CH_2, $C\underline{H}CH_3$), 1.39 – 1.27 (m, 2H, CH_2), 1.24 – 1.17 (m, 2H, CH_2), 1.03 (d, *J* = 5.9 Hz, 3H, CH_3); ^{13}C NMR (75 MHz, DMSO-d_6) δ 170.07, 169.73, 169.37, 169.16, 163.41, 162.81, 156.72, 143.25, 132.48, 130.81, 129.34, 125.84, 125.51, 123.09, 122.48, 114.99, 114.90, 83.56, 74.71, 73.84, 68.73, 62.15, 54.99, 53.33, 52.32, 49.33, 34.08, 30.33, 29.67, 29.28, 29.16,

27.61, 25.51, 22.73, 21.82, 20.57, 20.51, 20.44; HRMS (ESI) calcd for $C_{41}H_{53}N_6O_{10}S$ ($M+H^+$) 821.3544, found 821.3552.

6-(4-Methylpiperazin-1-yl)-2-[[1-[6-[(2-acetamido-3,4,6-tri-O-acetyl-β-D-glucopyranosyl) thio]hexyl]-1*H*-1,2,3-triazol-4-yl]methyl]-1*H*-benzo[*de*]isoquinoline-1,3(2*H*)-dione (**14x**): yellow syrup; (0.95 g, 76.9 %) yield; $[\alpha]_D^{25}$ -49.4 (c=0.5, DMSO); ^{1}H NMR (300 MHz, DMSO-d_6) δ 8.52 – 8.33 (m, 3H, ArH), 8.12 (d, J = 9.4 Hz, 1H, NH), 8.02 (s, 1H, ArH), 7.81 (dd, J = 8.4, 7.4 Hz, 1H, ArH), 7.35 (d, J = 8.2 Hz, 1H, ArH), 5.27 (s, 2H, $ArCH_2Ar$), 5.09 (t, J = 9.7 Hz, 1H, H-3), 4.83 (t, J = 9.7 Hz, 1H, H-4), 4.72 (d, J = 10.4 Hz, 1H, H-1), 4.27 (t, J = 7.1 Hz, 2H, CH_2), 4.14 (dd, J = 12.3, 5.1 Hz, 1H, H-6b), 4.03 – 3.97 (m, 1H, H-6a), 3.91 – 3.78 (m, 2H, H-2, H-5), 3.44 – 3.21 (m, 4H, 2 NCH_2), 2.95 – 2.73 (m, 4H, 2 NCH_2), 2.66 – 2.53 (m, 2H, SCH_2), 2.44 (s, 3H, NCH_3), 1.99 (s, 3H, OAc), 1.98 (s, 3H, OAc), 1.92 (s, 3H, OAc), 1.80 – 1.66 (m, 5H, NAc, CH_2), 1.60 – 1.43 (m, 2H, CH_2), 1.38 – 1.25 (m, 2H, CH_2), 1.21 – 1.13 (m, 2H, CH_2); ^{13}C NMR (75 MHz, DMSO-d_6) δ 170.08, 169.68, 169.40, 169.19, 163.40, 162.84, 155.44, 143.18, 132.42, 130.94, 130.75, 129.28, 126.25, 125.43, 123.12, 122.59, 115.79, 115.40, 83.56, 74.67, 73.87, 68.75, 62.15, 59.85, 54.01, 52.33, 51.62, 49.33, 44.69, 35.24, 29.65, 29.32, 29.16, 27.58, 25.49, 22.74, 20.59, 20.53, 20.46; HRMS (ESI) calcd for $C_{40}H_{52}N_7O_{10}S$ ($M+H^+$) 822.3496, found 822.3499.

6-(Azepan-1-yl)-2-[[1-[6-[(2-acetamido-3,4,6-tri-O-acetyl-β-D-glucopyranosyl)thio]hexyl]-1*H*-1,2,3-triazol-4-yl]methyl]-1*H*-benzo[*de*]isoquinoline-1,3(2*H*)-dione (**14y**): yellow syrup; (1.0 g, 81.4 %) yield; $[\alpha]_D^{25}$ -57.6 (c=0.5, DMSO); ^{1}H NMR (300 MHz, DMSO-d_6) δ 8.38 (t, J = 8.1 Hz, 2H, ArH), 8.22 (d, J = 8.5 Hz, 1H, ArH), 7.99 – 7.90 (m, 2H, ArH, NH), 7.63 (t, J = 7.9 Hz, 1H, ArH), 7.13 (d, J = 8.6 Hz, 1H, ArH), 5.23 (s, 2H, $ArCH_2Ar$), 5.06 (t, J = 9.8 Hz, 1H, H-3), 4.82 (t, J = 9.7 Hz, 1H, H-4), 4.65 (d, J = 10.4 Hz, 1H, H-1), 4.23 (t, J = 7.0 Hz, 2H, CH_2), 4.12 (dd, J = 12.2, 5.0 Hz, 1H, H-6b), 4.00 – 3.94 (m, 1H, H-6a), 3.89 – 3.76 (m, 2H, H-2, H-5), 3.60 – 3.48 (m, 4H, 2 CH_2), 2.65 – 2.49 (m, 2H, SCH_2), 1.96 (s, 3H, OAc), 1.94 (s, 3H, OAc), 1.90 (s, 3H, OAc), 1.87 – 1.78 (m, 4H, 2 CH_2), 1.77 – 1.69 (m, 5H, NAc, CH_2), 1.68 – 1.59 (m, 4H, 2 CH_2), 1.54 – 1.39 (m, 2H, CH_2), 1.33 – 1.23 (m, 2H, CH_2), 1.21 – 1.15 (m, 2H, CH_2); ^{13}C NMR (75 MHz, DMSO-d_6) δ 170.07, 169.73, 169.37, 169.16, 163.52, 162.68, 157.01, 143.36, 132.45, 131.99, 130.75, 130.12, 124.49, 124.24, 123.09, 122.16, 113.17, 112.21, 83.56, 74.72, 73.84, 68.74, 62.15, 59.85, 54.82, 52.33, 49.32, 35.08, 29.69, 29.29, 29.16, 27.89, 27.61, 27.31, 25.52, 22.73, 20.56, 20.51, 20.43; HRMS (ESI) calcd for $C_{41}H_{53}N_6O_{10}S$ ($M+H^+$) 821.3544, found 821.3536.

Compounds **15u-15y** were synthesized by deacetylation of **14u-14y** (1 mmol) using the procedure described for the synthesis of compounds **15a-15t** (from **14a-14t**).

6-(Pyrrolidin-1-yl)-2-[[1-[6-[(2-acetamido-β-D-glucopyranosyl)thio]hexyl]-1*H*-1,2,3-triazol-4-yl]methyl]-1*H*-benzo[*de*]isoquinoline-1,3(2*H*)-dione (**15u**): yellow solid; (0.56 g, 84.0 %) yield; $[\alpha]_D^{25}$ -25.8 (c=0.2, DMSO); ^{1}H NMR (300 MHz, DMSO-d_6) δ 8.65 (d, J = 8.2 Hz, 1H, ArH), 8.37 (d, J = 6.8 Hz, 1H, ArH), 8.15 (d, J = 8.7 Hz, 1H, ArH), 7.96 (s, 1H, ArH), 7.71 (d, J = 9.3 Hz, 1H, NH), 7.55 (dd, J = 8.5, 7.4 Hz, 1H, ArH), 6.77 (d, J = 8.9 Hz, 1H, ArH), 5.25 (s, 2H, $ArCH_2Ar$), 5.03 (d, J = 3.9 Hz, 1H, OH), 4.99 (d, J = 5.3 Hz, 1H, OH), 4.53 (t, J = 5.7 Hz, 1H, OH), 4.32 (d, J = 10.3 Hz, 1H, H-1), 4.26 (t, J = 7.1 Hz, 2H, H-3, H-4), 3.82 – 3.64 (m, 5H, 2 CH_2, H-6b), 3.60 – 3.44 (m, 2H, H-2, H-6a), 3.33 – 3.22 (m, 1H, H-5), 3.18 – 3.03 (m, 2H, CH_2), 2.66 – 2.53 (m, 2H, SCH_2), 2.09 – 1.93 (m, 4H, 2 CH_2), 1.85 – 1.67 (m, 5H, NAc, CH_2), 1.54 – 1.41 (m, 2H, CH_2), 1.36 – 1.26 (m, 2H, CH_2), 1.25 – 1.13 (m, 2H, CH_2); ^{13}C NMR (75 MHz, DMSO-d_6) δ 169.08, 163.65, 162.56, 152.28, 143.49, 133.07, 132.81, 130.75, 130.71, 123.14, 121.75, 121.46, 108.62, 108.48, 84.21, 81.28, 75.68, 70.66, 61.35, 54.67, 52.95, 49.32, 35.00, 29.70, 29.07, 28.98, 27.74, 25.66, 25.56, 23.16; HRMS (ESI) calcd for $C_{33}H_{43}N_6O_7S$ ($M+H^+$) 667.2914, found 667.2919.

6-Morpholino-2-[[1-[6-[(2-acetamido-β-D-glucopyranosyl)thio]hexyl]-1*H*-1,2,3-triazol-4-yl]methyl]-1*H*-benzo[*de*]isoquinoline-1,3(2*H*)-dione (**15v**): yellow solid; (0.55 g, 87.5 %) yield; $[\alpha]_D^{25}$ -33.1 (c=0.2, DMSO); ^{1}H NMR (300 MHz, DMSO-d_6) δ 8.45 (dd, J = 7.9, 2.1 Hz, 2H, ArH), 8.37 (d, J = 8.1 Hz, 1H, ArH), 8.01 (s, 1H, ArH), 7.85 – 7.68 (m, 2H, ArH, NH), 7.32 (d, J = 8.2 Hz, 1H, ArH), 5.27 (s, 2H, $ArCH_2Ar$), 4.39 (br s, 3H, 3 OH), 4.32 (d, J = 10.3 Hz, 1H, H-1), 4.26 (t, J = 7.1 Hz, 2H, H-3, H-4), 3.96 – 3.87 (m, 4H, 2 CH_2), 3.69 (d, J = 11.5 Hz, 1H, H-6b), 3.52 (d, J = 9.8 Hz, 1H, H-2), 3.47 – 3.39 (m, 1H, H-6a), 3.33 – 3.24 (m, 1H, H-5), 3.24 – 3.19 (m, 4H, 2 CH_2), 3.13 – 3.04 (m, 2H, CH_2), 2.62 – 2.54 (m, 2H, SCH_2), 1.80 (s, 3H, NAc), 1.78 – 1.68 (m, 2H, CH_2), 1.53 – 1.38 (m, 2H, CH_2), 1.36 – 1.24 (m, 2H, CH_2), 1.24 – 1.14 (m, 2H, CH_2); ^{13}C NMR (75 MHz, DMSO-d_6) δ 169.05, 163.38, 162.82, 155.69, 143.19, 132.44, 130.91, 130.79, 129.28, 126.17, 125.36, 123.10, 122.56, 115.77, 115.15, 84.23, 81.30, 75.68, 70.67, 66.31, 61.35, 54.67, 53.15, 48.73, 35.24, 29.66, 29.06, 28.97, 27.74, 25.55, 23.16; HRMS (ESI) calcd for $C_{33}H_{43}N_6O_7S$ ($M+H^+$) 683.2863, found 683.2874.

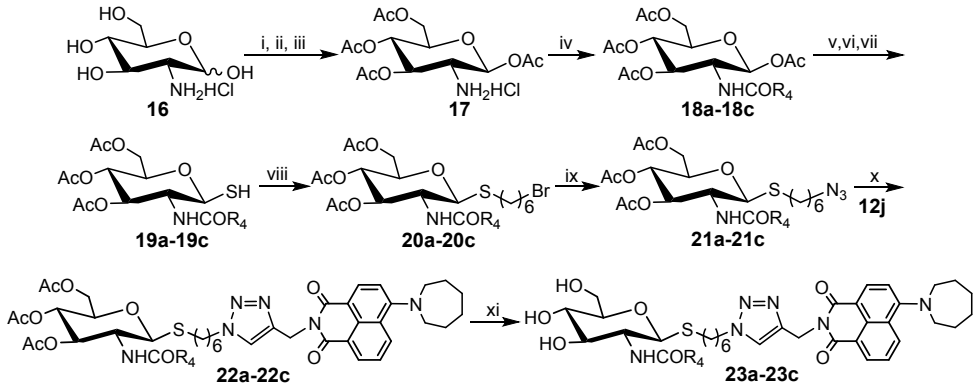
6-(4-Methylpiperidin-1-yl)-2-[[1-[6-[(2-acetamido-β-D-glucopyranosyl)thio]hexyl]-1*H*-1,2,3-triazol-4-yl]methyl]-1*H*-benzo[*de*]isoquinoline-1,3(2*H*)-dione (**15w**): yellow solid; (0.56 g, 80.6 %) yield; $[\alpha]_D^{25}$ -19.7 (c=0.2, DMSO); ^{1}H NMR (300 MHz, DMSO-d_6) δ 8.40 (d, J = 7.2 Hz, 1H, ArH), 8.32 (dd, J = 8.2, 3.6 Hz, 2H, ArH), 7.97 (s, 1H, ArH), 7.73 (m, 2H, ArH, NH), 7.23 (d, J = 8.2 Hz, 1H, ArH), 5.24 (s, 2H, $ArCH_2Ar$), 4.29 (d, J = 10.3 Hz, 1H, H-1), 4.27 – 4.13 (m, 5H, 3 OH, H-3, H-4), 3.65 (d, J = 11.5 Hz, 1H, H-6b), 3.55 – 3.34 (m, 4H, H-6a, H-2, CH_2), 3.29 – 3.19

(m, 1H, H-5), 3.12 – 2.99 (m, 2H, CH_2), 2.84 (t, *J* = 11.2 Hz, 2H, CH_2), 2.56 – 2.51 (m, 2H, SCH_2), 1.80 – 1.68 (m, 7H, NAc, 2 CH_2), 1.60 – 1.36 (m, 5H, 2 CH_2, C<u>H</u>CH_3), 1.34 – 1.22 (m, 2H, CH_2), 1.21 – 1.11 (m, 2H, CH_2), 0.99 (d, *J* = 5.9 Hz, 3H, CH_3); ^{13}C NMR (75 MHz, DMSO-d_6) δ 169.03, 163.43, 162.84, 156.74, 143.24, 132.51, 130.84, 129.36, 125.88, 125.52, 123.09, 122.49, 115.04, 114.90, 84.24, 81.31, 75.67, 70.67, 61.35, 54.66, 53.33, 49.34, 48.73, 34.09, 30.33, 29.67, 29.06, 28.97, 27.74, 25.56, 23.16, 21.84; HRMS (ESI) calcd for $C_{35}H_{47}N_6O_7S$ ($M+H^+$) 695.3227, found 695.3234.

6-(4-Methylpiperazin-1-yl)-2-[[1-[6-[(2-acetamido-β-D-glucopyranosyl)thio]hexyl]-1*H*-1,2,3-triazol-4-yl]methyl]-1*H*-benzo[*de*]isoquinoline-1,3(2*H*)-dione (**15x**): yellow solid; (0.36 g, 51.7 %) yield; $[\alpha]_D^{25}$ -21.4 (c=0.2, DMSO); ^{1}H NMR (300 MHz, DMSO-d_6) δ 8.54 – 8.37 (m, 3H, ArH), 8.01 (s, 1H, ArH), 7.83 (m, 2H, ArH, NH), 7.36 (d, *J* = 8.1 Hz, 1H, ArH), 5.28 (s, 2H, $ArCH_2Ar$), 4.35 – 4.22 (m, 3H, H-3, H-4, H-1), 3.64 (d, *J* = 11.9 Hz, 1H, H-6b), 3.51 – 3.45 (m, 2H, H-2, H-6a), 3.35 – 3.31 (m, 1H, H-5), 3.28 – 3.23 (m, 4H, 2 CH_2), 3.10 – 3.05 (m, 2H, CH_2), 2.69 – 2.60 (m, 4H, 2 CH_2), 2.58 – 2.54 (m, 2H, SCH_2), 2.31 (s, 3H, NCH_3), 1.78 (s, 3H, NAc), 1.73 – 1.69 (m, 2H, CH_2), 1.48 – 1.40 (m, 2H, CH_2), 1.35 – 1.27 (m, 2H, CH_2), 1.22 – 1.16 (m, 2H, CH_2); ^{13}C NMR (75 MHz, DMSO-d_6) δ 169.02, 163.47, 162.90, 156.01, 143.20, 132.54, 130.95, 130.86, 129.40, 126.17, 125.47, 123.09, 122.65, 115.48, 115.25, 84.30, 81.26, 75.54, 70.66, 61.25, 54.75, 54.54, 52.66, 48.67, 45.85, 35.26, 29.66, 29.10, 28.98, 27.73, 25.54, 23.15; HRMS (ESI) calcd for $C_{34}H_{46}N_7O_7S$ ($M+H^+$) 696.3179, found 696.3168.

6-(Azepan-1-yl)-2-[[1-[6-[(2-acetamido-β-D-glucopyranosyl)thio]hexyl]-1*H*-1,2,3-triazol-4-yl]methyl]-1*H*-benzo[*de*]isoquinoline-1,3(2*H*)-dione (**15y**): yellow solid; (0.57 g, 82.0 %) yield; $[\alpha]_D^{25}$ -39.6 (c=0.2, DMSO); ^{1}H NMR (300 MHz, DMSO-d_6) δ 8.45 (dd, *J* = 11.9, 7.8 Hz, 2H, ArH), 8.29 (d, *J* = 8.5 Hz, 1H, ArH), 7.98 (s, 1H, ArH), 7.70 (m, 2H, ArH, NH), 7.21 (d, *J* = 8.6 Hz, 1H, ArH), 5.27 (s, 2H, $ArCH_2Ar$), 4.42 (s, 3H, 3 OH), 4.32 (d, *J* = 10.3 Hz, 1H, H-1), 4.26 (t, *J* = 7.2 Hz, 2H, H-3, H-4), 3.68 (d, *J* = 11.5 Hz, 1H, H-6b), 3.64 – 3.56 (m, 4H, 2 CH_2), 3.55 – 3.40 (m, 2H, H-2, H-6b), 3.32 – 3.23 (m, 1H, H-5), 3.13 – 3.05 (m, 2H, CH_2), 2.62 – 2.55 (m, 2H, SCH_2), 1.94 – 1.82 (m, 4H, 2 CH_2), 1.79 (s, 3H, NAc), 1.78 – 1.62 (m, 6H, 3 CH_2), 1.54 – 1.40 (m, 2H, CH_2), 1.38 – 1.26 (m, 2H, CH_2), 1.26 – 1.15 (m, 2H, CH_2); ^{13}C NMR (75 MHz, DMSO-d_6) δ 169.02, 163.57, 162.72, 157.05, 143.35, 132.51, 132.08, 130.81, 130.18, 124.56, 124.26, 123.08, 122.19, 113.22, 112.19, 84.23, 81.31, 75.67, 70.67, 61.35, 54.84, 54.66, 49.33, 35.11, 29.68, 29.06, 28.98, 27.89, 27.74, 27.32, 25.56, 23.16; HRMS (ESI) calcd for $C_{35}H_{47}N_6O_7S$ ($M+H^+$) 695.3227, found 695.3223.

1.9 Synthesis of thioglycosyl-naphthalimide derivatives 23a-23c



23a: R_4=CH_2CH_3; **23b**: R_4=$NHCH_3$; **23c**: R_2=CF_3

Scheme S9. Synthesis of glycosylated naphthalimide derivatives **23a-23c**. (i) p-anisaladehyde, NaOH, H_2O; (ii) Py, Ac_2O; (iii) acetone, HCl, H_2O; (iv) Et_3N, CH_2Cl_2, RCOCl for **18a-18b**; Et_3N, CH_2Cl_2, TFAA for **18c**; (v) HBr, CH_3COOH, CH_2Cl_2; (vi) thiourea, acetone; (vii) $Na_2S_2O_5$, CH_2Cl_2, H_2O; (viii) 1,6-dibromoalkane, K_2CO_3, acetone, H_2O; (ix) NaN_3, acetone, H_2O; (x) **12j**, $CuSO_4$, sodium ascorbate, THF, H_2O; (xi) NH_3, MeOH.

Compound **17** was synthesized according to procedures described in the literature[13]. white solid; (60.2 % over three steps) yield; $[\alpha]_D^{25}$ +30.5 (c=1, MeOH); ^{1}H NMR (300 MHz, D_2O) δ 5.91 (d, *J* = 8.8 Hz, 1H, H-1), 5.45 (t, *J* = 9.4 Hz, 1H, H-3), 5.15 (t, *J* = 9.4 Hz, 1H, H-4), 4.29 (dd, *J* = 13.2, 4.5 Hz, 1H, H-6b), 4.18–4.12 (m, 2H, H-6a, H-5), 3.71 (d, *J* = 10.6, 8.8 Hz, 1H, H-2), 2.14, 2.07, 2.02 (3 s, 9H, 3 OAc).

Compounds **18a-18b** were prepared according to published methods[14].

1,3,4,6-tetra-O-acetyl-2-deoxy-2-propionamido-β-D-glucopyranose (**18a**): white solid; (87.3 %) yield; $[\alpha]_D^{25}$ + 67.4 (c=0.5, $CHCl_3$); ^{1}H NMR (300 MHz, $CDCl_3$) δ 5.68 (d, *J* = 8.8 Hz, 1H, H-1), 5.43 (d, *J* = 6.5 Hz, 1H, NH), 5.14 (t, *J* = 9.3 Hz, 1H, H-3), 5.12 (t, *J* = 9.3 Hz, 1H, H-4), 4.32 (d, *J* = 10.3, 8.7 Hz, 1H, H-2), 4.27 (dd, *J* = 12.5, 4.6 Hz, 1H, H-6b), 4.12 (dd, *J* = 12.3, 2.1 Hz, 1H, H-6a), 3.79-3.73 (m, 1H, H-5), 2.12 – 2.06 (m, 5H, CH_2, OAc), 2.05 (s, 3H, OAc), 2.02 (s, 3H, OAc), 0.91 (t, *J* = 7.6 Hz, 3H, CH_3).

1,3,4,6-tetra-O-acetyl-2-deoxy-2-[[(methylamino)carbonyl] amino]-β-D-glucopyranose (**18b**): white solid; (82.5 %) yield; $[\alpha]_D^{25}$ + 35.0 (c=0.5, $CHCl_3$); ^{1}H NMR (300 MHz, $CDCl_3$) δ 5.71 (d, *J* = 8.8 Hz, 1H, H-1), 5.20 (d, *J* = 8.5 Hz, 1H, NH), 5.17-5.14 (m, 2H, H-3, NH), 5.13 (t, *J* = 9.3 Hz, 1H, H-4), 4.25 (dd, *J* = 12.5, 4.6 Hz, 1H, H-6b), 4.17-4.02 (m, 2H, H-6a, H-2), 3.77-3.70 (m, 1H,

H-5), 2.75 – 2.67 (m, 3H, NCH_3), 2.09 (s, 3H, OAc), 2.05 (d, *J* = 7.0 Hz, 3H, OAc), 2.02 (s, 3H, OAc).

Compounds **18c** was prepared according to published methods[15].

1,3,4,6-tetra-O-acetyl-2-deoxy-2-trifluoroacetamido-β-D-glucopyranose (**18c**): white solid; (87.4 %) yield; $[\alpha]_D^{25}$ + 65.2 (c=0.5, $CHCl_3$); ^{1}H NMR (300 MHz, CD_3OD) δ 5.81 (d, *J* = 8.8 Hz, 1H, H-1), 5.30 (t, *J* = 9.4 Hz, 1H, H-3), 5.03 (t, *J* = 9.3 Hz, 1H, H-4), 4.25 (dd, *J* = 12.5, 4.6 Hz, 1H, H-6b), 4.09-4.07 (m, 2H, H-6a, H-2), 3.95-3.87 (m, 1H, H-5), 2.04 (s, 3H, OAc), 2.02 (s, 3H, OAc), 1.98 (s, 3H, OAc), 1.95 (s, 3H, OAc).

A solution of compound **18a-18c** (10 mmol) in anhydrous CH_2Cl_2 (30 mL) at 0°C, then 33% HBr/HOAc was added (8 mL) was added dropwise. The solution was stirred for 3 h at room temperature and the completion of the reaction was confirmed by TLC (petroleum ether/EtOAc, 1:1 v/v) analysis. The reaction was then quenched with chilled H_2O (200 mL), and the mixture was extracted with CH_2Cl_2 (3×100 ml). The organic phase was washed with water (2×40 mL), sat. $NaHCO_3$ (50 mL) and dried over Na_2SO_4. The resulting solution was concentrated to a white foam and carried on without further purification. The resulting white foam was dissolved in 80 mL acetone, and thiourea (0.91 g, 12 mmol) was then added. The mixture was heated to reflux for 4 h until a white precipitate was observed. The solid precipitate was then filtered and washed with acetone (2×20 mL). Subsequently, the precipitate was dissolved in CH_2Cl_2 (60 mL) and H_2O (40 mL), then $Na_2S_2O_5$ (2.1 g, 11.0 mmol) was added. The resulting mixture was stirred vigorously and heated to reflux for 5 h, until TLC (EtOAc) indicated that the reaction was complete. The mixture was extracted with CH_2Cl_2 (3×30 mL). The combined organic layers were dried over Na_2SO_4 and concentrated. Finally, the resulting compounds **19a-19c** were harvested by recrystallized from petroleum ether/EtOAc.

2-Propionamido-3,4,6-tri-O-acetyl-2-deoxy-1-thio-β-D-glucopyranose (**19a**): white solid; (2.3g, 61.5 % over three steps) yield; $[\alpha]_D^{25}$ -20.4 (c=1.0, $CHCl_3$); ^{1}H NMR (300 MHz, DMSO-d_6) δ 7.94 (d, *J* = 9.4 Hz, 1H, NH), 5.06 (t, *J* = 9.8 Hz, 1H, H-3), 4.91 – 4.74 (m, 2H, H-4, H-1), 4.14 (dd, *J* = 12.4, 4.9 Hz, 1H, H-6b), 3.99 (dd, *J* = 12.4, 2.0 Hz, 1H, H-6a), 3.88 – 3.74 (m, 2H, H-5, H-2), 3.35 (d, J = 7.9 Hz, 1H, SH), 2.09 – 1.99 (m, 5H, CH_2, OAc), 1.97 (d, *J* = 7.0 Hz, 3H, OAc), 1.89 (s, 3H, OAc), 0.96 (t, *J* = 7.6 Hz, 3H, CH_3); ^{13}C NMR (75 MHz, DMSO-d_6) δ 173.18, 170.16, 169.69, 169.34, 78.84, 74.96, 73.51, 68.53, 62.14, 55.53, 28.95, 20.64, 20.49, 20.41, 10.02.

2-[[(Methylamino)carbonyl]amino]- 3,4,6- tri- O- acetyl-2- deoxy -1- thio- β-D- glucopyranose (**19b**): white solid; (2.0 g, 52.9 % over three steps) yield; $[\alpha]_D^{25}$ -17.9 (c=1.0, $CHCl_3$); ^{1}H NMR (300 MHz, DMSO-d_6) δ 5.96 (s, 1H, NH), 5.89 (d, *J* = 5.1 Hz, 1H, NH), 5.20 – 5.03 (m, 3H, H-3, H-4, H-1), 4.15 (dd, *J* = 12.2, 4.3 Hz, 1H, H-6b), 4.05 – 3.76 (m, 3H, H-6a, H-2, H-5), 3.26 (s, 1H, SH),

2.48 (d, J = 2.1 Hz, 3H, NCH_3), 1.98 (s, 3H, OAc), 1.94 (s, 3H, OAc), 1.88 (s, 3H, OAc); ^{13}C NMR (75 MHz, DMSO-d_6) δ 172.78, 170.11, 169.60, 161.24, 78.81, 75.03, 73.44, 68.51, 62.07, 55.42, 26.37, 20.62, 20.48, 20.43.

2-Trifluoroacetamido-3,4,6-tri-O-acetyl-2-deoxy-1-thio-β-D-glucopyranose (**19c**): white solid; (2.6 g, 62.3 % over three steps) yield; $[\alpha]_D^{25}$ -63.5 (c=1.0, $CHCl_3$); ^1H NMR (300 MHz, DMSO-d_6) δ 9.67 (d, J = 9.2 Hz, 1H, NH), 5.15 (t, J = 9.8 Hz, 1H, H-3), 4.98 – 4.81 (m, 2H, H-4, H-1), 4.16 (dd, J = 12.5, 4.9 Hz, 1H, H-6b), 4.01 (dd, J = 12.5, 1.7 Hz, 1H, H-6a), 3.97 – 3.82 (m, 2H, H-2, H-5), 3.75 (d, J = 7.5 Hz, 1H, SH), 2.02 (s, 3H, OAc), 1.97 (s, 3H, OAc), 1.91 (s, 3H, OAc); ^{13}C NMR (75 MHz, DMSO-d_6) δ 170.15, 169.70, 169.30, 156.62, 117.67, 113.85, 85.35, 75.43, 72.74, 68.25, 62.01, 52.58, 20.58, 20.42, 20.12.

Compounds **20a-20c** were synthesized from **19a-19c** (3 mmol) using the procedure described for the synthesis of compounds **9a-9d** (from **8a-8b**).

6-Bromohexyl 2-propionamido-3,4,6-tri-O-acetyl-2-deoxy-1-thio-β-D-glucopyranoside (**20a**): white solid; (1.2 g, 74.1 %) yield; $[\alpha]_D^{25}$ -51.7 (c=0.5, $CHCl_3$); ^1H NMR (300 MHz, DMSO-d_6) δ 7.88 (d, J = 9.4 Hz, 1H, NH), 5.06 (t, J = 9.8 Hz, 1H, H-3), 4.82 (t, J = 9.7 Hz, 1H, H-4), 4.66 (d, J = 10.4 Hz, 1H, H-1), 4.13 (dd, J = 12.4, 5.0 Hz, 1H, H-6b), 3.99 (dd, J = 12.1, 1.5 Hz, 1H, H-6a), 3.91 – 3.76 (m, 2H, H-2, H-5), 3.50 (t, J = 6.7 Hz, 2H, CH_2Br), 2.70 – 2.50 (m, 2H, SCH_2), 2.06 – 1.96 (m, 5H, OAc, CH_2), 1.95 (s, 3H, OAc), 1.88 (s, 3H, OAc), 1.82 – 1.70 (m, 2H, CH_2), 1.60 – 1.43 (m, 2H, CH_2), 1.42 – 1.24 (m, 4H, 2 CH_2), 0.94 (t, J = 7.6 Hz, 3H, CH_3); ^{13}C NMR (75 MHz, DMSO-d_6) δ 173.56, 170.17, 169.81, 169.43, 91.00, 70.66, 69.23, 66.60, 62.43, 51.46, 35.06, 32.22, 28.31, 27.41, 27.20, 27.08, 26.29, 20.63, 20.52, 20.47, 10.10; HRMS (ESI) calcd for $C_{21}H_{35}BrNO_8S$ ($M+H^+$) 540.1267, found 540.1256.

6-Bromohexyl 2-[[(methylamino) carbonyl] amino] -3,4,6-tri- O-acetyl- 2-deoxy-1-thio-β-D-glucopyranoside (**20b**): white solid; (1.1 g, 67.9 %) yield; $[\alpha]_D^{25}$ -58.3 (c=0.5, $CHCl_3$); ^1H NMR (300 MHz, $CDCl_3$) δ 5.20 (t, J = 9.7 Hz, 1H, H-3), 5.15 – 4.99 (m, 3H, 2 NH, H-4), 4.65 (d, J = 10.3 Hz, 1H, H-1), 4.25 (dd, J = 12.3, 5.1 Hz, 1H, H-6b), 4.13 (dd, J = 12.5, 2.0 Hz, 1H, H-6a), 3.90 (dd, J = 19.4, 10.0 Hz, 1H, H-2), 3.77 – 3.67 (m, 1H, H-5), 3.41 (t, J = 6.7 Hz, 2H, CH_2Br), 2.80 – 2.65 (m, 5H, NCH_3, SCH_2), 2.09 (s, 3H, OAc), 2.05 (s, 3H, OAc), 2.03 (s, 3H, OAc), 1.94 – 1.77 (m, 2H, CH_2), 1.72 – 1.56 (m, 2H, CH_2), 1.52 – 1.36 (m, 4H, 2 CH_2); ^{13}C NMR (75 MHz, $CDCl_3$) δ 170.12, 169.70, 168.43, 157.33, 84.28, 74.78, 73.47, 67.84, 61.57, 53.44, 32.79, 31.59, 28.99, 28.46, 26.90, 26.67, 26.21, 19.82, 19.79, 19.64; HRMS (ESI) calcd for $C_{20}H_{34}BrN_2O_8S$ ($M+H^+$) 541.1219, found 541.1231.

6-Bromohexyl 2-trifluoroacetamido-3,4,6-tri-O-acetyl-2-deoxy-1-thio-β-D-glucopyranoside (**20c**): white solid; (1.3 g, 74.7 %) yield; $[\alpha]_D^{25}$ -42.6 (c=0.5, $CHCl_3$); ^1H NMR (300 MHz, $CDCl_3$)

δ 7.12 (d, *J* = 9.4 Hz, 1H, NH), 5.33 (t, *J* = 9.8 Hz, 1H, H-3), 5.09 (t, *J* = 9.7 Hz, 1H, H-4), 4.64 (d, *J* = 10.4 Hz, 1H, H-1), 4.26 (dd, *J* = 12.4, 5.0 Hz, 1H, H-6b), 4.22 – 4.11 (m, 2H, H-6a, H-2), 3.89 – 3.74 (m, 1H, H-5), 3.41 (t, *J* = 6.7 Hz, 2H, CH_2Br), 2.81 – 2.61 (m, 2H, SCH_2), 2.10 (s, 3H, OAc), 2.04 (s, 6H, 2 OAc), 1.93 – 1.79 (m, 2H, CH_2), 1.68 – 1.56 (m, 2H, CH_2), 1.51 – 1.34 (m, 4H, 2 CH_2); ^{13}C NMR (75 MHz, $CDCl_3$) δ 171.05, 170.42, 169.00, 83.16, 75.60, 72.89, 68.19, 61.98, 53.06, 33.40, 32.15, 29.32, 28.92, 27.40, 27.23, 20.41, 20.24, 20.07; HRMS (ESI) calcd for $C_{20}H_{30}BrF_3NO_8S$ ($M+H^+$) 580.0828, found 580.0815.

Compounds **21a-21c** were synthesized from **20a-20c** (2 mmol) using the procedure described for the synthesis of compounds **13a-13d** (from **9a-9d**).

6-Azidohexyl 2-propionamido-3,4,6-tri-O-acetyl-2-deoxy-1-thio-β-D-glucopyranoside (**21a**): white solid; (0.82 g, 82.0 %) yield; $[\alpha]_D^{25}$ -59.3 (c=0.5, $CHCl_3$); ^1H NMR (300 MHz, $CDCl_3$) δ 6.07 (d, *J* = 9.3 Hz, 1H, NH), 5.24 (t, *J* = 9.8 Hz, 1H, H-3), 5.09 (t, *J* = 9.7 Hz, 1H, H-4), 4.67 (d, *J* = 10.4 Hz, 1H, H-1), 4.25 (dd, *J* = 12.3, 5.0 Hz, 1H, H-6b), 4.18 – 4.04 (m, 2H, H-6a, H-2), 3.75 (ddd, *J* = 9.9, 4.9, 2.3 Hz, 1H, H-5), 3.27 (t, *J* = 6.8 Hz, 2H, CH_2N_3), 2.80 – 2.60 (m, 2H, SCH_2), 2.25 – 2.13 (m, 2H, CH_2), 2.09 (s, 3H, OAc), 2.03 (s, 6H, 2 OAc), 1.72 – 1.52 (m, 4H, 2 CH_2), 1.49 – 1.32 (m, 4H, 2 CH_2), 1.13 (t, *J* = 7.6 Hz, 3H, CH_3); ^{13}C NMR (75 MHz, $CDCl_3$) δ 173.54, 170.47, 170.23, 168.93, 83.99, 75.41, 73.46, 68.32, 62.09, 52.73, 50.92, 29.39, 29.34, 29.02, 28.29, 27.85, 25.84, 20.32, 20.26, 20.19, 9.42; HRMS (ESI) calcd for $C_{21}H_{35}N_4O_8S$ ($M+H^+$) 503.2176, found 503.2179.

6-Azidohexyl 2-[[(methylamino)carbonyl]amino]-3,4,6-tri-O-acetyl-2-deoxy-1-thio-β-D-glucopyranoside (**21b**): white solid; (0.81 g, 80.5 %) yield; $[\alpha]_D^{25}$ -47.1(c=0.5, $CHCl_3$); ^1H NMR (300 MHz, $CDCl_3$) δ 5.21 (t, *J* = 9.7 Hz, 1H, H-3), 5.16 – 5.04 (m, 2H, H-4, NH), 4.98 (q, *J* = 4.5 Hz, 1H, NH), 4.67 (d, *J* = 10.3 Hz, 1H, H-1), 4.25 (dd, *J* = 12.3, 5.1 Hz, 1H, H-6b), 4.13 (dd, *J* = 12.5, 2.1 Hz, 1H, H-6a), 3.98 – 3.83 (m, 1H, H-2), 3.75 – 3.66 (m, 1H, H-5), 3.27 (t, *J* = 6.8 Hz, 2H, CH_2N_3), 2.82 – 2.66 (m, 5H, NCH_3, SCH_2), 2.08 (s, 3H, OAc), 2.05 (s, 3H, OAc), 2.03 (s, 3H, OAc), 1.66 – 1.51 (m, 4H, 2 CH_2), 1.46 – 1.32 (m, 4H, 2 CH_2); ^{13}C NMR (75 MHz, $CDCl_3$) δ 170.68, 170.30, 169.06, 157.83, 84.92, 75.39, 74.06, 68.52, 62.22, 54.07, 50.97, 29.62, 29.13, 28.34, 27.93, 26.78, 25.90, 20.44, 20.37, 20.25; HRMS (ESI) calcd for $C_{20}H_{34}N_5O_8S$ ($M+H^+$) 504.2128, found 504.2137.

6-Azidohexyl 2-trifluoroacetamido-3,4,6-tri-O-acetyl-2-deoxy-1-thio-β-D-glucopyranoside (**21c**): white solid; (0.88 g, 81.1 %) yield; $[\alpha]_D^{25}$ -66.7(c=0.5, $CHCl_3$); ^1H NMR (300 MHz, $CDCl_3$) δ 7.01 (d, *J* = 9.2 Hz, 1H, NH), 5.30 (t, *J* = 9.8 Hz, 1H, H-3), 5.10 (t, *J* = 9.7 Hz, 1H, H-4), 4.63 (d, *J* = 10.4 Hz, 1H, H-1), 4.26 (dd, *J* = 12.4, 5.0 Hz, 1H, H-6b), 4.22 – 4.10 (m, 2H, H-6a, H-2), 3.78 (ddd, *J* = 10.1, 4.9, 2.4 Hz, 1H, H-5), 3.27 (t, *J* = 6.8 Hz, 2H, CH_2N_3), 2.80 – 2.62 (m, 2H, SCH_2), 2.10 (s, 3H, OAc), 2.04 (s, 6H, 2 OAc), 1.69 – 1.54 (m, 4H, 2 CH_2), 1.48 – 1.32 (m, 4H, 2 CH_2);

^{13}C NMR (75 MHz, $CDCl_3$) δ 170.89, 170.33, 168.95, 157.22, 156.72, 156.22, 120.96, 117.14, 113.33, 83.22, 75.70, 72.88, 68.10, 61.93, 53.18, 50.96, 29.32, 28.92, 28.30, 27.77, 25.83, 20.34, 20.19, 20.02; HRMS (ESI) calcd for $C_{20}H_{30}F_3N_4O_8S$ ($M+H^+$) 543.1736, found 543.1723.

Compounds **22a-22c** were synthesized from **21a-21c** (1 mmol) using the procedure described for the synthesis of compounds **14a-14t** (from **13a-13d**).

6-(Azepan-1-yl)-2- [[1-[6- [(2-propionamido- 3,4,6- tri-O-acetyl-β- D-glucopyranosyl)thio] hex yl]-1*H*-1,2,3-triazol-4-yl]methyl]-1*H*-benzo[*de*]isoquinoline-1,3(2*H*)-dione (**22a**): yellow syrup; (0.62 g, 74.3 %) yield; $[\alpha]_D^{25}$ -67.1 (c=0.5, DMSO); ^{1}H NMR (300 MHz, DMSO-d_6) δ 8.43 – 8.29 (m, 2H, ArH), 8.20 (d, *J* = 8.3 Hz, 1H, ArH), 7.95 (s, 1H, ArH), 7.86 (d, *J* = 9.3 Hz, 1H, NH), 7.61 (t, *J* = 8.0 Hz, 1H, ArH), 7.10 (d, *J* = 8.5 Hz, 1H, ArH), 5.23 (s, 2H, $ArCH_2Ar$), 5.08 (t, *J* = 9.8 Hz, 1H, H-3), 4.83 (t, *J* = 9.7 Hz, 1H, H-3), 4.66 (d, *J* = 10.3 Hz, 1H, H-1), 4.23 (t, *J* = 6.8 Hz, 2H, CH_2), 4.13 (dd, *J* = 12.5, 5.1 Hz, 1H, H-6b), 4.01 – 3.94 (m, 1H, H-6a), 3.92 – 3.73 (m, 2H, H-2, H-5), 3.51 (s, 4H, 2 CH_2), 2.66 – 2.48 (m, 2H, SCH_2), 2.05 – 1.97 (m, 2H, CH_2), 1.96 (s, 6H, 2 OAc), 1.89 (s, 3H, NAc), 1.85 – 1.76 (m, 4H, 2 CH_2), 1.74 – 1.67 (m, 2H, CH_2), 1.66 – 1.57 (m, 4H, 2 CH_2), 1.52 – 1.39 (m, 2H, CH_2), 1.33 – 1.21 (m, 2H, CH_2), 1.18 – 1.09 (m, 2H, CH_2), 0.93 (t, *J* = 7.6 Hz, 3H, CH_3); ^{13}C NMR (75 MHz, DMSO-d_6) δ 172.94, 170.06, 169.71, 169.37, 163.48, 162.64, 156.96, 143.36, 132.40, 131.92, 130.69, 130.07, 124.43, 124.21, 123.11, 122.12, 113.11, 112.19, 83.56, 74.76, 73.88, 68.71, 62.16, 54.80, 52.21, 49.32, 35.05, 29.70, 29.25, 29.15, 28.97, 27.88, 27.60, 27.30, 25.53, 20.55, 20.50, 20.41, 10.04; HRMS (ESI) calcd for $C_{42}H_{55}N_6O_{10}S$ ($M+H^+$) 835.3700, found 835.3713.

6-(Azepan-1-yl)-2-[[1-[6-[[2-[[(methylamino)carbonyl]amino]-3,4,6-tri-O-acetyl-β-D-gluco pyranosyl]thio]hexyl]-1*H*-1,2,3-triazol-4-yl]methyl]-1*H*-benzo[*de*]isoquinoline-1,3(2*H*)-dione (**22b**): yellow syrup; (0.64 g, 76.6 %) yield; $[\alpha]_D^{25}$ -58.2 (c=0.5, DMSO); ^{1}H NMR (300 MHz, DMSO-d_6) δ 8.38 (t, *J* = 7.7 Hz, 2H, ArH), 8.21 (d, *J* = 8.4 Hz, 1H, ArH), 7.95 (s, 1H, ArH), 7.68 – 7.58 (m, 1H, ArH), 7.13 (d, *J* = 8.5 Hz, 1H, ArH), 5.93 – 5.75 (m, 2H, 2 NH), 5.23 (s, 2H, $ArCH_2Ar$), 5.08 (t, *J* = 9.7 Hz, 1H, H-3), 4.80 (t, *J* = 9.7 Hz, 1H, H-4), 4.69 (d, *J* = 10.3 Hz, 1H, H-1), 4.23 (t, *J* = 7.1 Hz, 2H, CH_2), 4.12 (dd, *J* = 12.3, 5.1 Hz, 1H, H-6b), 3.99 – 3.93 (m, 1H, H-6a), 3.85 – 3.76 (m, 1H, H-5), 3.70 (q, *J* = 10.1 Hz, 1H, H-2), 3.61 – 3.48 (m, 4H, 2 CH_2), 2.64 – 2.48 (m, 5H, CH_2, NCH_3), 1.96 (s, 3H, OAc), 1.95 (s, 3H, OAc), 1.89 (s, 3H, OAc), 1.87 – 1.77 (m, 4H, 2 CH_2), 1.76 – 1.67 (m, 2H, CH_2), 1.67 – 1.59 (m, 4H, 2 CH_2), 1.53 – 1.39 (m, 2H, CH_2), 1.34 – 1.22 (m, 2H, CH_2), 1.22 – 1.15 (m, 2H, CH_2); ^{13}C NMR (75 MHz, DMSO-d_6) δ 170.07, 169.79, 169.39, 163.52, 162.67, 157.90, 157.00, 143.36, 132.44, 131.97, 130.73, 130.11, 124.48, 124.23, 123.10, 122.15, 113.16, 112.20, 84.35, 74.55, 74.33, 69.00, 62.26, 59.84, 54.82, 53.36, 49.32, 35.07,

29.70, 29.25, 29.17, 27.89, 27.66, 27.30, 26.50, 25.54, 20.56, 20.52, 20.51; HRMS (ESI) calcd for $C_{41}H_{54}N_7O_{10}S$ ($M+H^+$) 836.3653, found 836.3658.

6-(Azepan-1-yl)-2- [[1-[6- [(2-trifluoroacetamido- 3,4,6- tri-O-acetyl-β- D-glucopyranosyl) thio] hexyl]-1*H*-1,2,3-triazol-4-yl]methyl]-1*H*-benzo[*de*]isoquinoline-1,3(2*H*)-dione (**22c**): yellow syrup; (0.67 g, 76.6 %) yield; $[\alpha]_D^{25}$ -60.9 (c=0.5, DMSO); ^{1}H NMR (300 MHz, DMSO-d_6) δ 9.63 (d, *J* = 9.2 Hz, 1H, NH), 8.36 (t, *J* = 6.9 Hz, 2H, ArH), 8.20 (d, *J* = 8.5 Hz, 1H, ArH), 7.95 (s, 1H, ArH), 7.66 – 7.57 (m, 1H, ArH), 7.11 (d, *J* = 8.6 Hz, 1H, ArH), 5.28 – 5.13 (m, 3H, $ArCH_2Ar$, H-3), 4.91 (t, *J* = 9.7 Hz, 1H, H-4), 4.78 (d, *J* = 10.4 Hz, 1H, H-1), 4.22 (t, *J* = 7.1 Hz, 2H, CH_2), 4.12 (d, *J* = 4.9 Hz, 1H, H-6b), 4.05 – 4.01 (m, 1H, H-6a), 3.97 – 3.80 (m, 2H, H-2, H-5), 3.60 – 3.45 (m, 4H, 2 CH_2), 2.67 – 2.49 (m, 2H, SCH_2), 1.97 (s, 3H, OAc), 1.97 (s, 3H, OAc), 1.90 (s, 3H, OAc), 1.88 – 1.77 (m, 4H, 2 CH_2), 1.76 – 1.67 (m, 2H, CH_2), 1.66 – 1.59 (m, 4H, 2 CH_2), 1.53 – 1.40 (m, 2H, CH_2), 1.34 – 1.21 (m, 2H, CH_2), 1.20 – 1.14 (m, 2H, CH_2); ^{13}C NMR (75 MHz, DMSO-d_6) δ 170.06, 169.66, 169.35, 163.50, 162.65, 156.98, 156.60, 156.12, 143.37, 132.40, 131.93, 130.70, 130.09, 124.44, 124.23, 123.10, 122.14, 117.75, 113.93, 113.13, 112.21, 82.55, 74.95, 73.09, 68.37, 62.03, 59.83, 54.81, 53.05, 49.31, 35.06, 29.69, 29.38, 29.19, 27.88, 27.48, 27.30, 25.50, 20.54, 20.47, 20.17; HRMS (ESI) calcd for $C_{41}H_{50}F_3N_6O_{10}S$ ($M+H^+$) 875.3261, found 875.3247.

Compounds **23a-23c** were synthesized from **22a-22c** (1 mmol) using the procedure described for the synthesis of compounds **15a-15t** (from **14a-14t**).

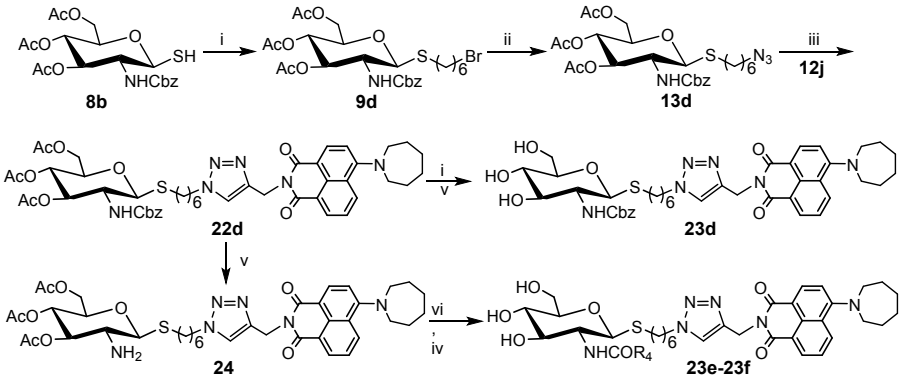
6-(Azepan-1-yl)-2- [[1- [6- [(2-propionamido-β- D-glucopyranosyl) thio] hexyl]-1*H*-1,2,3-triazol-4-yl]methyl]-1*H*-benzo[*de*]isoquinoline-1,3(2*H*)-dione (**23a**): yellow solid; (0.62 g, 87.4 %) yield; $[\alpha]_D^{25}$ -37.2 (c=0.2, DMSO); ^{1}H NMR (300 MHz, DMSO-d_6) δ 8.39 (t, *J* = 8.4 Hz, 2H, ArH), 8.23 (d, *J* = 8.4 Hz, 1H, ArH), 7.94 (s, 1H, ArH), 7.69 – 7.60 (m, 1H, ArH), 7.56 (d, *J* = 9.2 Hz, 1H, NH), 7.14 (d, *J* = 8.5 Hz, 1H, ArH), 5.23 (s, 2H, $ArCH_2Ar$), 4.31 (d, *J* = 10.3 Hz, 1H, H-1), 4.22 (t, *J* = 7.1 Hz, 2H, H-3, H-4), 3.66 (d, *J* = 11.5 Hz, 1H, H-6b), 3.58 – 3.51 (m, 4H, 2 CH_2), 3.50 – 3.36 (m, 2H, H-2, H-6a), 3.32 – 3.22 (m, 1H, H-5), 3.12 – 3.02 (m, 2H, CH_2), 2.62 – 2.50 (m, 2H, SCH_2), 2.03 (q, *J* = 7.5 Hz, 2H, $C\underline{H_2}CH_3$), 1.92 – 1.78 (m, 4H, 2 CH_2), 1.76 – 1.67 (m, 2H, CH_2), 1.67 – 1.57 (m, 4H, 2 CH_2), 1.50 – 1.36 (m, 2H, CH_2), 1.34 – 1.22 (m, 2H, CH_2), 1.20 – 1.09 (m, 2H, CH_2), 0.96 (t, *J* = 7.6 Hz, 3H, CH_3); ^{13}C NMR (75 MHz, DMSO-d_6) δ 172.74, 163.53, 162.68, 157.01, 143.34, 132.46, 132.02, 130.76, 130.13, 124.51, 124.22, 123.10, 122.14, 113.16, 112.16, 84.27, 81.32, 75.64, 70.71, 61.37, 54.81, 54.50, 49.33, 35.09, 29.70, 29.02, 28.97, 27.88, 27.71, 27.31, 25.56, 9.94; HRMS (ESI) calcd for $C_{36}H_{49}N_6O_7S$ ($M+H^+$) 709.3383, found 709.3389.

6-(Azepan-1-yl)-2-[[1-[6-[[2-[[(methylamino)carbonyl] amino]-β-D-gluco pyranosyl]thio]hex yl]-1*H*-1,2,3-triazol-4-yl]methyl]-1*H*-benzo[*de*]isoquinoline-1,3(2*H*)-dione (**23b**): yellow solid; (0.61 g, 85.9 %) yield; $[\alpha]_D^{25}$ -30.3 (c=0.2, DMSO); ^{1}H NMR (300 MHz, DMSO-d_6) δ 8.39 (t, *J* =

8.3 Hz, 2H, ArH), 8.22 (d, *J* = 8.5 Hz, 1H, ArH), 7.95 (s, 1H, ArH), 7.69 – 7.57 (m, 1H, ArH), 7.14 (d, *J* = 8.6 Hz, 1H, ArH), 5.82 (d, *J* = 8.5 Hz, 1H, NH), 5.72 (d, *J* = 4.6 Hz, 1H, NH), 5.23 (s, 2H, $ArCH_2Ar$), 4.33 (d, *J* = 9.8 Hz, 1H, H-1), 4.22 (t, *J* = 7.1 Hz, 2H, H-3, H-4), 3.65 (d, *J* = 11.5 Hz, 1H, H-6b), 3.59 – 3.49 (m, 4H, 2 CH_2), 3.40 (dd, *J* = 11.3, 4.3 Hz, 1H, H-6a), 3.35 – 3.25 (m, 1H, H-2), 3.24 – 3.18 (m, 1H, H-5), 3.10 – 3.01 (m, 2H, CH_2), 2.59 – 2.50 (m, 5H, CH_2, NCH_3), 1.90 – 1.78 (m, 4H, 2 CH_2), 1.75 – 1.68 (m, 2H, CH_2), 1.67 – 1.57 (m, 4H, 2 CH_2), 1.51 – 1.35 (m, 2H, CH_2), 1.33 – 1.22 (m, 2H, CH_2), 1.20 – 1.09 (m, 2H, CH_2); ^{13}C NMR (75 MHz, DMSO-d_6) δ 169.65, 163.54, 162.69, 158.65, 157.01, 143.34, 132.47, 132.03, 130.77, 130.13, 124.51, 124.22, 123.10, 122.15, 113.17, 112.16, 84.77, 81.10, 76.55, 70.96, 61.42, 55.69, 54.81, 49.33, 35.09, 29.69, 29.03, 27.88, 27.79, 27.31, 26.53, 25.57, 22.56; HRMS (ESI) calcd for $C_{35}H_{47}N_7NaO_7S$ ($M+Na^+$) 732.3155 found 732.3152.

6-(Azepan-1-yl)-2- [[1- [6- [(2-trifluoroacetamido -β- D-glucopyranosyl) thio] hex yl]-1*H*-1,2,3-triazol-4-yl]methyl]-1*H*-benzo[*de*]isoquinoline-1,3(2*H*)-dione (**23c**): yellow syrup; (0.45 g, 60.1 %) yield; $[\alpha]_D^{25}$ -39.1 (c=0.2, DMSO); ^1H NMR (300 MHz, DMSO-d_6) δ 9.25 (d, *J* = 9.2 Hz, 1H, NH), 8.46 (dd, *J* = 11.7, 7.9 Hz, 2H, ArH), 8.30 (d, *J* = 8.5 Hz, 1H, ArH), 7.98 (s, 1H, ArH), 7.72 – 7.67 (m, 1H, ArH), 7.22 (d, *J* = 8.6 Hz, 1H, ArH), 5.41 – 5.24 (m, 3H, $ArCH_2Ar$, OH), 5.16 (s, 1H, OH), 4.58 (s, 1H, OH), 4.48 (d, *J* = 10.2 Hz, 1H, H-1), 4.26 (t, *J* = 7.2 Hz, 2H, H-3, H-4), 3.78 – 3.66 (m, 1H, H-6b), 3.65 – 3.59 (m, 4H, 2 CH_2), 3.59 – 3.52 (m, 1H, H-6a), 3.51 – 3.41 (m, 2H, H-2, H-5), 3.19 – 3.08 (m, 2H, CH_2), 2.66 – 2.57 (m, 2H, SCH_2), 1.94 – 1.86 (m, 4H, 2 CH_2), 1.78 – 1.73 (m, 2H, CH_2), 1.72 – 1.66 (m, 4H, 2 CH_2), 1.55 – 1.41 (m, 2H, CH_2), 1.38 – 1.26 (m, 2H, CH_2), 1.25 – 1.17 (m, 2H, CH_2); ^{13}C NMR (75 MHz, DMSO-d_6) δ 163.62, 162.77, 157.11, 143.36, 132.57, 132.17, 130.87, 130.25, 124.63, 124.32, 123.06, 122.26, 114.24, 113.29, 112.23, 82.99, 81.48, 74.64, 70.42, 61.16, 55.43, 54.86, 49.32, 35.13, 29.66, 29.11, 28.99, 27.89, 27.59, 27.33, 25.54; HRMS (ESI) calcd for $C_{35}H_{44}F_3N_6O_7S$ ($M+H^+$) 749.2944 found 749.2927.

1.10 Synthesis of thioglycosyl-naphthalimide derivatives 23d-23f.



23e: R_4=$CH_2CH_2CH_3$; **23f**: R_4=$CH(CH_3)_2$

Scheme S10. Synthesis of glycosylated naphthalimide derivatives **23d-23f**. (i) 1,6-dibromoalkane, K_2CO_3, acetone,

H_2O; (ii) NaN_3, acetone, H_2O; (iii) **12j**, $CuSO_4$, sodium ascorbate, THF, H_2O; (iv) NH_3, MeOH; (v) Pd/C, H_2, THF, MeOH, HCl; (vi) R_4COCl, Et_3N, CH_2Cl_2, DMAP.

Compound **22d** was synthesized from **13d** (1 mmol) using the procedure described for the synthesis of compounds **14a-14t** (from **13a-13d**).

6-(Azepan-1-yl)-2-[[1-[6-[[2-[[(phenylmethoxy)carbonyl]amino]-3,4,6-tri-O-acetyl-β-D-glu copyranosyl]thio]hexyl]-1*H*-1,2,3-triazol-4-yl]methyl]-1*H*-benzo[*de*]isoquinoline-1,3(2*H*)-dione (**22d**): yellow syrup; (0.78 g, 85.4 %) yield; $[\alpha]_D^{25}$ -72.4 (c=0.5, DMSO); ^{1}H NMR (300 MHz, DMSO-d_6) δ 8.45 (dd, J = 10.1, 8.0 Hz, 2H, ArH), 8.28 (d, J = 8.4 Hz, 1H, ArH), 8.00 (s, 1H, ArH), 7.74 – 7.63 (m, 1H, ArH), 7.48 (d, J = 9.6 Hz, 1H, NH), 7.39 – 7.24 (m, 5H, ArH), 7.20 (d, J = 8.5 Hz, 1H, ArH), 5.27 (s, 2H, $ArCH_2Ar$), 5.14 – 4.96 (m, 3H, OCH_2, H-3), 4.87 (t, J = 9.8 Hz, 1H, H-4), 4.65 (d, J = 10.3 Hz, 1H, H-1), 4.26 (t, J = 7.1 Hz, 2H, CH_2), 4.15 (dd, J = 12.3, 5.0 Hz, 1H, H-6b), 4.03 – 3.95 (m, 1H, H-6a), 3.83 – 3.73 (m, 1H, H-5), 3.69 – 3.54 (m, 5H, H-2, 2 CH_2), 2.68 – 2.52 (m, 2H, SCH_2), 2.00 (s, 3H, OAc), 1.98 (s, 3H, OAc), 1.86 (s, 7H, OAc, 2 CH_2), 1.78 – 1.61 (m, 6H, 3 CH_2), 1.56 – 1.40 (m, 2H, CH_2), 1.36 – 1.25 (m, 2H, CH_2), 1.24 – 1.18 (m, 2H, CH_2); ^{13}C NMR (75 MHz, DMSO-d_6) δ 170.08, 169.63, 169.38, 163.56, 162.71, 157.04, 155.86, 137.28, 132.49, 132.05, 130.79, 130.17, 128.36, 127.79, 127.41, 124.53, 124.27, 122.20, 113.20, 112.22, 83.77, 74.77, 73.88, 68.72, 65.37, 62.11, 59.85, 54.83, 54.56, 49.34, 35.13, 29.67, 29.32, 29.13, 27.88, 27.58, 27.32, 25.53, 20.58, 20.51, 20.38; HRMS (ESI) calcd for $C_{47}H_{57}N_6O_{11}S$ ($M+H^+$) 913.3806 found 913.3817.

Compound **23d** was synthesized from **22d** (1 mmol) using the procedure described for the synthesis of compounds **15a-15t** (from **14a-14t**).

6-(Azepan-1-yl)-2-[[1-[6-[[2-[[(phenylmethoxy)carbonyl]amino]-β-D-glucopyranosyl]thio] hexyl]-1*H*-1,2,3-triazol-4-yl]methyl]-1*H*-benzo[*de*]isoquinoline-1,3(2*H*)-dione (**23d**): yellow solid; (0.65 g, 82.6 %) yield; $[\alpha]_D^{25}$ -27.2 (c=0.2, DMSO); ^{1}H NMR (300 MHz, DMSO-d_6) δ 8.46 (dd, J = 12.6, 7.9 Hz, 2H, ArH), 8.30 (d, J = 8.5 Hz, 1H, ArH), 7.97 (s, 1H, ArH), 7.79 – 7.62 (m, 1H, ArH), 7.40 – 7.20 (m, 6H, ArH), 7.18 (d, J = 8.8 Hz, 1H, NH), 5.27 (s, 2H, $ArCH_2Ar$), 5.13 – 4.90 (m, 4H, H-3, H-4, H-1, OH), 4.50 (t, J = 5.5 Hz, 1H, OH), 4.32 (d, J = 9.8 Hz, 1H, OH), 4.24 (t, J = 7.1 Hz, 2H, $PhCH_2$), 3.67 (dd, J = 11.6, 5.2 Hz, 1H, H-6b), 3.64 – 3.54 (m, 4H, H-6a, H-2, CH_2), 3.50 – 3.38 (m, 1H, H-5), 3.30 – 3.20 (m, 2H, CH_2), 3.15 – 2.99 (m, 2H, CH_2), 2.75 – 2.52 (m, 2H, SCH_2), 2.00 – 1.82 (m, 4H, 2 CH_2), 1.77 – 1.60 (m, 6H, 3 CH_2), 1.56 – 1.38 (m, 2H, CH_2), 1.36 – 1.25 (m, 2H, CH_2), 1.23 – 1.10 (m, 2H, CH_2); ^{13}C NMR (75 MHz, DMSO) δ 163.59, 162.75, 157.08,

156.11, 143.35, 137.44, 132.53, 132.11, 130.84, 130.21, 128.32, 127.71, 127.59, 124.59, 124.29, 123.09, 122.23, 113.25, 112.23, 84.44, 81.33, 75.51, 70.72, 65.13, 61.32, 56.77, 54.85, 49.33, 35.12, 29.68, 29.07, 28.95, 27.89, 27.72, 27.33, 25.58; HRMS (ESI) calcd for $C_{41}H_{51}N_6O_8S$ ($M+H^+$) 787.3489 found 787.3482.

To a solution of compound **23d** (0.91 g, 1 mmol) and 10% Pd/C (0.1 g) in THF/MeOH (1:1, 30 mL), a drop of concentrated HCl was added. The reaction was then stirred vigorously under hydrogen atmosphere for 12 h at room temperature, the completion of the reaction was confirmed by TLC (DCM /MeOH, 15:1 v/v) analysis. The reaction mixture was filtered through celite. The filtrate was concentrated under reduced pressure to afford compound **24** (0.65 g, 83.4%) as a yellow syrup. $[\alpha]_D^{25}$ -45.5 (c=0.5, DMSO); ^{1}H NMR (300 MHz, $CDCl_3$) δ 8.57 (d, *J* = 7.2 Hz, 1H, ArH), 8.44 (dd, *J* = 8.1, 4.4 Hz, 2H, ArH), 7.60 (t, *J* = 7.9 Hz, 2H, ArH), 7.13 (d, *J* = 8.4 Hz, 1H, ArH), 5.48 (s, 2H, $ArCH_2Ar$), 5.06 – 4.91 (m, 2H, H-3, H-4), 4.30 – 4.20 (m, 3H, H-1, H-2, H-6b), 4.08 (d, *J* = 9.7 Hz, 1H, H-6a), 3.73 – 3.63 (m, 1H, H-5), 3.62 – 3.53 (m, 4H, 2 CH_2), 2.77 – 2.53 (m, 4H, 2 CH_2), 2.07 (s, 3H, OAc), 2.04 (s, 3H, OAc), 2.01 (s, 3H, OAc), 1.98 – 1.89 (m, 4H, 2 CH_2), 1.89 – 1.81 (m, 2H, CH_2), 1.81 – 1.73 (m, 4H, 2 CH_2), 1.66 – 1.53 (m, 2H, CH_2), 1.45 – 1.35 (m, 2H, CH_2), 1.35 – 1.24 (m, 4H, NH_2, CH_2); HRMS (ESI) calcd for $C_{39}H_{51}N_6O_9S$ ($M+H^+$) 779.3438 found 779.3431.

A solution of **24** (0.78 g, 1 mmol) in dry CH_2Cl_2 (20 mL) was mixed with Et_3N (0.15 g, 1.5 mmol) and DMAP (0.05 g, 0.41 mmol) at 0 ℃ in a N_2 environment, R_4COCl (1.1 mmol) in dry CH_2Cl_2 (20 mL) was added dropwise. The resultant mixture was stirred for 5 h, and the completion of the reaction was confirmed by TLC (DCM /MeOH, 20:1 v/v) analysis. The reaction was then quenched with chilled H_2O (100 mL), and extracted with CH_2Cl_2 (2×50 mL). The organic phases were combined, dried over Na_2SO_4, and concentrated. The residue was purified by flash column chromatography to yield acetyl-protected precursors.

6-(Azepan-1-yl)-2- [[1-[6- [(2-butyryl- 3,4,6-tri-O-acetyl-β- D-glucopyranosyl)thio] hexyl]-1*H*-1,2,3-triazol-4-yl]methyl]-1*H*-benzo[*de*]isoquinoline-1,3(2*H*)-dione: yellow syrup; (0.67 g, 81.6 %) yield; $[\alpha]_D^{25}$ -48.3 (c=0.5, DMSO); ^{1}H NMR (300 MHz, DMSO-d_6) δ 8.39 (dd, *J* = 12.6, 5.3 Hz, 2H, ArH), 8.23 (d, *J* = 8.4 Hz, 1H, ArH), 7.99 – 7.82 (m, 2H, ArH, NH), 7.70 – 7.58 (m, 1H, ArH), 7.15 (d, *J* = 8.6 Hz, 1H, ArH), 5.23 (s, 2H, $ArCH_2Ar$), 5.07 (t, *J* = 9.7 Hz, 1H, H-3), 4.82 (t, *J* = 9.7 Hz, 1H, H-4), 4.64 (d, *J* = 10.4 Hz, 1H, H-1), 4.23 (t, *J* = 6.9 Hz, 2H, CH_2), 4.13 (dd, *J* = 12.3, 4.8 Hz, 1H, H-6b), 4.00 – 3.94 (m, 1H, H-6a), 3.92 – 3.73 (m, 2H, H-2, H-5), 3.62 – 3.48 (m, 4H, 2 CH_2), 2.65 – 2.48 (m, 2H, SCH_2), 1.97 (s, 3H, OAc), 1.96 – 1.91 (m, 5H, CH_2, OAc), 1.88 (s, 3H, OAc), 1.87 – 1.78 (m, 4H, 2 CH_2), 1.76 – 1.57 (m, 6H, 3 CH_2), 1.54 – 1.34 (m, 4H, 2 CH_2),

1.33 – 1.21 (m, 2H, CH_2), 1.18 – 1.10 (m, 2H, CH_2), 0.78 (t, *J* = 7.4 Hz, 3H, CH_3); ^{13}C NMR (75 MHz, DMSO-d_6) δ 171.95, 170.08, 169.66, 169.38, 163.53, 162.68, 157.02, 143.36, 132.46, 132.02, 130.76, 130.14, 124.51, 124.25, 123.09, 122.17, 113.18, 112.21, 83.59, 74.73, 73.82, 68.78, 62.15, 54.83, 52.06, 49.32, 37.65, 29.70, 29.22, 29.13, 27.89, 27.59, 27.31, 25.53, 20.58, 20.52, 20.46, 18.74, 13.51; HRMS (ESI) calcd for $C_{43}H_{57}N_6O_{10}S$ ($M+H^+$) 849.3857 found 849.3855.

6-(Azepan-1-yl)-2- [[1-[6- [(2-isobutyryl- 3,4,6-tri-O-acetyl-β- D-glucopyranosyl)thio] hexyl]-1*H*-1,2,3-triazol-4-yl]methyl]-1*H*-benzo[*de*]isoquinoline-1,3(2*H*)-dione: yellow syrup; (0.63 g, 76.7 %) yield; $[\alpha]_D^{25}$ -45.9 (c=0.5, DMSO); ^{1}H NMR (300 MHz, DMSO-d_6) δ 8.58 – 8.39 (m, 2H, ArH), 8.28 (d, *J* = 8.5 Hz, 1H, ArH), 7.95 (s, 1H, ArH), 7.82 (d, *J* = 9.5 Hz, 1H, NH), 7.73 – 7.67 (m, 1H, ArH), 7.21 (d, *J* = 8.6 Hz, 1H, ArH), 5.24 (s, 2H, $ArCH_2Ar$), 5.06 (t, *J* = 9.8 Hz, 1H, H-3), 4.81 (t, *J* = 9.7 Hz, 1H, H-4), 4.64 (d, *J* = 10.4 Hz, 1H, H-1), 4.24 (t, *J* = 7.1 Hz, 2H, CH_2), 4.12 (dd, *J* = 12.4, 5.0 Hz, 1H, H-6b), 3.97 (dd, *J* = 12.0, 1.7 Hz, 1H, H-6a), 3.89 – 3.73 (m, 2H, H-2, H-5), 3.67 – 3.52 (m, 4H, 2 CH_2), 2.63 – 2.49 (m, 2H, SCH_2), 2.28 – 2.15 (m, 1H, C<u>H</u>CH_3), 1.96 (s, 3H, OAc), 1.95 (s, 3H, OAc), 1.91 – 1.80 (m, 7H, OAc, 2 CH_2), 1.75 – 1.61 (m, 6H, 3 CH_2), 1.55 – 1.41 (m, 2H, CH_2), 1.33 – 1.24 (m, 2H, CH_2), 1.23 – 1.16 (m, 2H, CH_2), 0.92 (d, *J* = 2.3 Hz, 3H, CH_3), 0.89 (d, *J* = 2.8 Hz, 3H, CH_3); ^{13}C NMR (75 MHz, DMSO-d_6) δ 175.92, 170.10, 169.69, 169.37, 163.59, 162.75, 157.09, 143.37, 132.54, 132.14, 131.62, 130.85, 130.23, 128.78, 124.60, 124.31, 123.07, 122.24, 113.26, 112.24, 83.52, 74.77, 73.85, 68.66, 65.13, 62.16, 54.86, 51.95, 49.32, 34.42, 30.13, 29.70, 29.13, 27.89, 27.56, 27.33, 25.52, 20.60, 20.53, 20.42, 19.52, 19.15; HRMS (ESI) calcd for $C_{42}H_{57}N_6O_9S$ ($M+H^+$) 849.3857 found 849.3848.

Compounds **23e-23f** were synthesized by deacetylation of acetyl-protected precursors (1 mmol) using the procedure described for the synthesis of compounds **15a-15t** (from 14a-14t).

6-(Azepan-1-yl)-2- [[1- [6- [(2-butyryl-β- D-glucopyranosyl)thio] hexyl]-1*H*-1,2,3-triazol-4-yl]methyl]-1*H*-benzo[*de*]isoquinoline-1,3(2*H*)-dione (**23e**): yellow solid; (0.60 g, 83.0 %) yield; $[\alpha]_D^{25}$ -28.3 (c=0.2, DMSO); ^{1}H NMR (300 MHz, DMSO-d_6) δ 8.40 (dd, *J* = 9.6, 8.0 Hz, 2H, ArH), 8.23 (d, *J* = 8.5 Hz, 1H, ArH), 7.95 (s, 1H, ArH), 7.71 – 7.54 (m, 2H, NH, ArH), 7.15 (d, *J* = 8.6 Hz, 1H, ArH), 5.23 (s, 2H, $ArCH_2Ar$), 4.98 (s, 1H, OH), 4.90 (d, *J* = 5.2 Hz, 1H, OH), 4.49 (s, 1H, OH), 4.30 (d, *J* = 10.3 Hz, 1H, H-1), 4.22 (t, *J* = 7.1 Hz, 2H, H-3, H-4), 3.66 (dd, *J* = 12.2, 3.0 Hz, 1H, H-6b), 3.61 – 3.53 (m, 4H, 2 CH_2), 3.52 – 3.37 (m, 2H, H-2, H-6a), 3.30 – 3.20 (m, 1H, H-5), 3.12 – 3.00 (m, 2H, CH_2), 2.63 – 2.50 (m, 2H, SCH_2), 1.99 (t, *J* = 7.1 Hz, 2H, CH_2), 1.90 – 1.77 (m, 4H, 2 CH_2), 1.74 – 1.58 (m, 6H, 3 CH_2), 1.55 – 1.35 (m, 4H, 2 CH_2), 1.35 – 1.22 (m, 2H, CH_2), 1.22 – 1.08 (m, 2H, CH_2), 0.83 (t, *J* = 7.4 Hz, 3H, CH_3); ^{13}C NMR (75 MHz, DMSO-d_6) δ 171.88, 163.55, 162.70, 157.02, 143.35, 132.48, 132.04, 130.78, 130.15, 124.53, 124.24, 123.09, 122.16, 113.19,

112.18, 84.23, 81.32, 75.66, 70.75, 61.36, 54.82, 54.45, 49.33, 37.93, 35.09, 29.72, 28.95, 27.88, 27.71, 27.32, 25.57, 18.78, 13.75; HRMS (ESI) calcd for $C_{37}H_{51}N_6O_7S$ ($M+H^+$) 723.3540 found 723.3546.

6-(Azepan-1-yl)-2- [[1- [6- [(2-isobutyryl-β- D-glucopyranosyl)thio] hexyl]-1*H*-1,2,3- triazol-4-yl]methyl]-1*H*-benzo[*de*]isoquinoline-1,3(2*H*)-dione (**23f**): yellow solid; (0.59 g, 81.6 %) yield; $[\alpha]_D^{25}$ -32.7 (c=0.2, DMSO); ^{1}H NMR (300 MHz, DMSO-d_6) δ 8.54 – 8.39 (m, 2H, ArH), 8.29 (d, *J* = 8.5 Hz, 1H, ArH), 7.95 (s, 1H, ArH), 7.70 (dd, *J* = 8.5, 7.4 Hz, 1H, ArH), 7.51 (d, *J* = 9.3 Hz, 1H, NH), 7.22 (d, *J* = 8.6 Hz, 1H, ArH), 5.25 (s, 2H, $ArCH_2Ar$), 4.98 (d, *J* = 4.8 Hz, 1H, OH), 4.88 (d, *J* = 5.6 Hz, 1H, OH), 4.48 (t, *J* = 5.8 Hz, 1H, OH), 4.31 (d, *J* = 10.3 Hz, 1H, H-1), 4.23 (t, *J* = 7.1 Hz, 2H, H-3, H-4), 3.69 – 3.55 (m, 5H, H-6b, 2 CH_2), 3.53 – 3.35 (m, 2H, H-2, H-6a), 3.30 – 3.19 (m, 1H, H-5), 3.09 – 3.00 (m, 2H, CH_2), 2.60 – 2.49 (m, 2H, SCH_2), 2.34 – 2.19 (m, 1H, C<u>H</u>CH_3), 1.94 – 1.79 (m, 4H, 2 CH_2), 1.78 – 1.61 (m, 6H, 3 CH_2), 1.52 – 1.35 (m, 2H, CH_2), 1.33 – 1.22 (m, 2H, CH_2), 1.21 – 1.09 (m, 2H, CH_2), 0.97 (d, *J* = 3.4 Hz, 3H, CH_3), 0.94 (d, *J* = 3.3 Hz, 3H, CH_3); ^{13}C NMR (75 MHz, DMSO-d_6) δ 175.81, 163.60, 162.76, 157.10, 143.35, 132.55, 132.15, 130.86, 130.23, 124.61, 124.30, 123.07, 122.24, 113.27, 112.23, 84.26, 81.35, 75.58, 70.75, 61.36, 54.86, 54.24, 49.33, 35.13, 34.46, 29.71, 28.96, 27.89, 27.67, 27.33, 25.57, 19.79, 19.36; HRMS (ESI) calcd for $C_{37}H_{51}N_6O_7S$ ($M+H^+$) 723.3540 found 723.3549.

2. Molecular docking and MD simulations results

2.1 The binding mode of inhibitor 15b with OfHex1

To further explain the SAR results, the additional compound **15b** was selected for molecular docking and MD simulations. Inhibitors **15b** and **15r** possess the same parent structure, the difference is that **15b** bearing a 4-bromo substituent on naphthalimide and **15r** bearing a large 4-piperidyl group. In order to reveal the basis for the similar potency of **15b** and **15r** against OfHex1, the conformations of **15b** (red colored carbon atoms) and **15r** (green colored carbon atoms) with OfHex1 at 30 ns of MD simulations have been superimposed (Figure S1a). Both of the naphthalimide moieties of **15b** and **15r** could bind well at the +1 subsite of OfHex1 pocket, forming π-π stacking interactions with Trp490 and van der Waals interactions with Val327. Howerver, the naphthalimide moieties showed the different conformations affected by the 4-position substituents (Figure S1a). Specifically, the naphthalimide moiety of **15r** rotated anticlockwise around 90°

relative to the naphthalimide moiety of **15b**, resulting in the triazole ring of **15r** could bind deeper into active pocket and formed the H-bonding interaction with Tyr475 at a distance of 2.1 Å. As a comparison, the triazole ring of **15b** was closer to the +1 subsite and formed the H-bonding interaction with Trp490 at a distance of 2.6 Å (Figures S1a and S1b). On the other hand, the glycosyl moieties of **15b** and **15r** bound to -1 subsite of OfHex1 pocket at the similar depth, but exhibited different binding patterns. The glycosyl moieties of **15b** formed four hydrogen bonds fewer than that of **15r** (five hydrogen bonds) with residues Arg220, Glu297 (Figures 3d and S1b). On the basis of these observations, **15b** (IC_{50}= 8.3 μM) ultimately displayed the slightly lower inhibitory potency against OfHex1 than **15r** (IC_{50}= 6.4 μM).

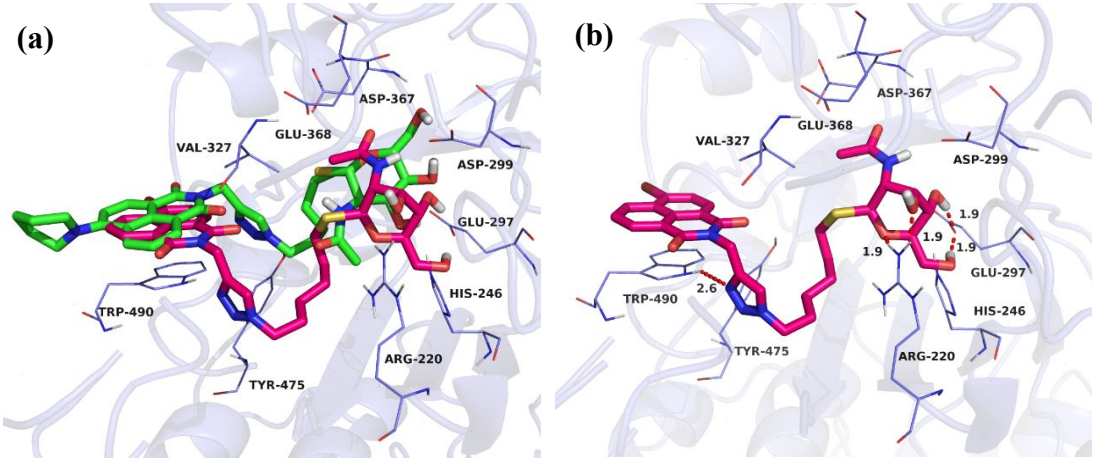


Figure S1. (a) Superimposition of the conformations of **15b** (red colored carbon atoms) and **15r** (green colored carbon atoms) with OfHex1 after 30 ns of MD simulations. (b) Specific binding mode of **15b** with OfHex1 after 30 ns of MD simulations.

2.2 The binding modes of inhibitor 15y with HsHexB and hOGA

To investigate the basis for the selectivity of these glycosylated naphthalimides against OfHex1, the binding modes of the representative compound **15y** with HsHexB and hOGA were performed using molecular docking. The complex crystal structures of HsHexB-pyrimethamine (PDB ID: 3LMY)[16] and hOGA-PUGNAc-type inhibitor (PDB ID: 5M7T)[17] were used as the starting model for molecular docking employing the Sybyl Software (Version 7.3). As shown in Figure S2a, the glycosyl moiety of **15y** bound to the -1 subsite of HsHexB pocket and only interacted with the residue Arg 211. The triazole-linked naphthalimide group extended out from the active pocket, and the oxygen of naphthalimide group formed hydrogen bond with Ser427. As shown in Figure S2b,

the glycosyl moiety of **15y** also buried at the -1 subsite of hOGA pocket and formed two hydrogen bonds with Tyr219 and Asp285, and the naphthalimide group interacted with residues outside the pocket. These results suggested that **15y** could not bind well with HsHexB and hOGA, which explained the basis for the lower inhibitory potencies of **15y** towards HsHexB and hOGA. Accordingly, compound **15y** (IC_{50} = 3.1 μM against OfHex1, IC_{50} >100 μM against HsHexB, IC_{50} = 90.5 μM against hOGA) exhibited excellent selectivity against OfHex1 over HsHex and hOGA.

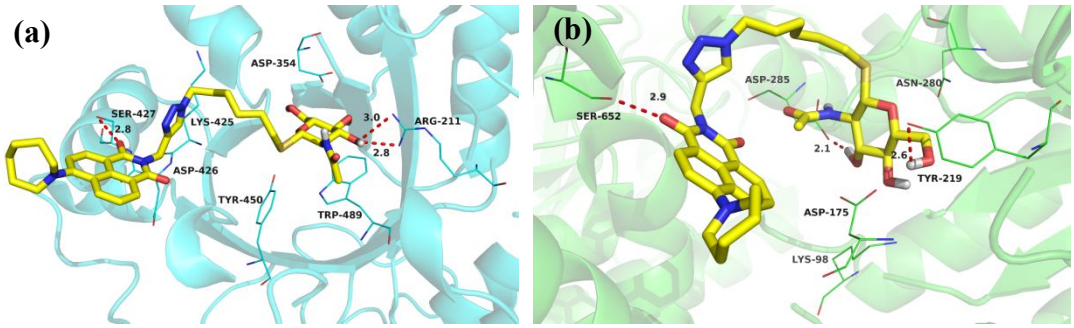


Figure S2. Specific binding mode of **15y** with HsHexB (a) and hOGA (b) revealed by molecular docking.

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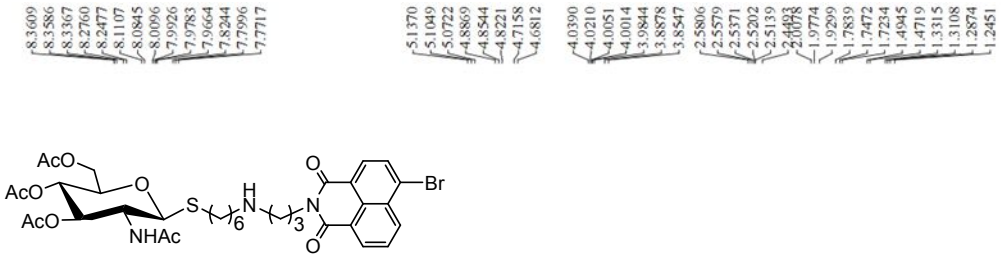
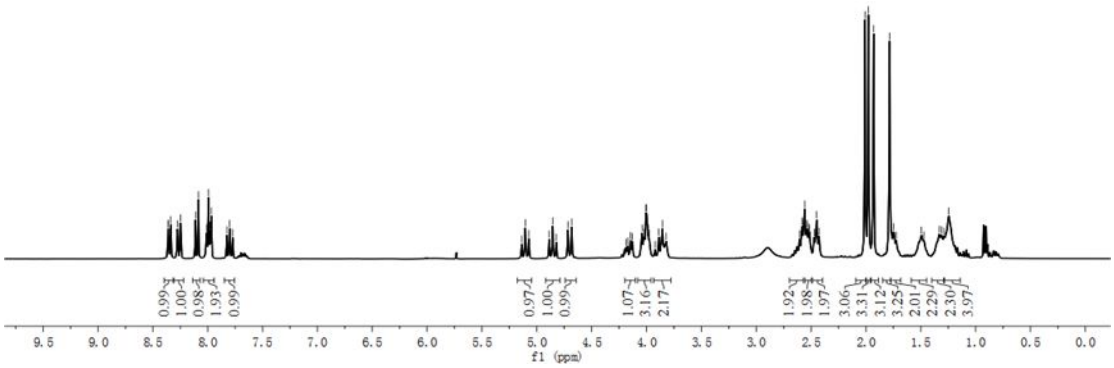
^{1}H NMR and ^{13}C NMR spectrum

^{1}H NMR spectrum of 10a (300 MHz, DMSO-d_6)





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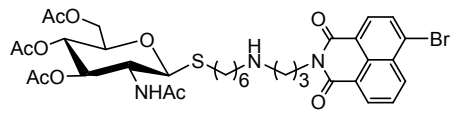

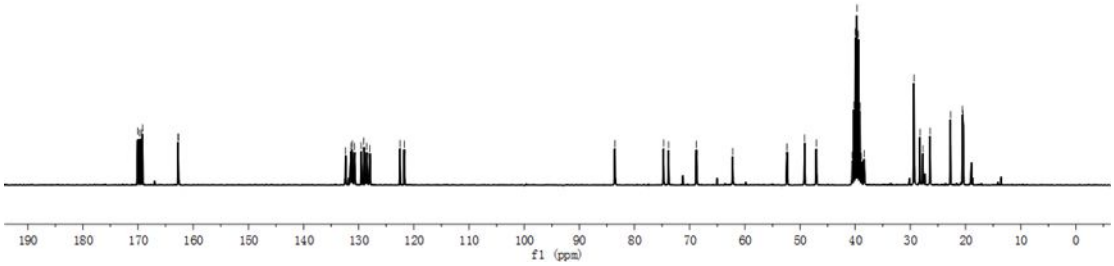

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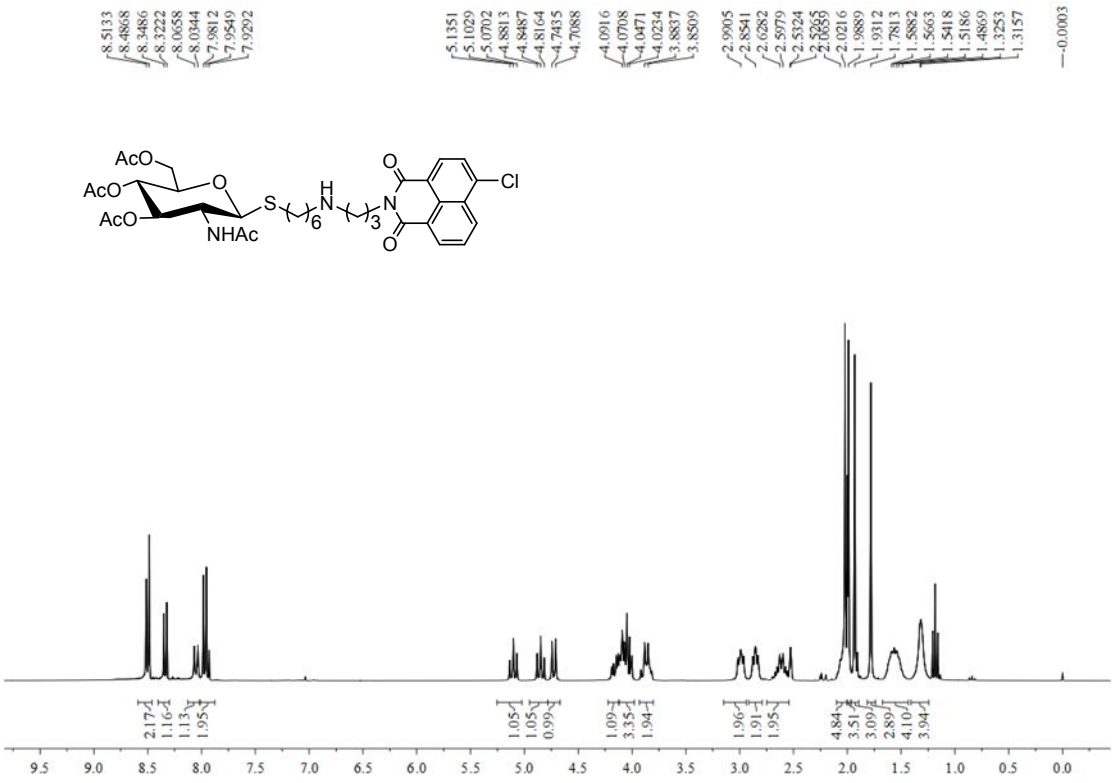

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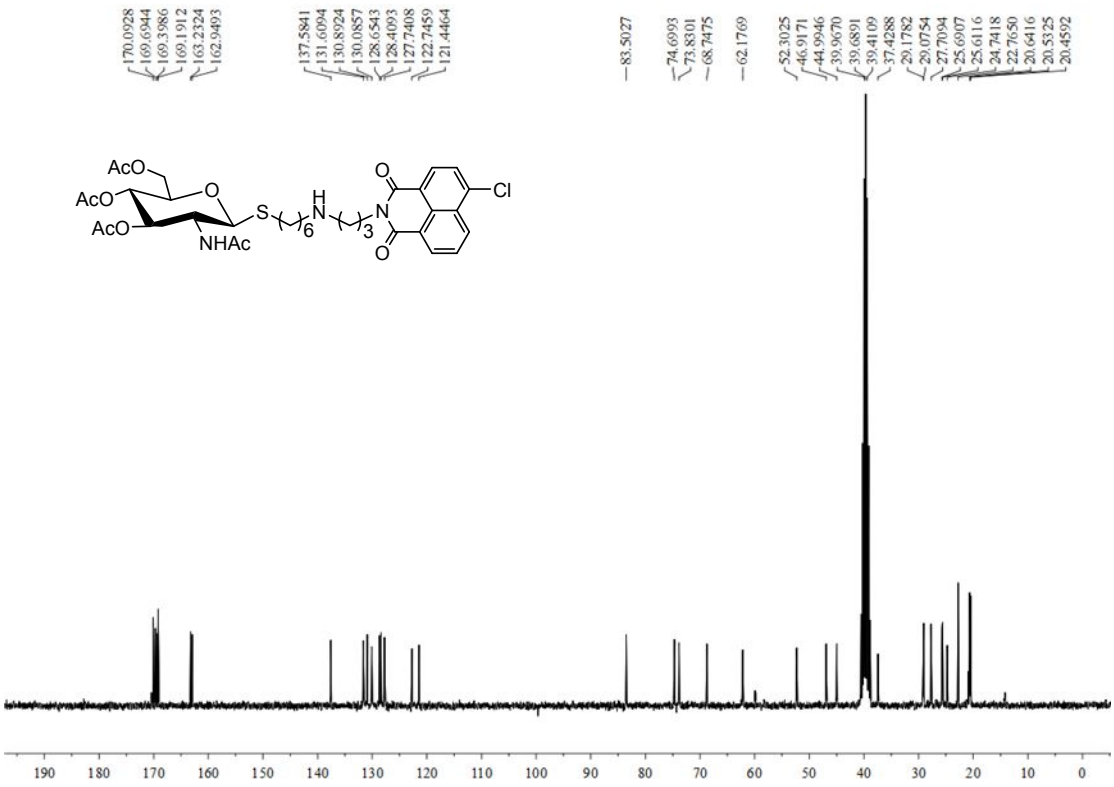

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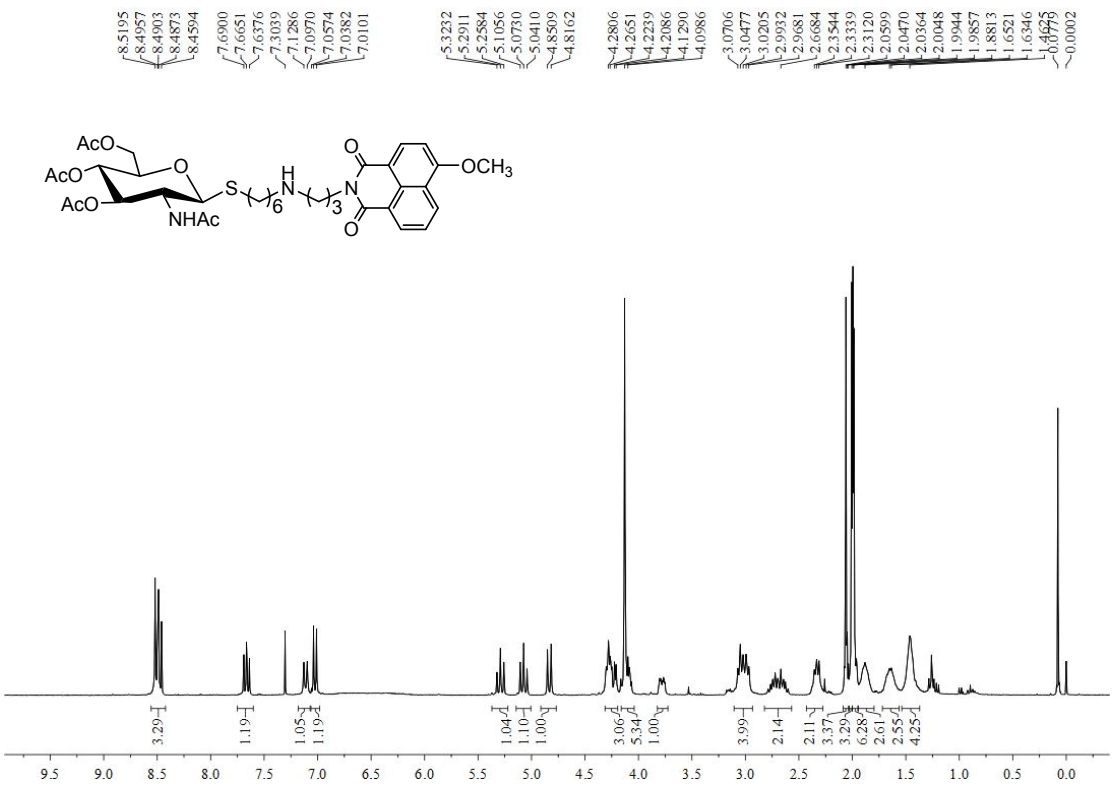

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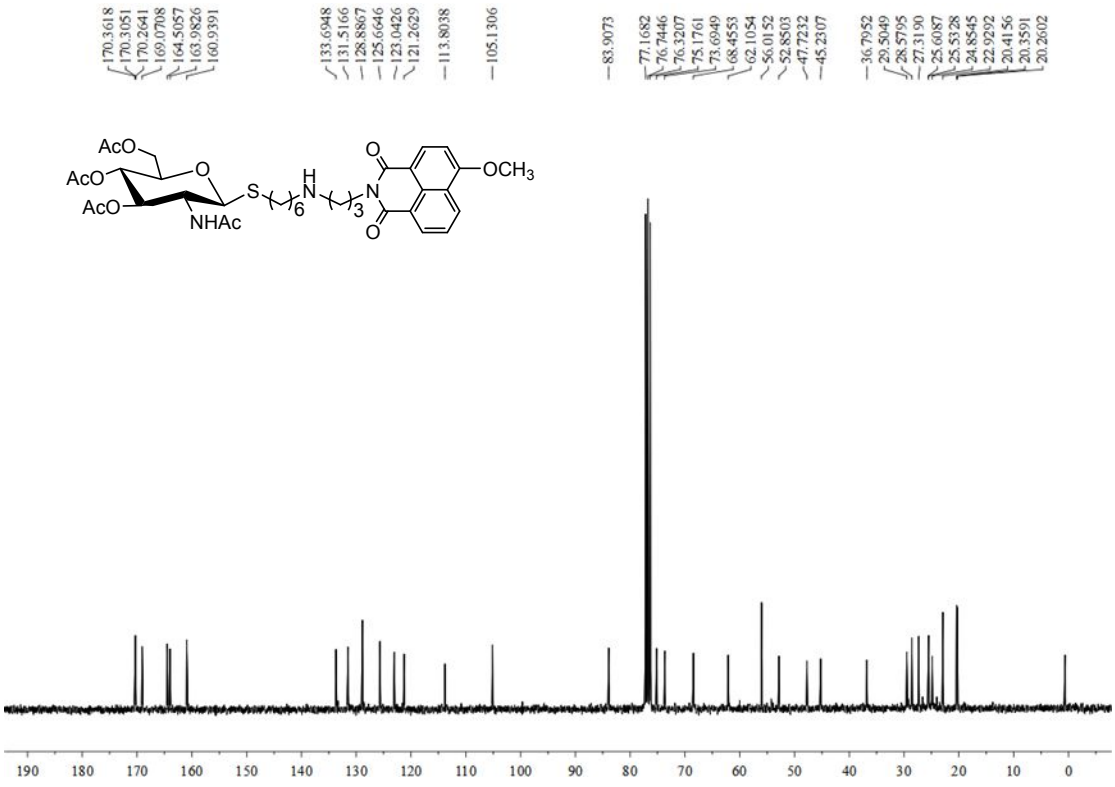

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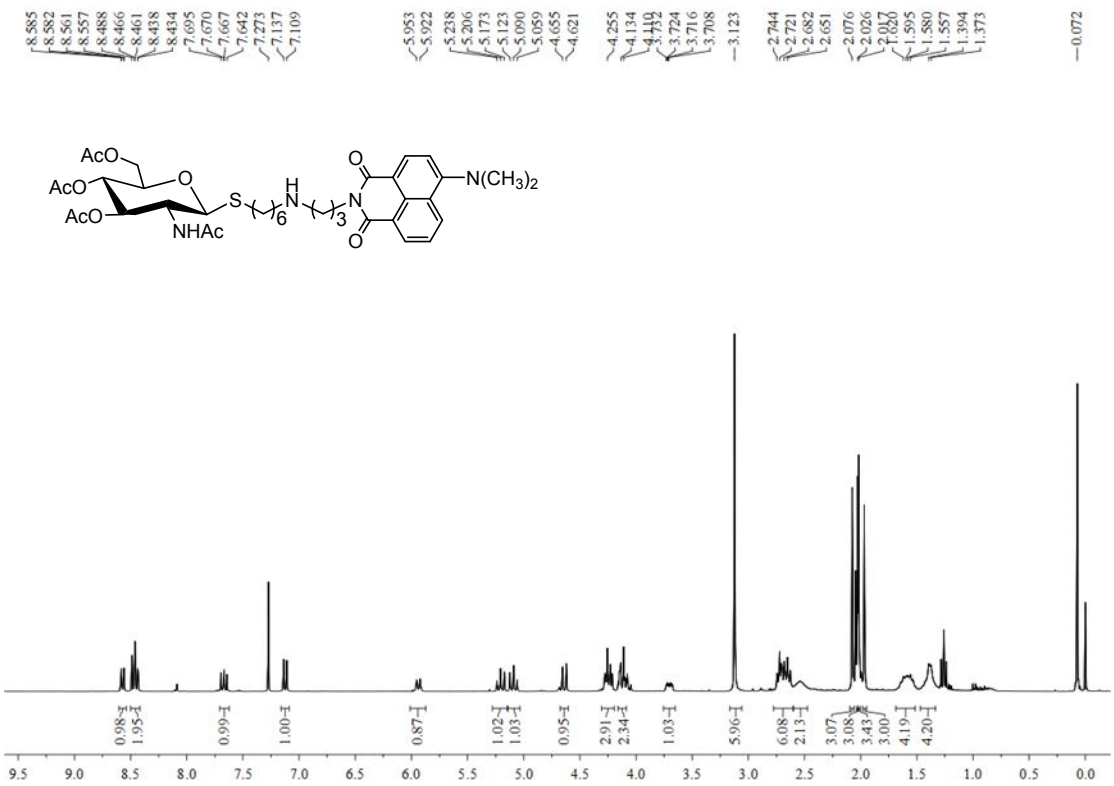

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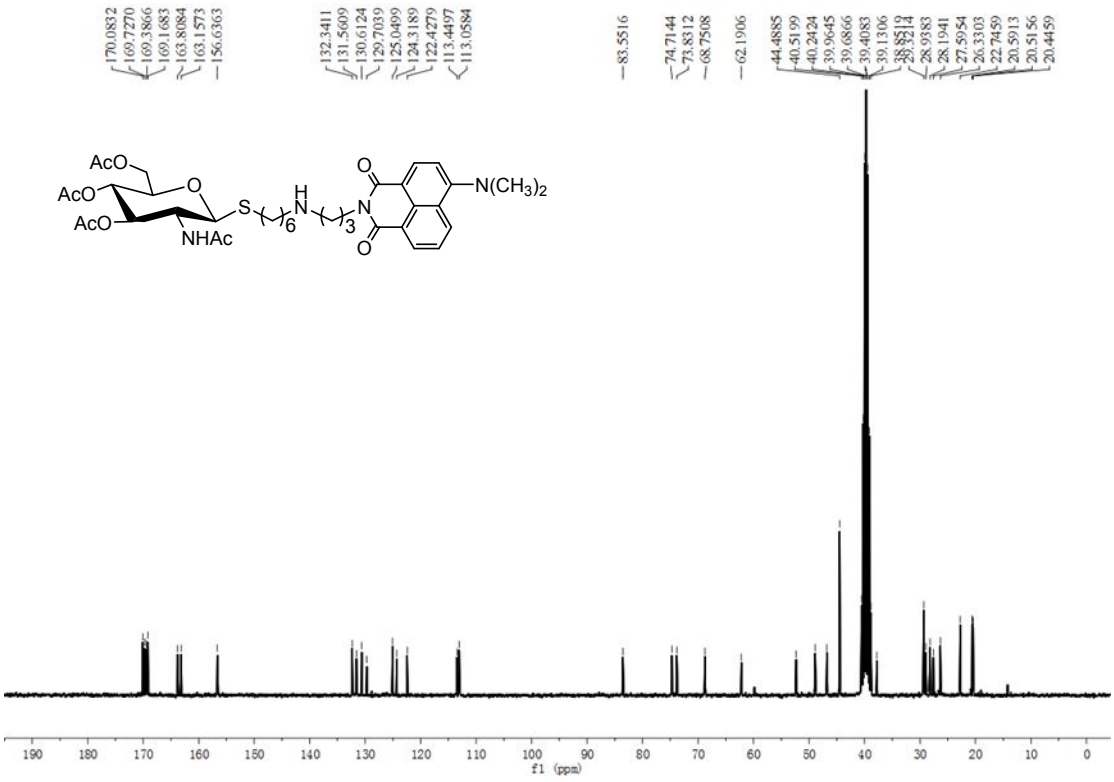

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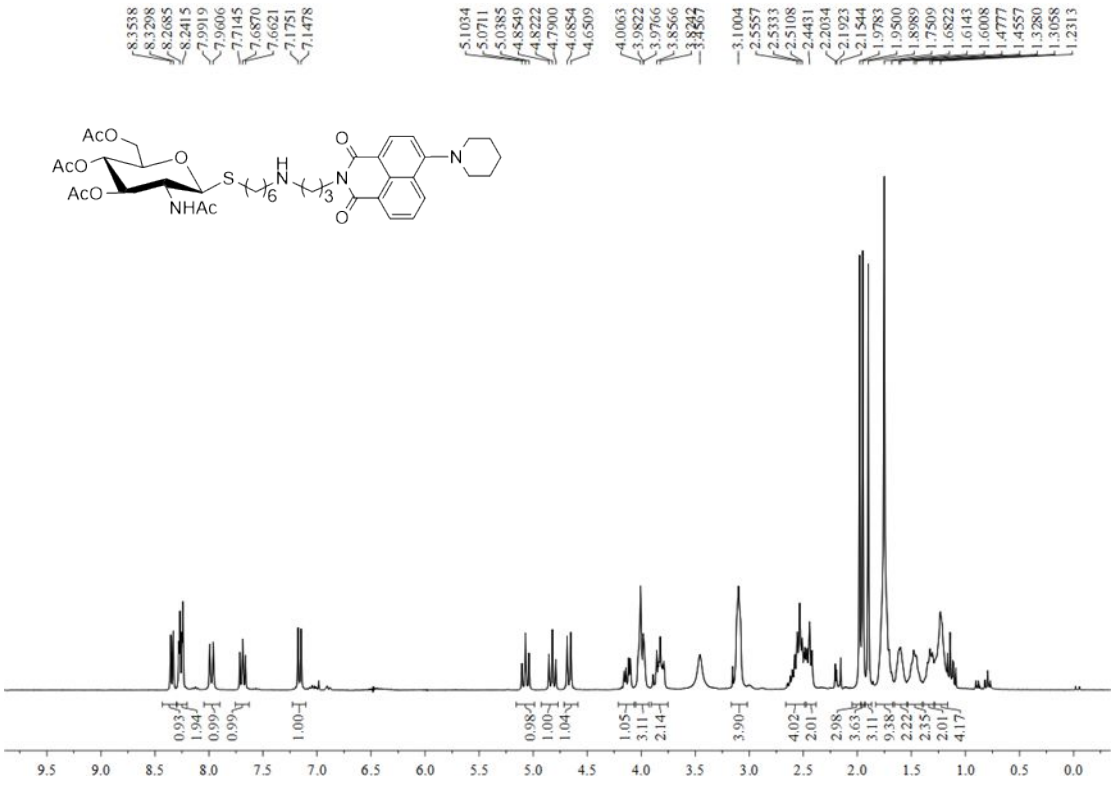

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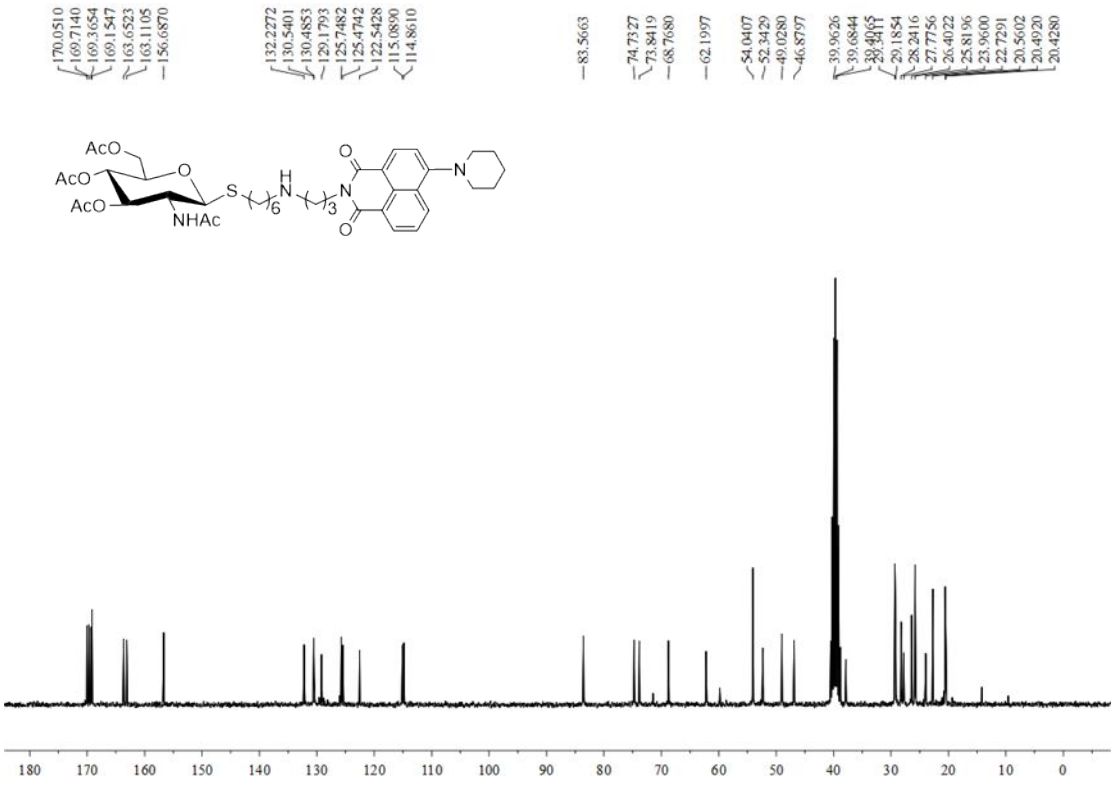

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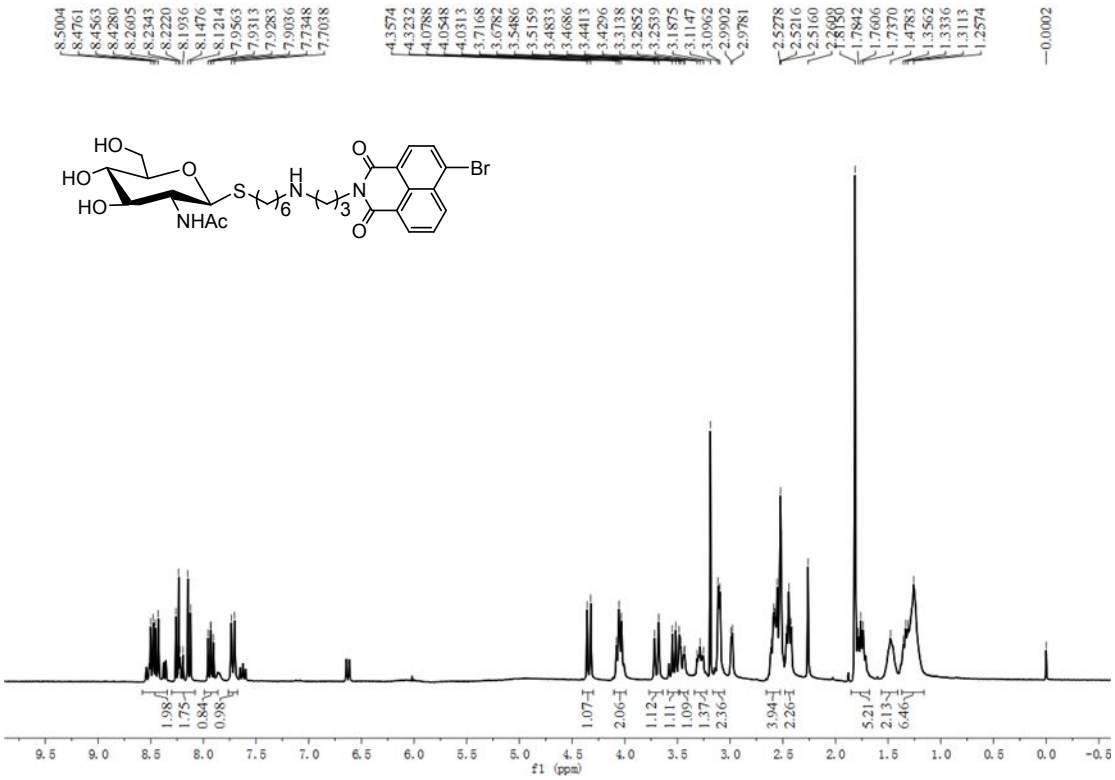
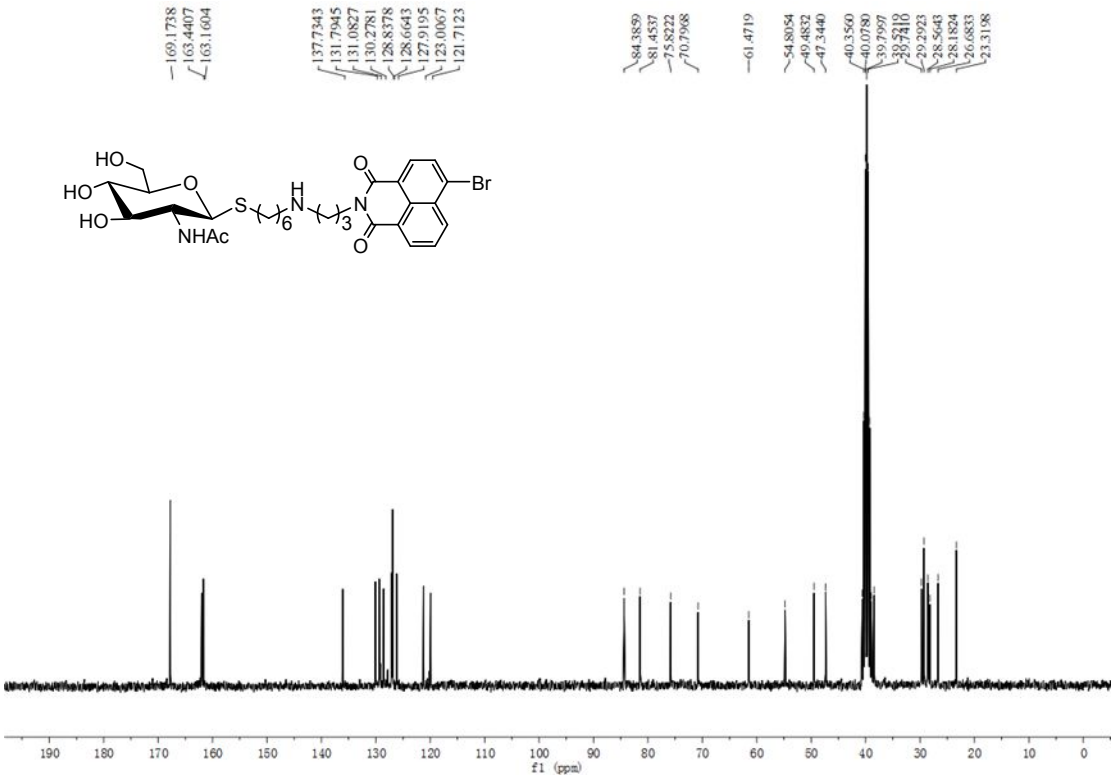
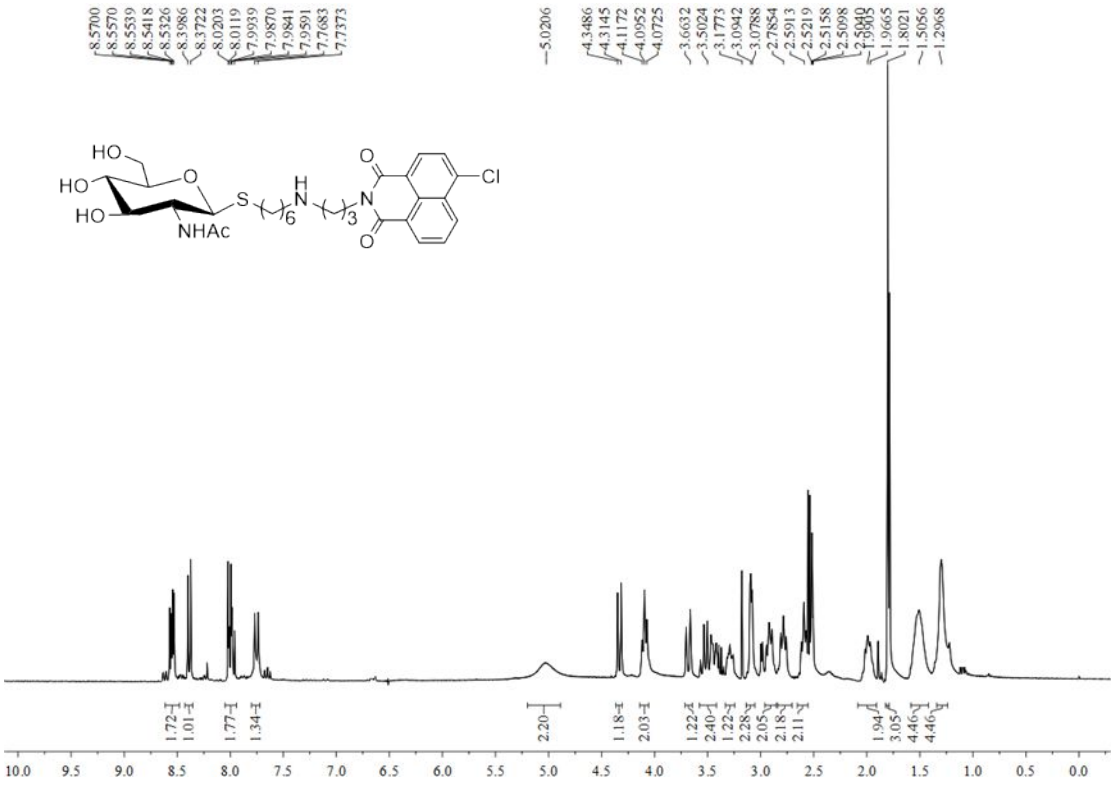


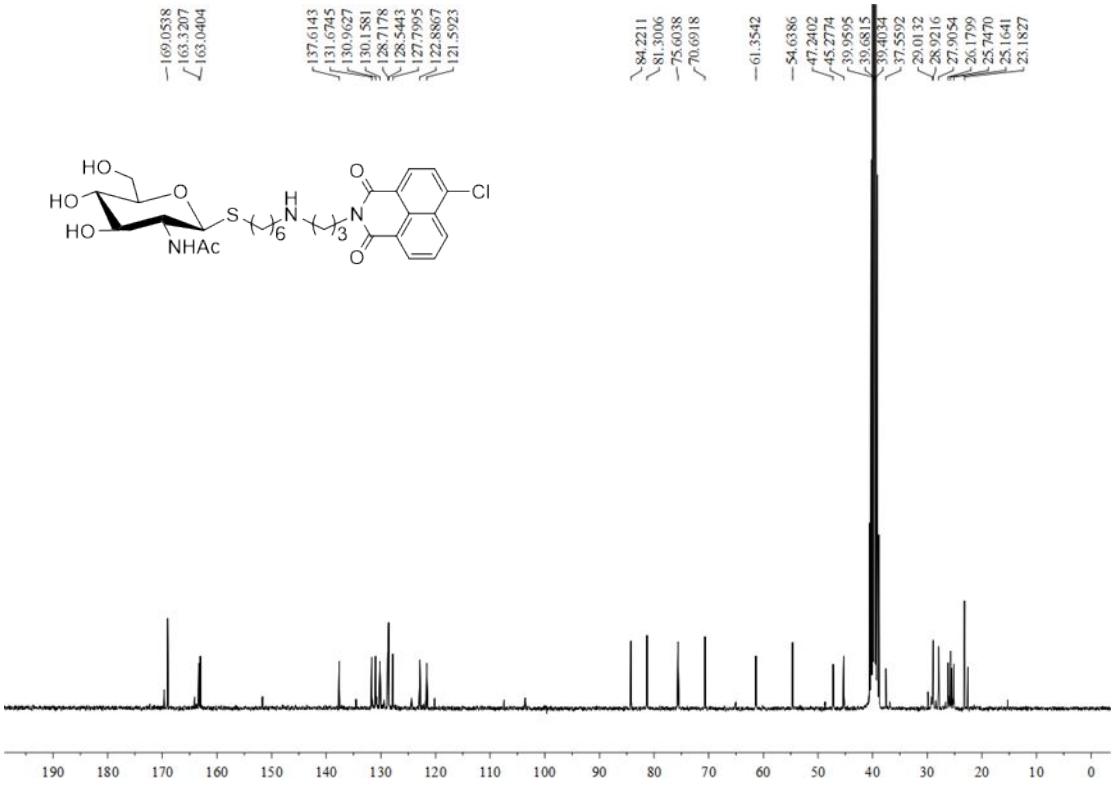
^{13}C NMR spectrum of 11a (75 MHz, DMSO-d_6)



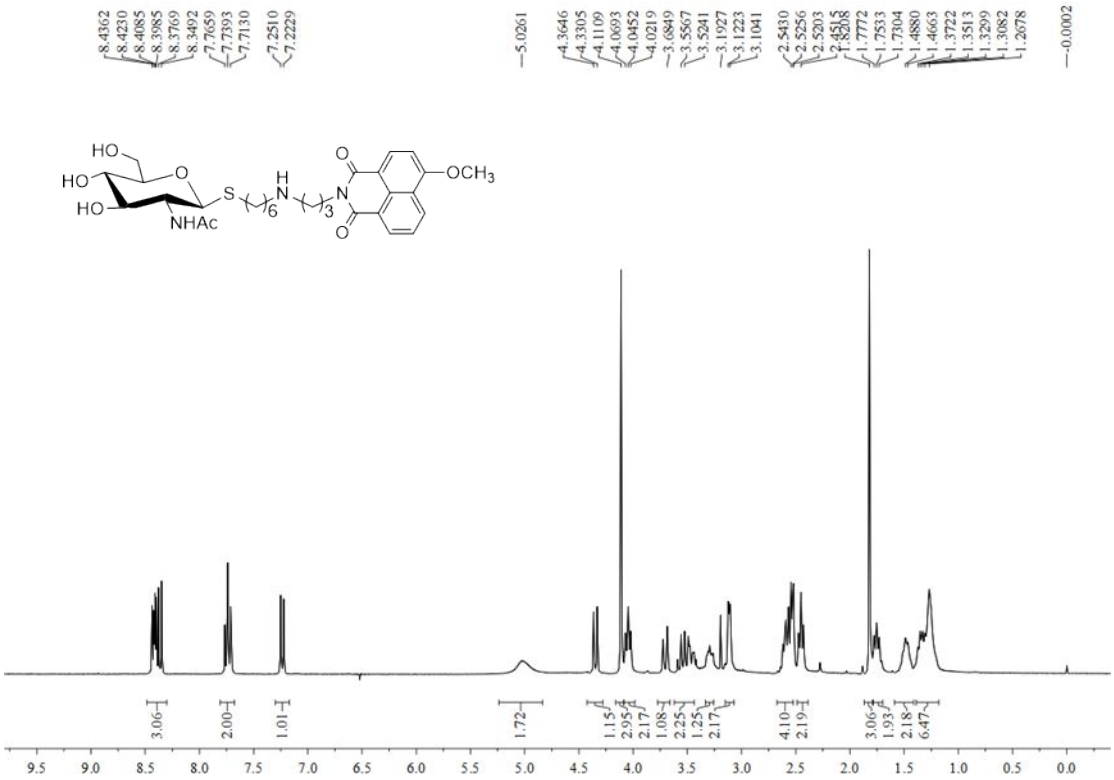
^{1}H NMR spectrum of 11b (300 MHz, DMSO-d_6)



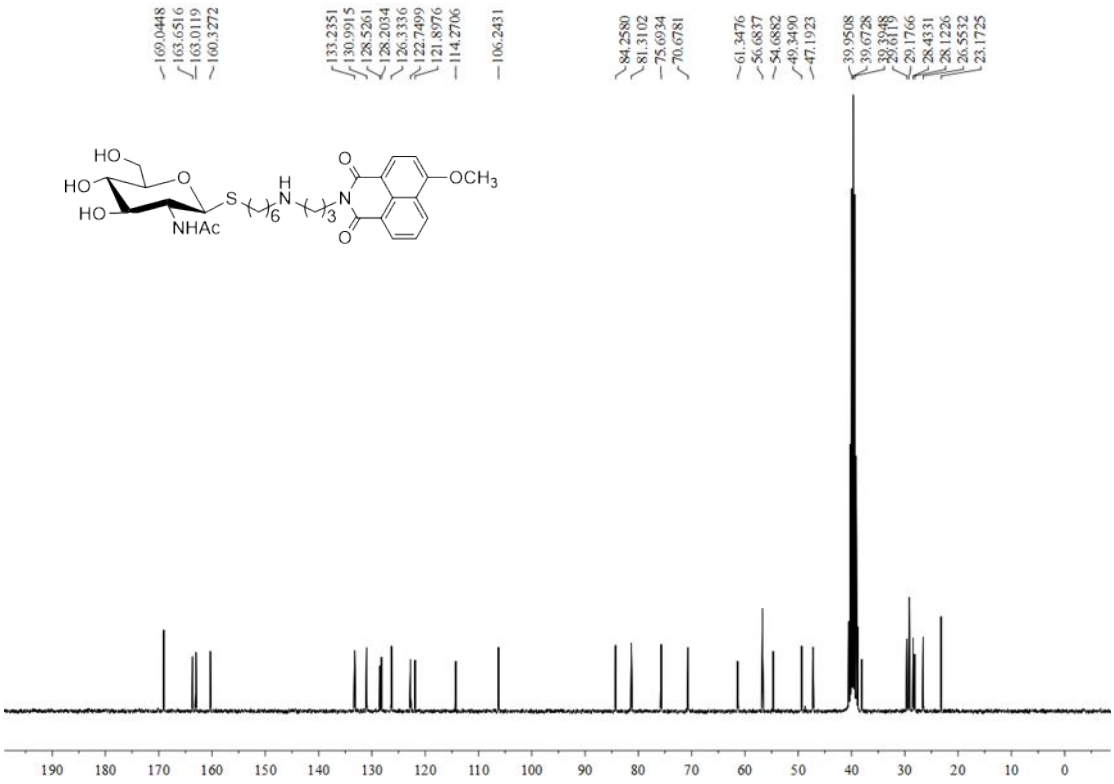
^{13}C NMR spectrum of 11b (75 MHz, DMSO-d_6)



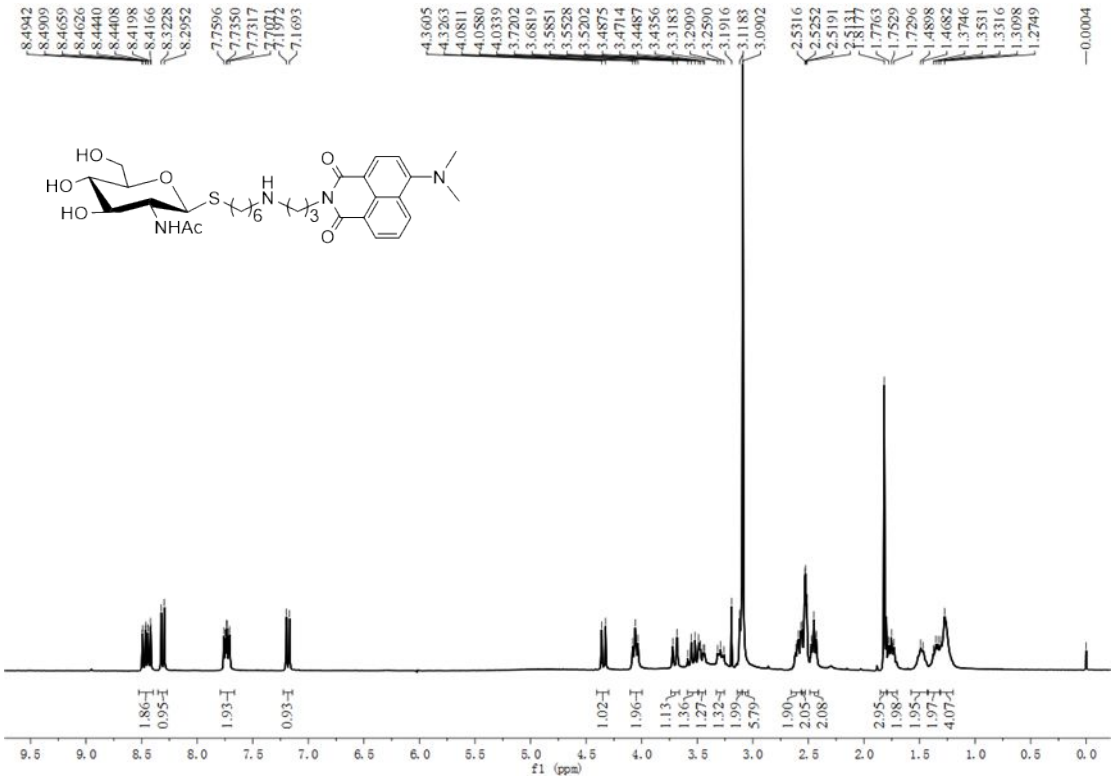
^{1}H NMR spectrum of 11c (300 MHz, DMSO-d_6)



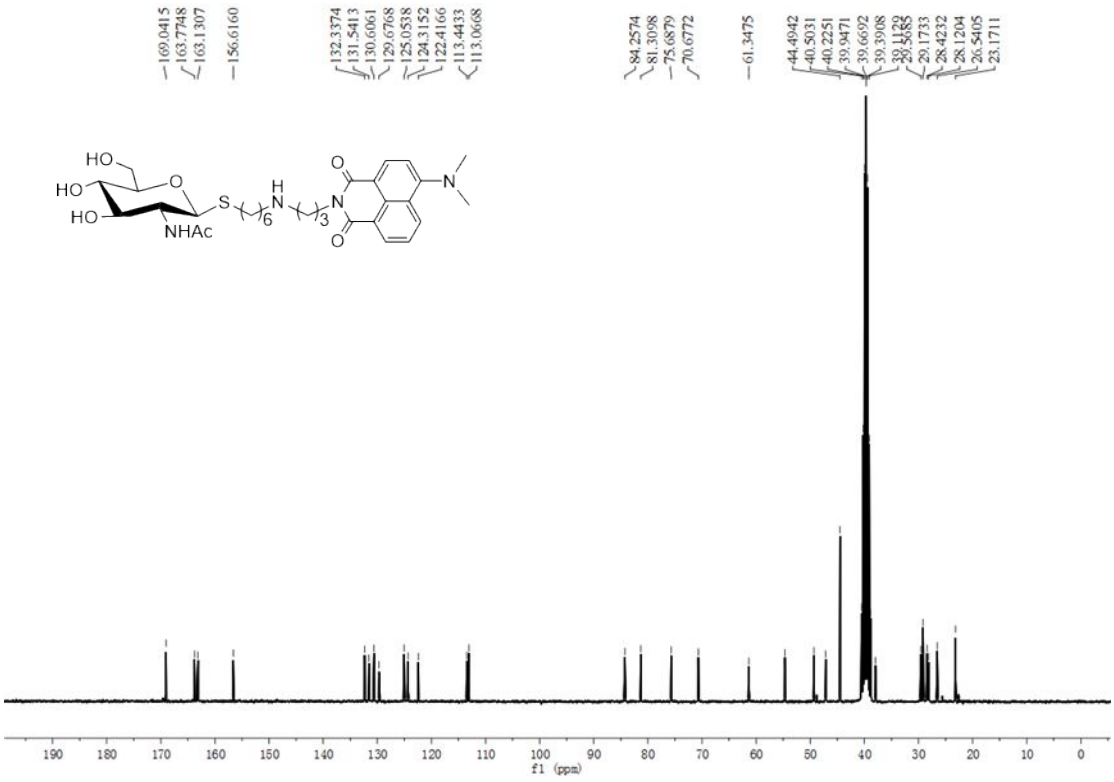
^{13}C NMR spectrum of 11c (75 MHz, DMSO-d_6)



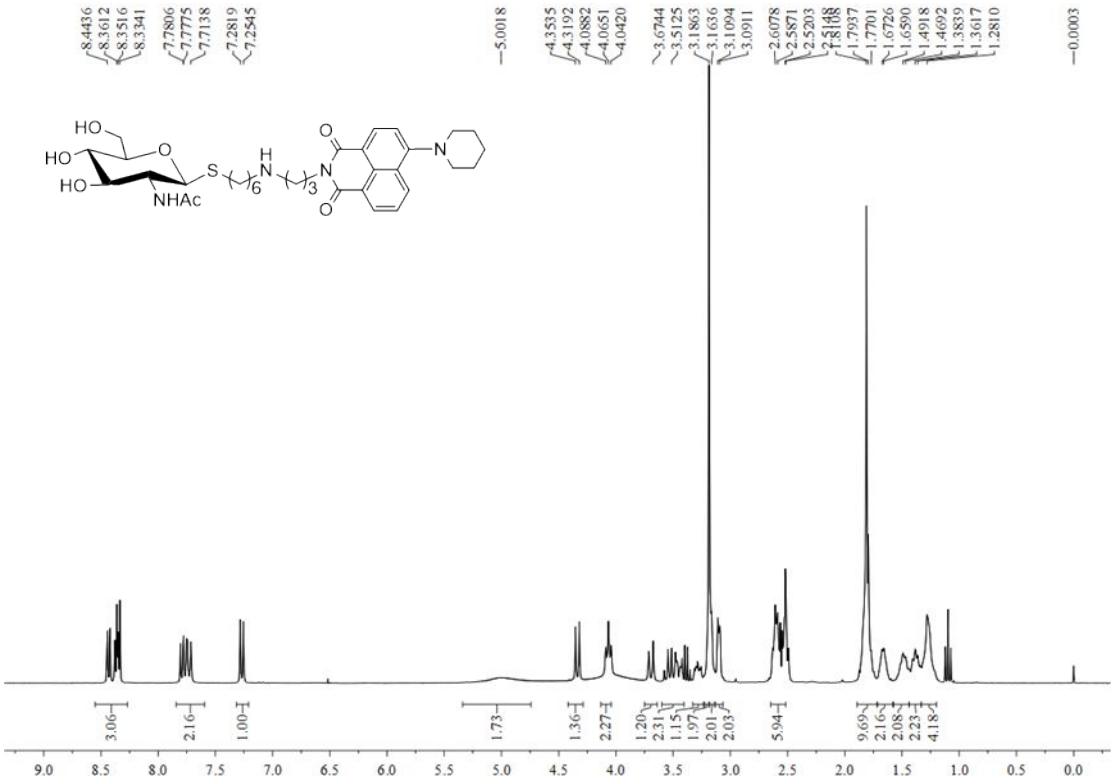
^{1}H NMR spectrum of 11d (300 MHz, DMSO-d_6)



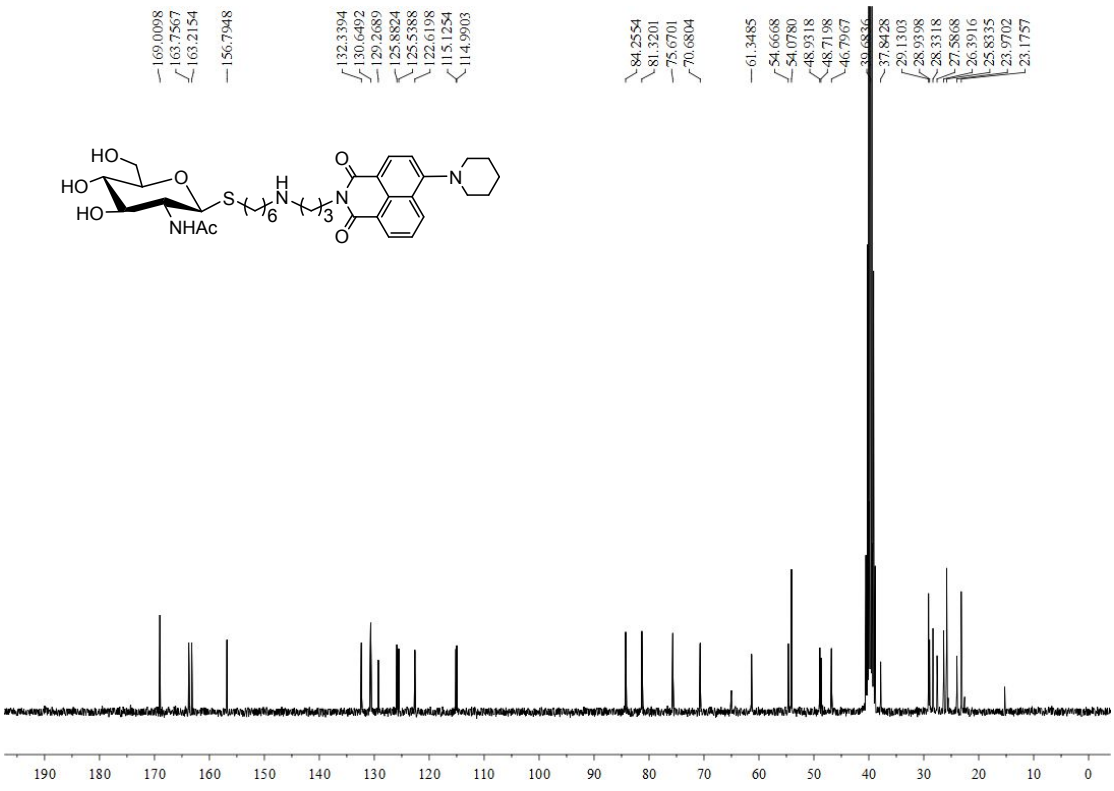
^{13}C NMR spectrum of 11d (75 MHz, DMSO-d_6)



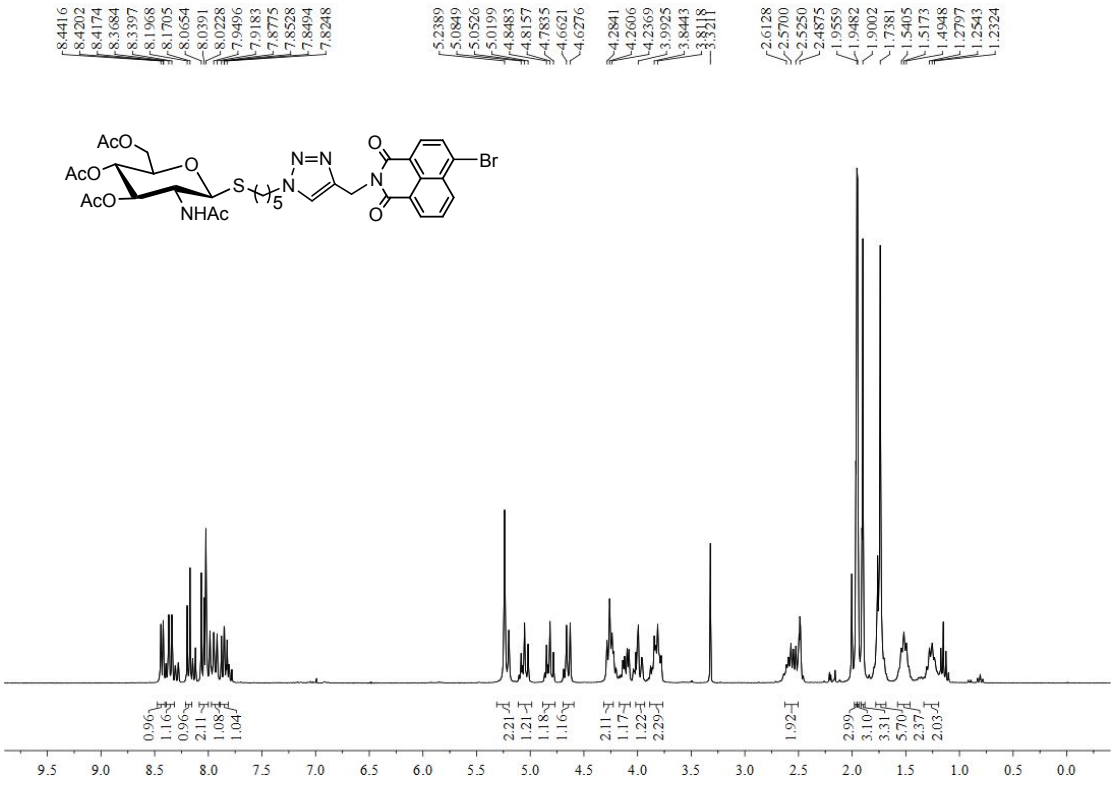
^{1}H NMR spectrum of 11e (300 MHz, DMSO-d_6)



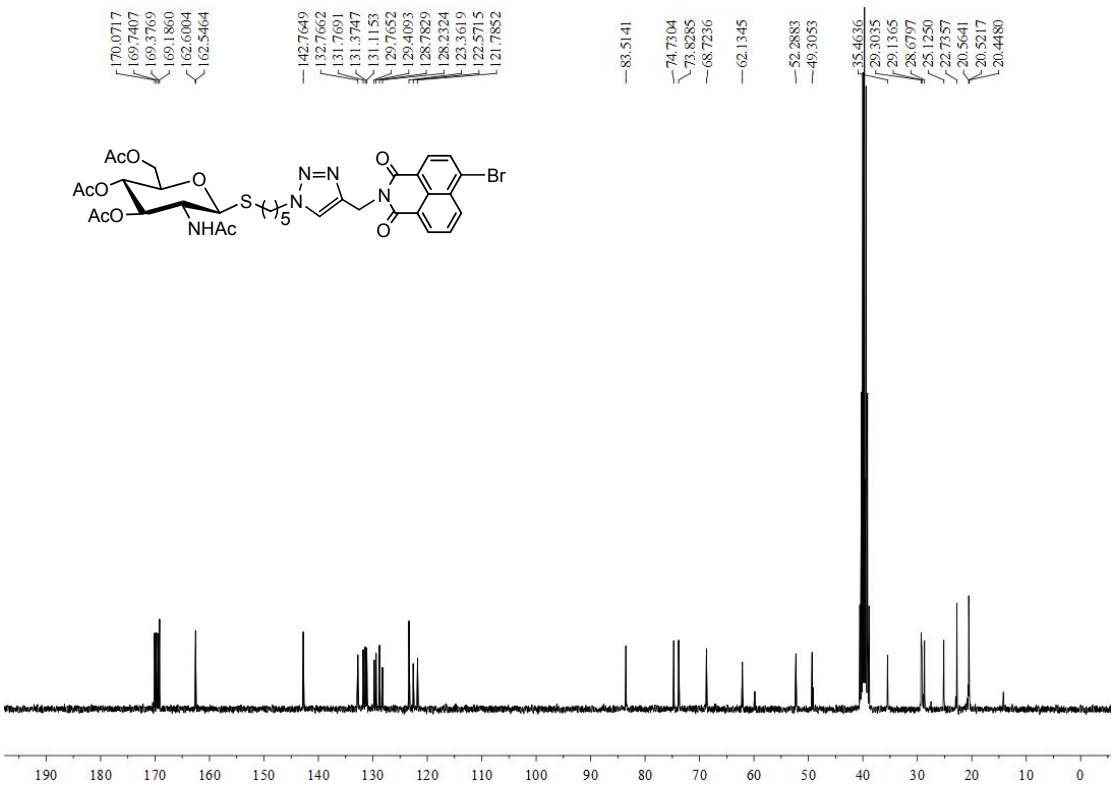
^{13}C NMR spectrum of 11e (75 MHz, DMSO-d_6)



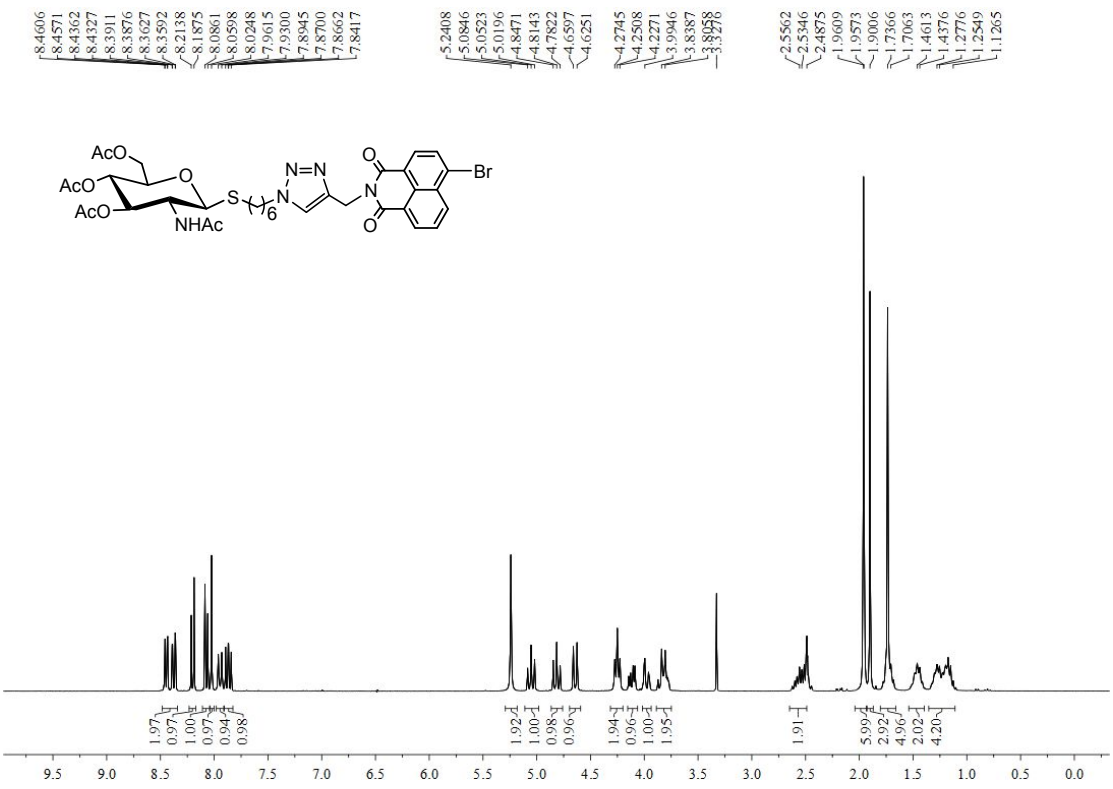
^{1}H NMR spectrum of 14a (300 MHz, DMSO-d_6)



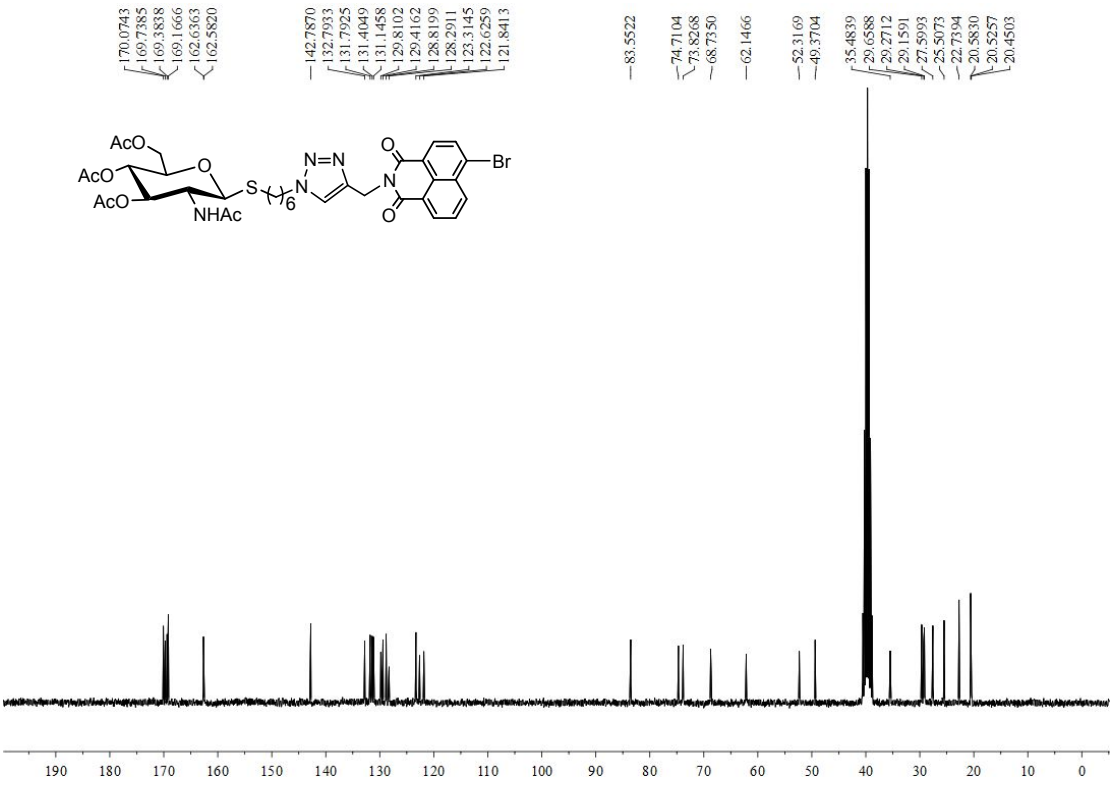
^{13}C NMR spectrum of 14a (75 MHz, DMSO-d_6)



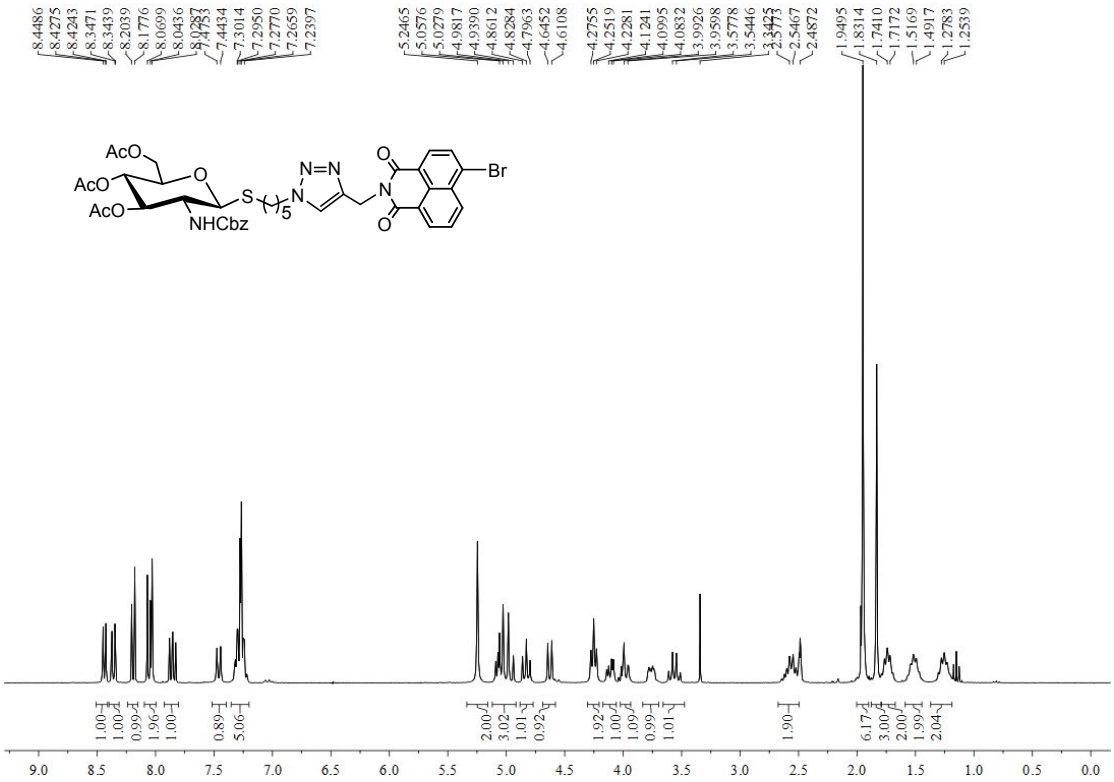
^{1}H NMR spectrum of 14b (300 MHz, DMSO-d_6)



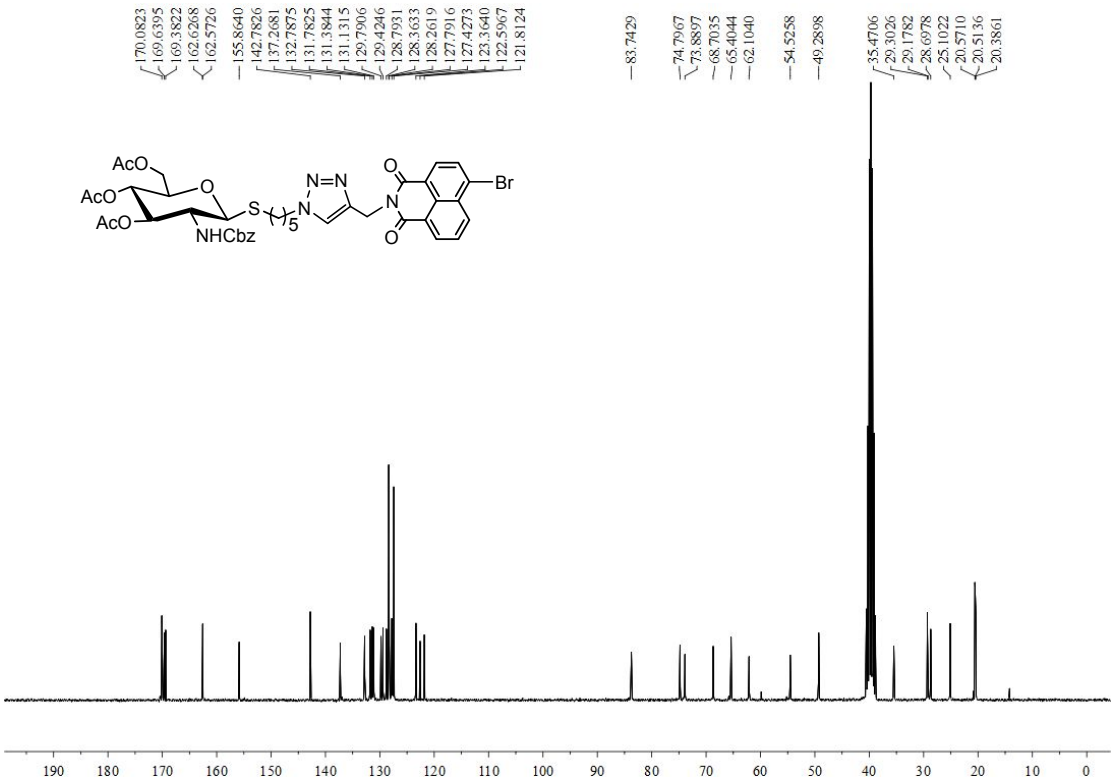
^{13}C NMR spectrum of 14b (75 MHz, DMSO-d_6)



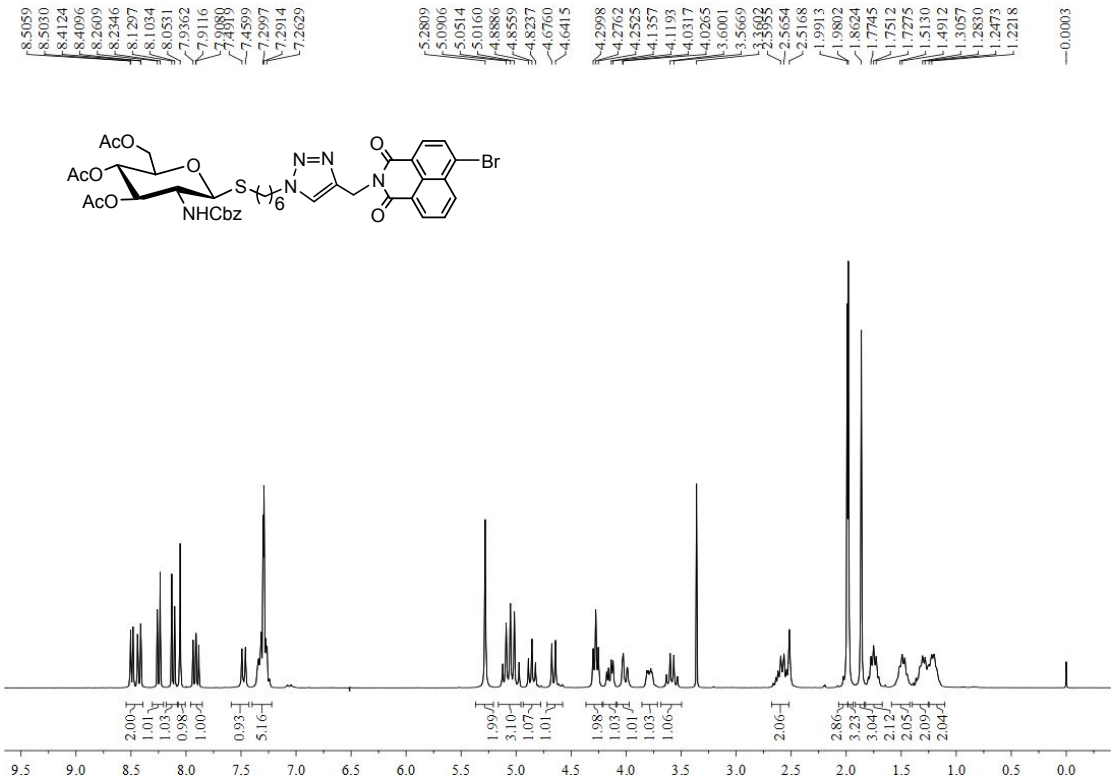
^{1}H NMR spectrum of 14c (300 MHz, DMSO-d_6)



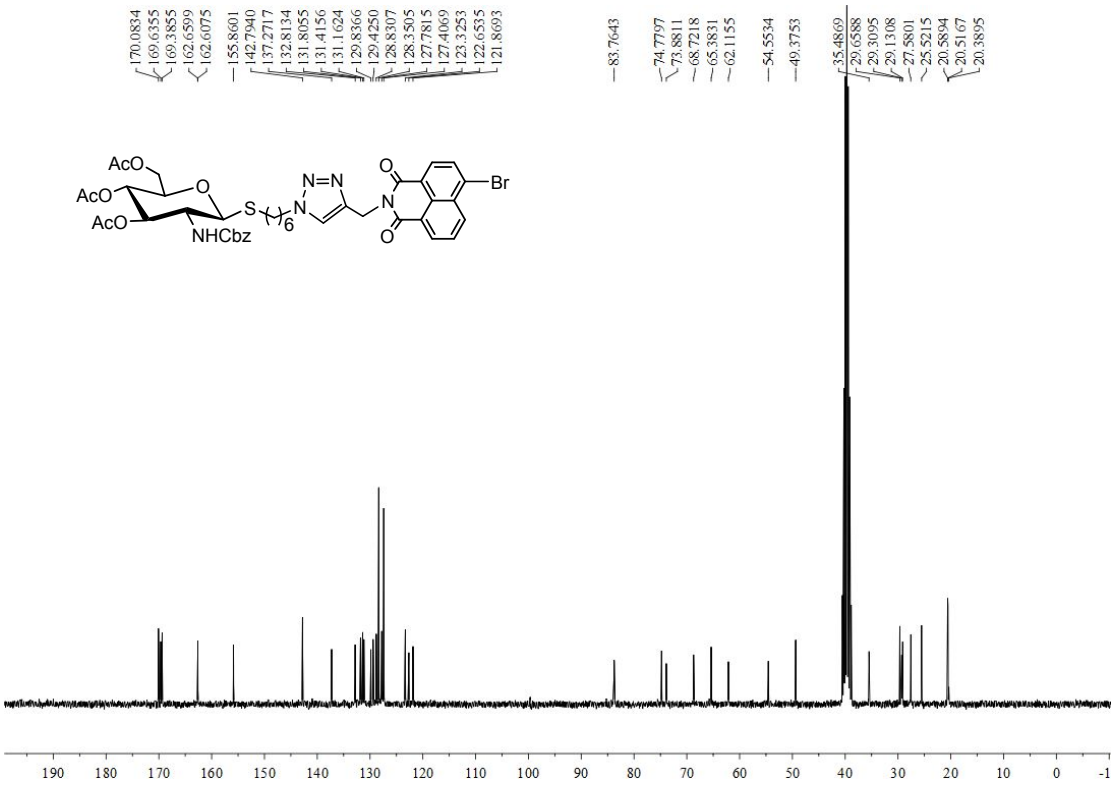
^{13}C NMR spectrum of 14c (75 MHz, DMSO-d_6)



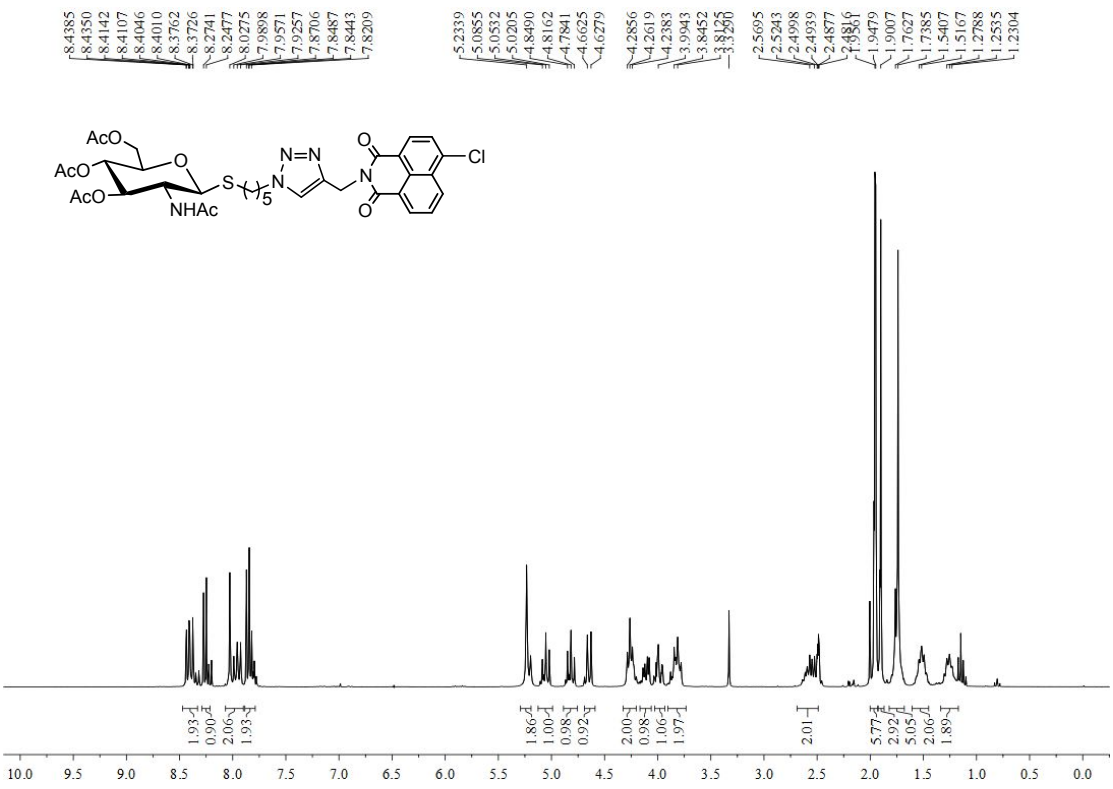
^{1}H NMR spectrum of 14d (300 MHz, DMSO-d_6)



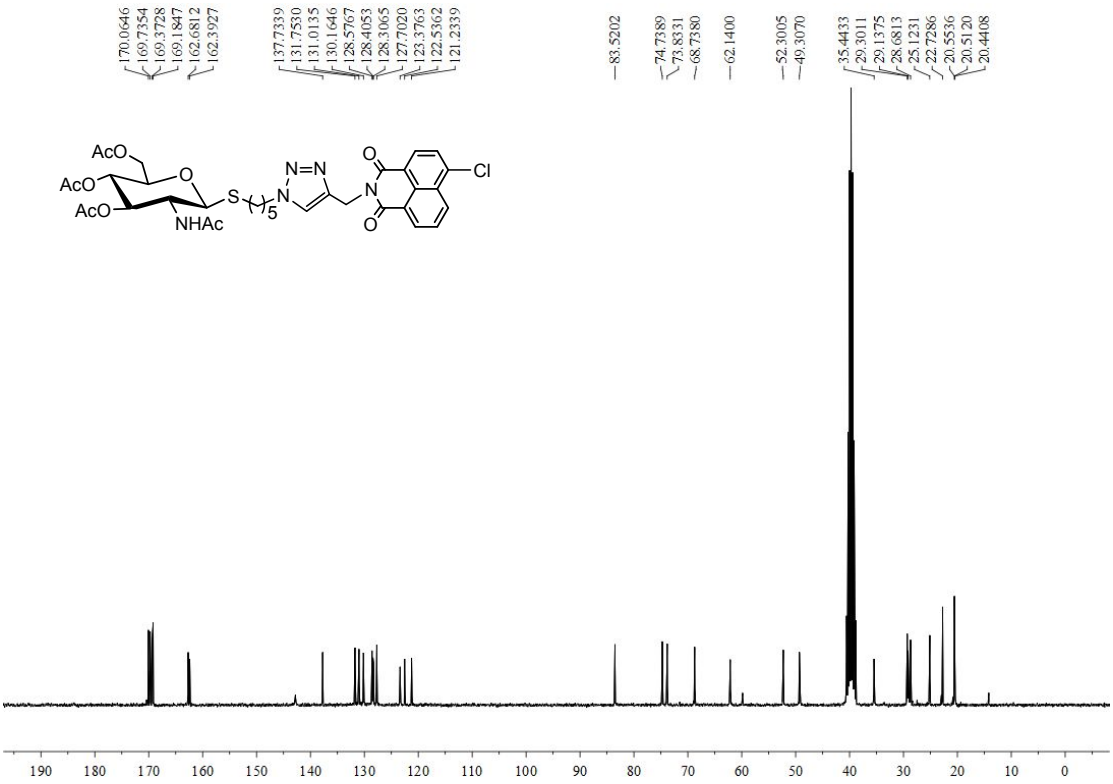
^{13}C NMR spectrum of 14d (75 MHz, DMSO-d_6)



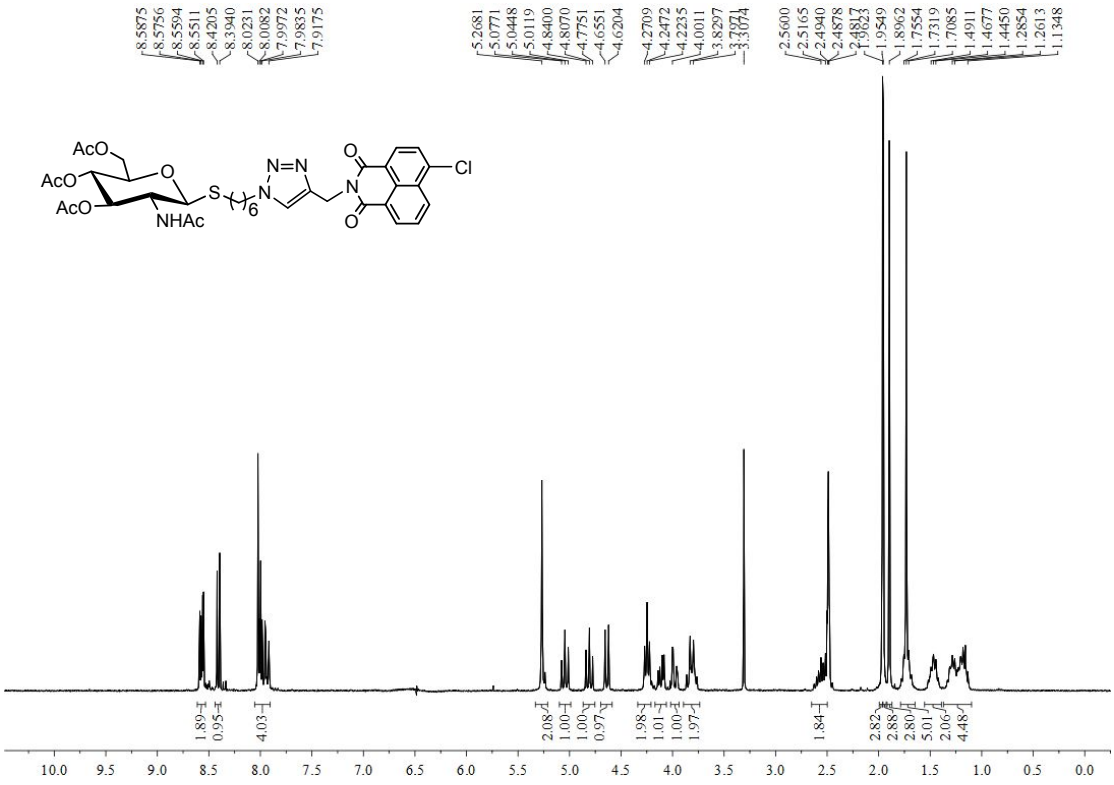
^{1}H NMR spectrum of 14e (300 MHz, DMSO-d_6)



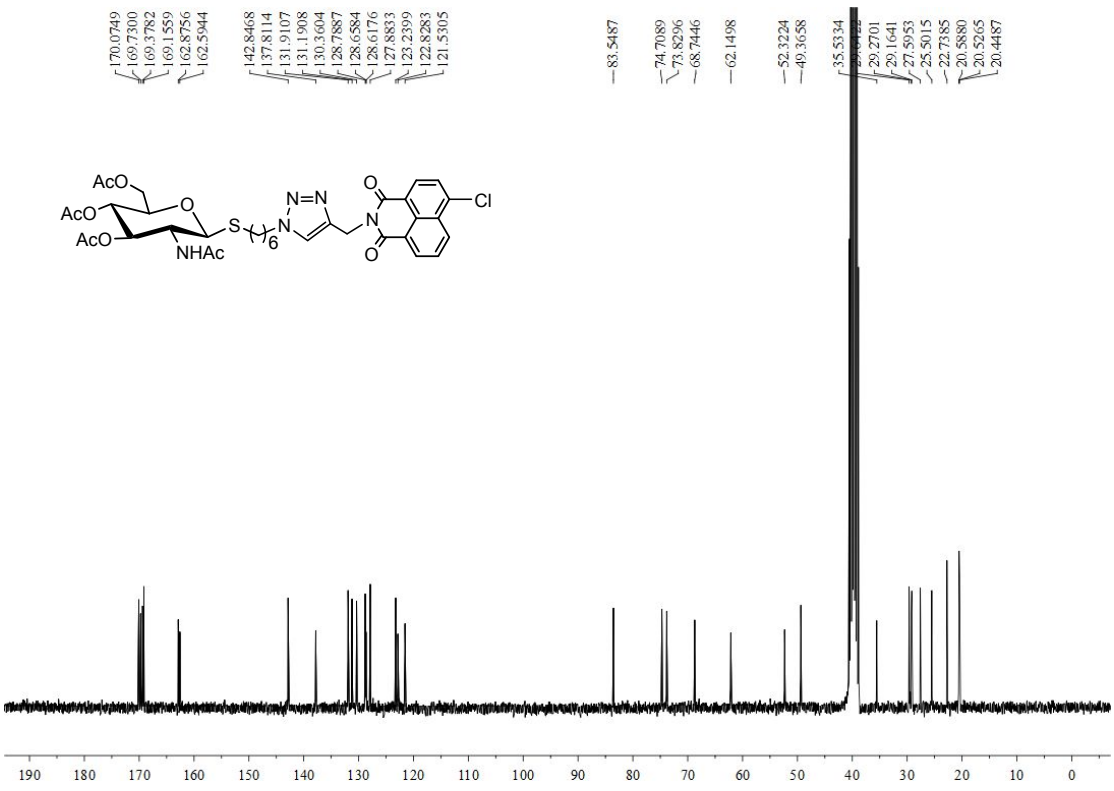
^{13}C NMR spectrum of 14e (75 MHz, DMSO-d_6)



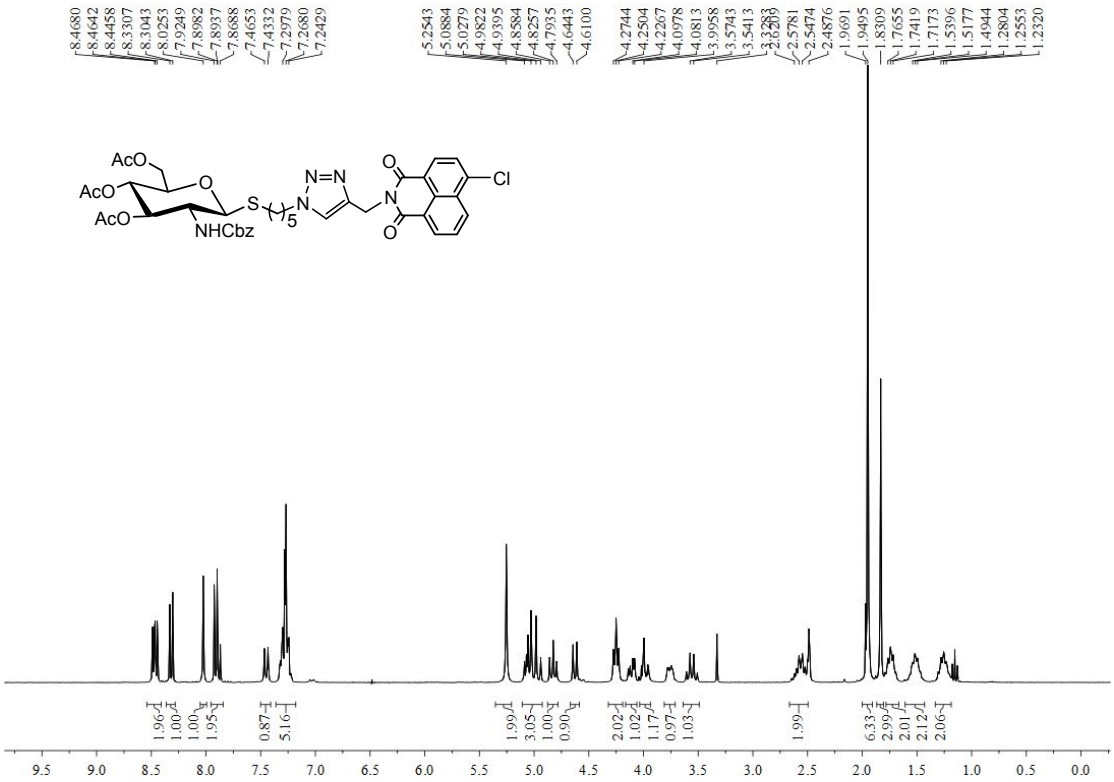
^{1}H NMR spectrum of 14f (300 MHz, DMSO-d_6)



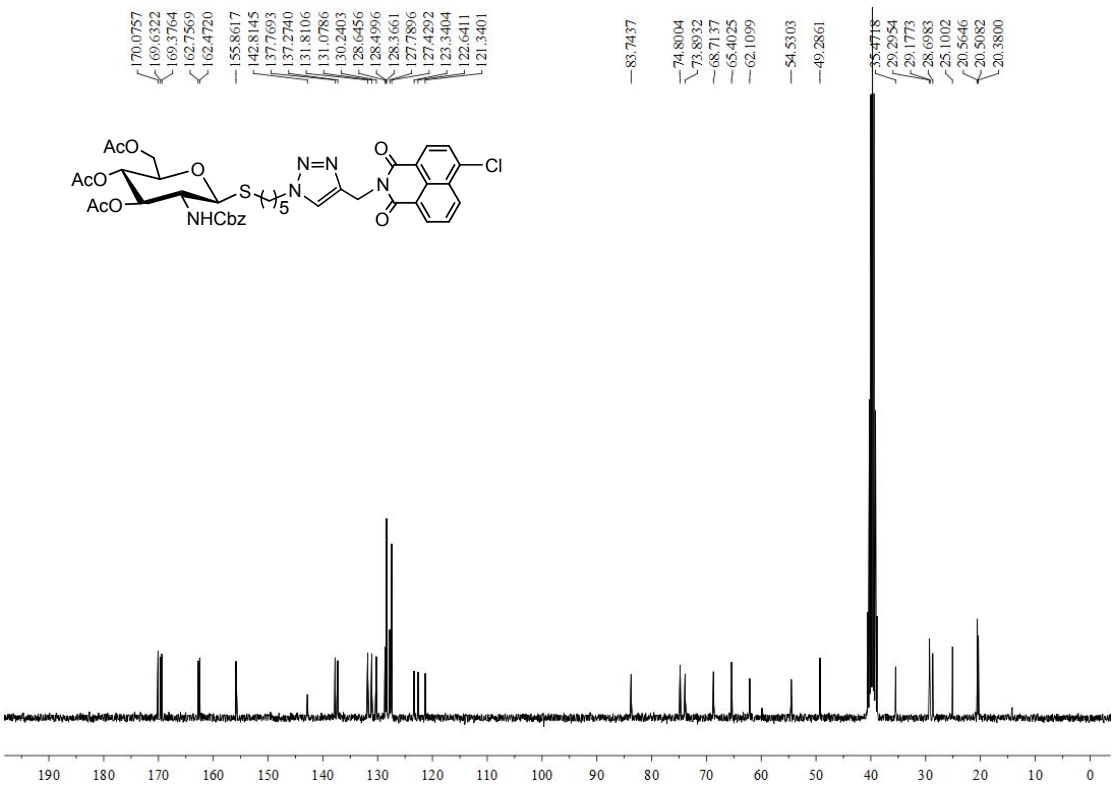
^{13}C NMR spectrum of 14f (75 MHz, DMSO-d_6)



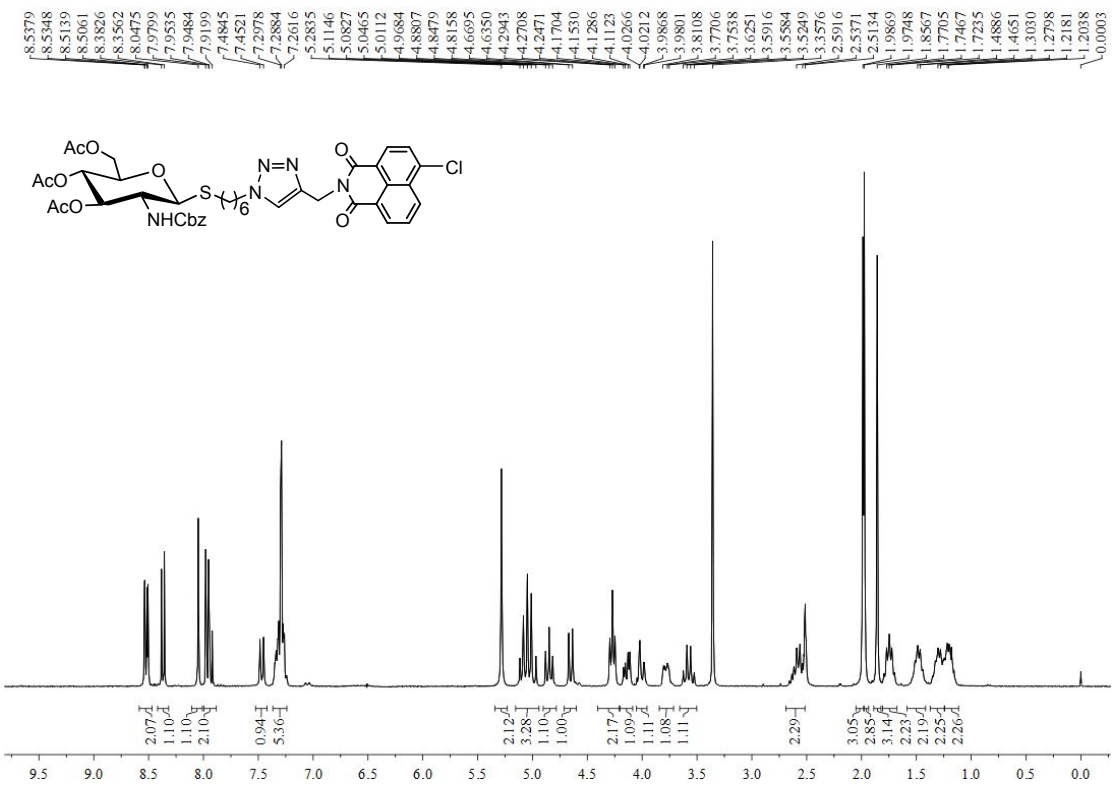
^{1}H NMR spectrum of 14g (300 MHz, DMSO-d_6)



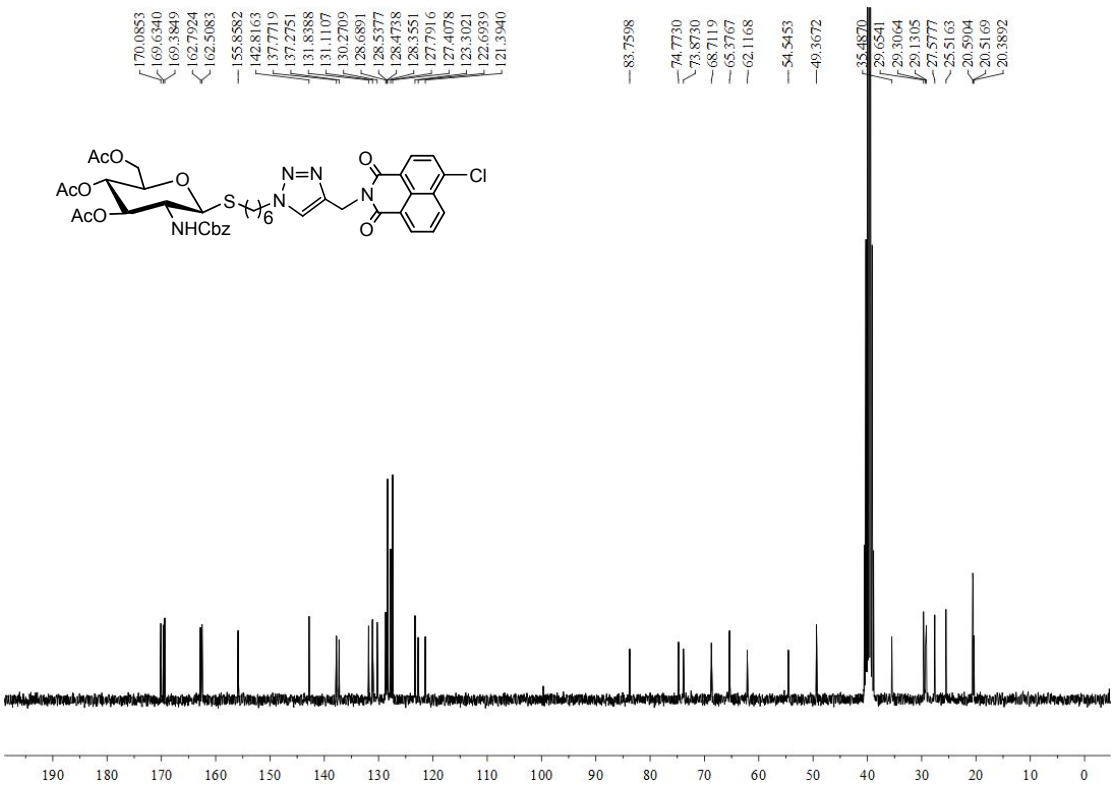
^{13}C NMR spectrum of 14g (75 MHz, DMSO-d_6)



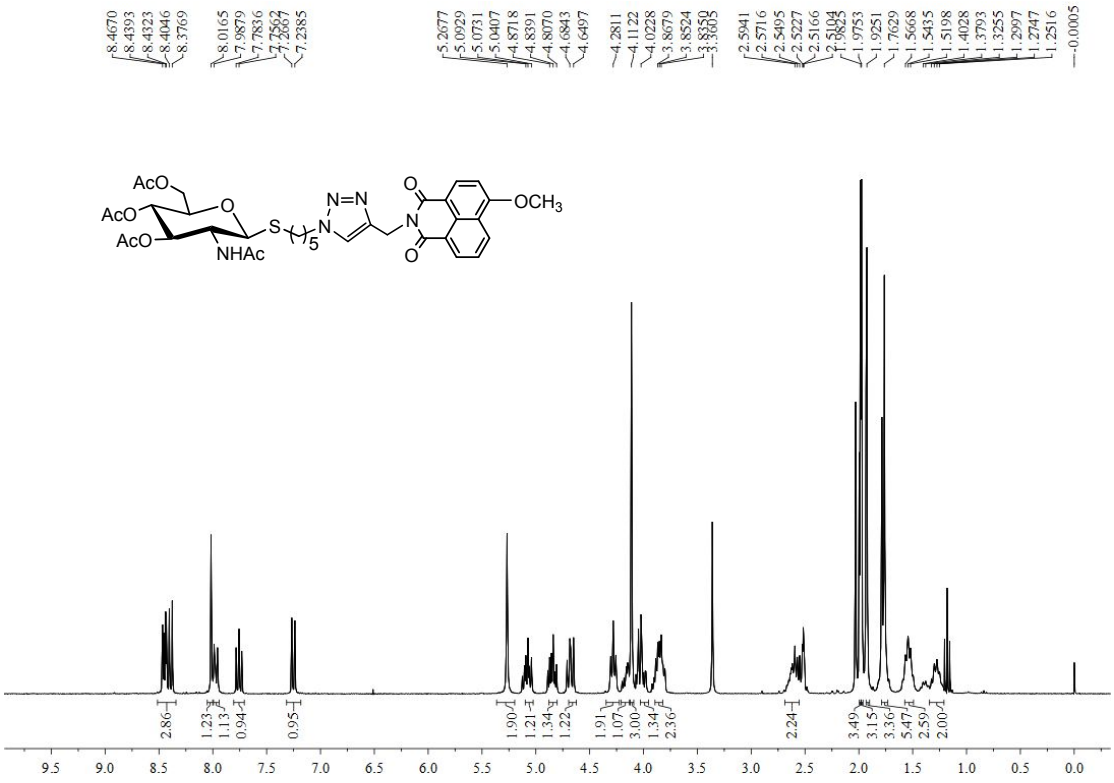
^{1}H NMR spectrum of 14h (300 MHz, DMSO-d_6)



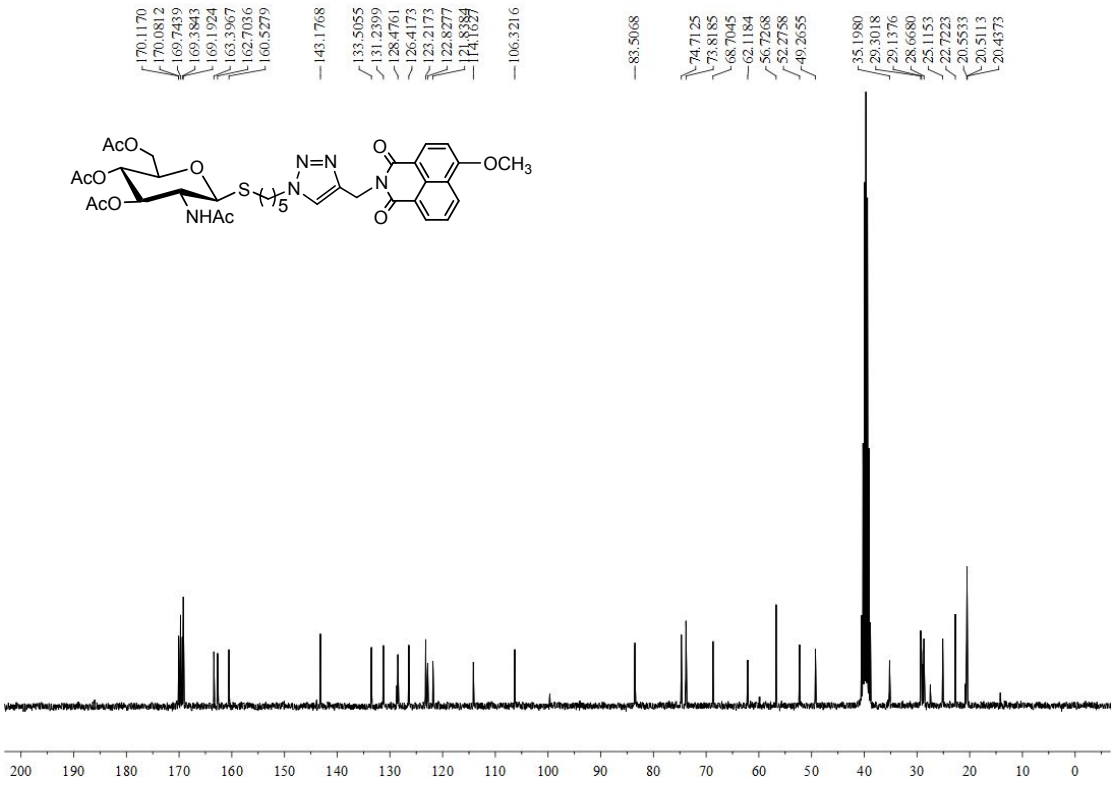
^{13}C NMR spectrum of 14h (75 MHz, DMSO-d_6)



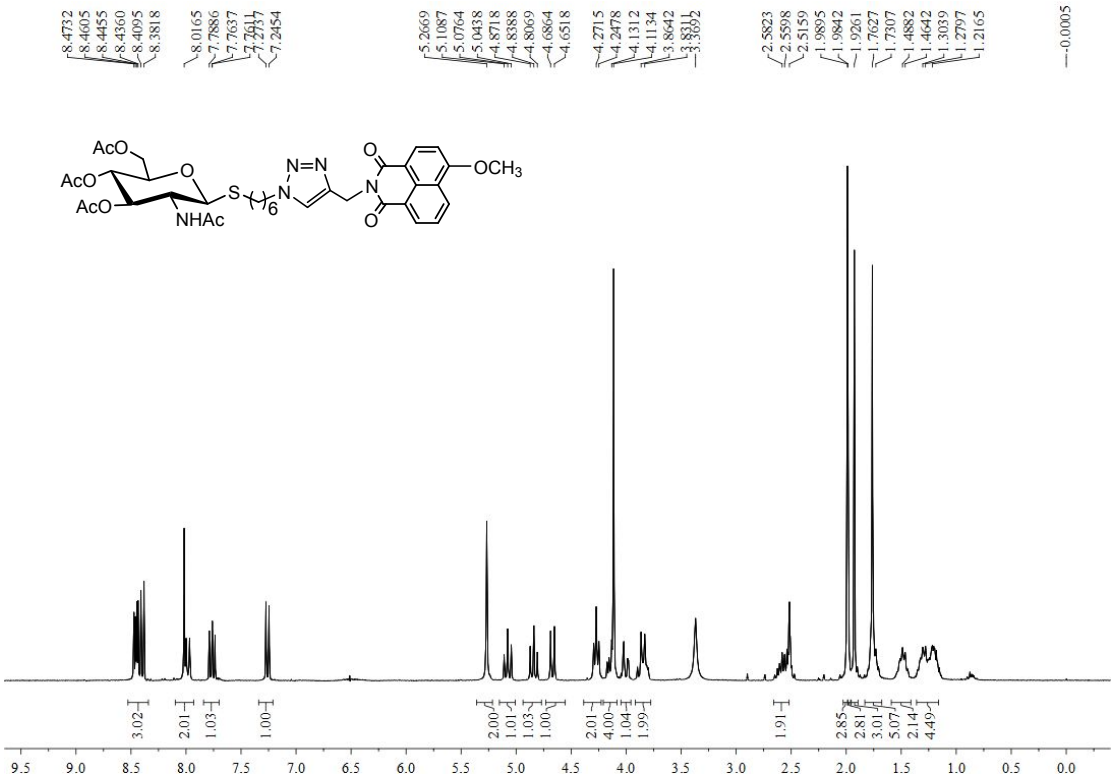
^{1}H NMR spectrum of 14i (300 MHz, DMSO-d_6)



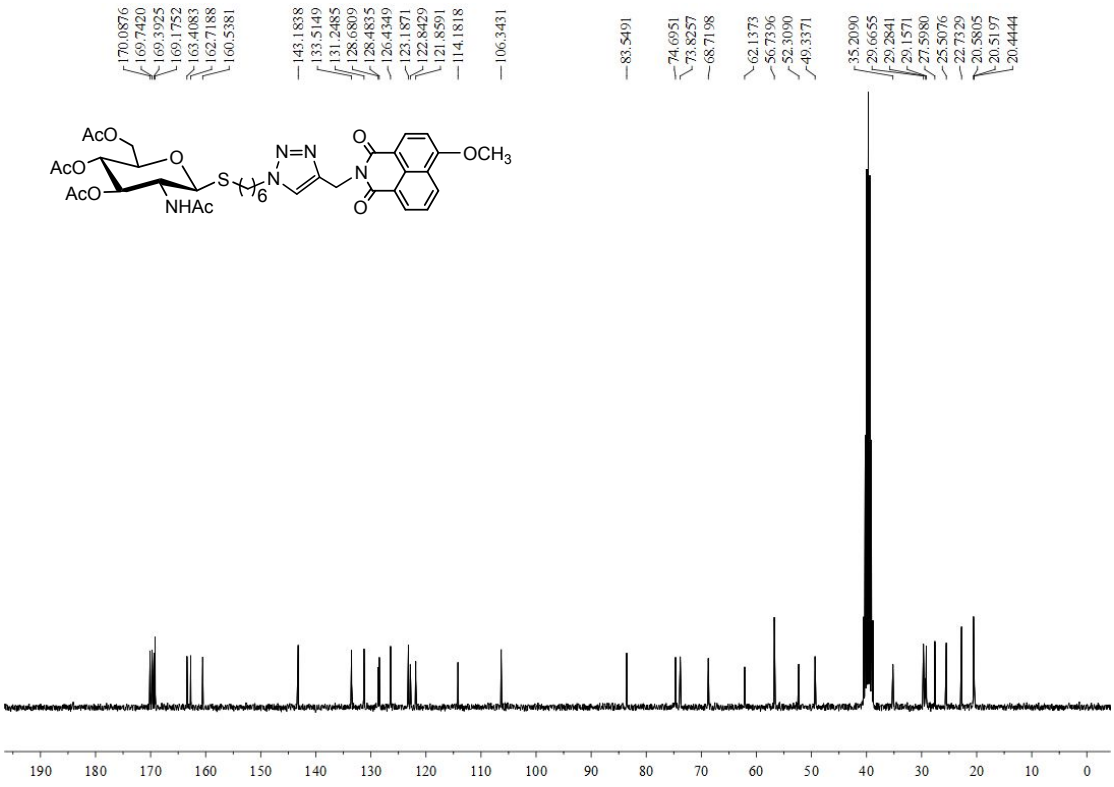
^{13}C NMR spectrum of 14i (75 MHz, DMSO-d_6)



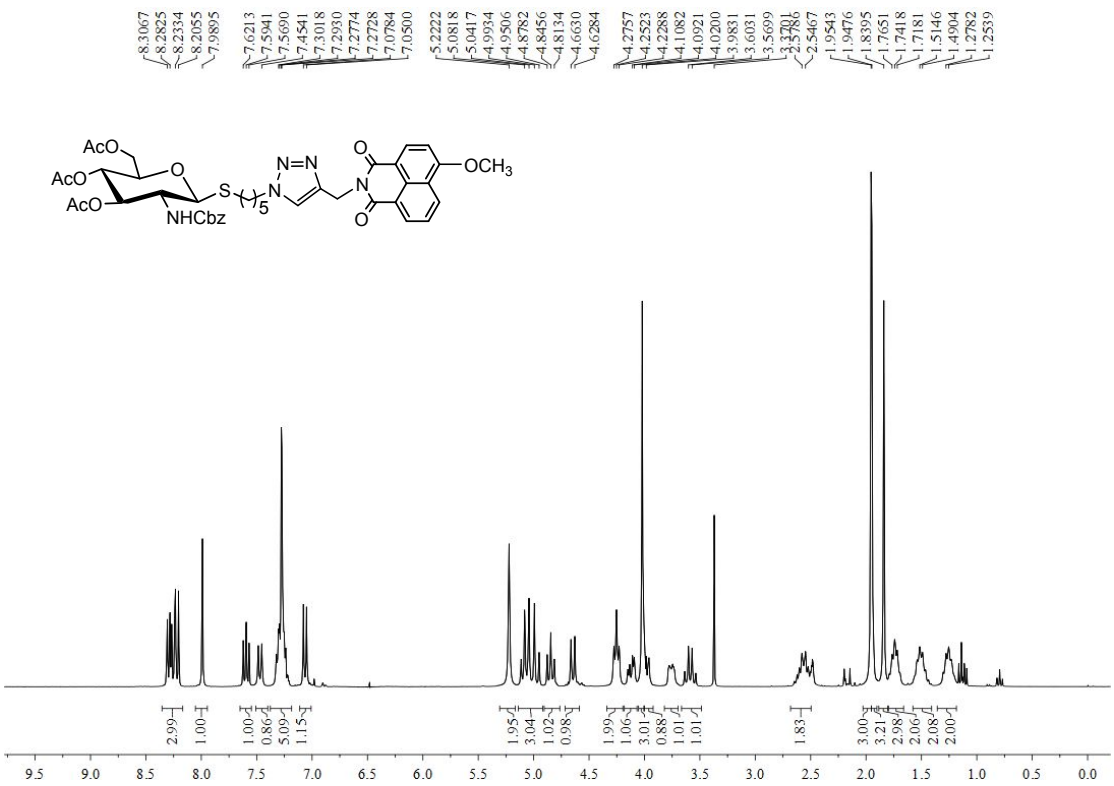
^{1}H NMR spectrum of 14j (300 MHz, DMSO-d_6)



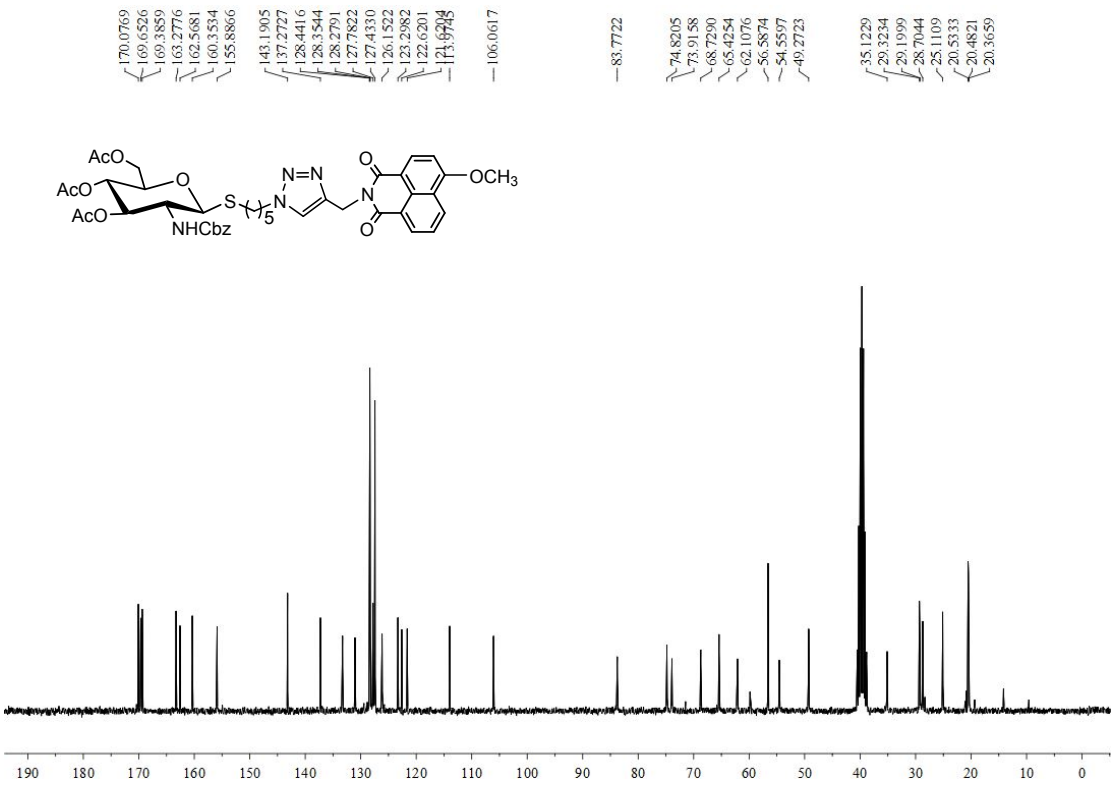
^{13}C NMR spectrum of 14j (75 MHz, DMSO-d_6)



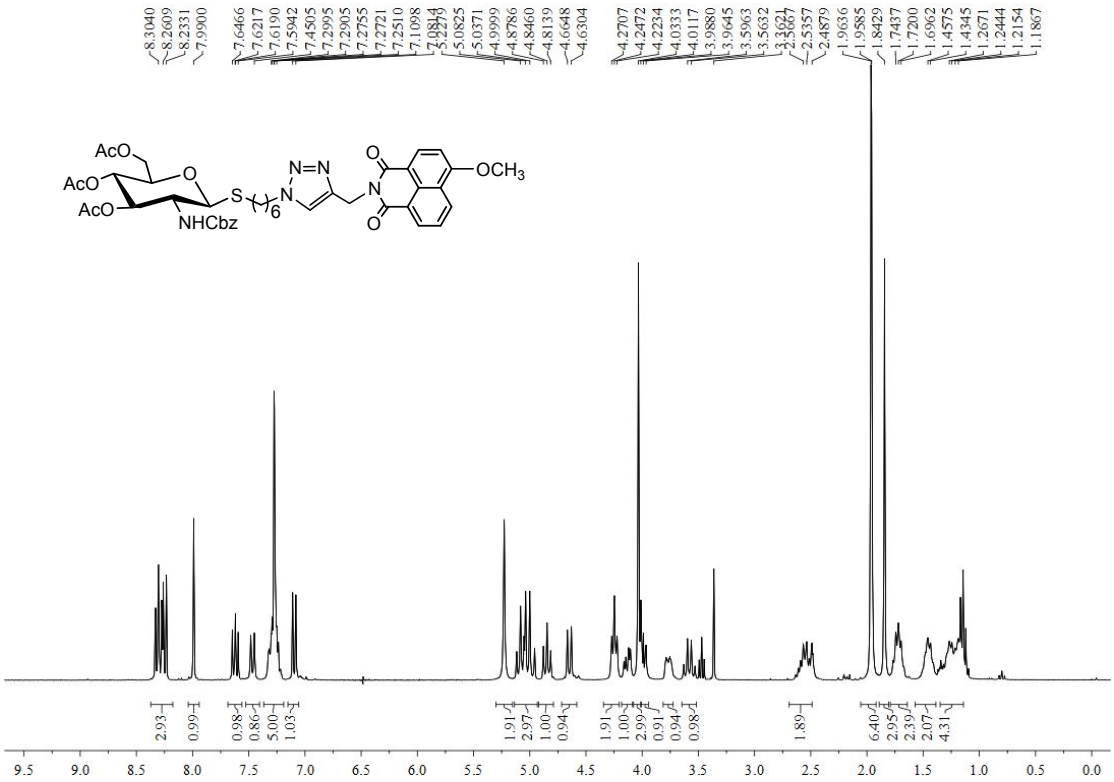
^{1}H NMR spectrum of 14k (300 MHz, DMSO-d_6)



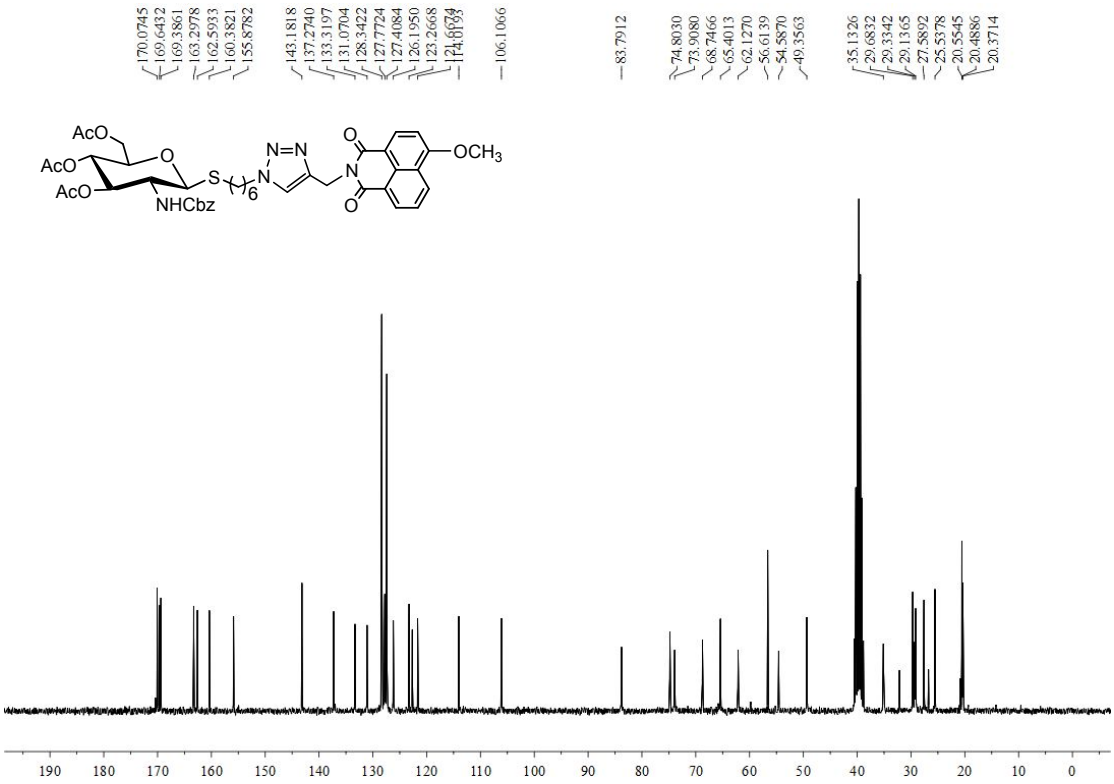
^{13}C NMR spectrum of 14k (75 MHz, DMSO-d_6)



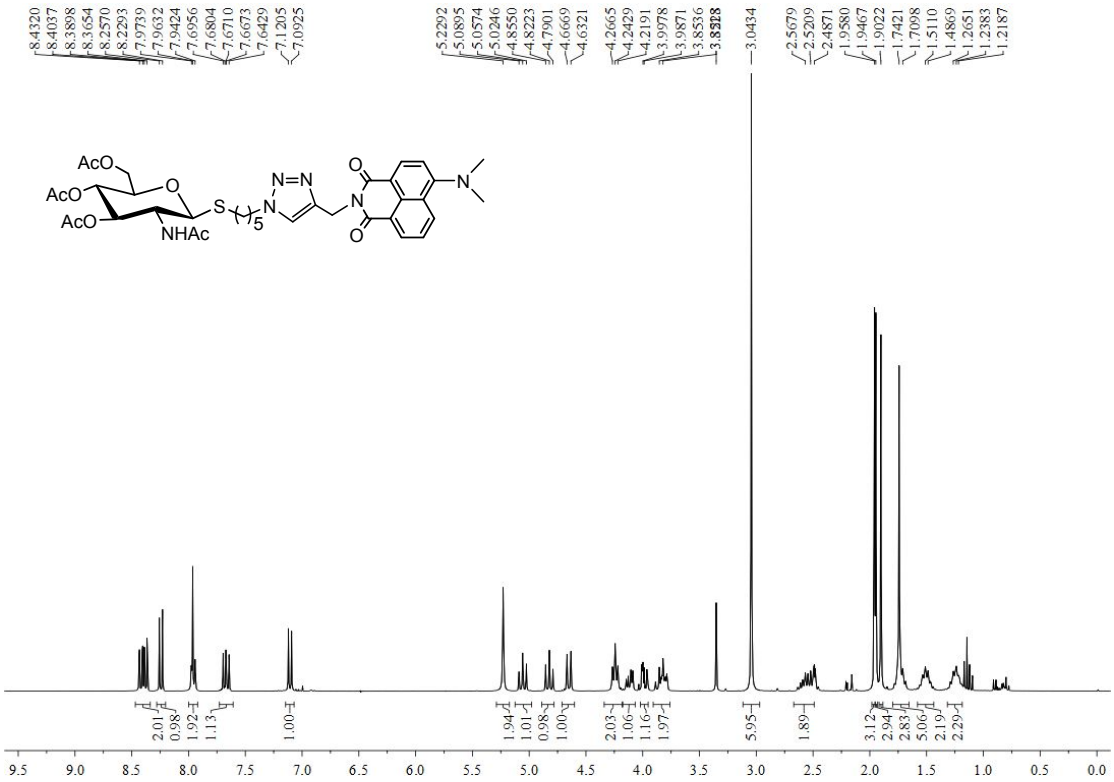
^{1}H NMR spectrum of 14l (300 MHz, DMSO-d_6)



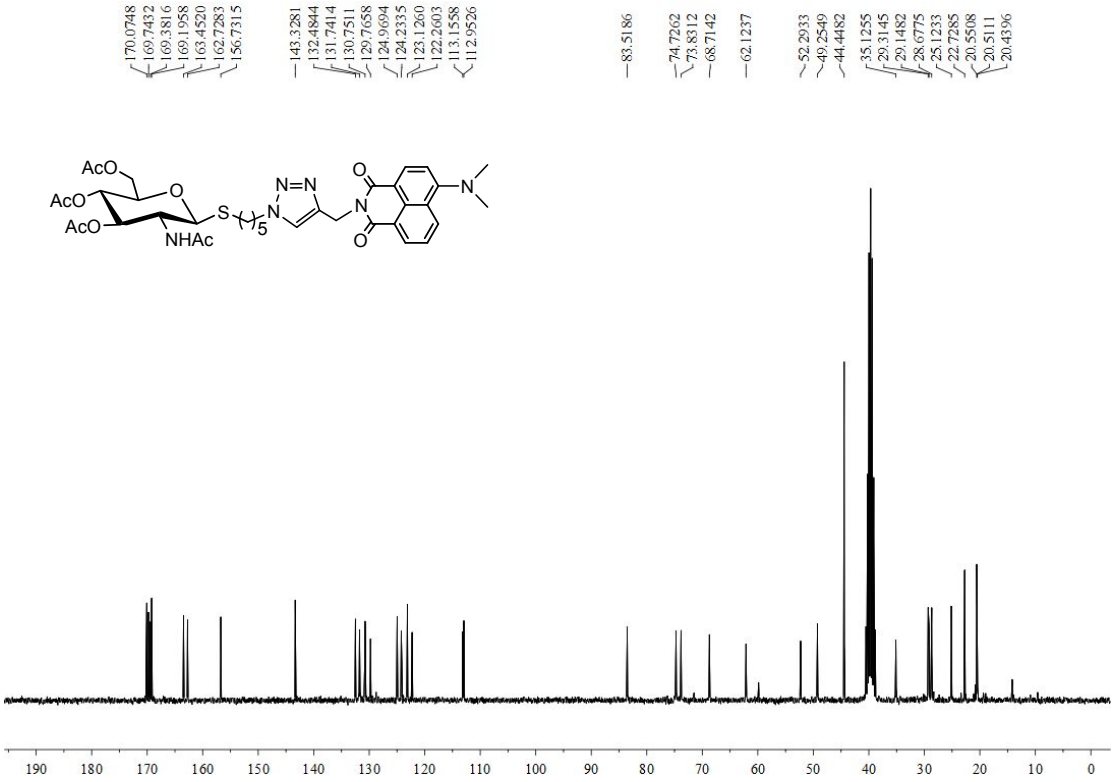
^{13}C NMR spectrum of 14l (75 MHz, DMSO-d_6)



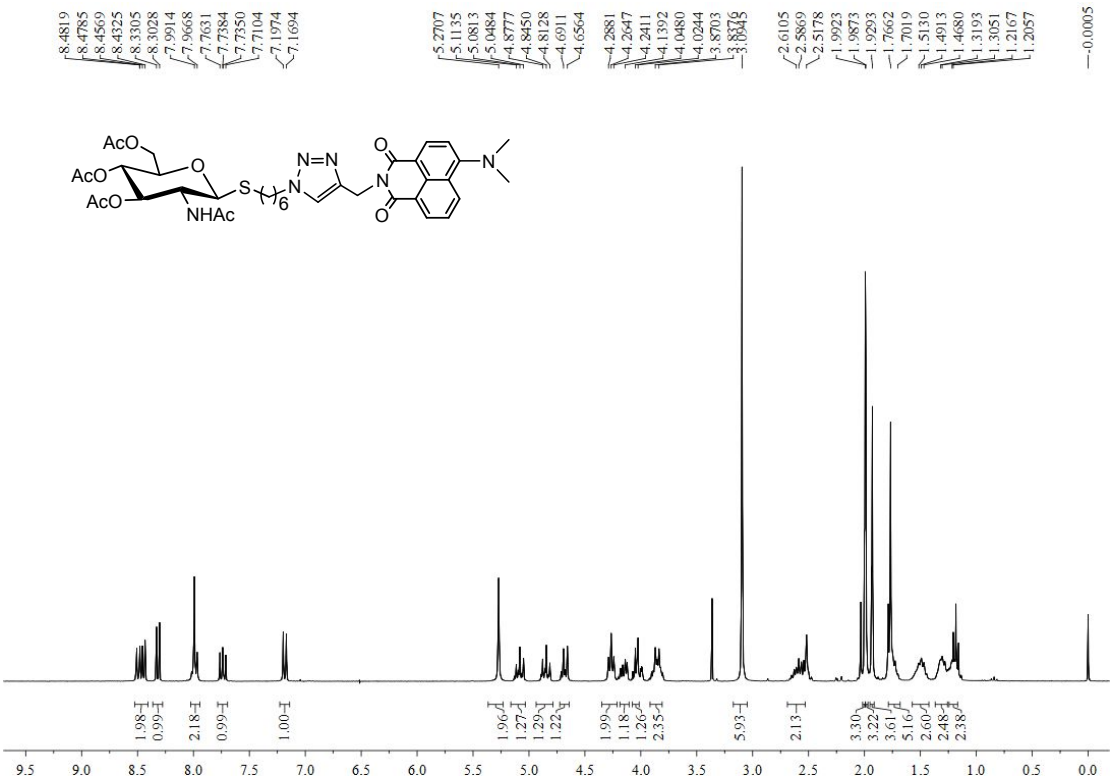
^{1}H NMR spectrum of 14m (300 MHz, DMSO-d_6)



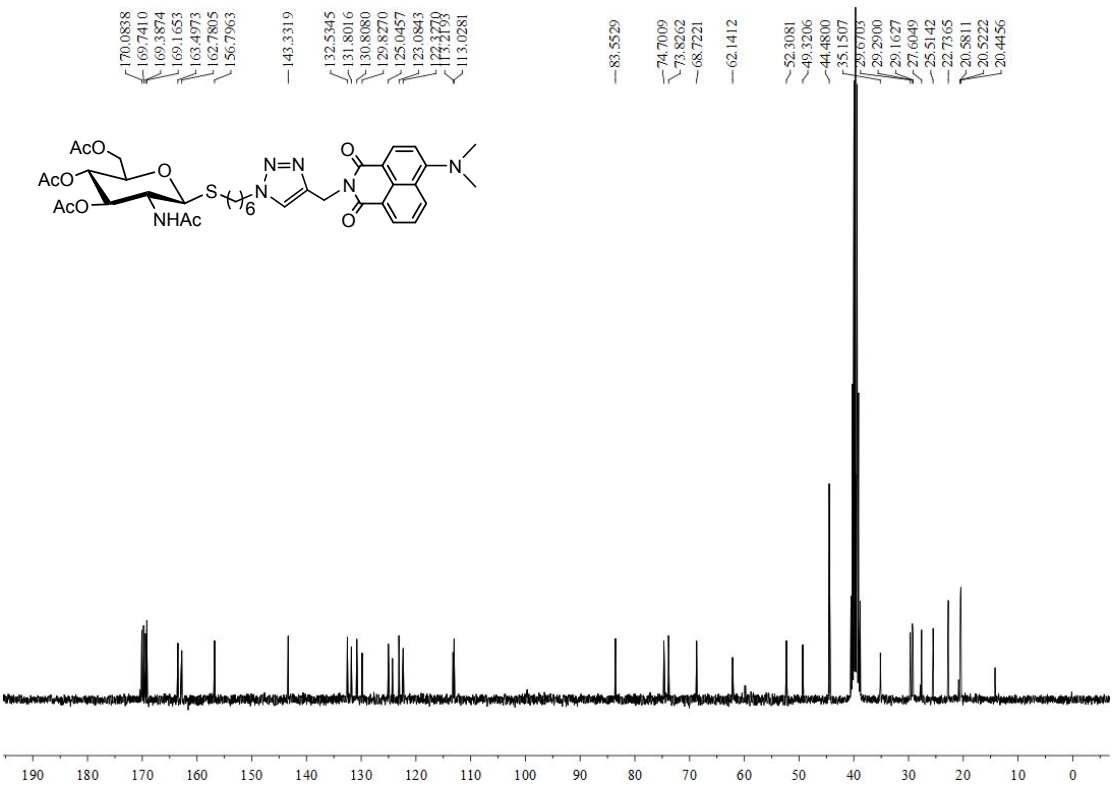
^{13}C NMR spectrum of 14m (75 MHz, DMSO-d_6)



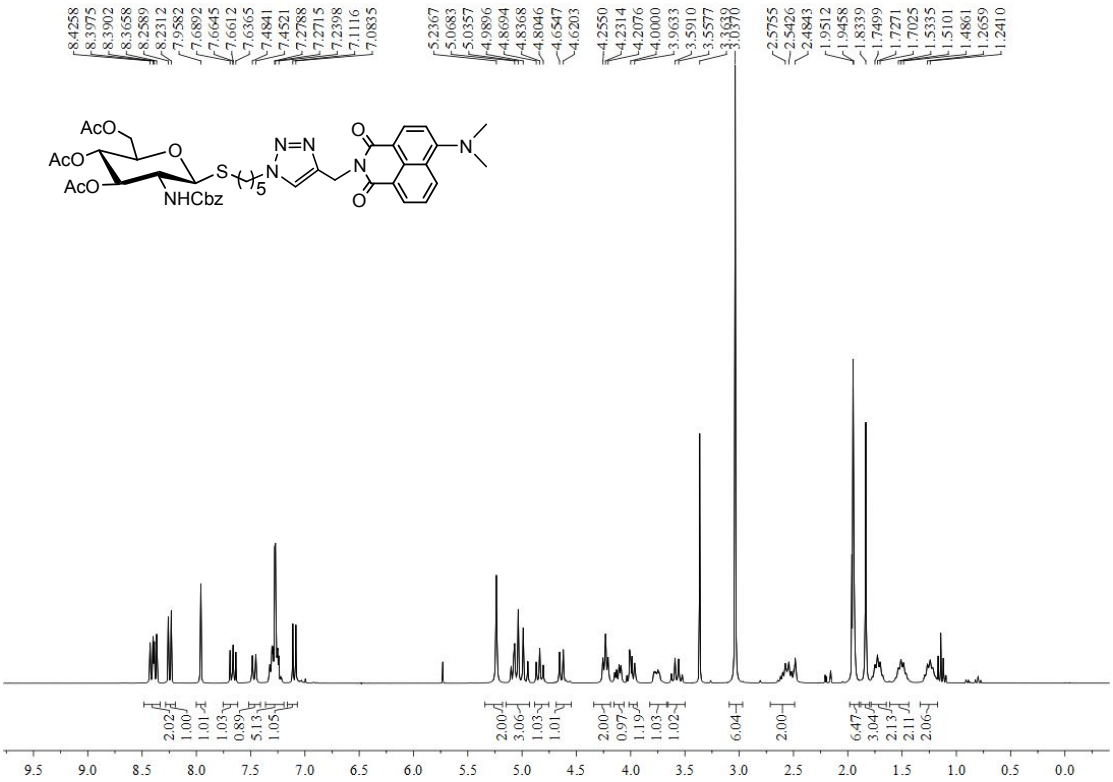
^{1}H NMR spectrum of 14n (300 MHz, DMSO-d_6)



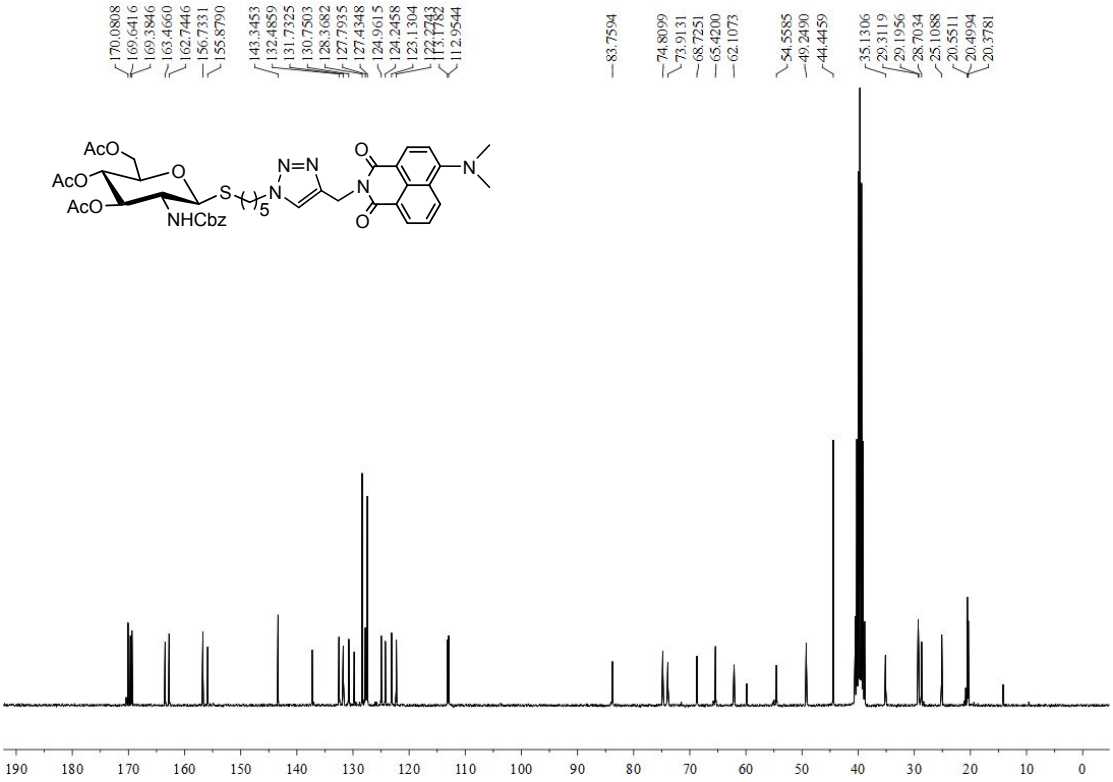
^{13}C NMR spectrum of 14n (75 MHz, DMSO-d_6)



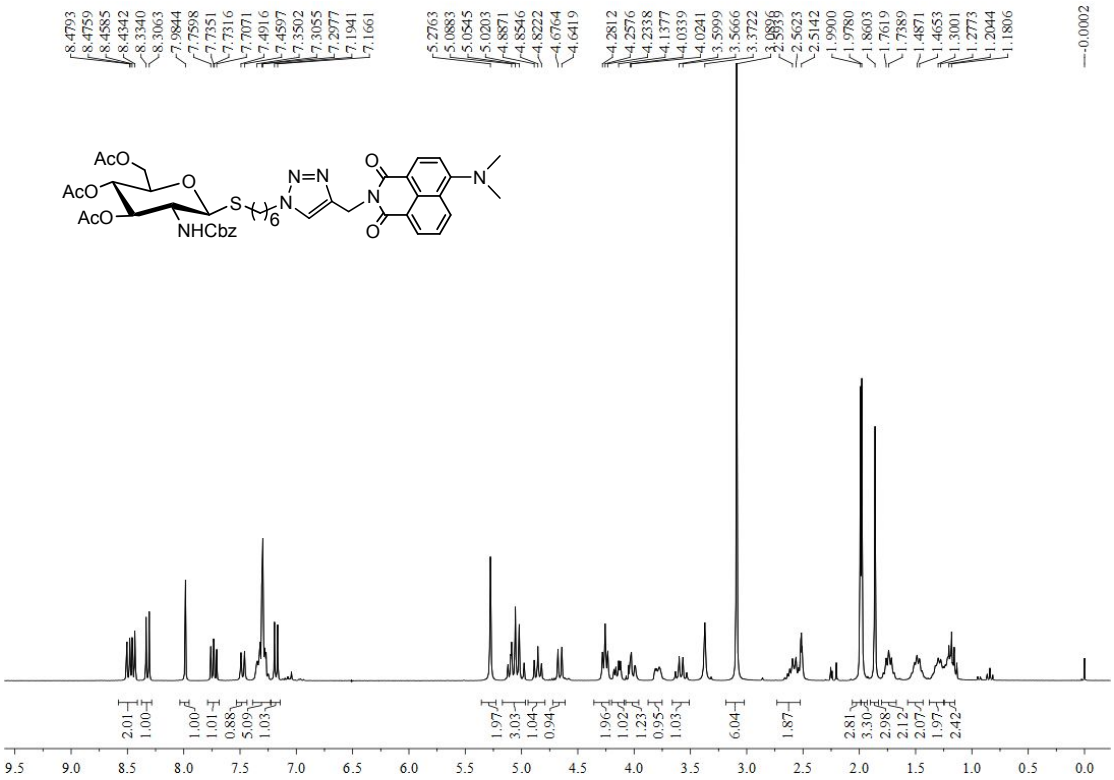
^{1}H NMR spectrum of 14o (300 MHz, DMSO-d_6)



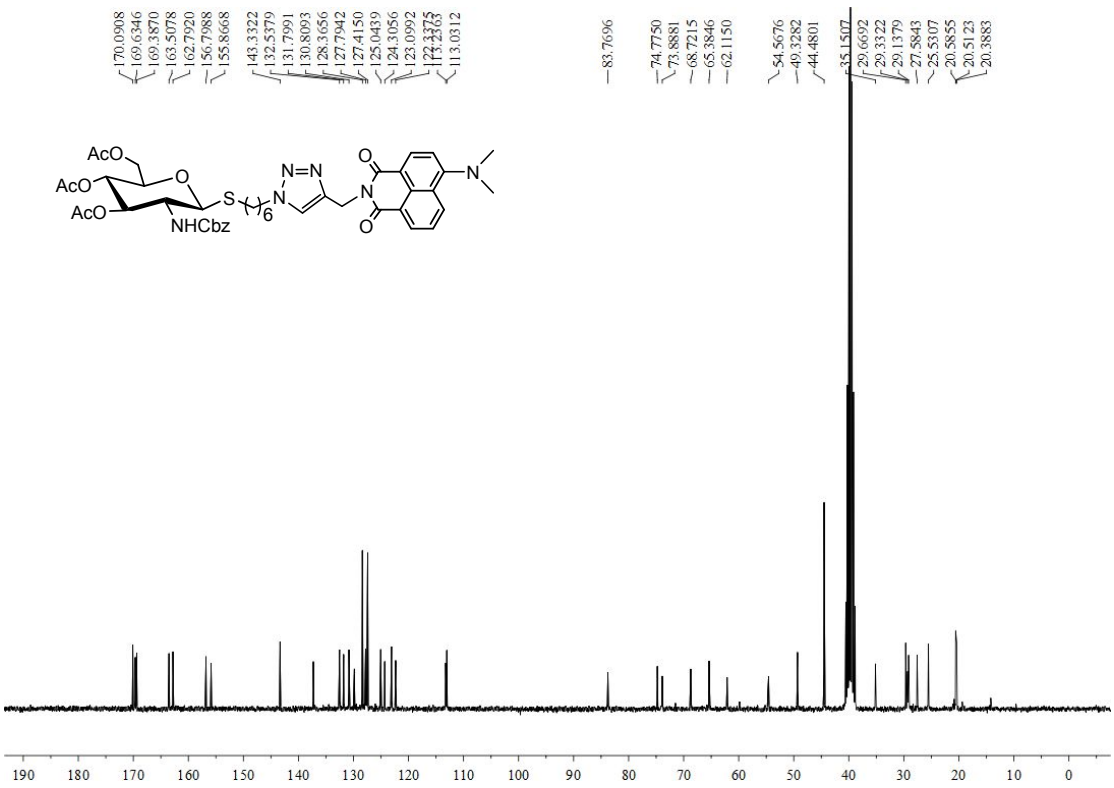
^{13}C NMR spectrum of 14o (75 MHz, DMSO-d_6)



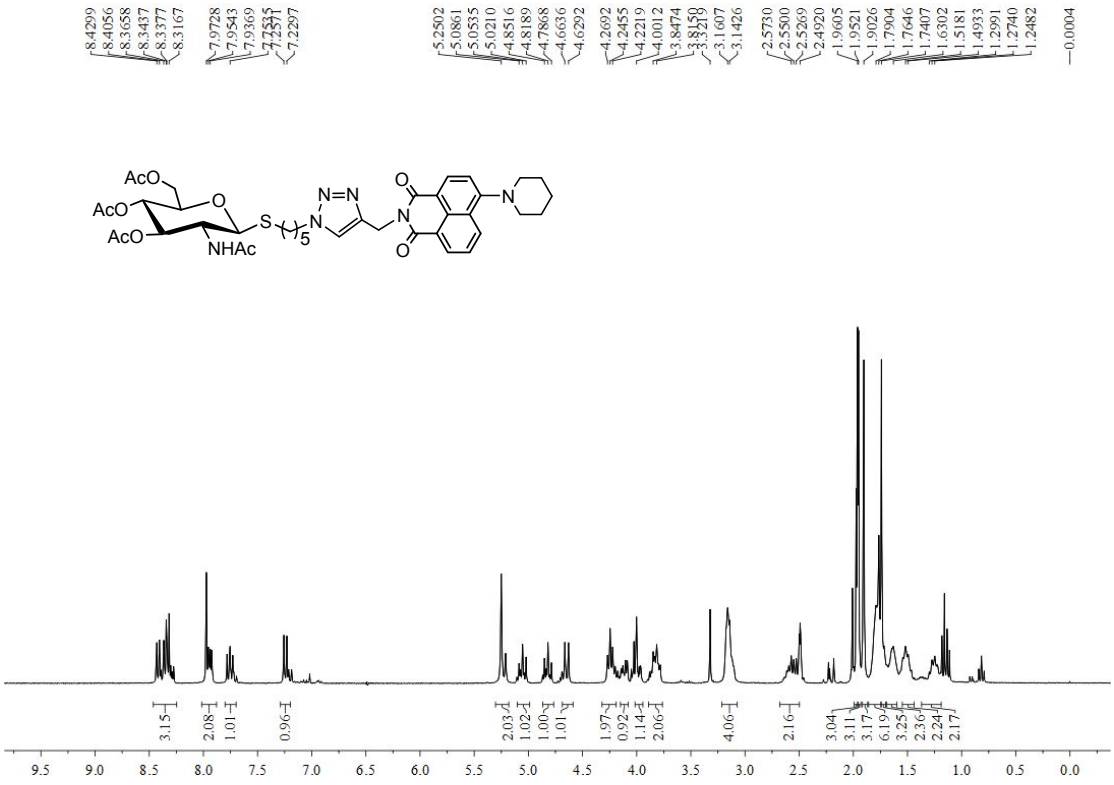
^{1}H NMR spectrum of 14p (300 MHz, DMSO-d_6)



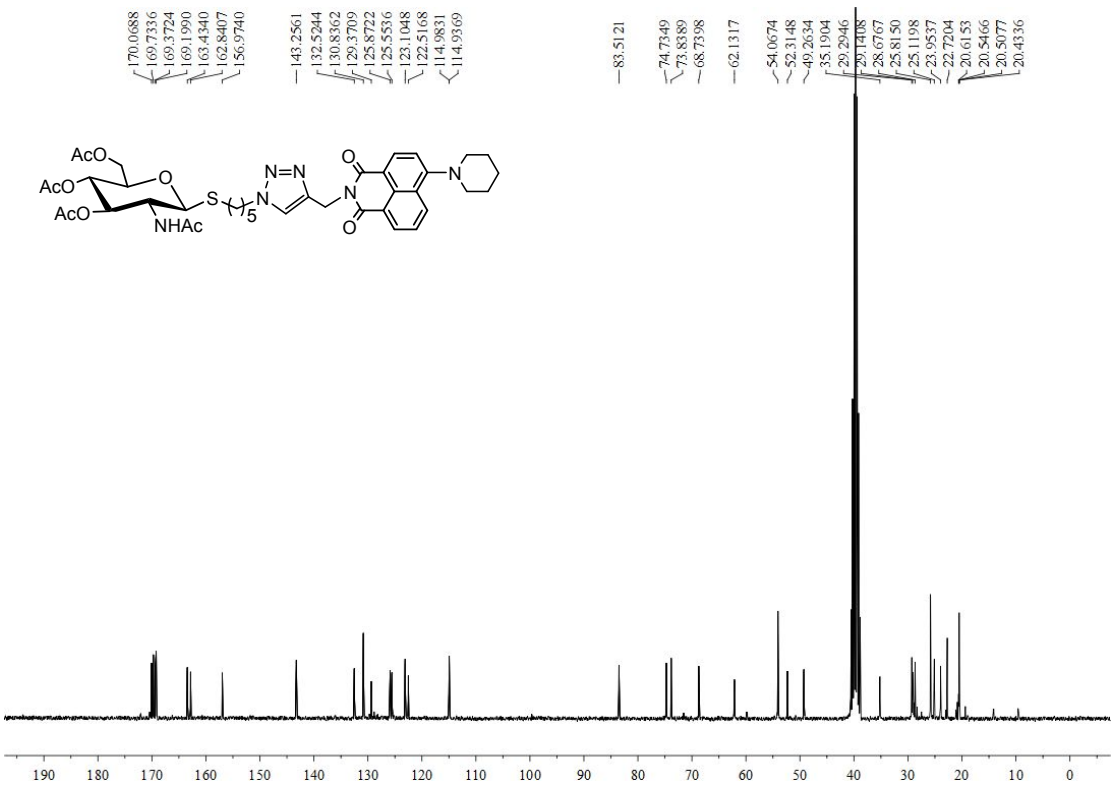
^{13}C NMR spectrum of 14p (75 MHz, DMSO-d_6)



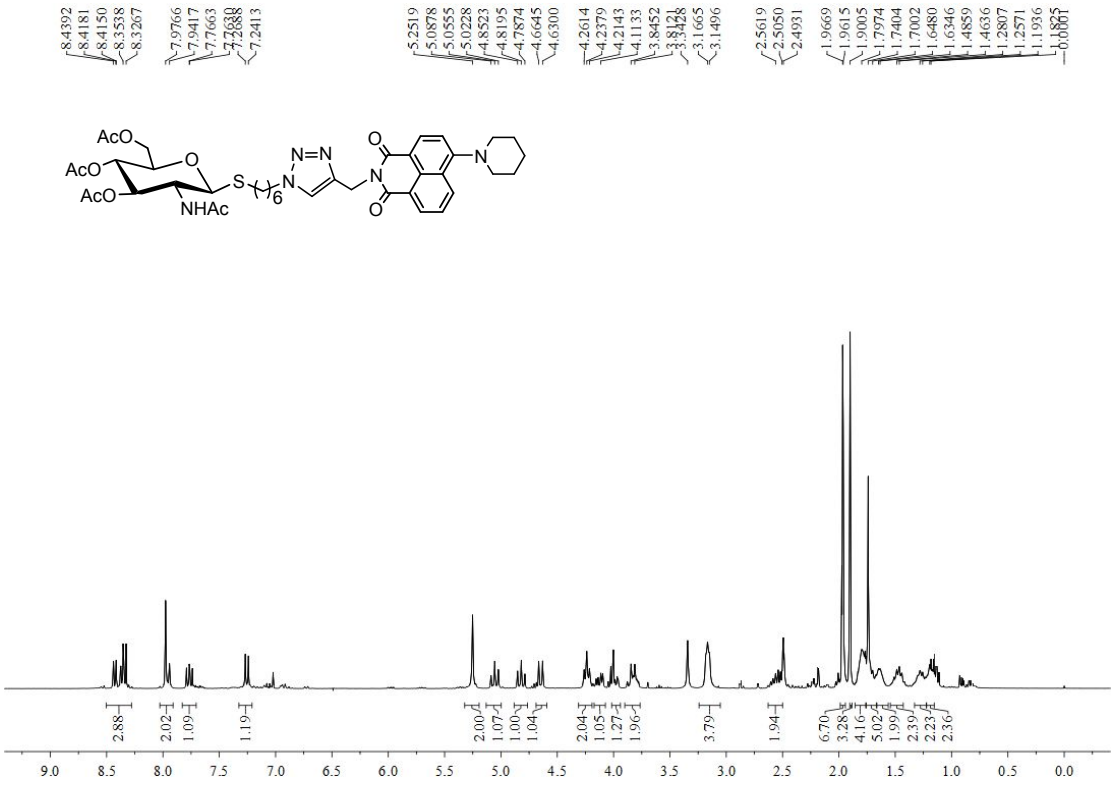
^{1}H NMR spectrum of 14q (300 MHz, DMSO-d_6)



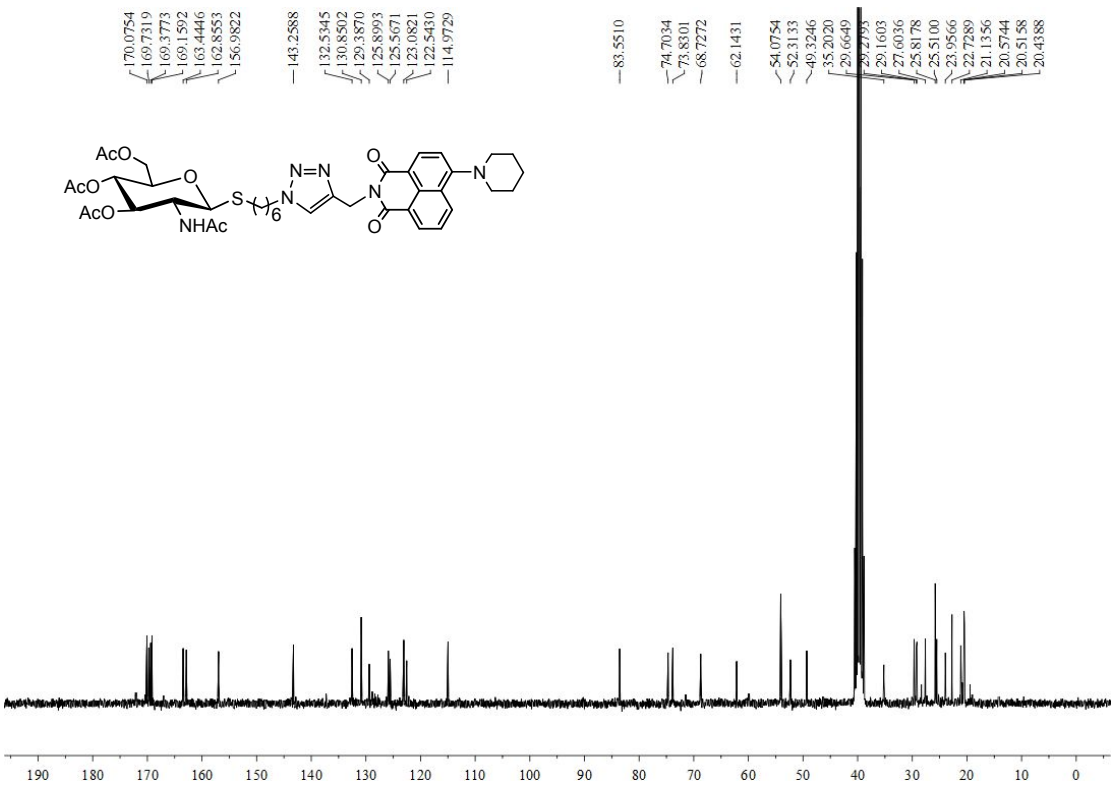
^{13}C NMR spectrum of 14q (75 MHz, DMSO-d_6)



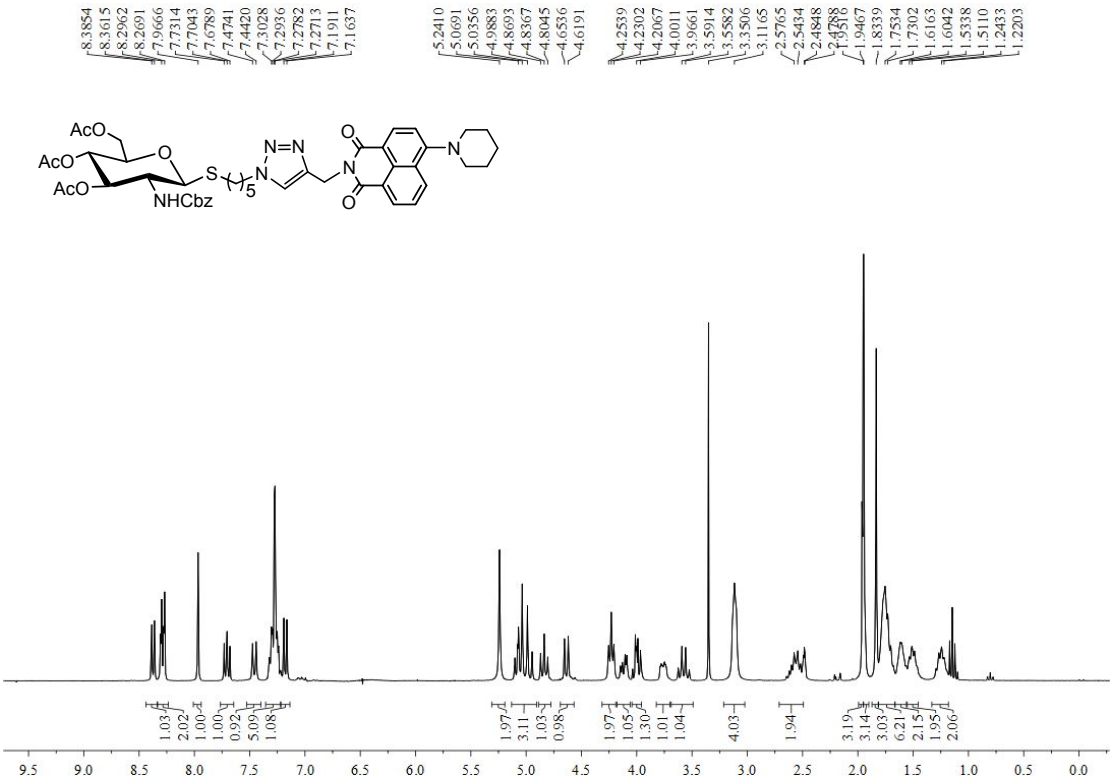
^{1}H NMR spectrum of 14r (300 MHz, DMSO-d_6)



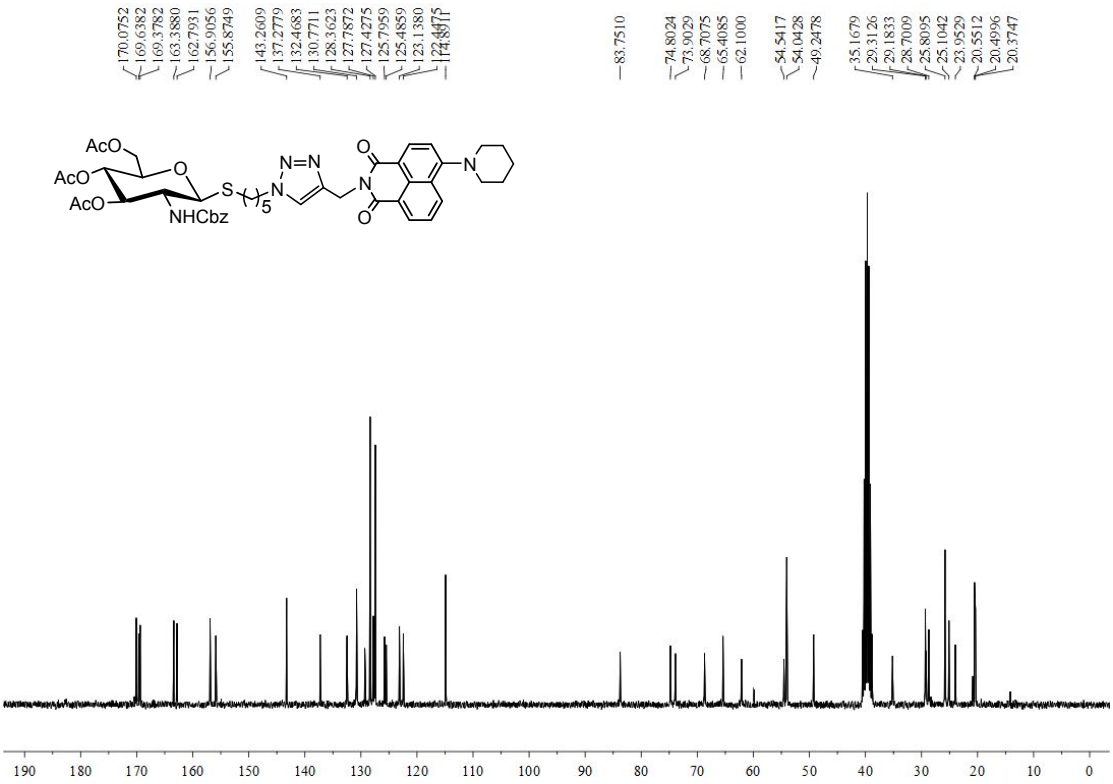
^{13}C NMR spectrum of 14r (75 MHz, DMSO-d_6)



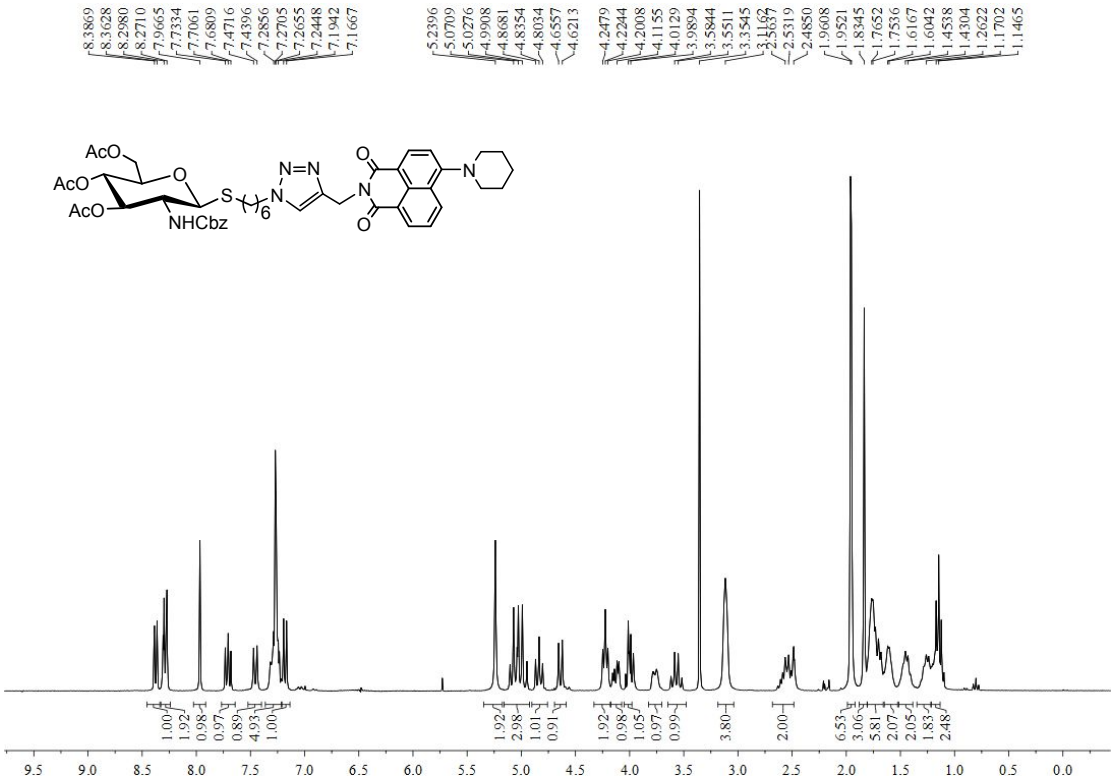
^{1}H NMR spectrum of 14s (300 MHz, DMSO-d_6)



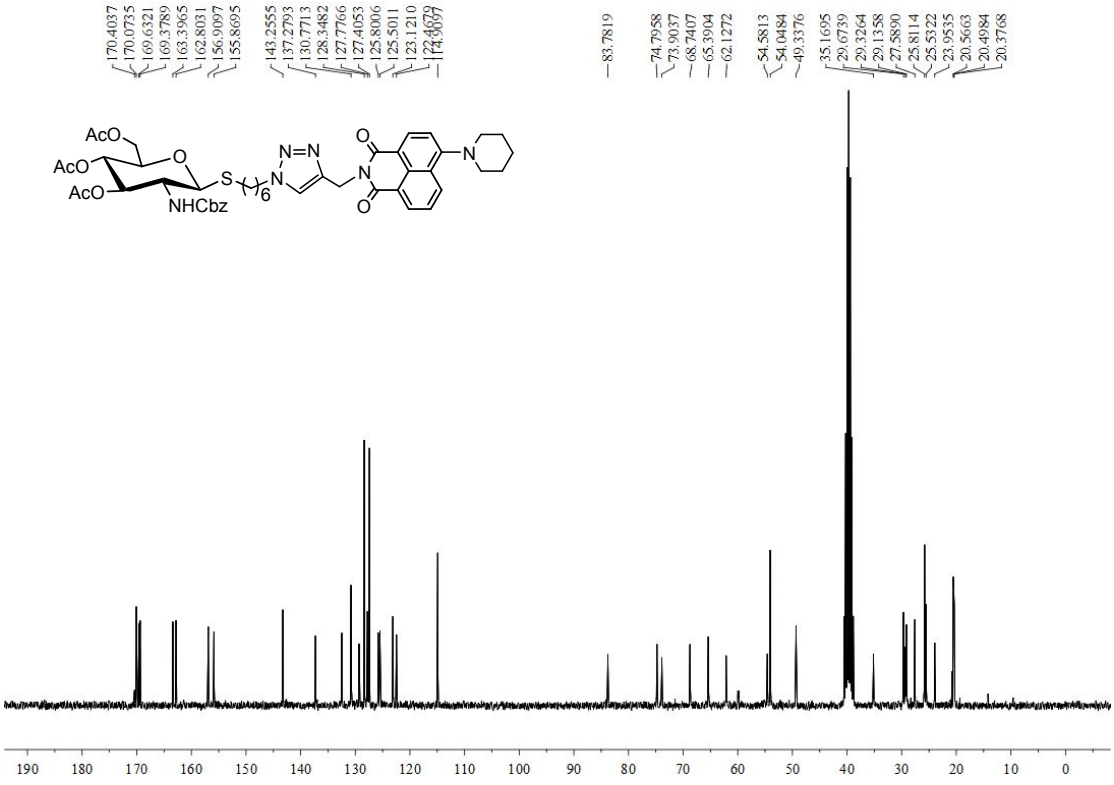
^{13}C NMR spectrum of 14s (75 MHz, DMSO-d_6)



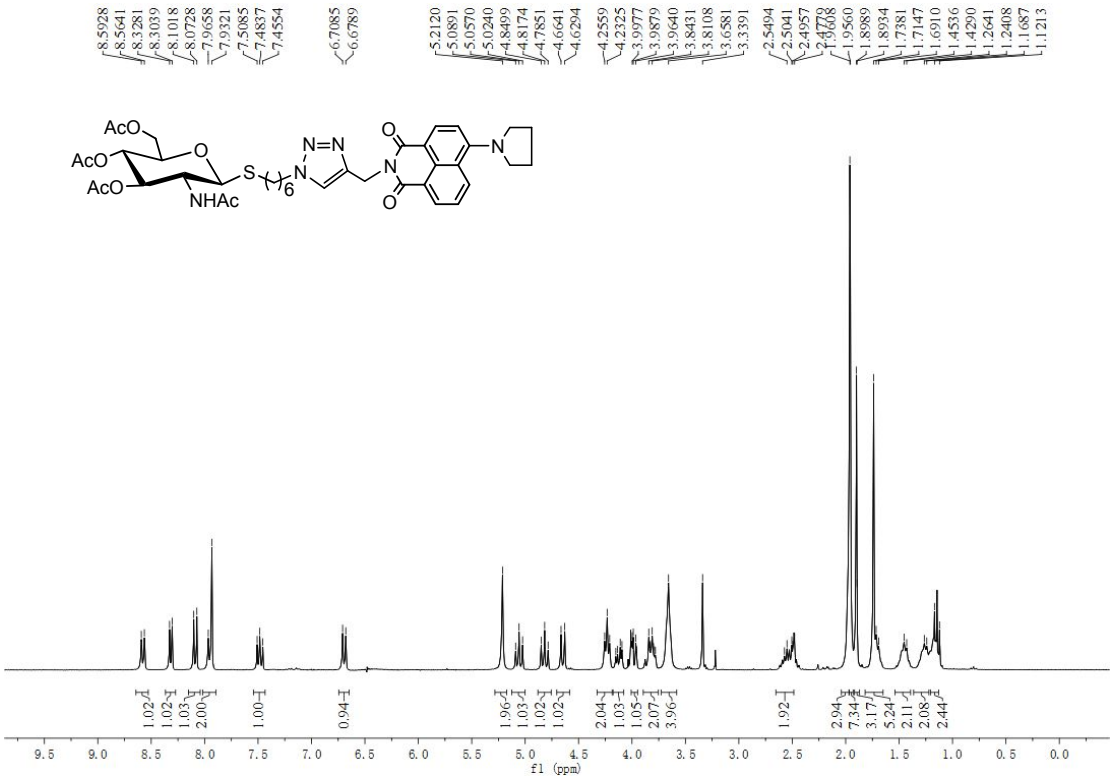
^{1}H NMR spectrum of 14t (300 MHz, DMSO-d_6)



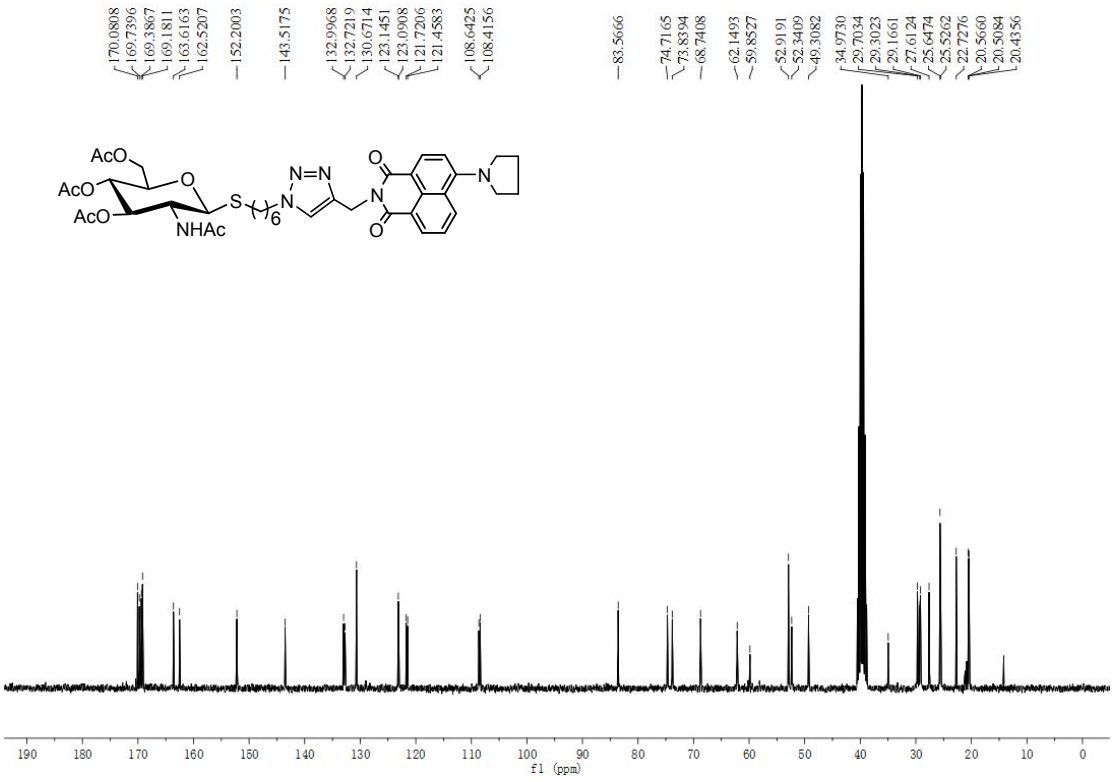
^{13}C NMR spectrum of 14t (75 MHz, DMSO-d_6)



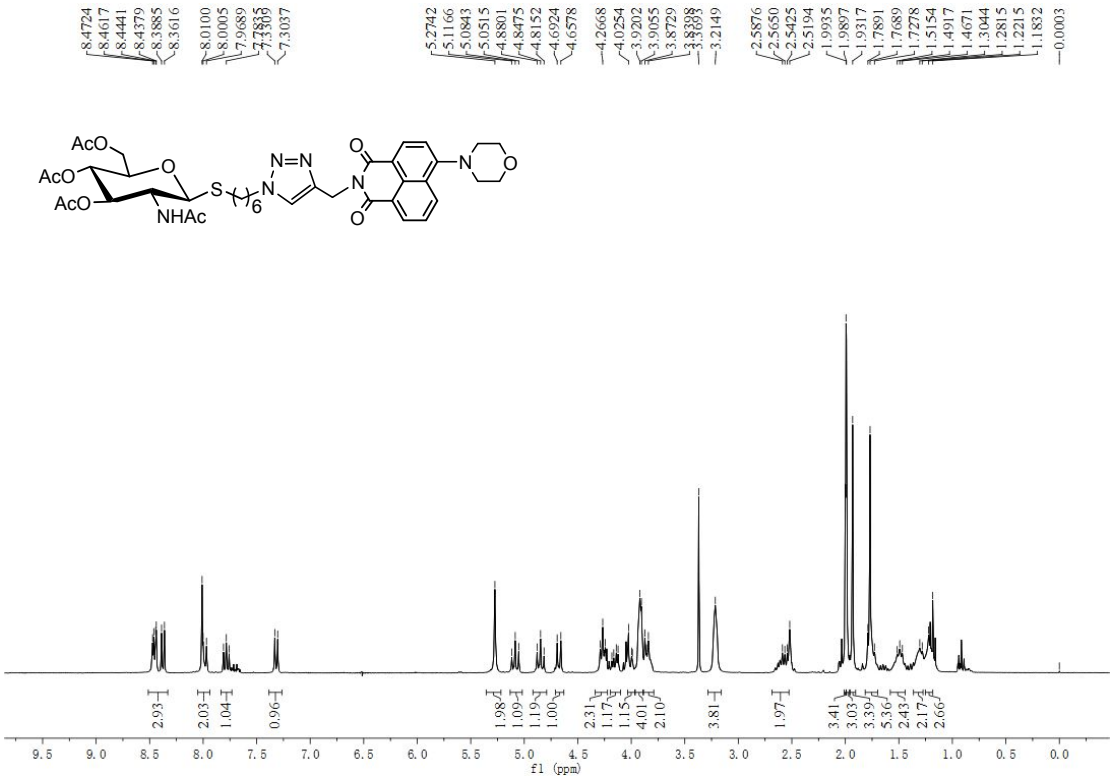
^{1}H NMR spectrum of 14u (300 MHz, DMSO-d_6)



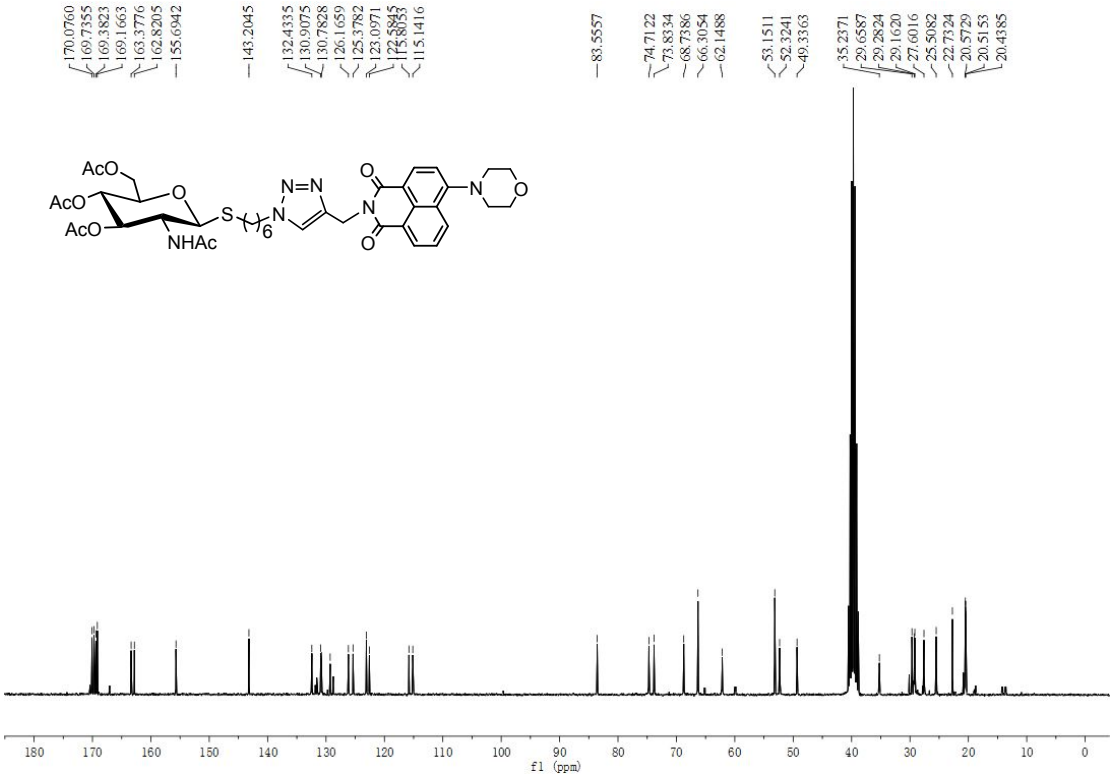
^{13}C NMR spectrum of 14u (75 MHz, DMSO-d_6)



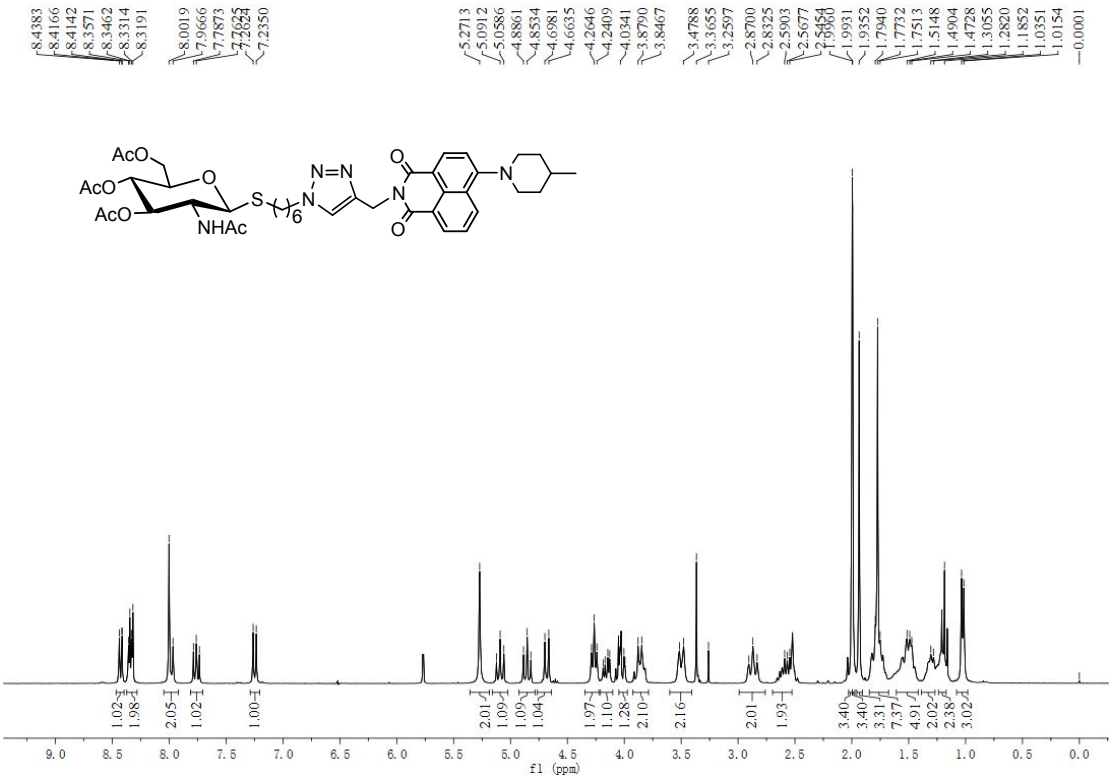
^{1}H NMR spectrum of 14v (300 MHz, DMSO-d_6)



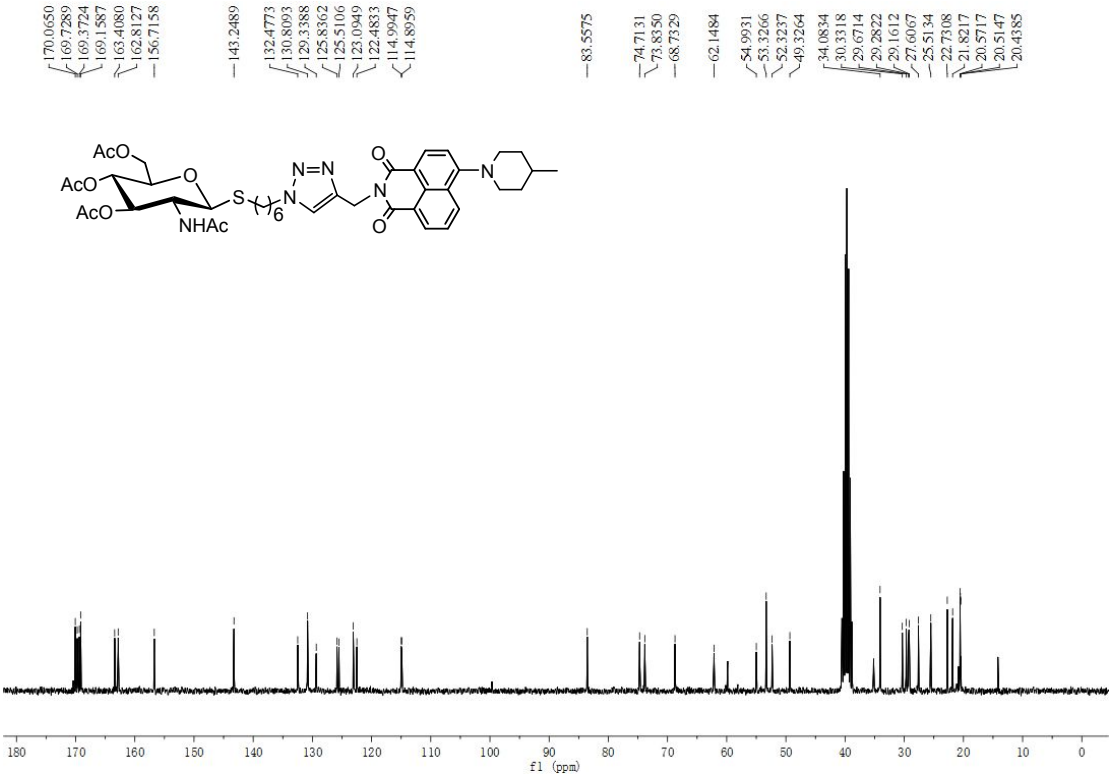
^{13}C NMR spectrum of 14v (75 MHz, DMSO-d_6)



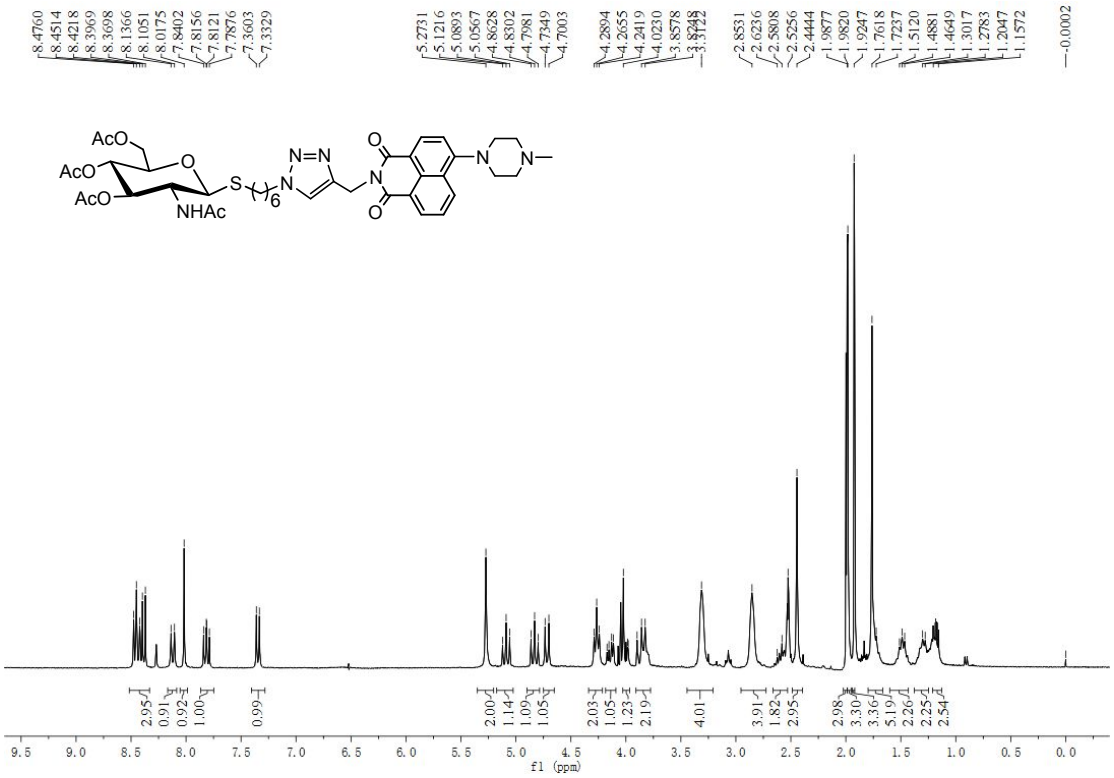
^{1}H NMR spectrum of 14w (300 MHz, DMSO-d_6)



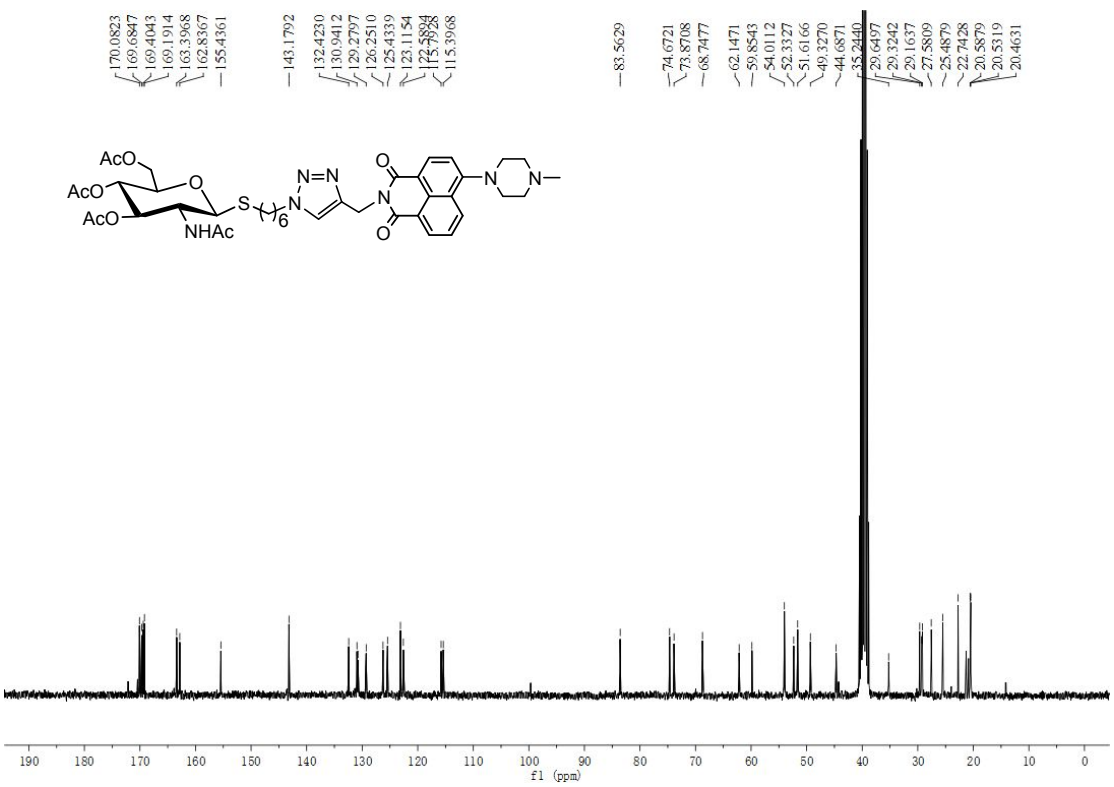
^{13}C NMR spectrum of 14w (75 MHz, DMSO-d_6)



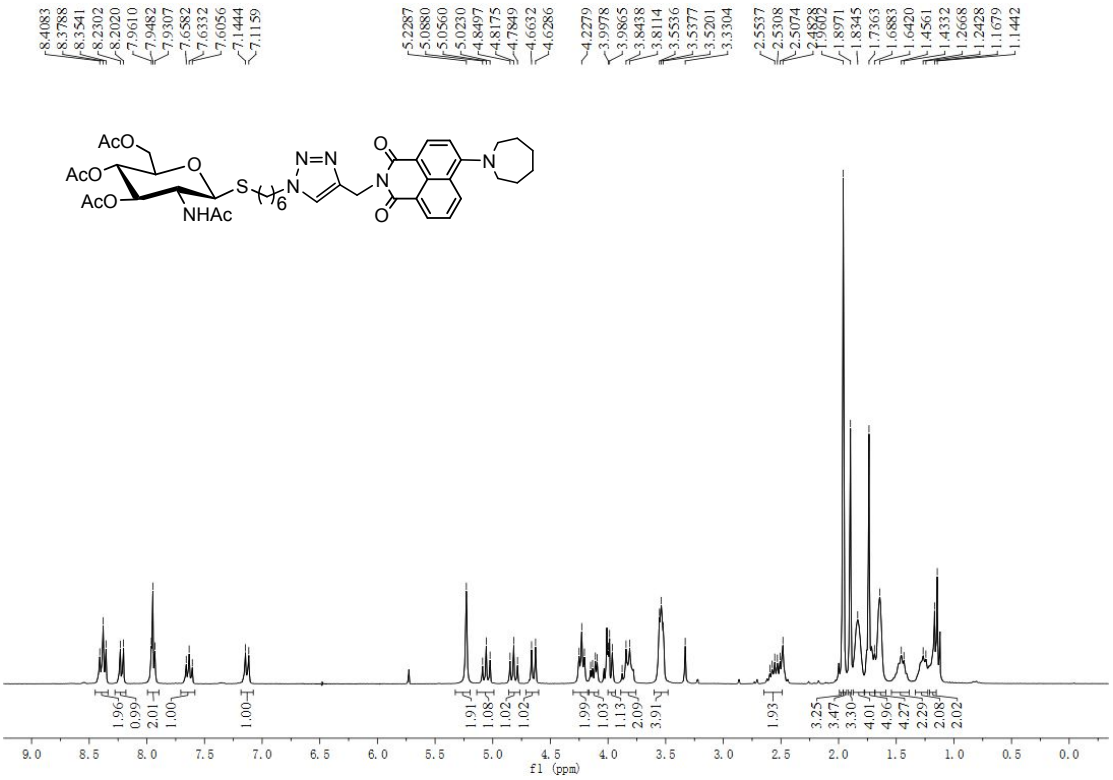
^{1}H NMR spectrum of 14x (300 MHz, DMSO-d_6)



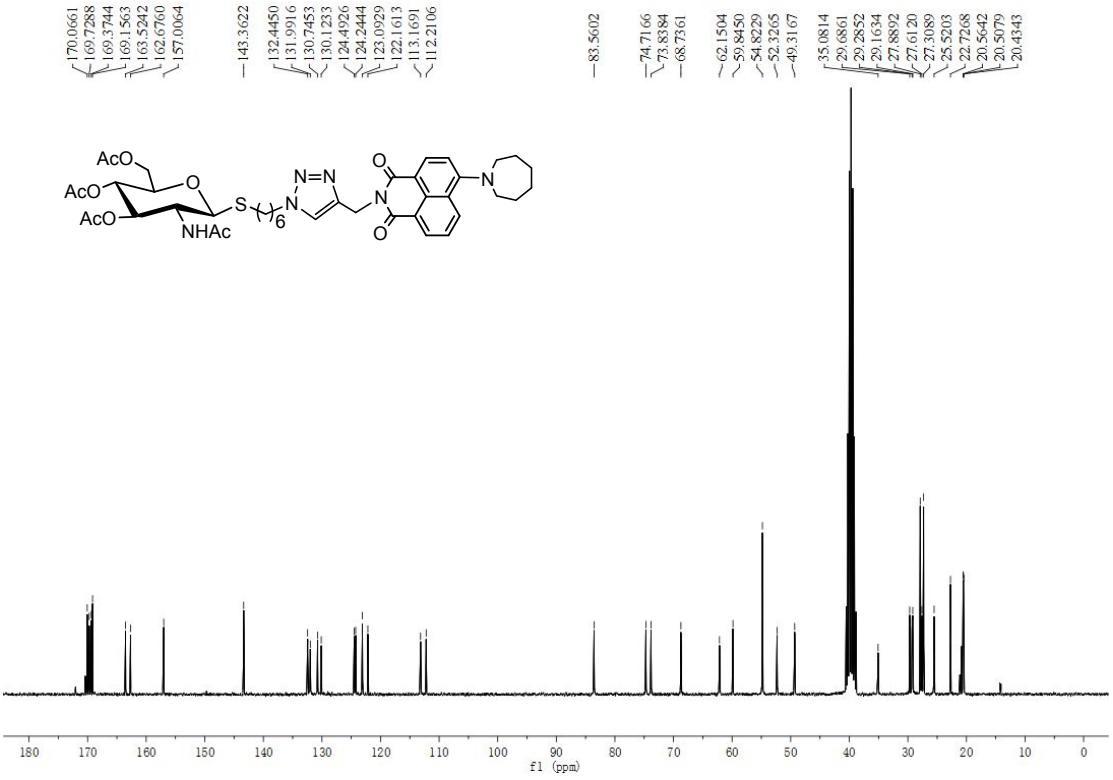
^{13}C NMR spectrum of 14x (75 MHz, DMSO-d_6)



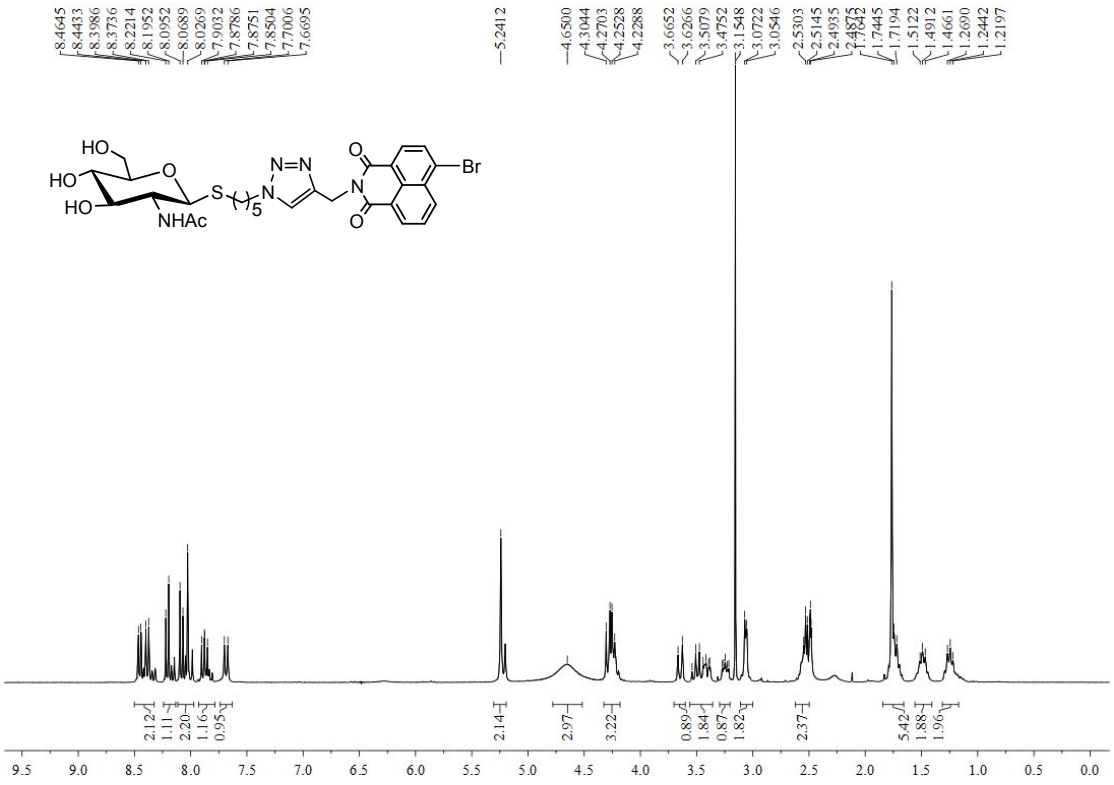
^{1}H NMR spectrum of 14y (300 MHz, DMSO-d_6)



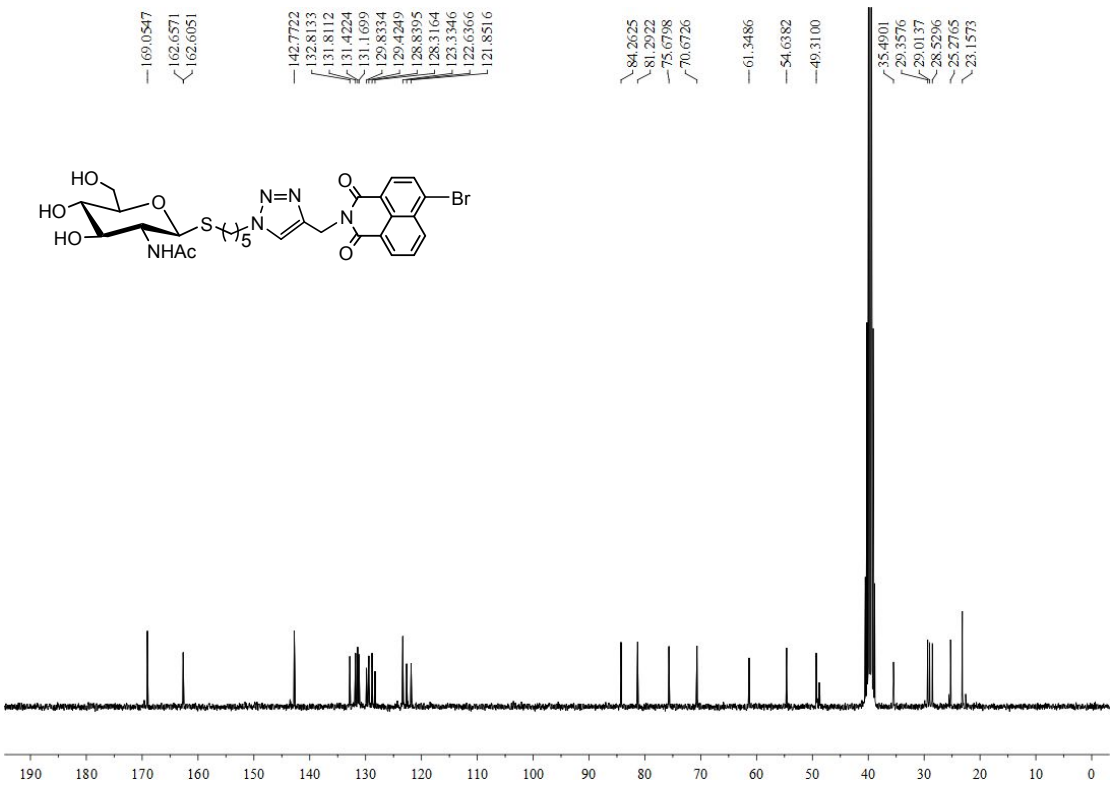
^{13}C NMR spectrum of 14y (75 MHz, DMSO-d_6)



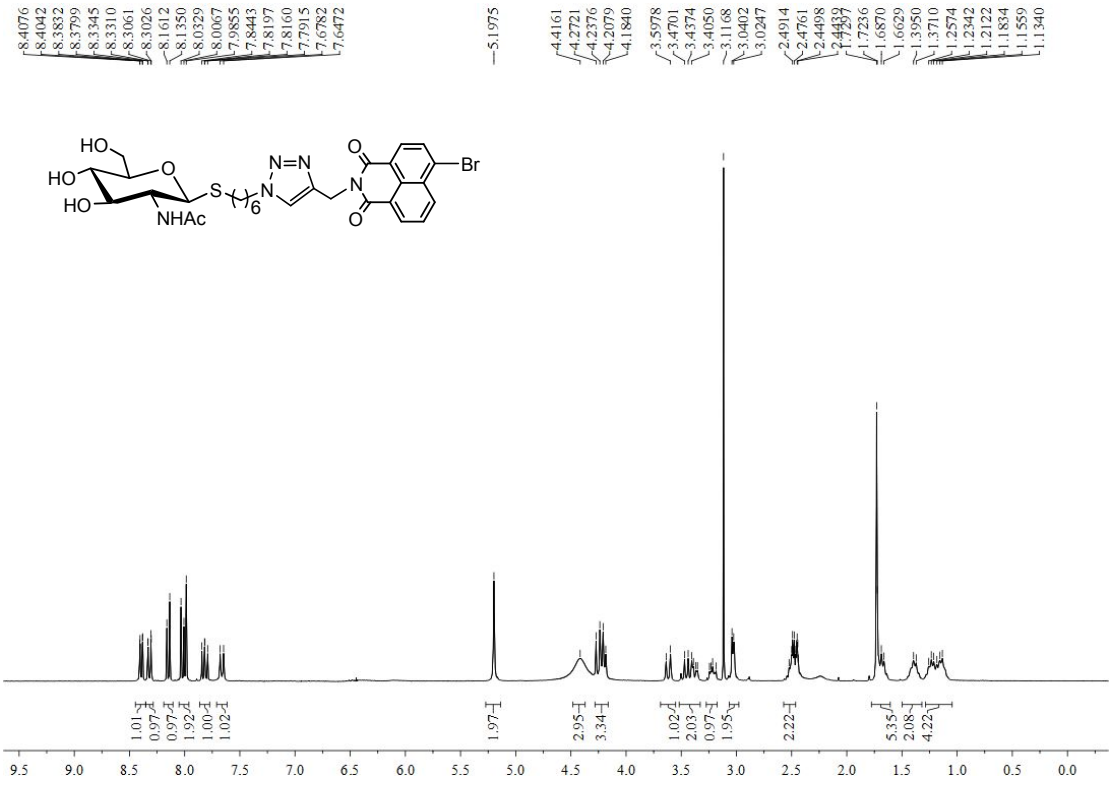
^{1}H NMR spectrum of 15a (300 MHz, DMSO-d_6)



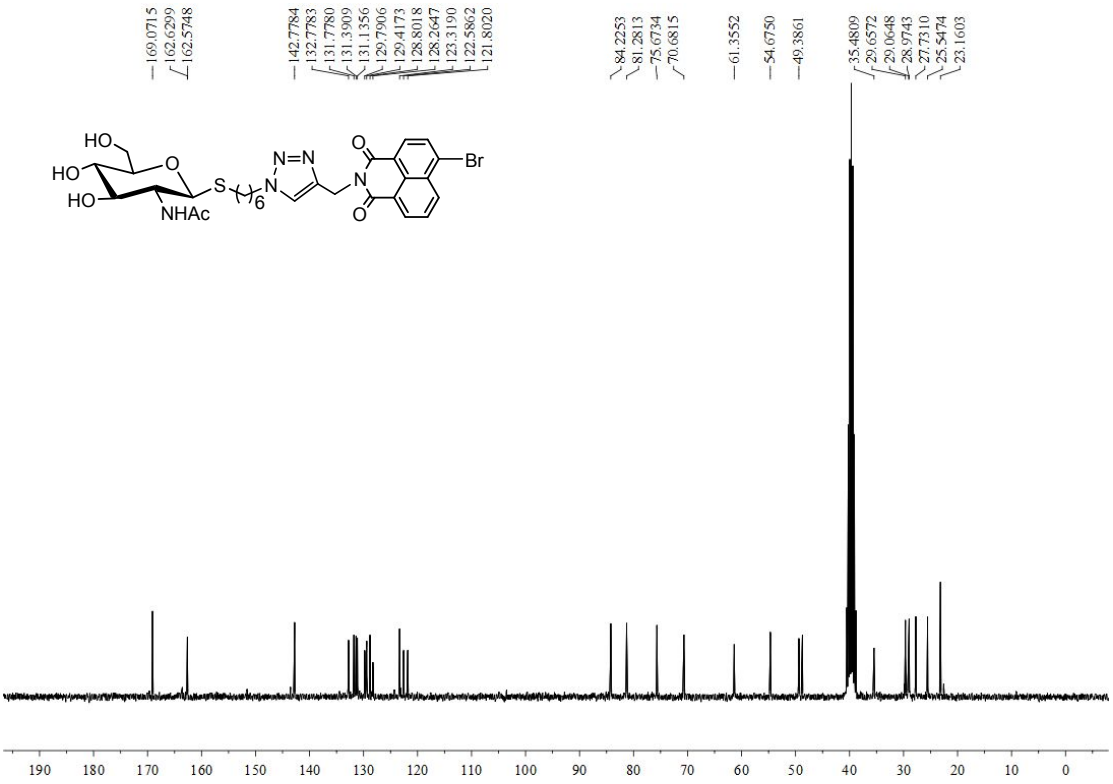
^{13}C NMR spectrum of 15a (75 MHz, DMSO-d_6)



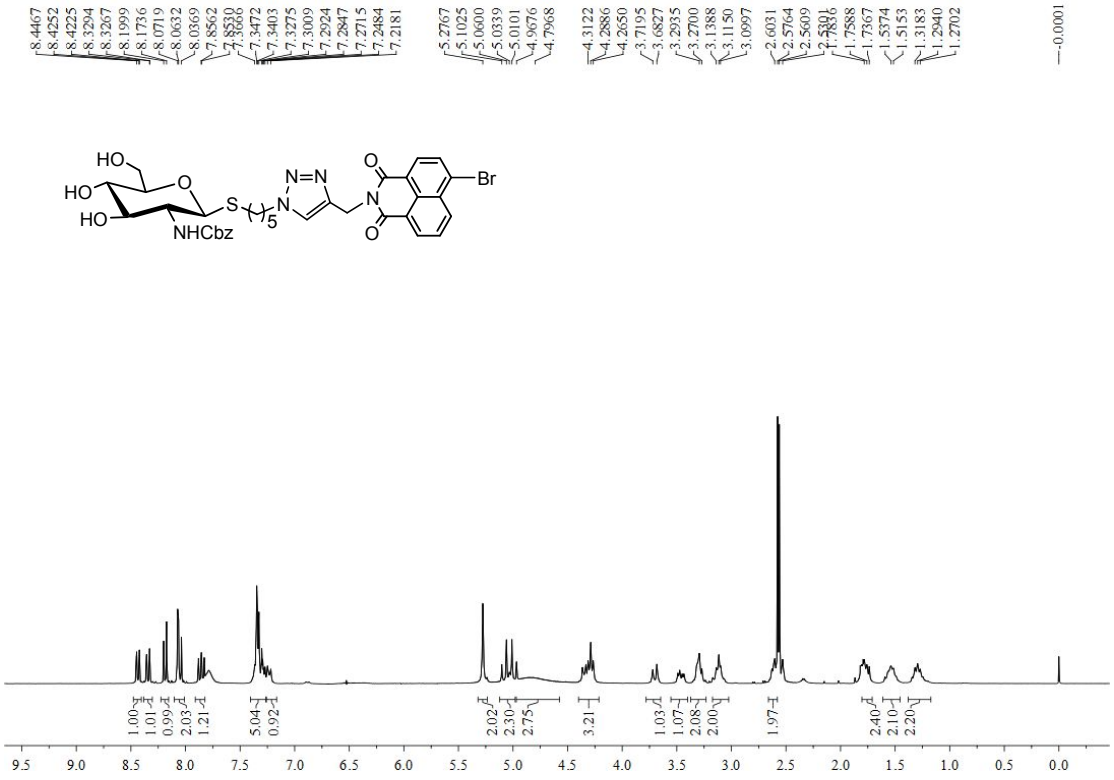
^{1}H NMR spectrum of 15b (300 MHz, DMSO-d_6)



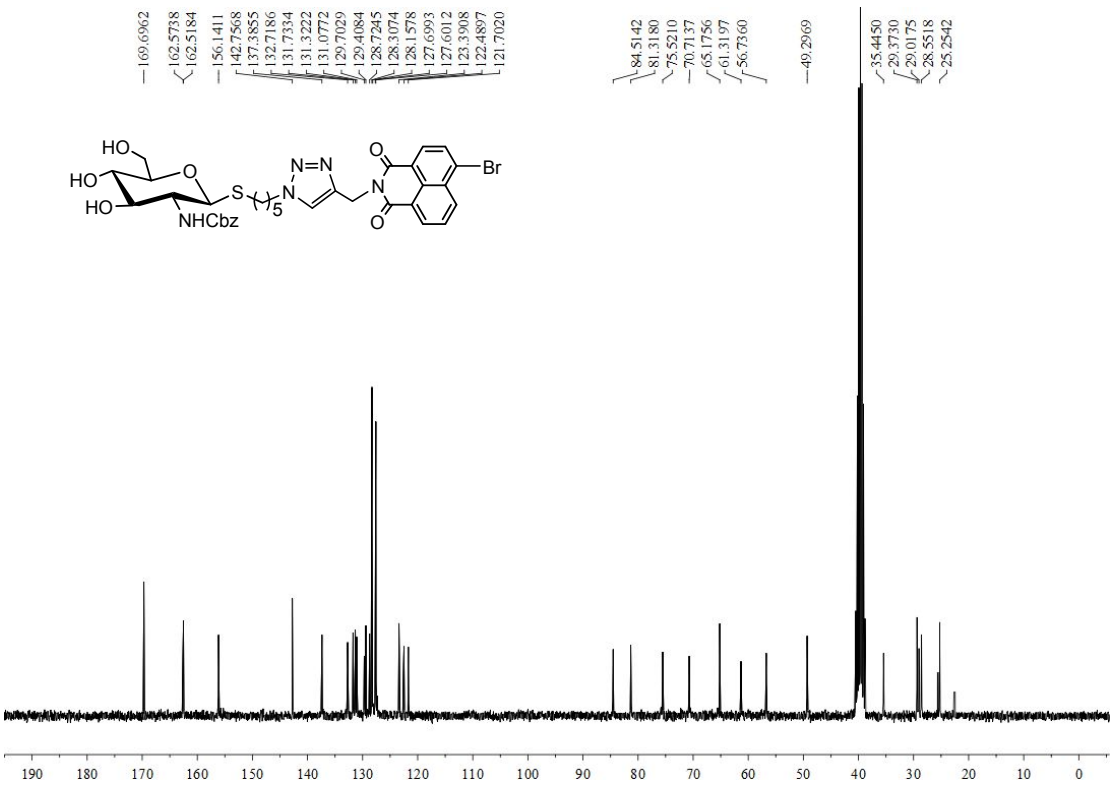
^{13}C NMR spectrum of 15b (75 MHz, DMSO-d_6)



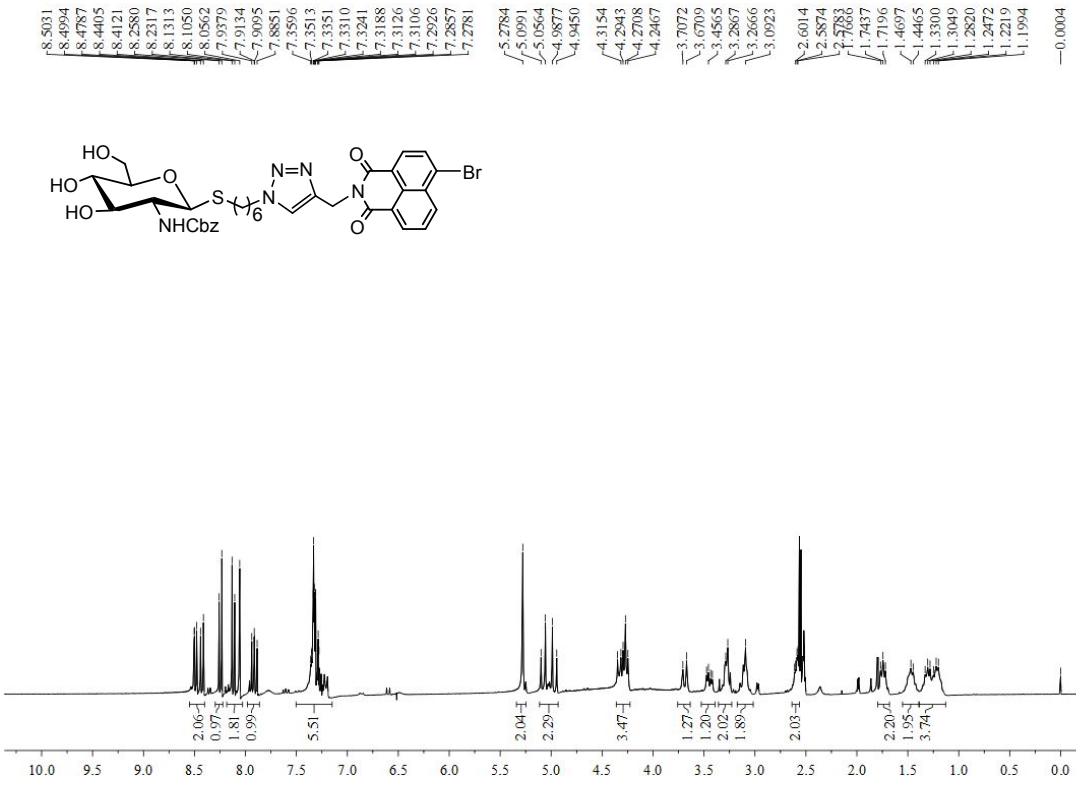
^{1}H NMR spectrum of 15c (300 MHz, DMSO-d_6)



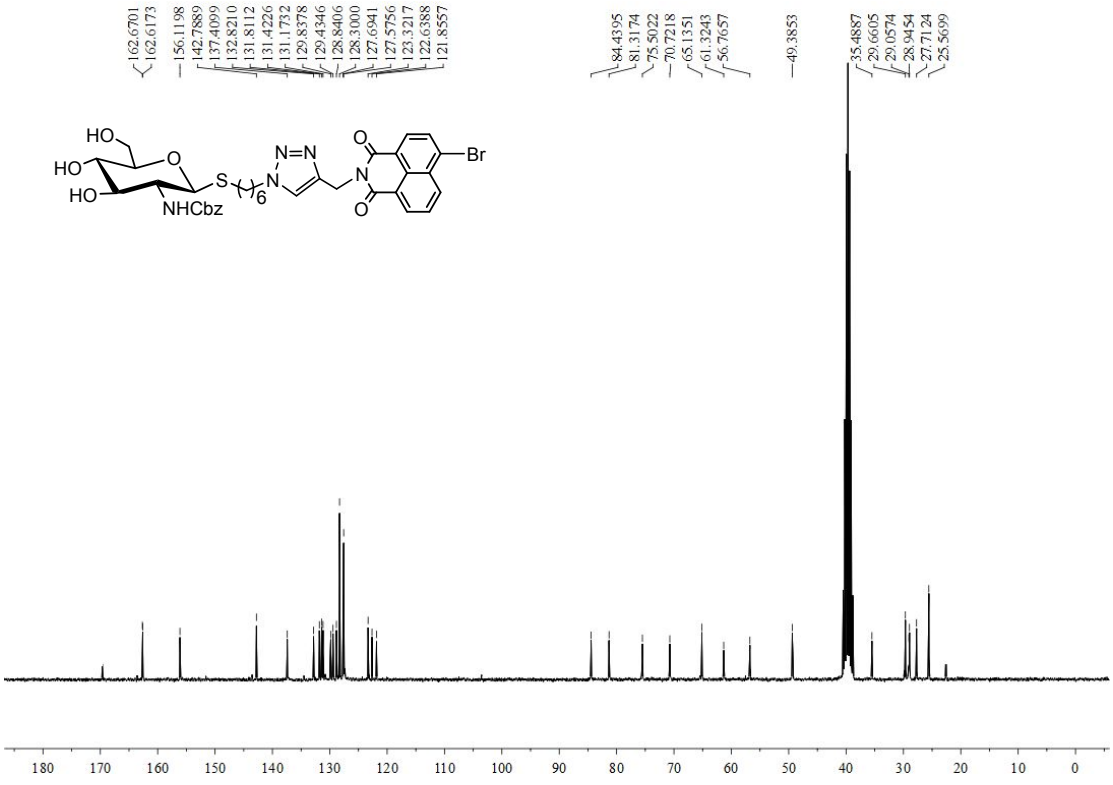
^{13}C NMR spectrum of 15c (75 MHz, DMSO-d_6)



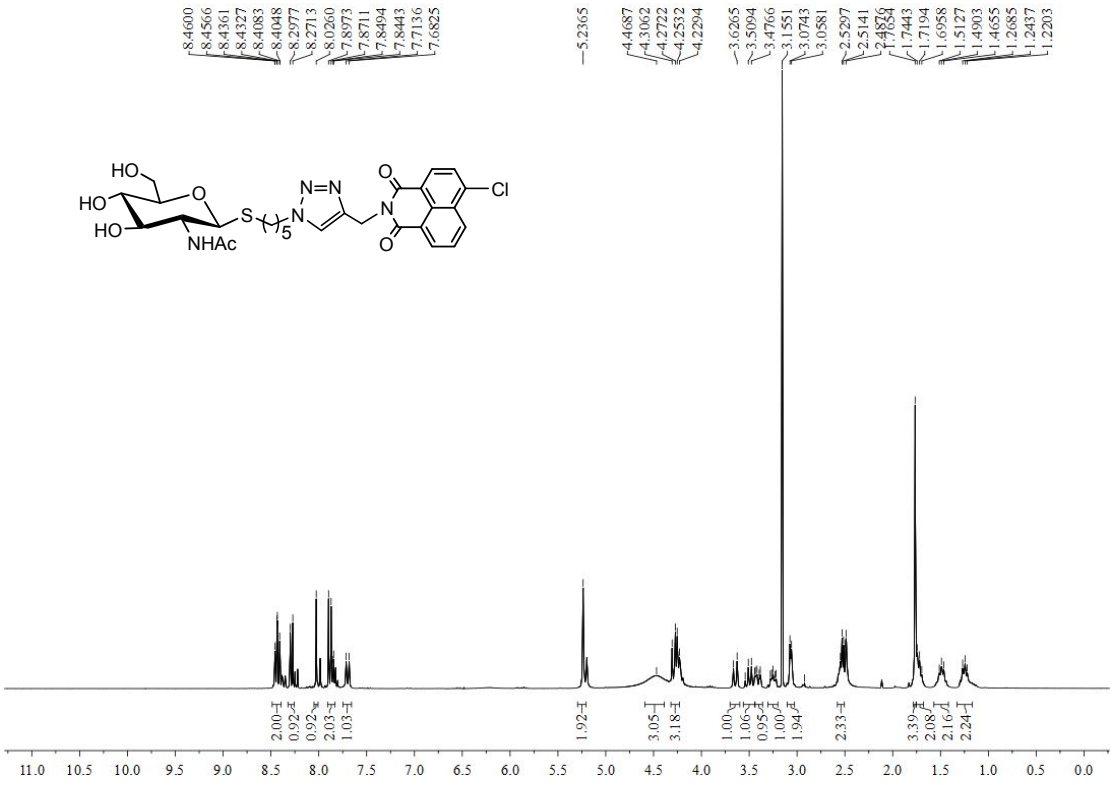
^{1}H NMR spectrum of 15d (300 MHz, DMSO-d_6)



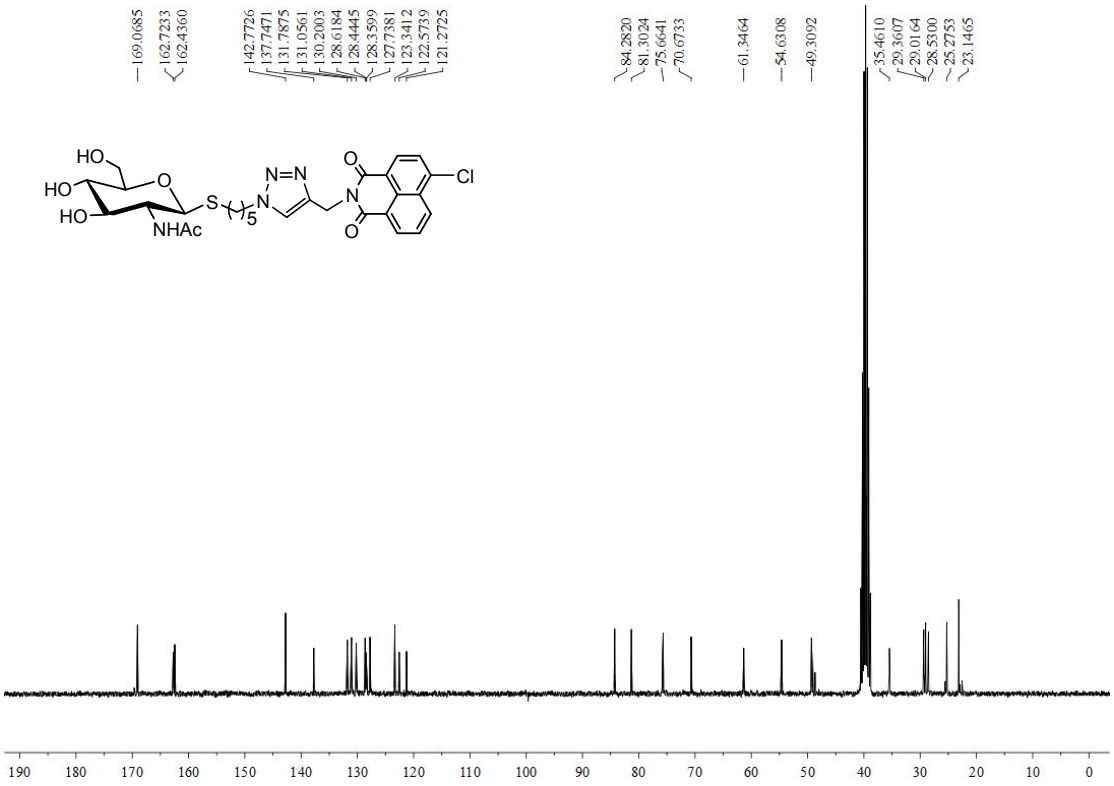
^{13}C NMR spectrum of 15d (75 MHz, DMSO-d_6)



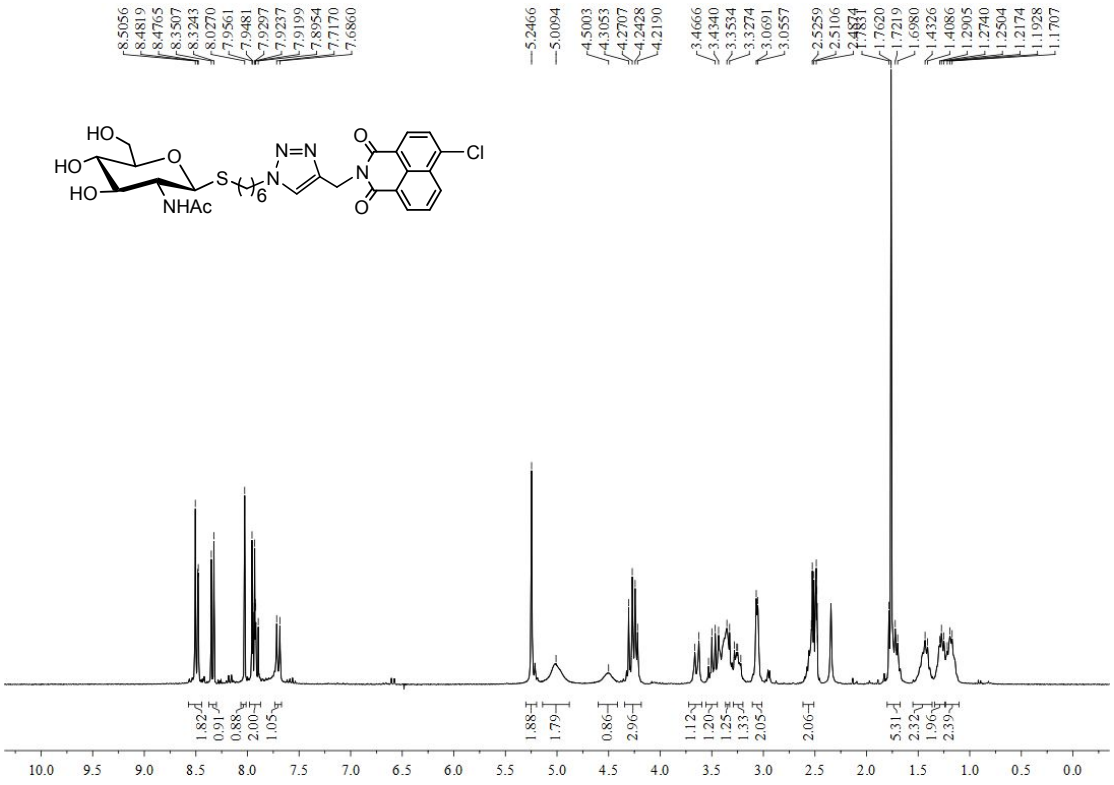
^{1}H NMR spectrum of 15e (300 MHz, DMSO-d_6)



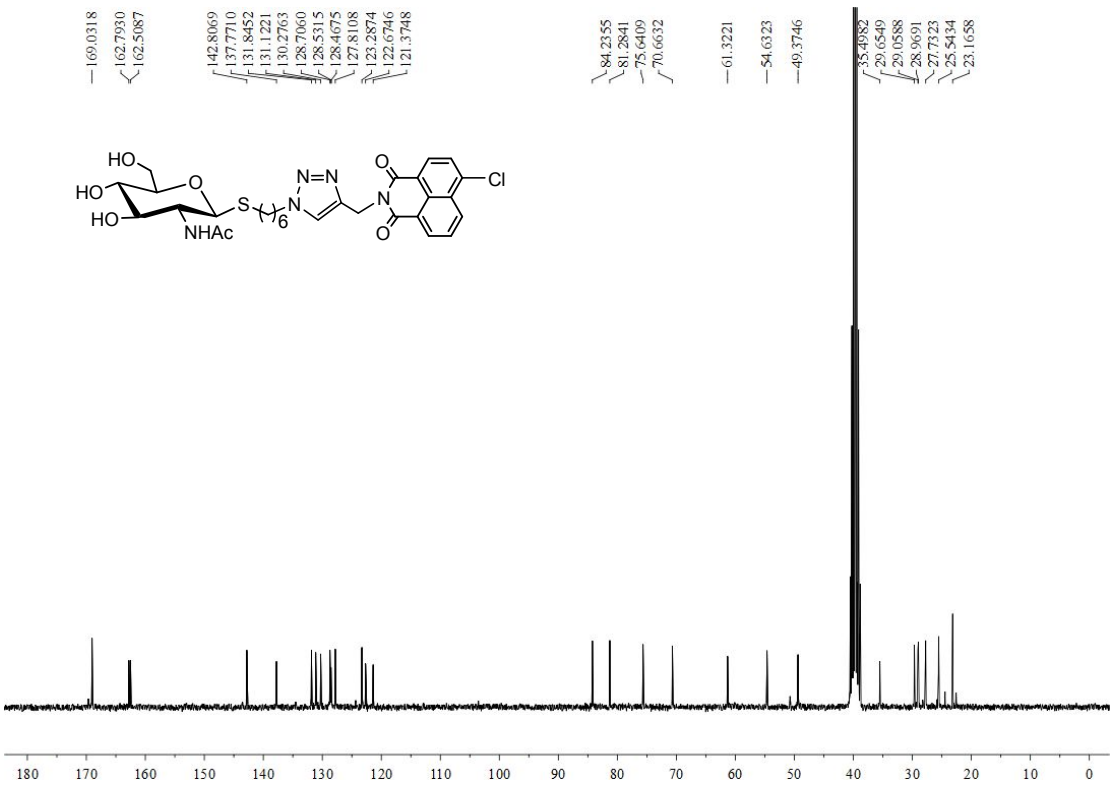
^{13}C NMR spectrum of 15e (75 MHz, DMSO-d_6)



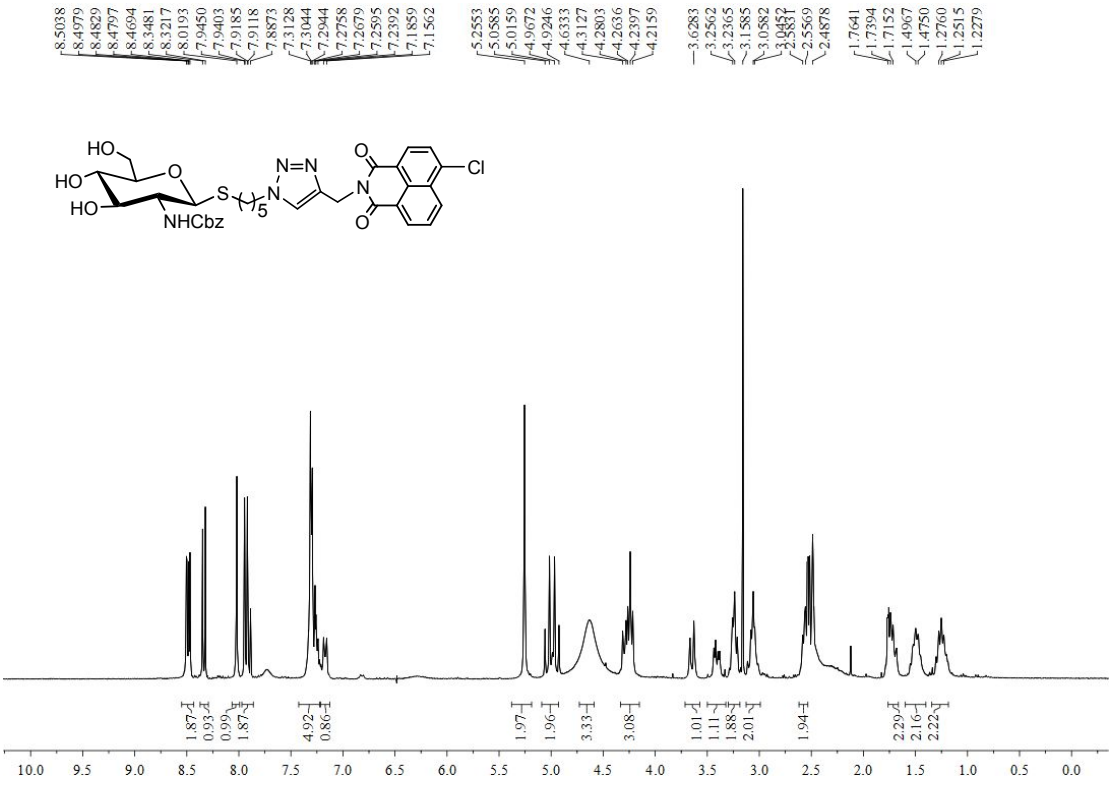
^{1}H NMR spectrum of 15f (300 MHz, DMSO-d_6)



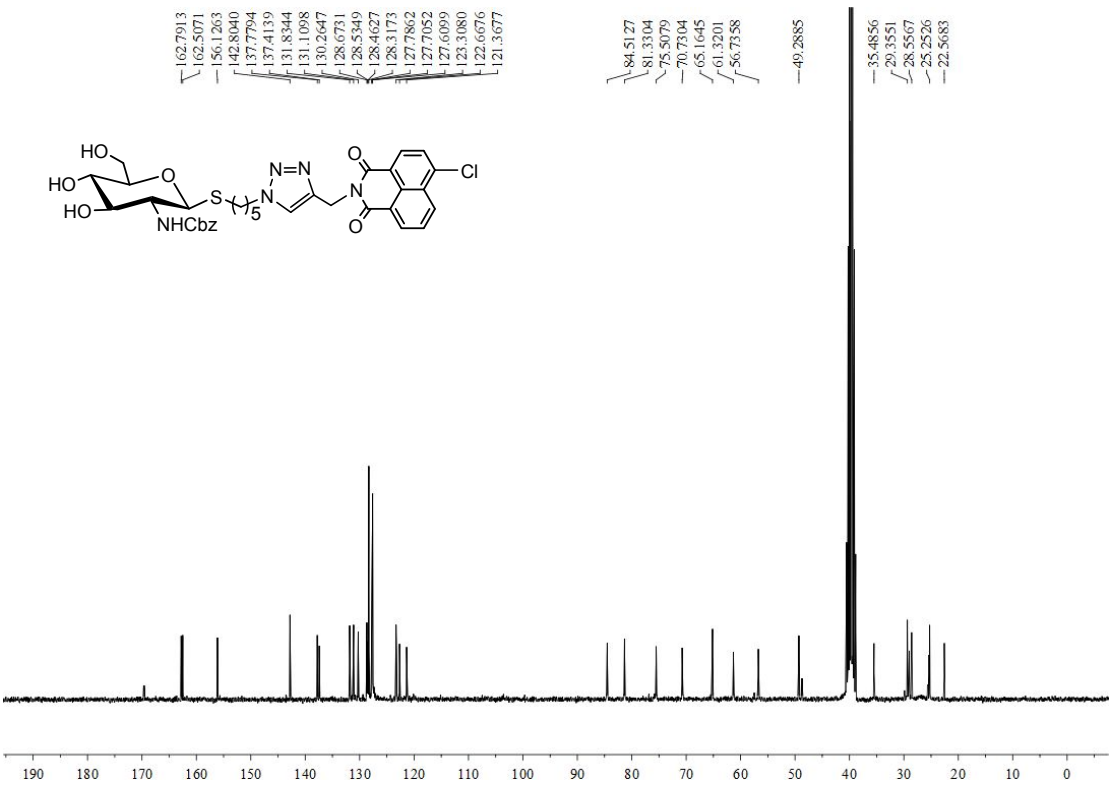
^{13}C NMR spectrum of 15f (75 MHz, DMSO-d_6)



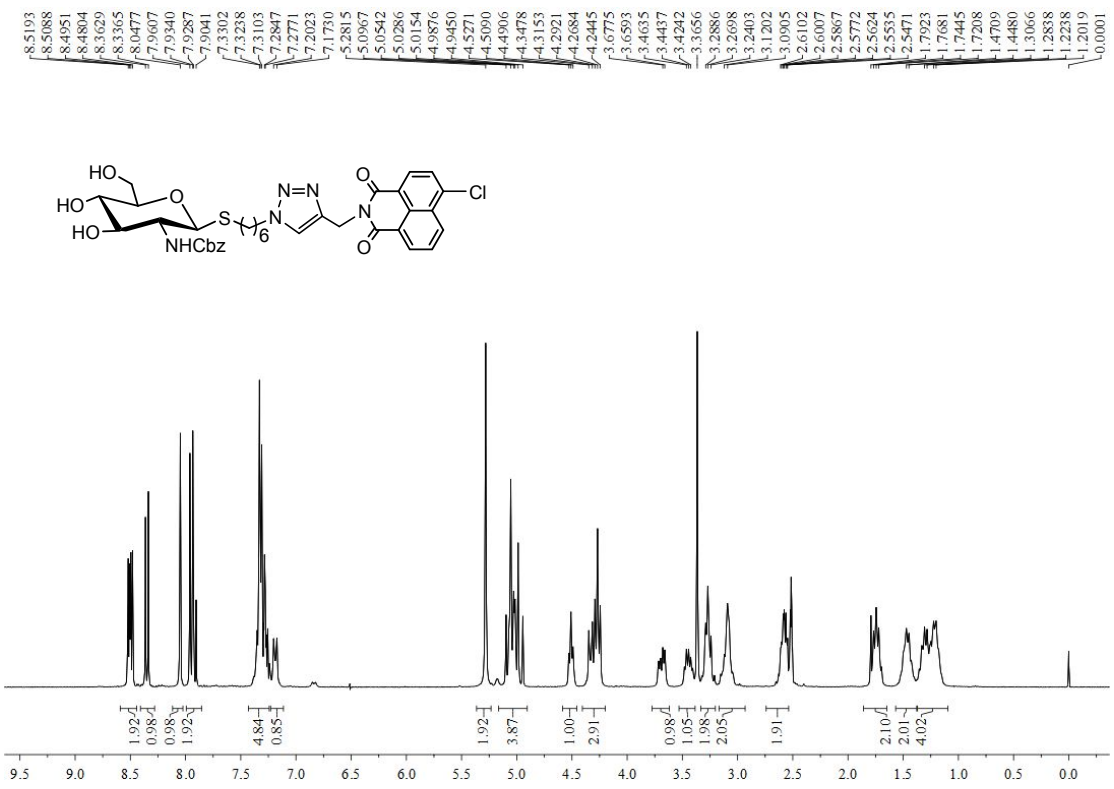
^{1}H NMR spectrum of 15g (300 MHz, DMSO-d_6)



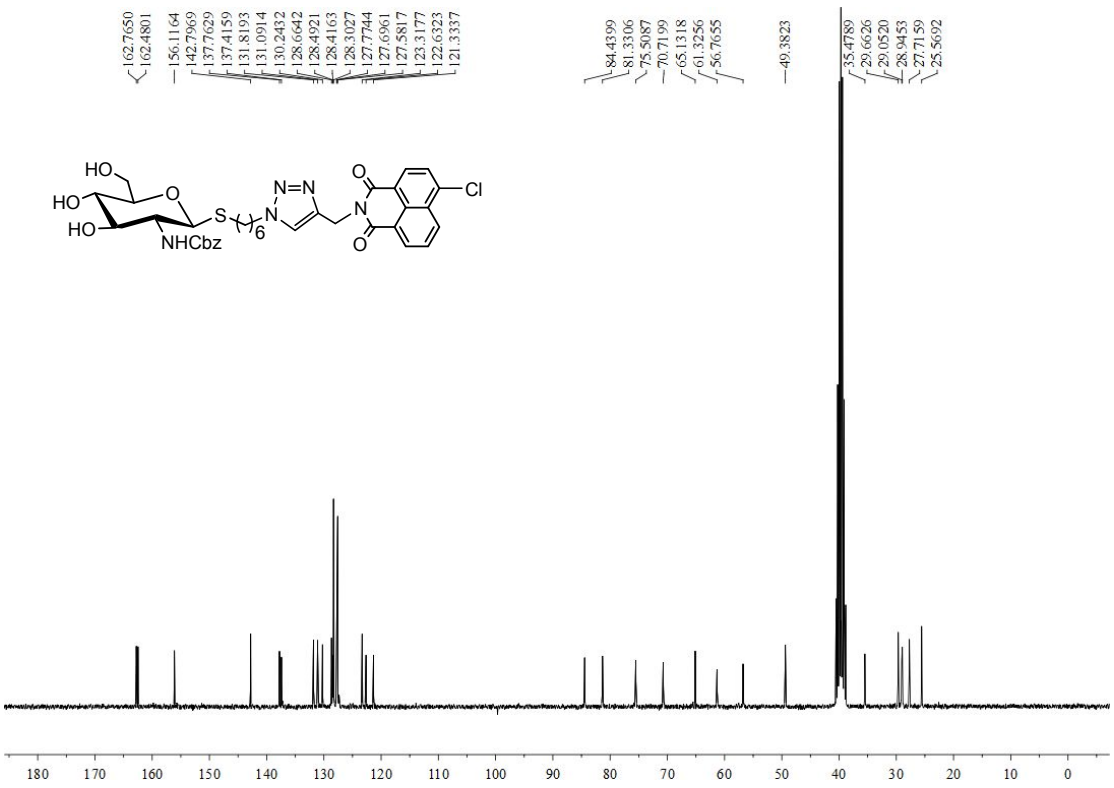
^{13}C NMR spectrum of 15g (75 MHz, DMSO-d_6)



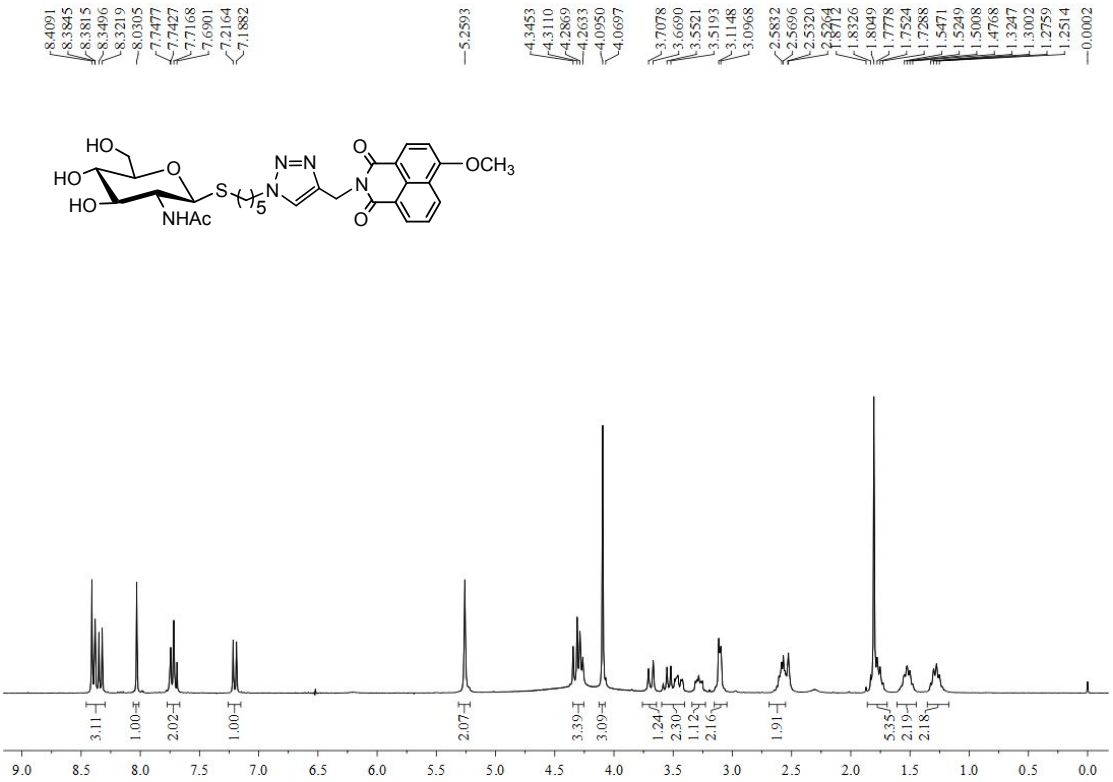
^{1}H NMR spectrum of 15h (300 MHz, DMSO-d_6)



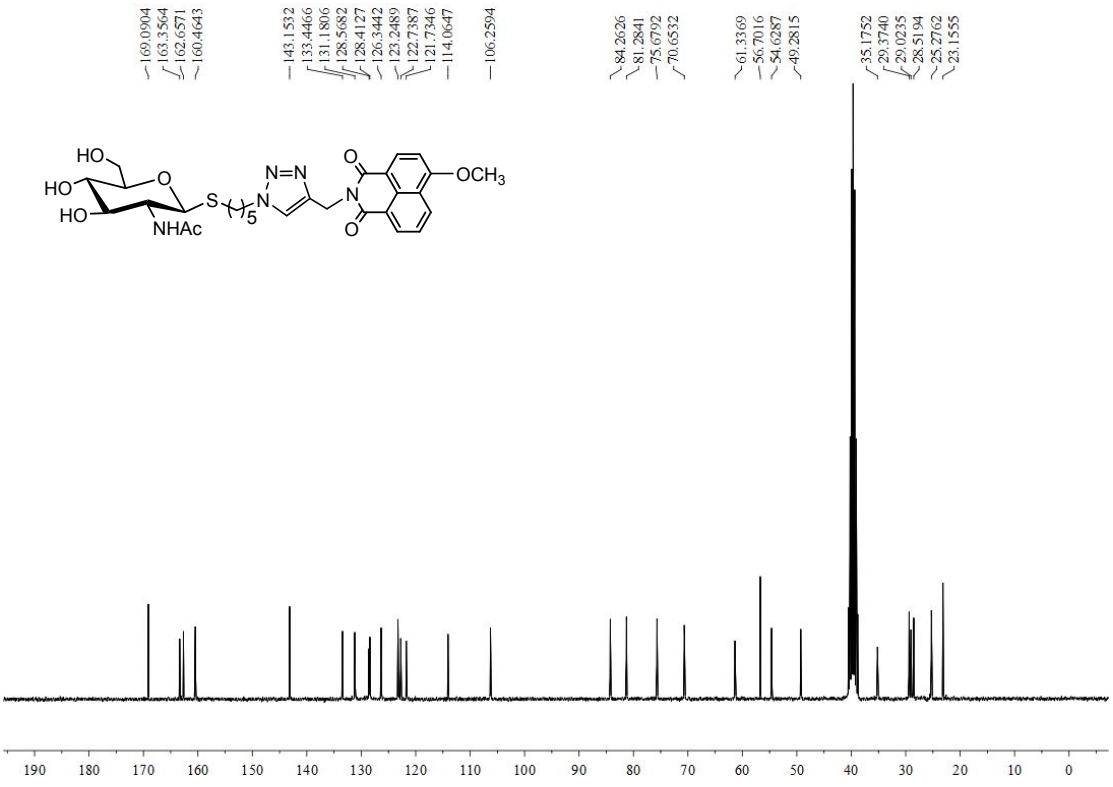
^{13}C NMR spectrum of 15h (75 MHz, DMSO-d_6)



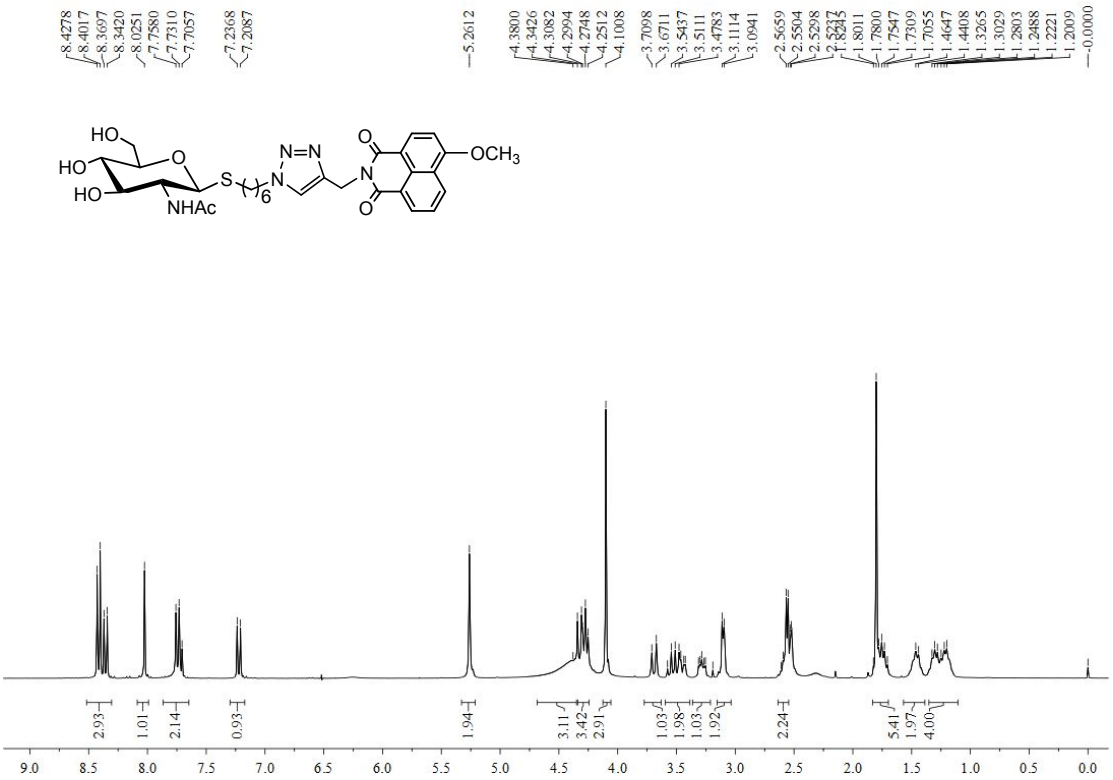
^{1}H NMR spectrum of 15i (300 MHz, DMSO-d_6)



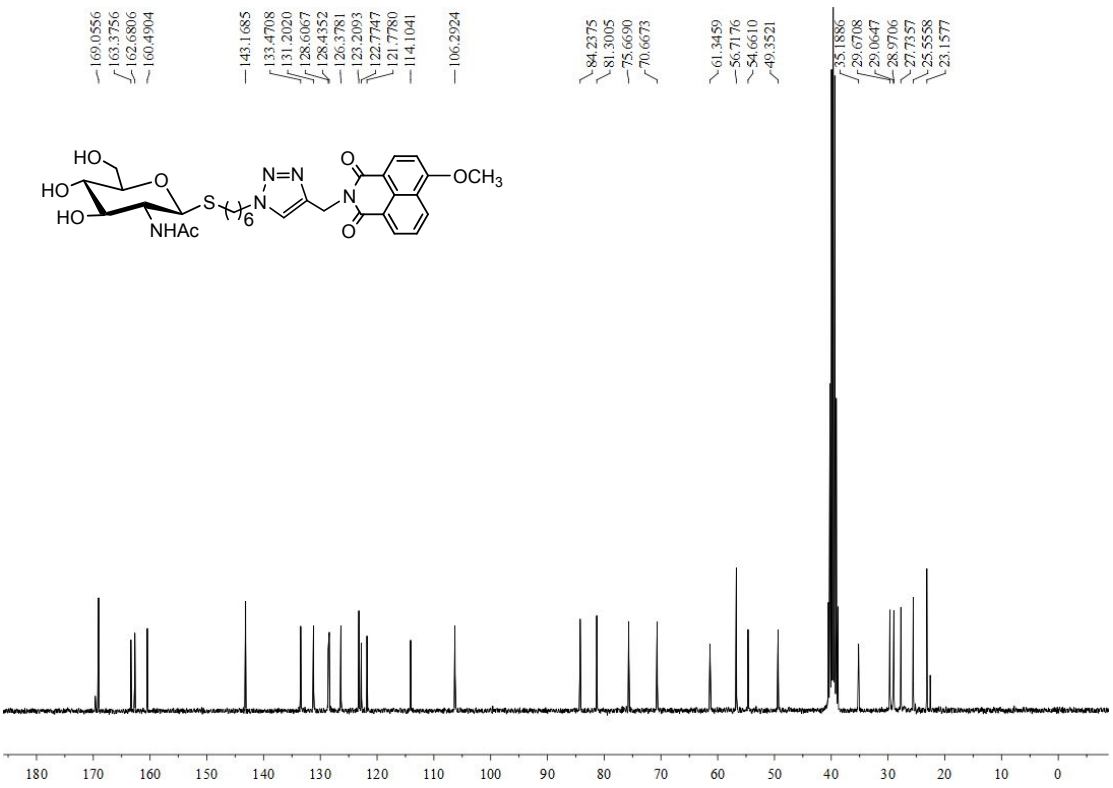
^{13}C NMR spectrum of 15i (75 MHz, DMSO-d_6)



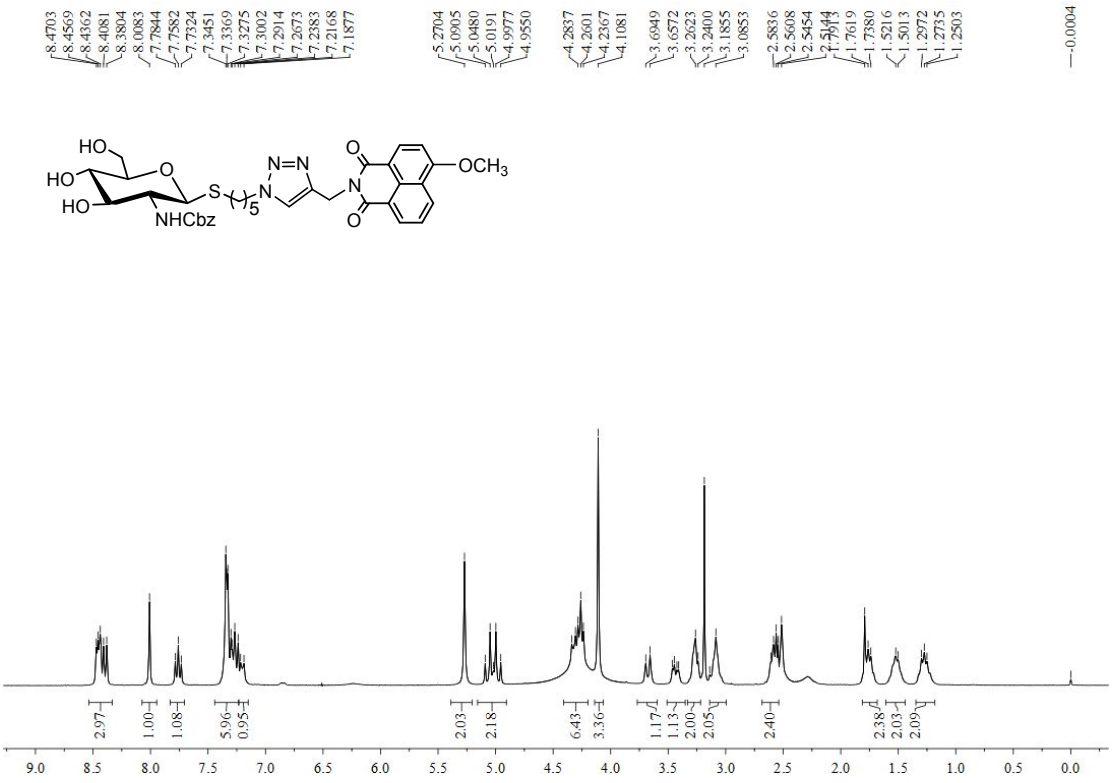
^{1}H NMR spectrum of 15j (300 MHz, DMSO-d_6)



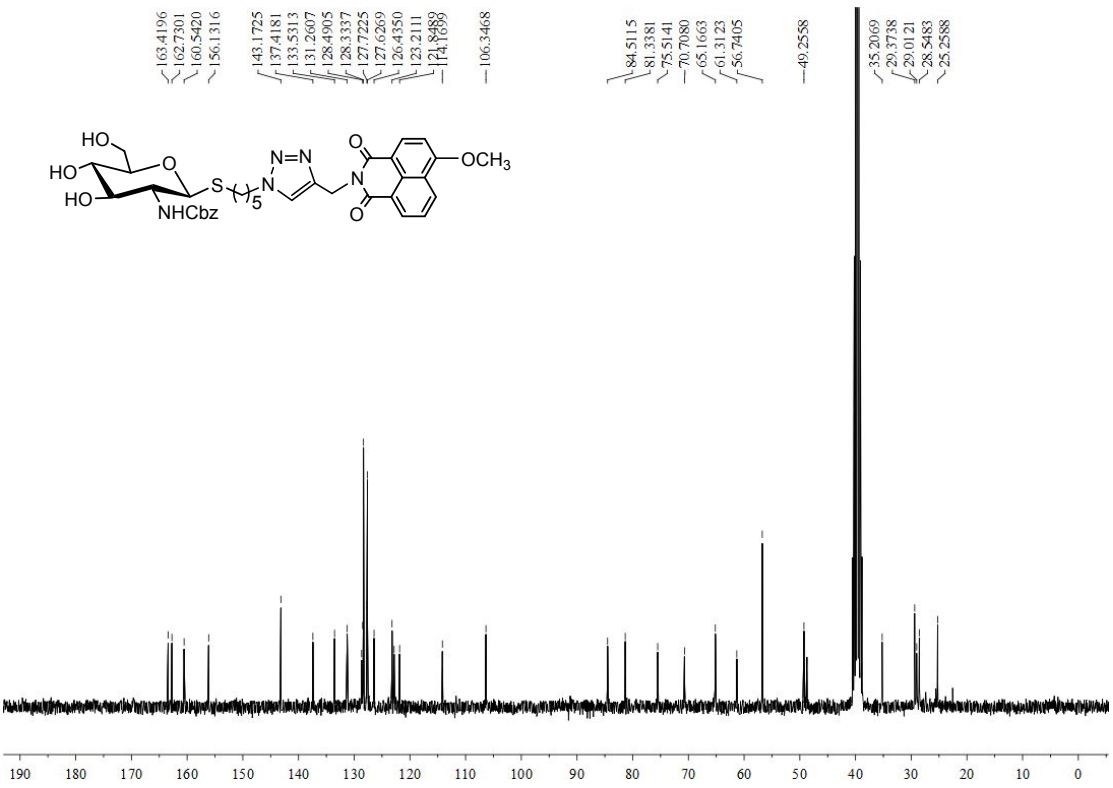
^{13}C NMR spectrum of 15j (75 MHz, DMSO-d_6)



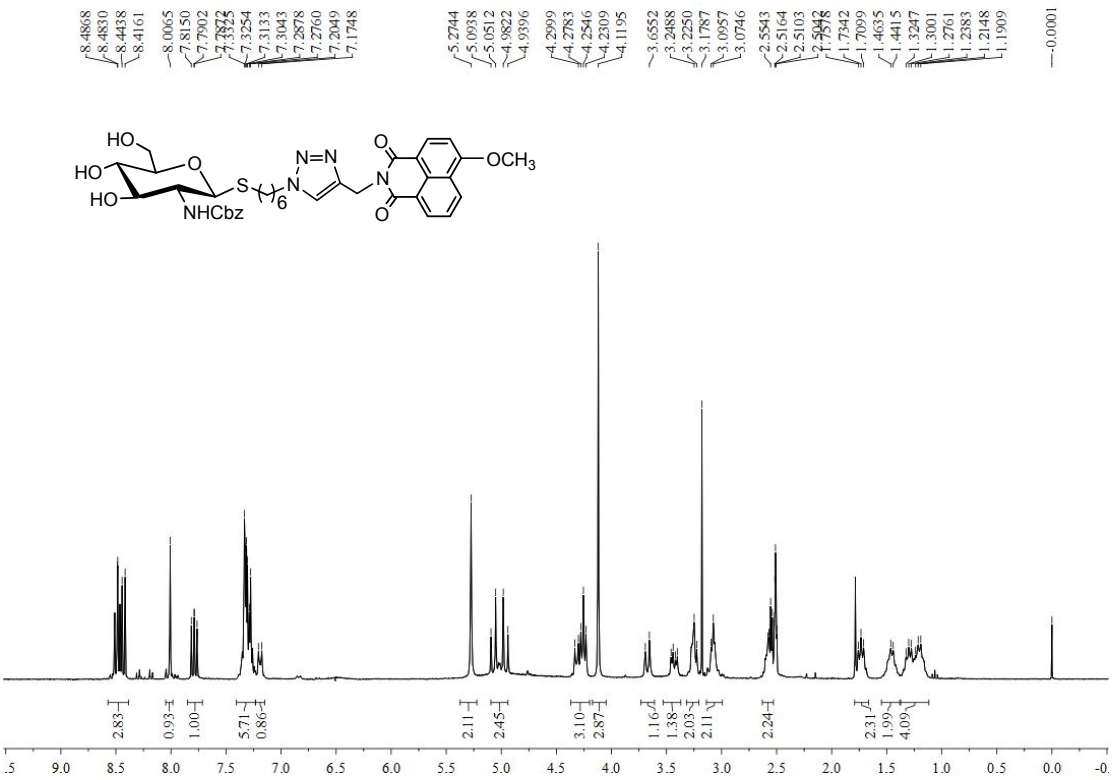
^{1}H NMR spectrum of 15k (300 MHz, DMSO-d_6)



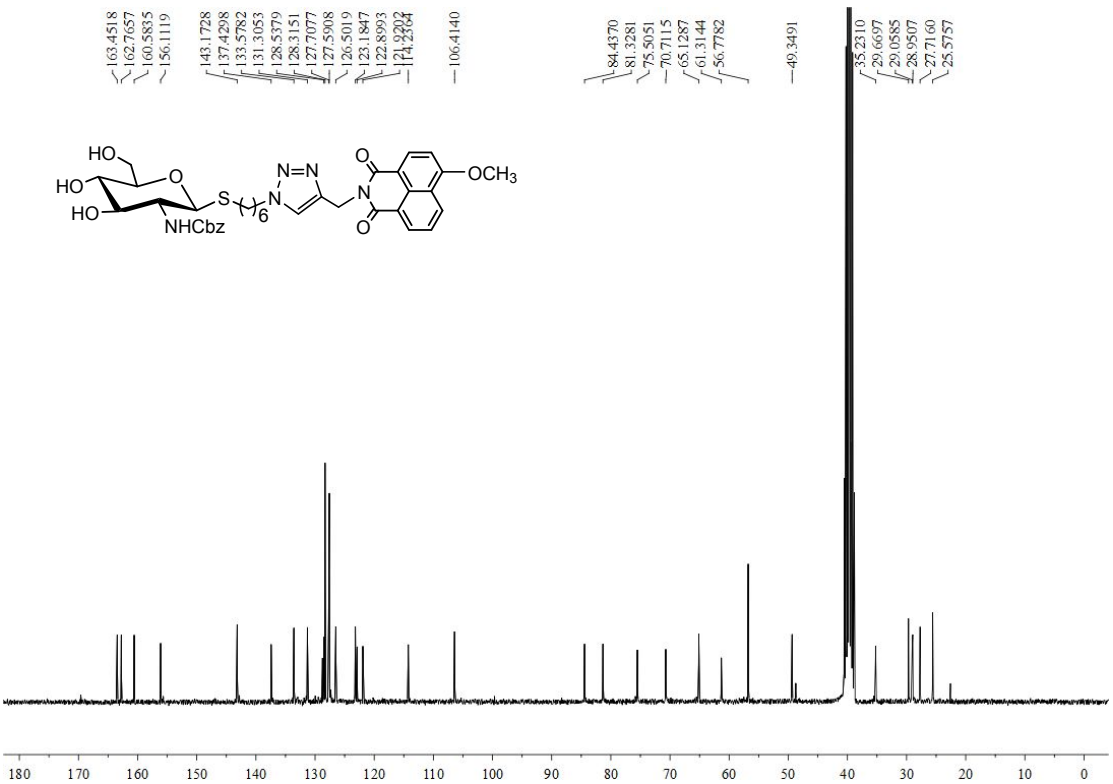
^{13}C NMR spectrum of 15k (75 MHz, DMSO-d_6)



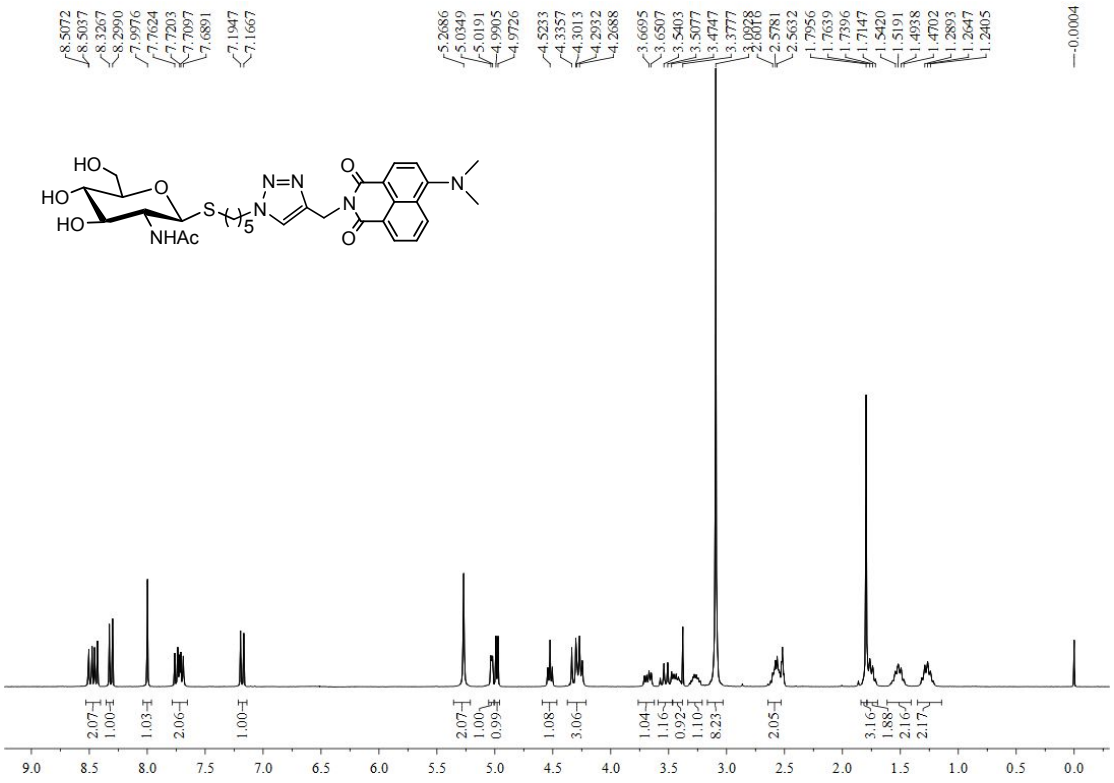
^{1}H NMR spectrum of 15l (300 MHz, DMSO-d_6)



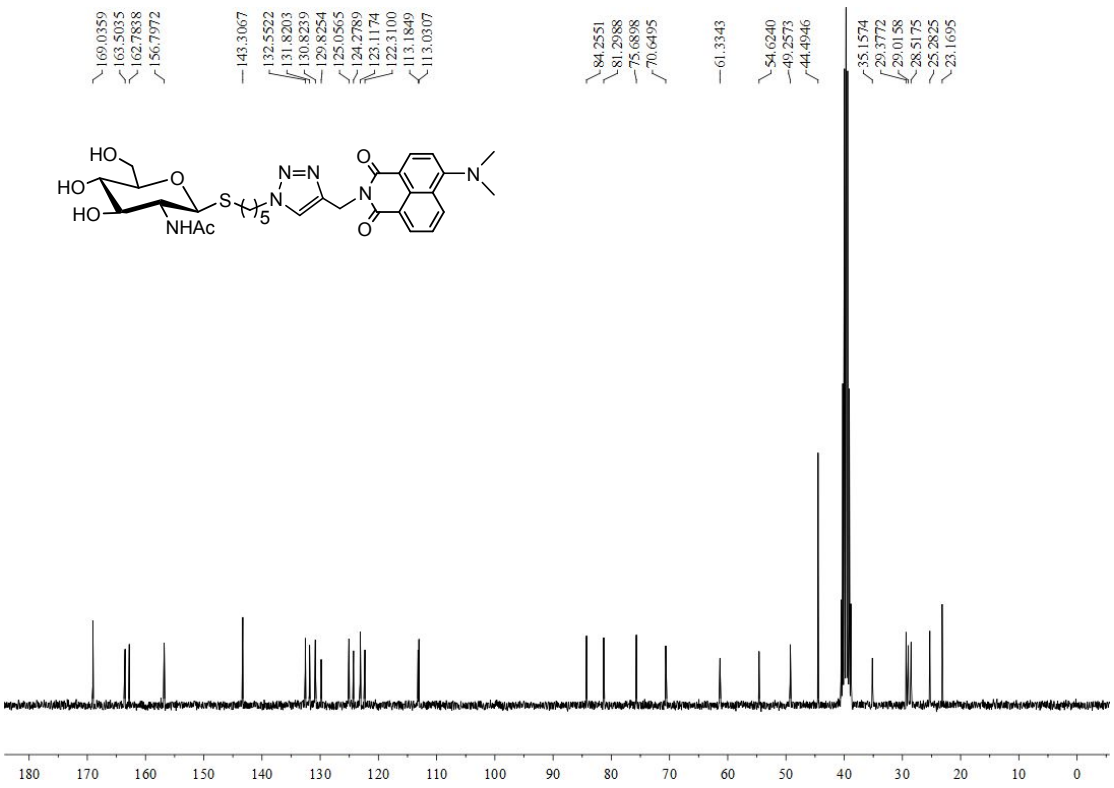
^{13}C NMR spectrum of 15l (75 MHz, DMSO-d_6)



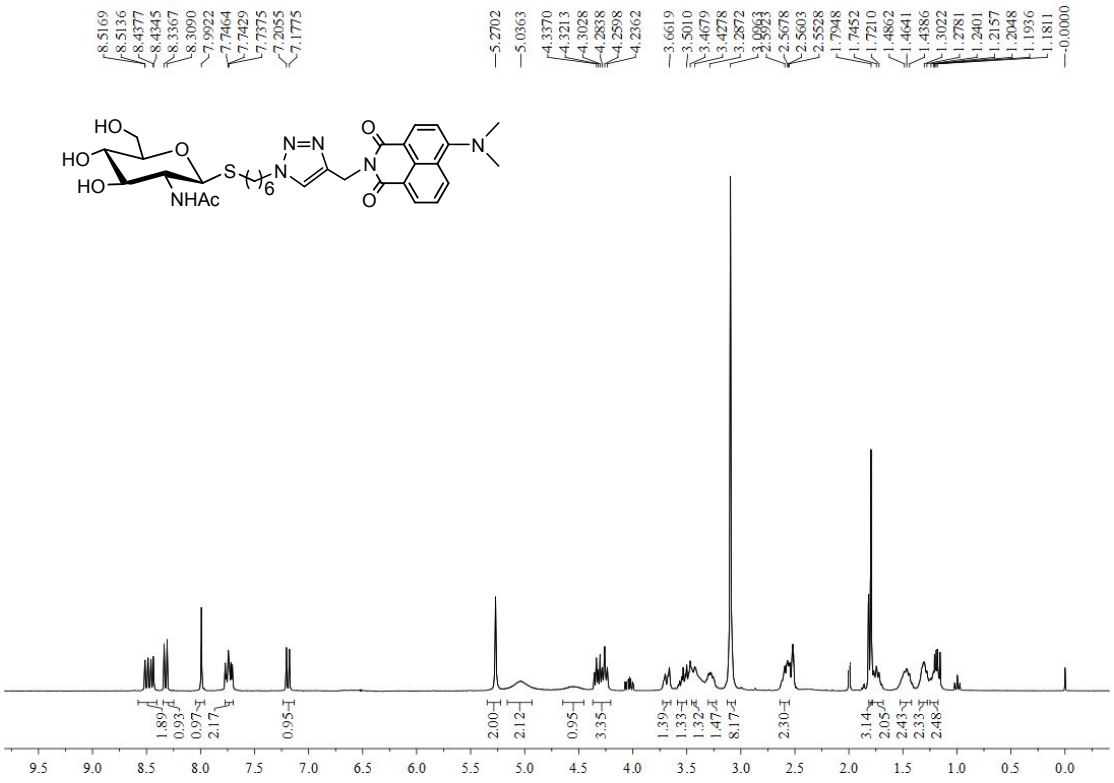
^{1}H NMR spectrum of 15m (300 MHz, DMSO-d_6)



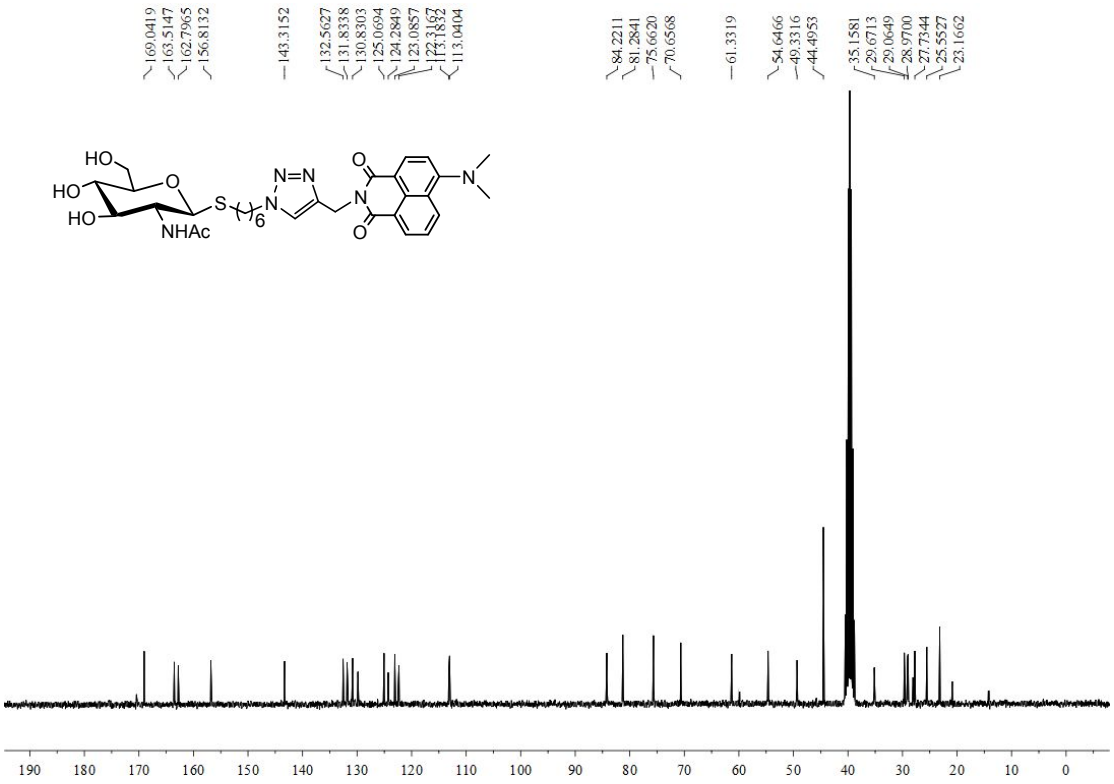
^{13}C NMR spectrum of 15m (75 MHz, DMSO-d_6)



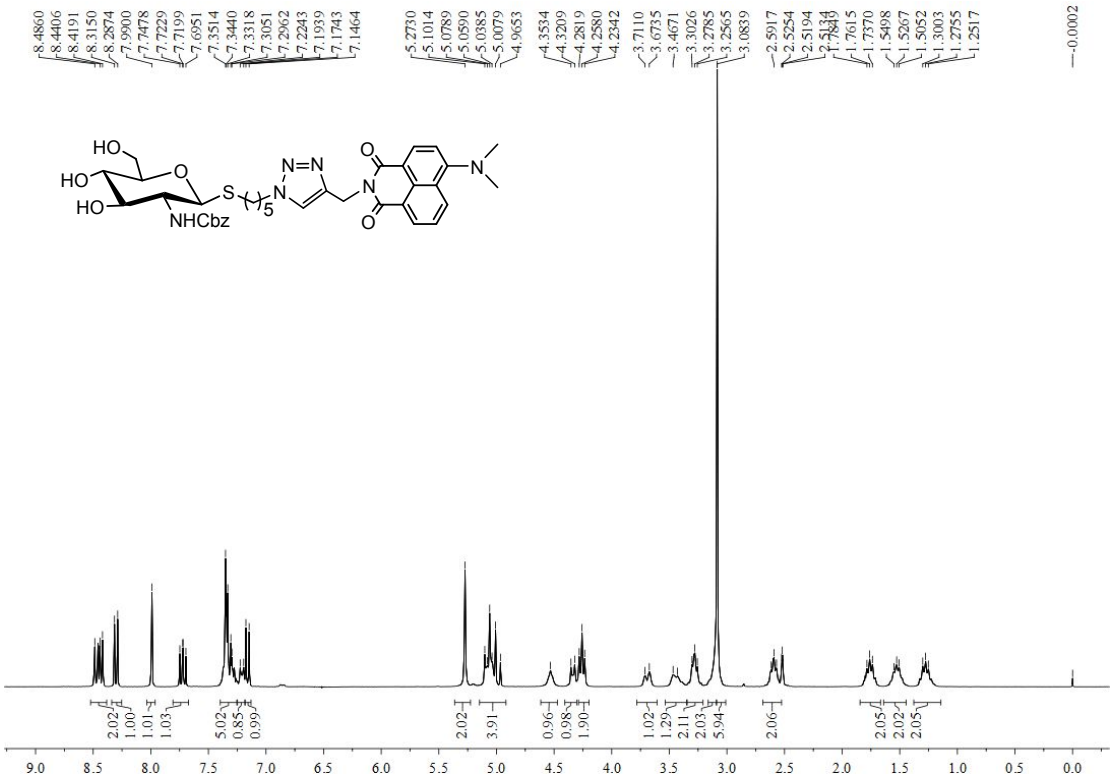
^{1}H NMR spectrum of 15n (300 MHz, DMSO-d_6)



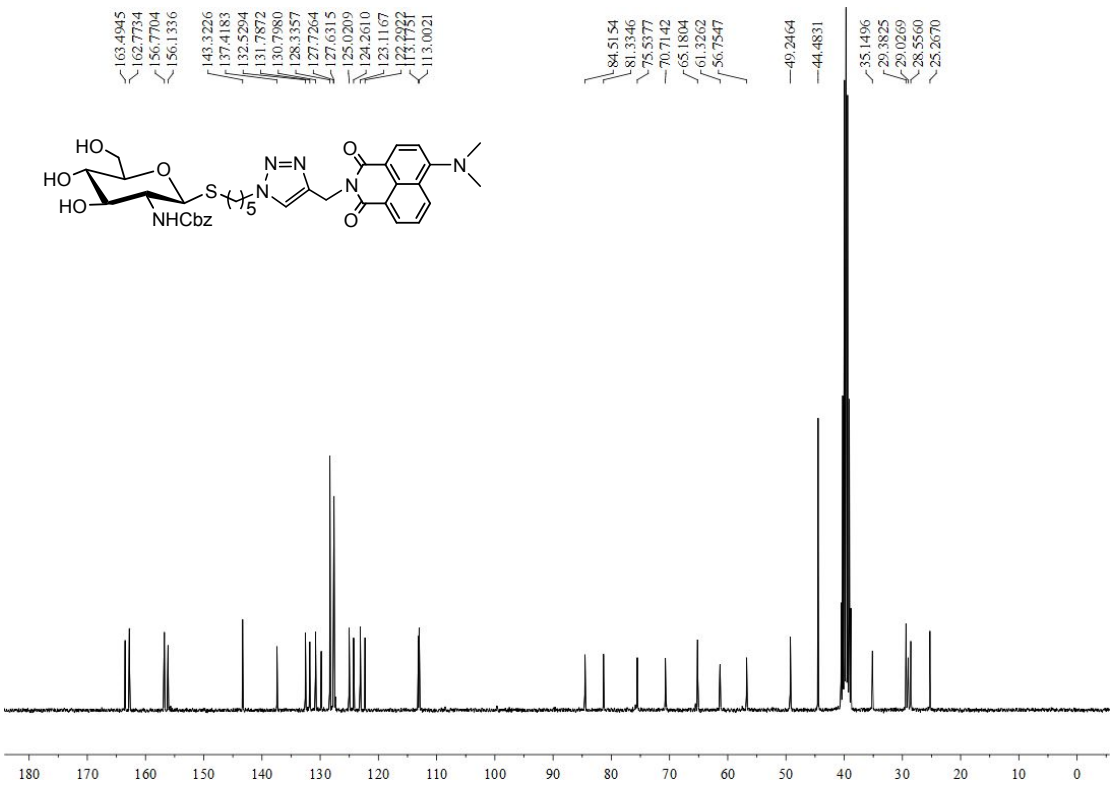
^{13}C NMR spectrum of 15n (75 MHz, DMSO-d_6)



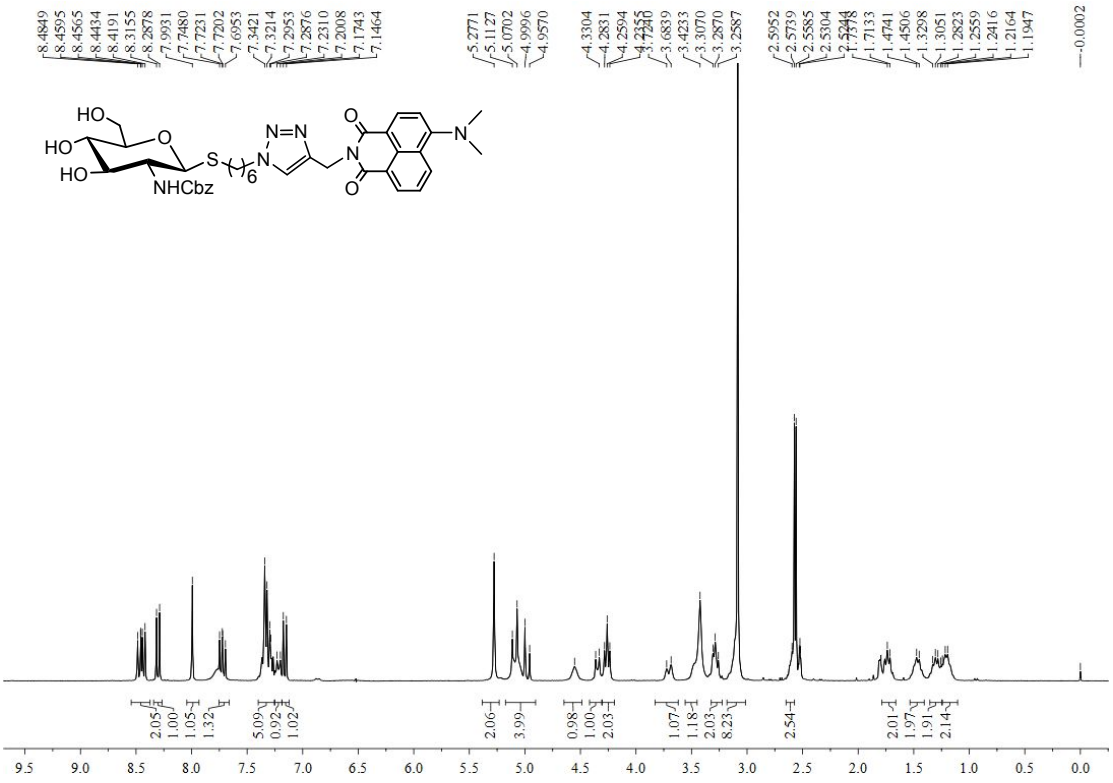
^{1}H NMR spectrum of 15o (300 MHz, DMSO-d_6)



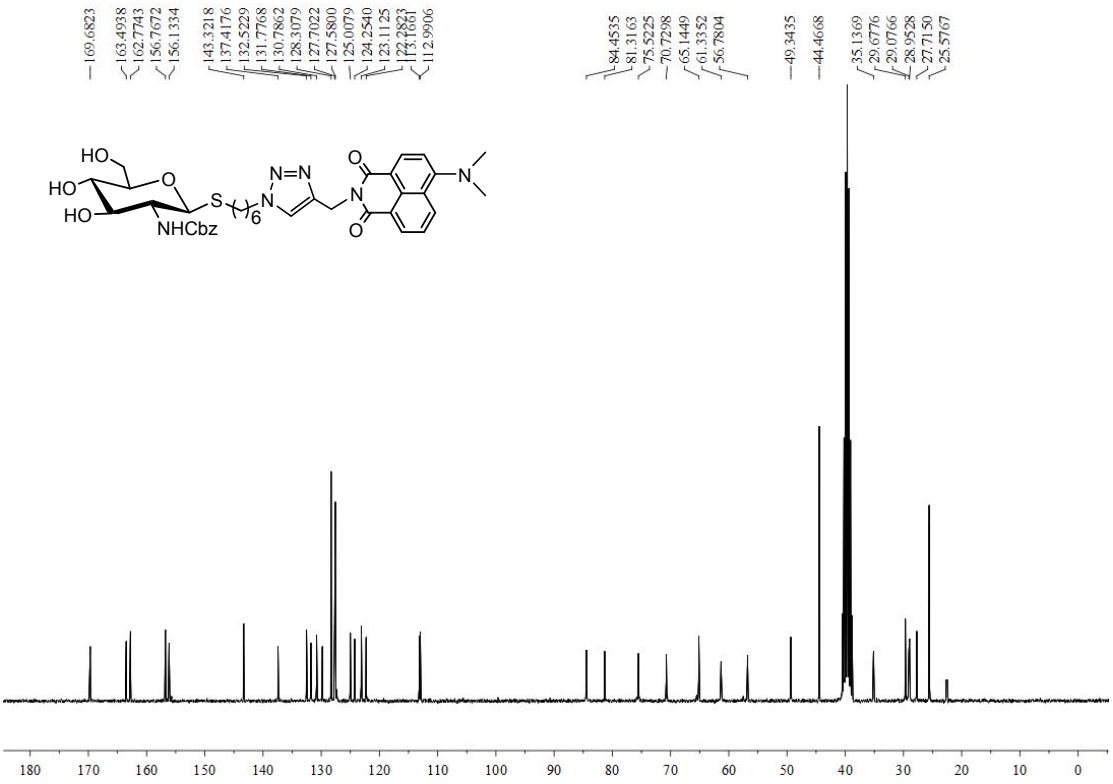
^{13}C NMR spectrum of 15o (75 MHz, DMSO-d_6)



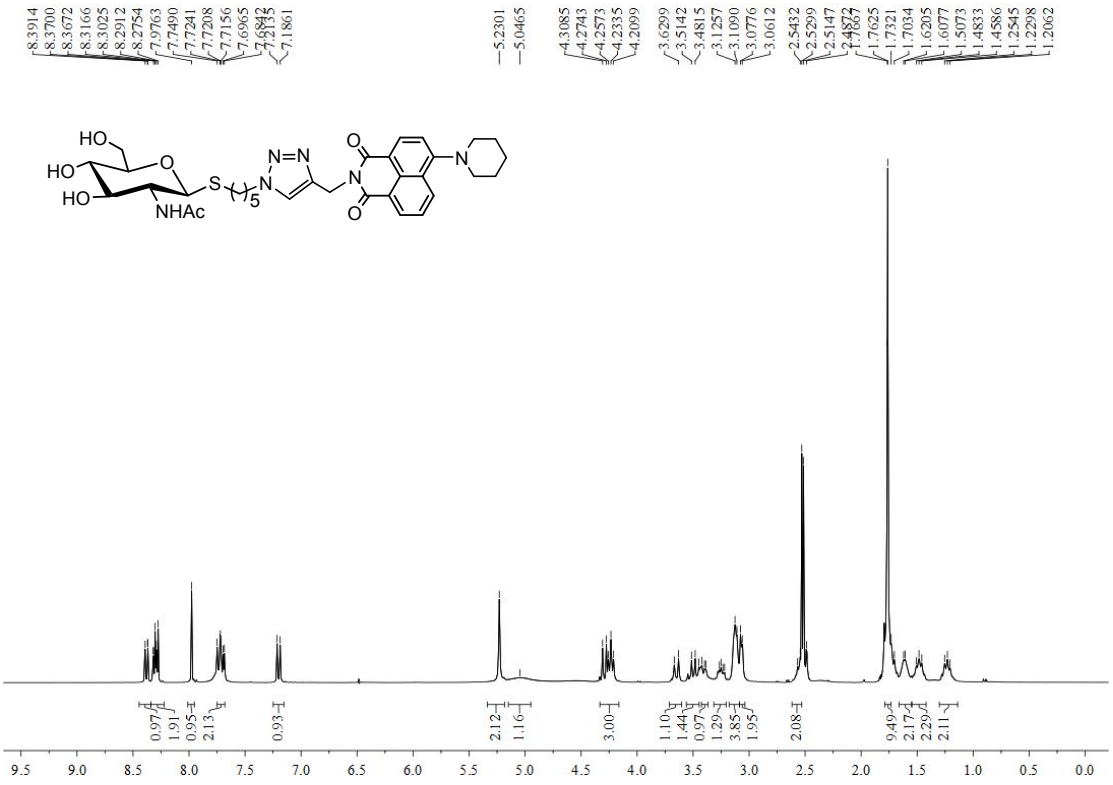
^{1}H NMR spectrum of 15p (300 MHz, DMSO-d_6)



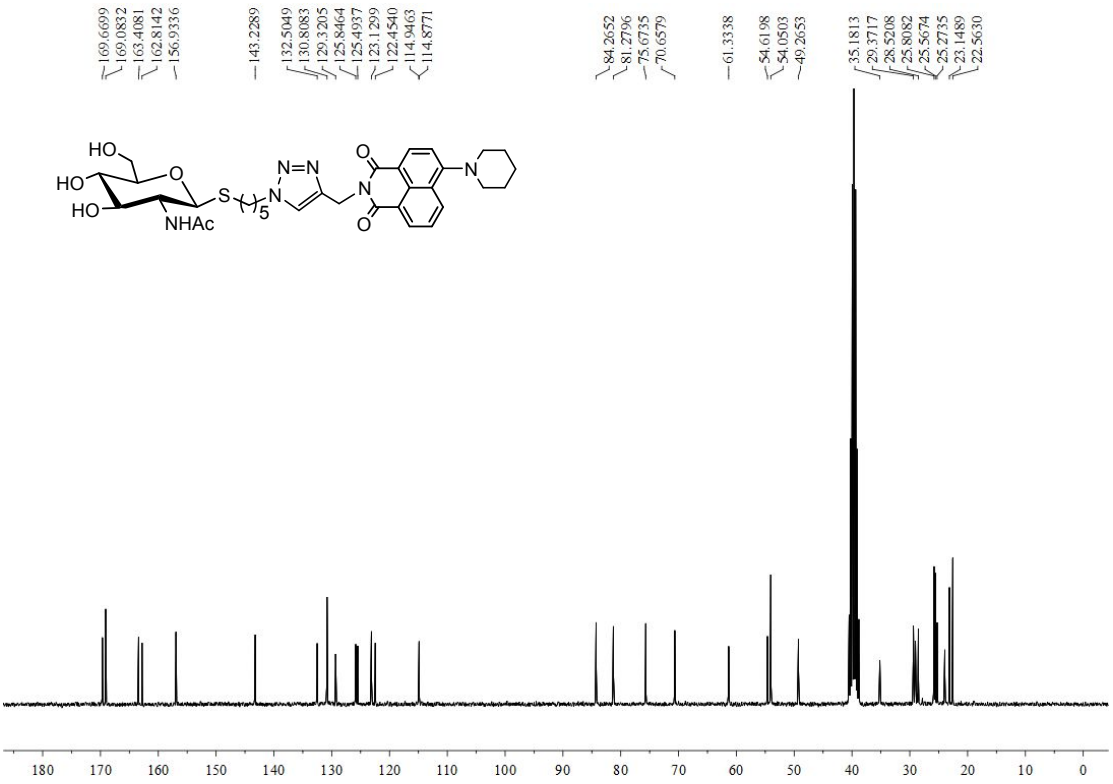
^{13}C NMR spectrum of 15p (75 MHz, DMSO-d_6)



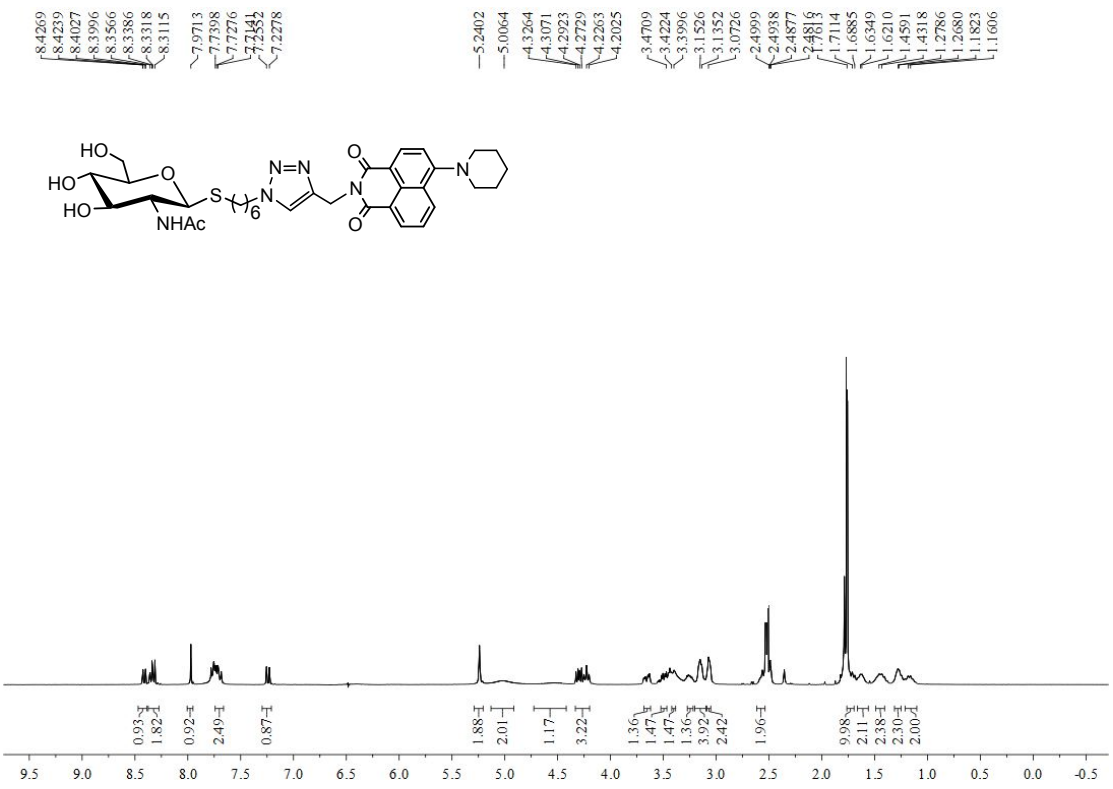
^{1}H NMR spectrum of 15q (300 MHz, DMSO-d_6)



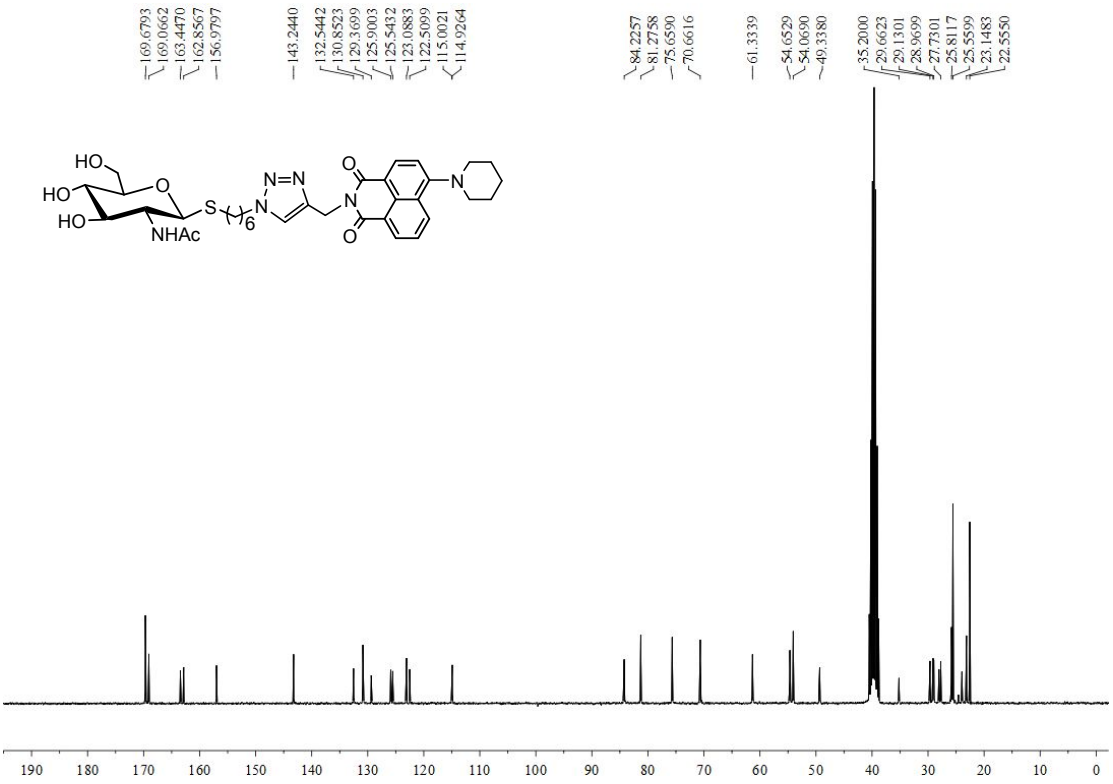
^{13}C NMR spectrum of 15q (75 MHz, DMSO-d_6)



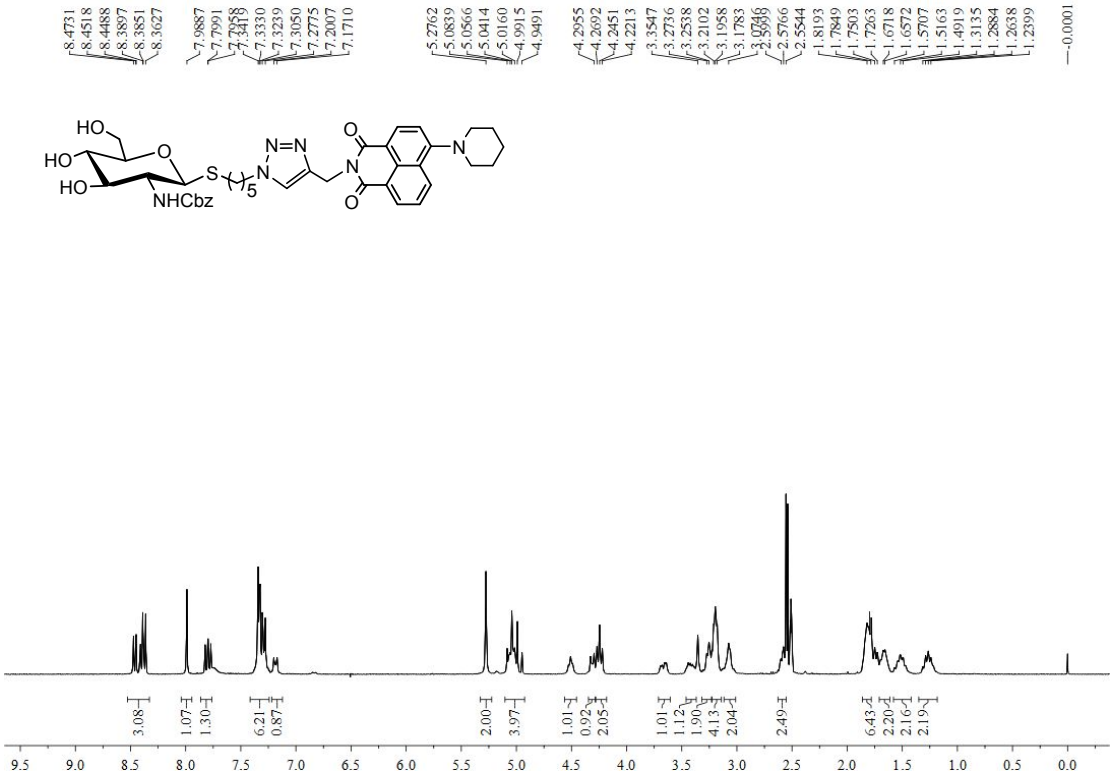
^{1}H NMR spectrum of 15r (300 MHz, DMSO-d_6)



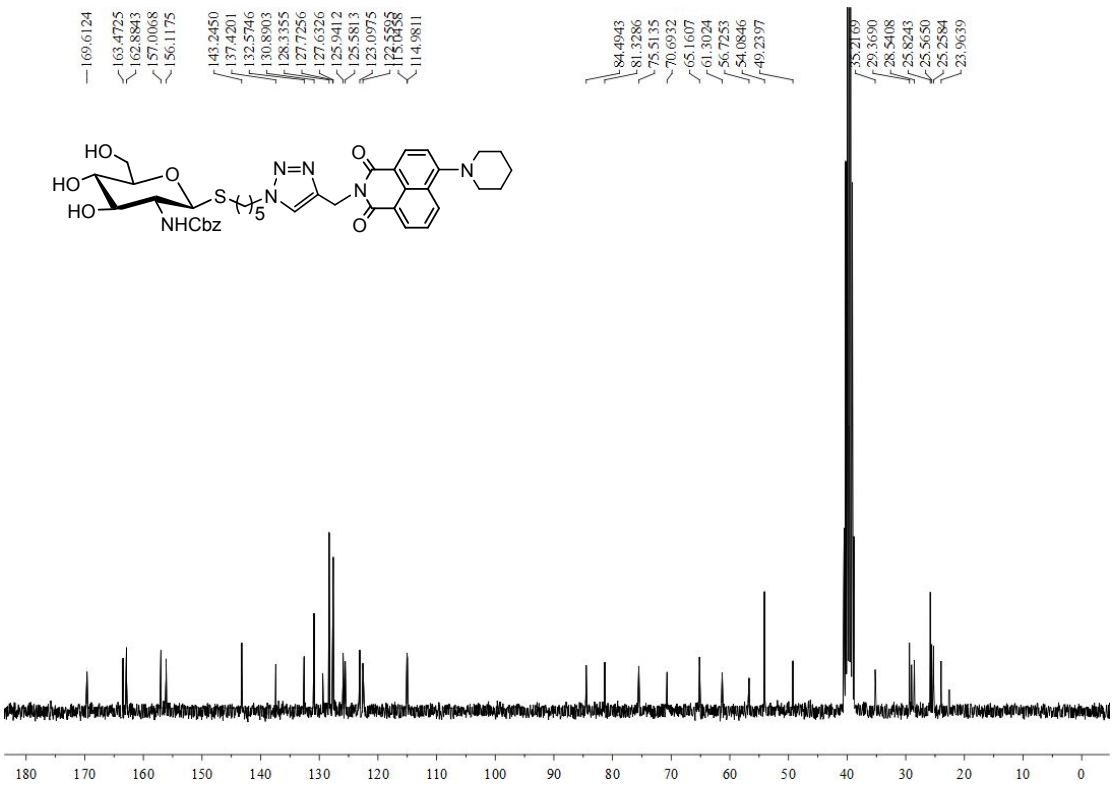
^{13}C NMR spectrum of 15r (75 MHz, DMSO-d_6)



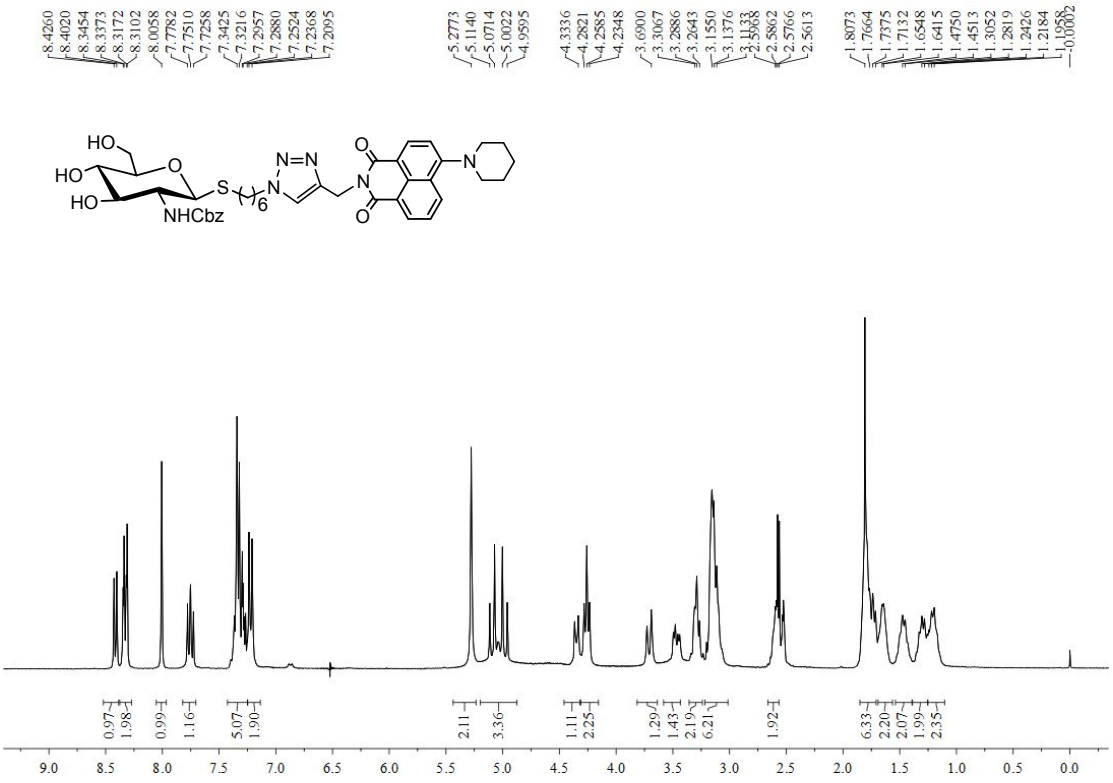
^{1}H NMR spectrum of 15s (300 MHz, DMSO-d_6)



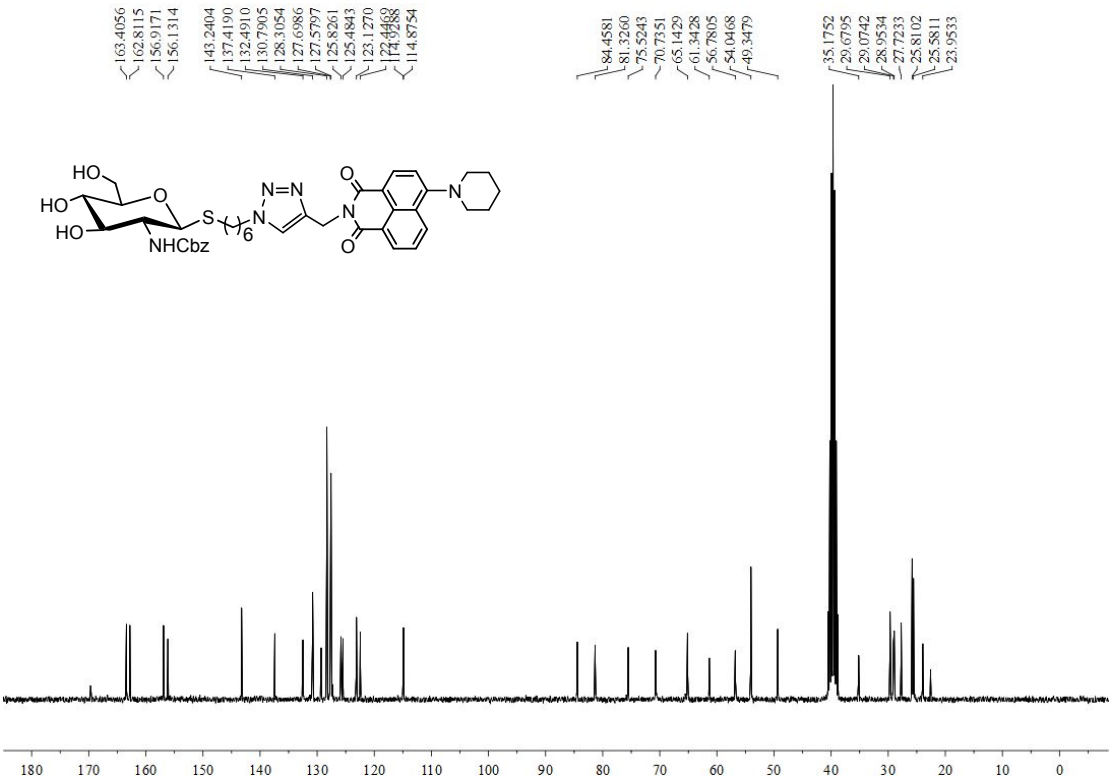
^{13}C NMR spectrum of 15s (75 MHz, DMSO-d_6)



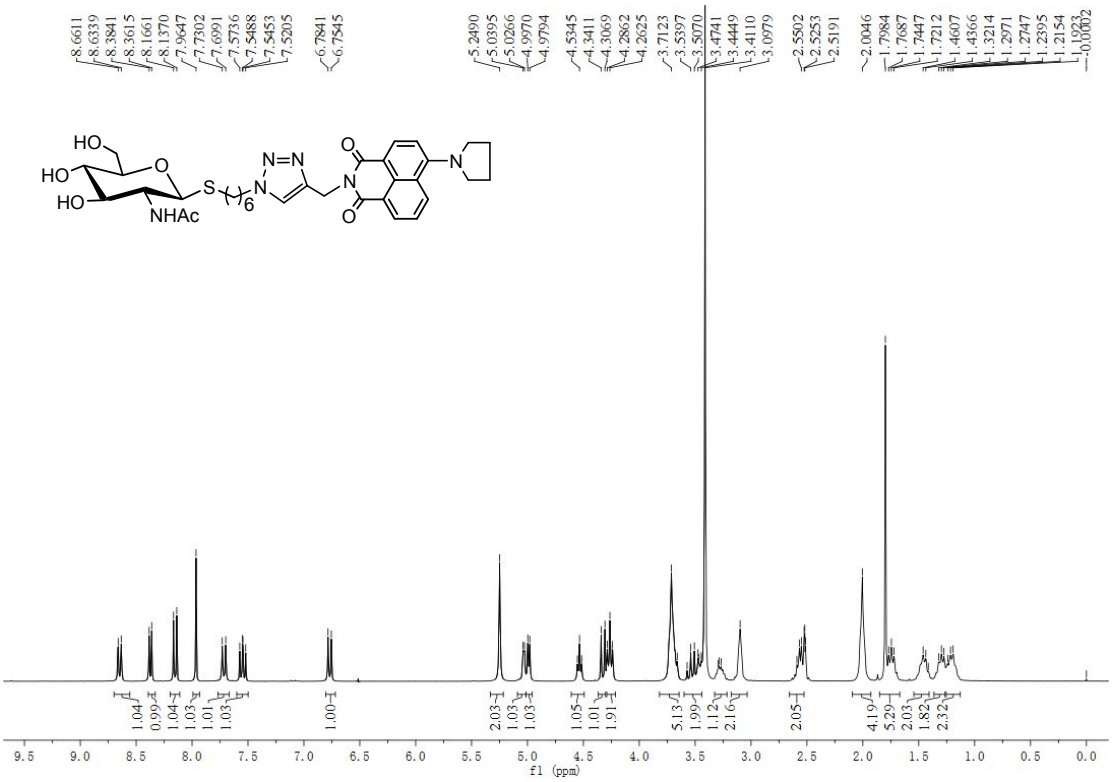
^{1}H NMR spectrum of 15t (300 MHz, DMSO-d_6)



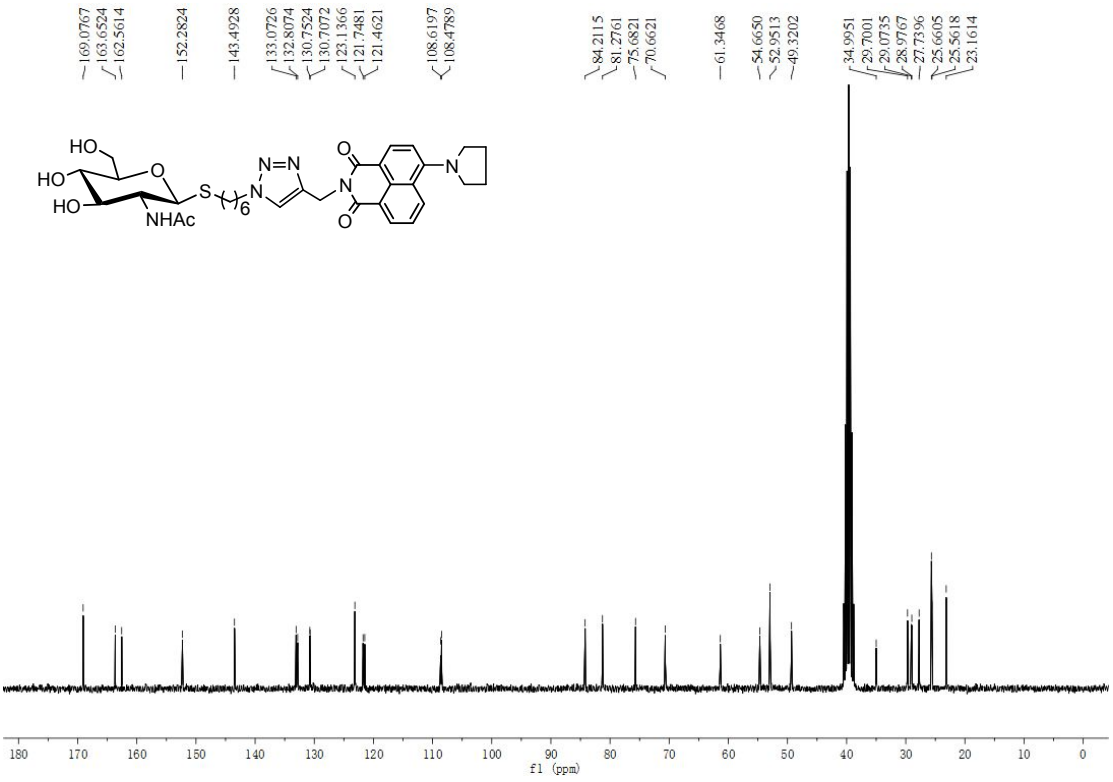
^{13}C NMR spectrum of 15t (75 MHz, DMSO-d_6)



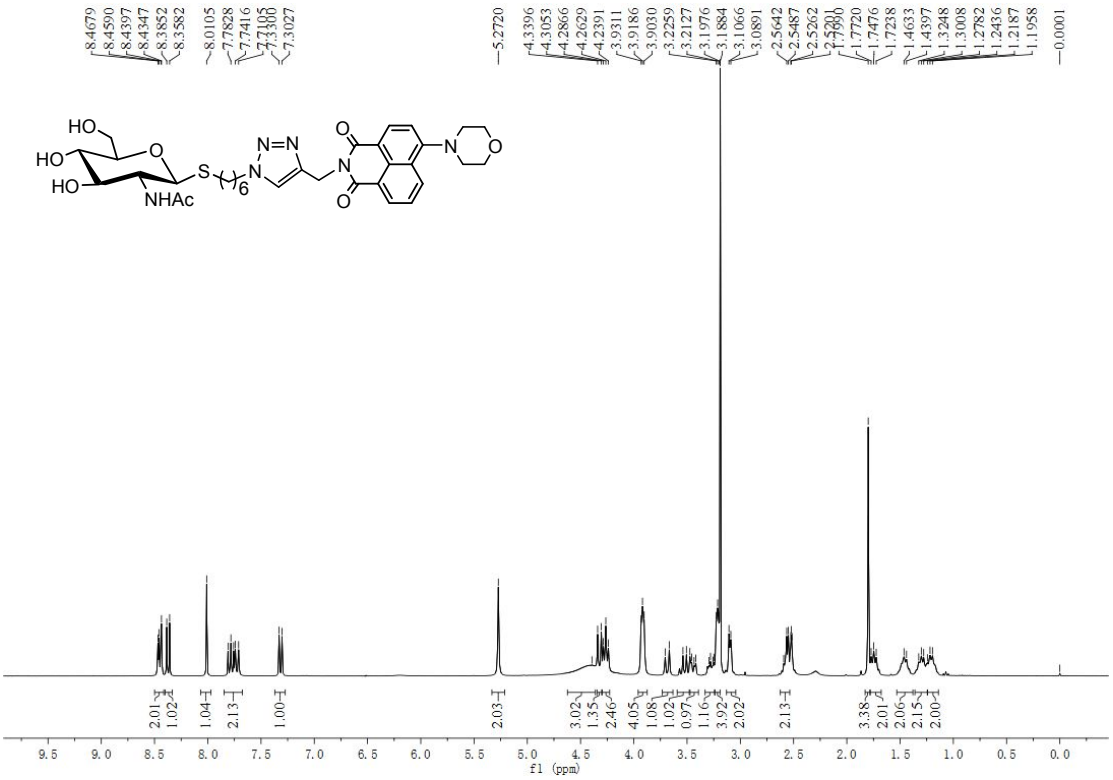
^{1}H NMR spectrum of 15u (300 MHz, DMSO-d_6)



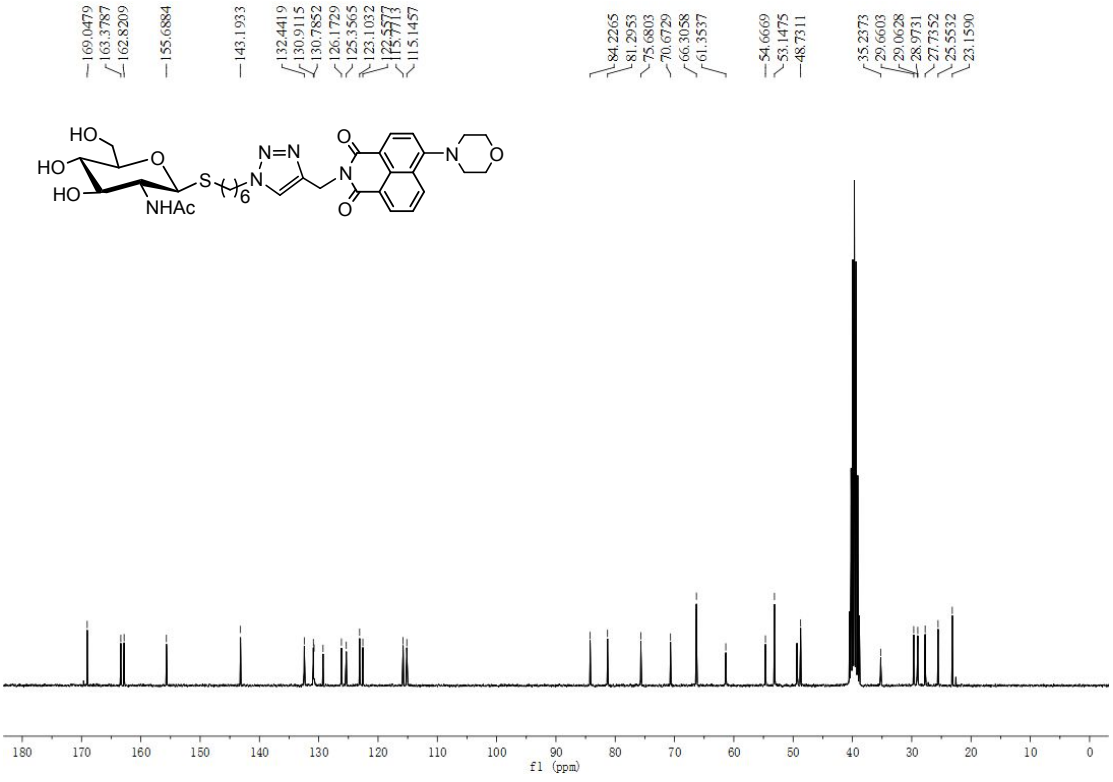
^{13}C NMR spectrum of 15u (75 MHz, DMSO-d_6)



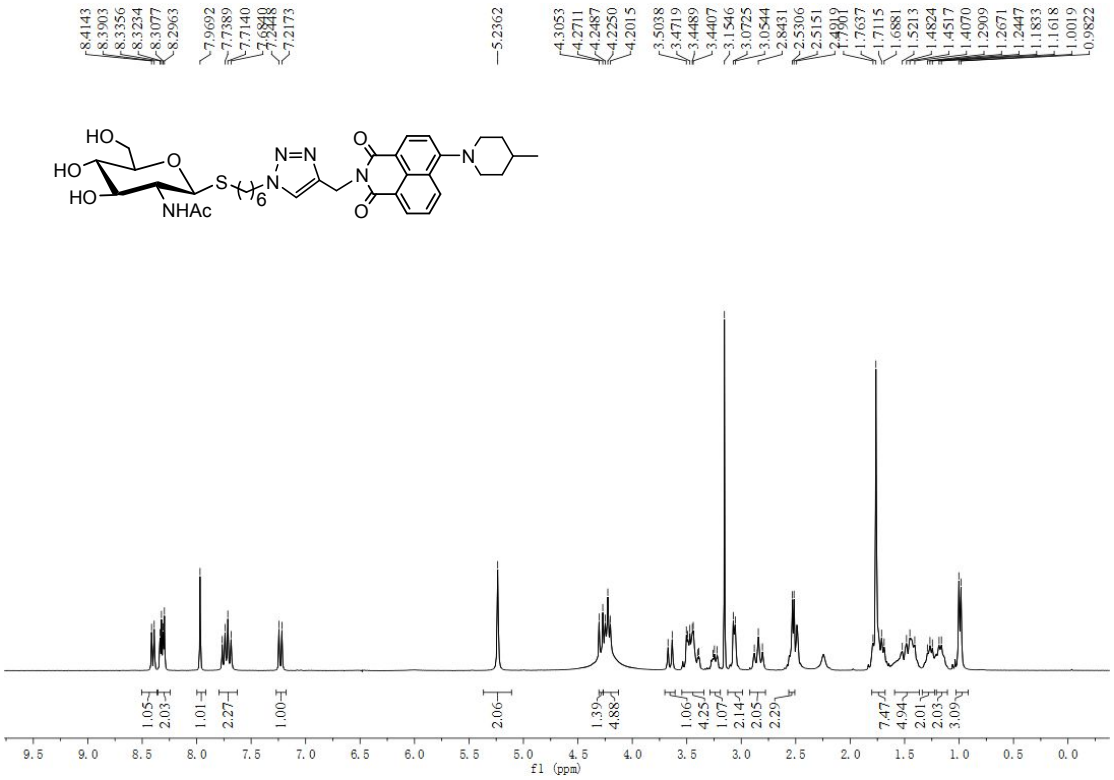
^{1}H NMR spectrum of 15v (300 MHz, DMSO-d_6)



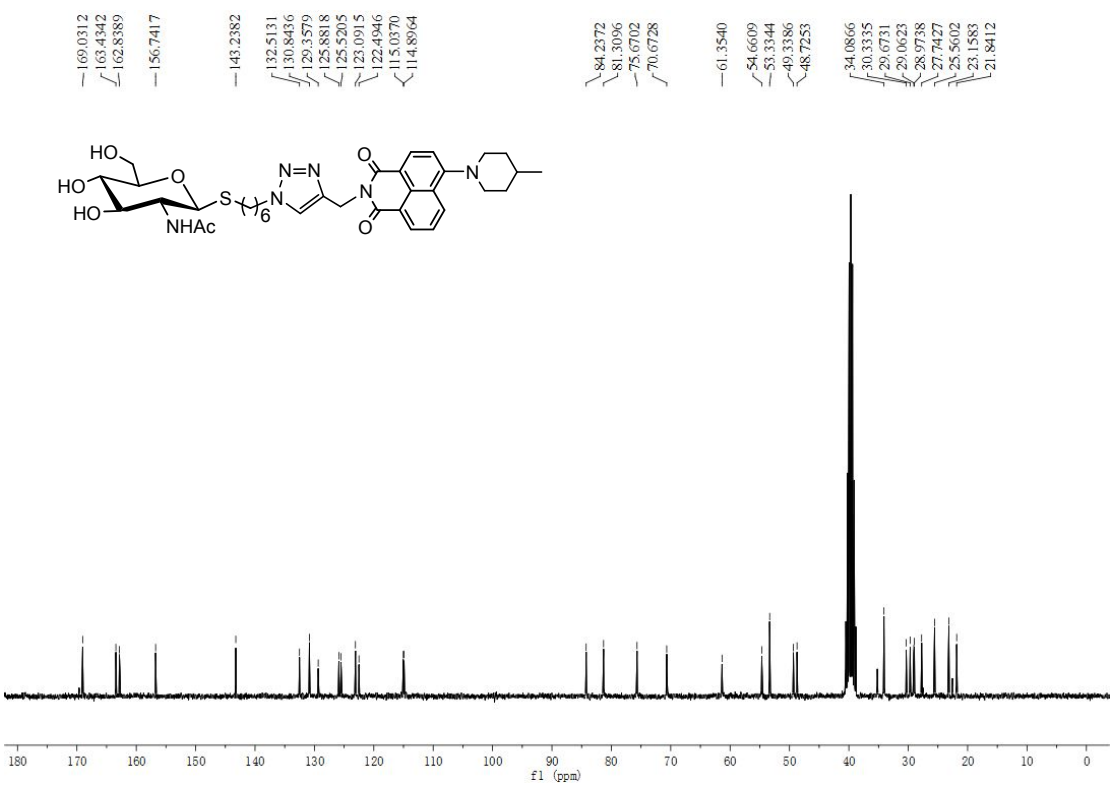
^{13}C NMR spectrum of 15v (75 MHz, DMSO-d_6)



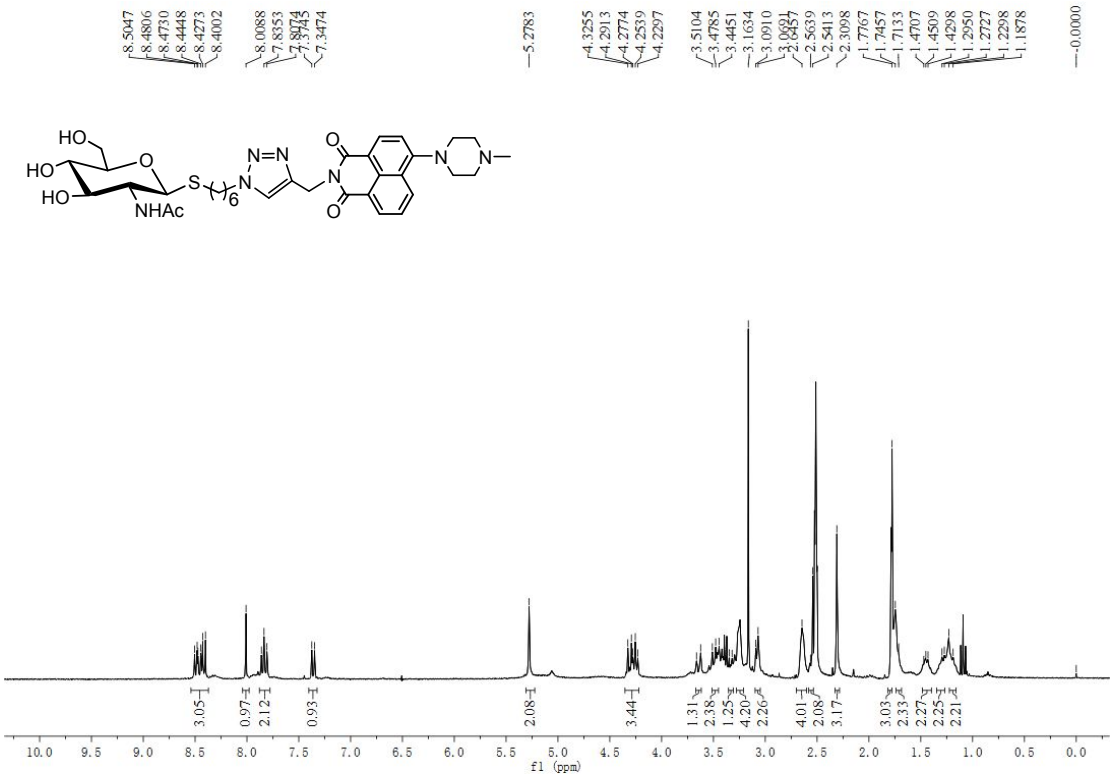
^{1}H NMR spectrum of 15w (300 MHz, DMSO-d_6)



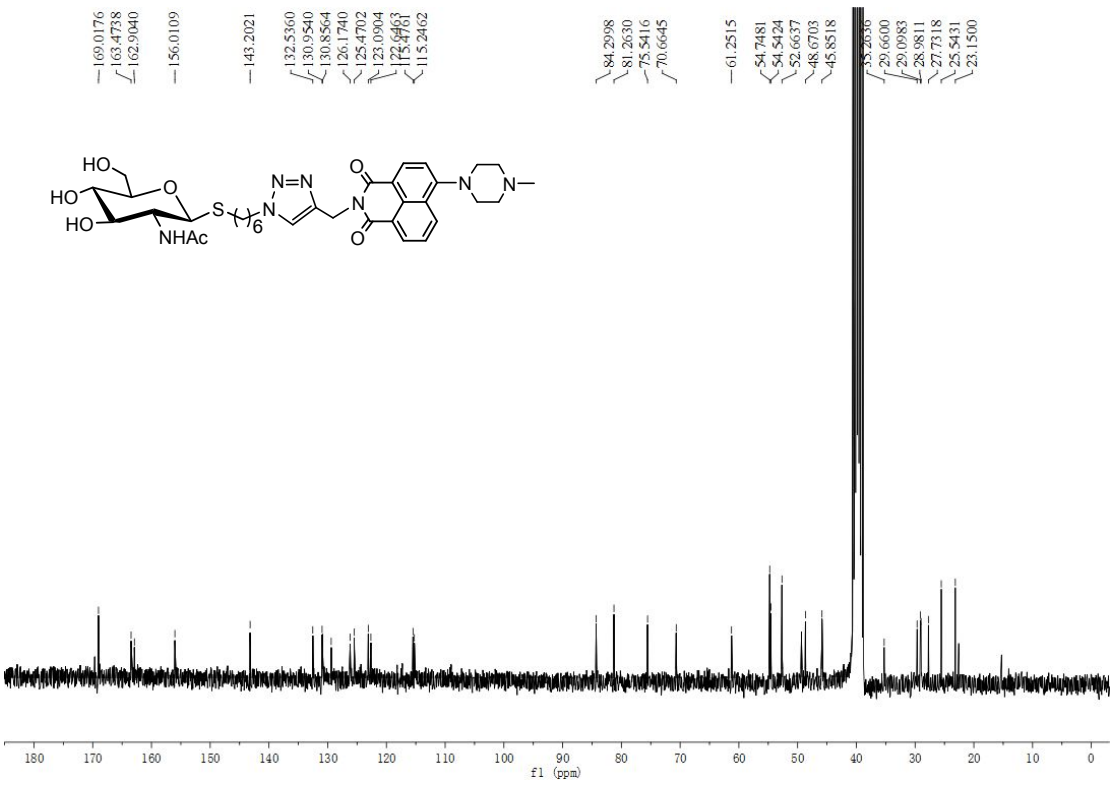
^{13}C NMR spectrum of 15w (75 MHz, DMSO-d_6)



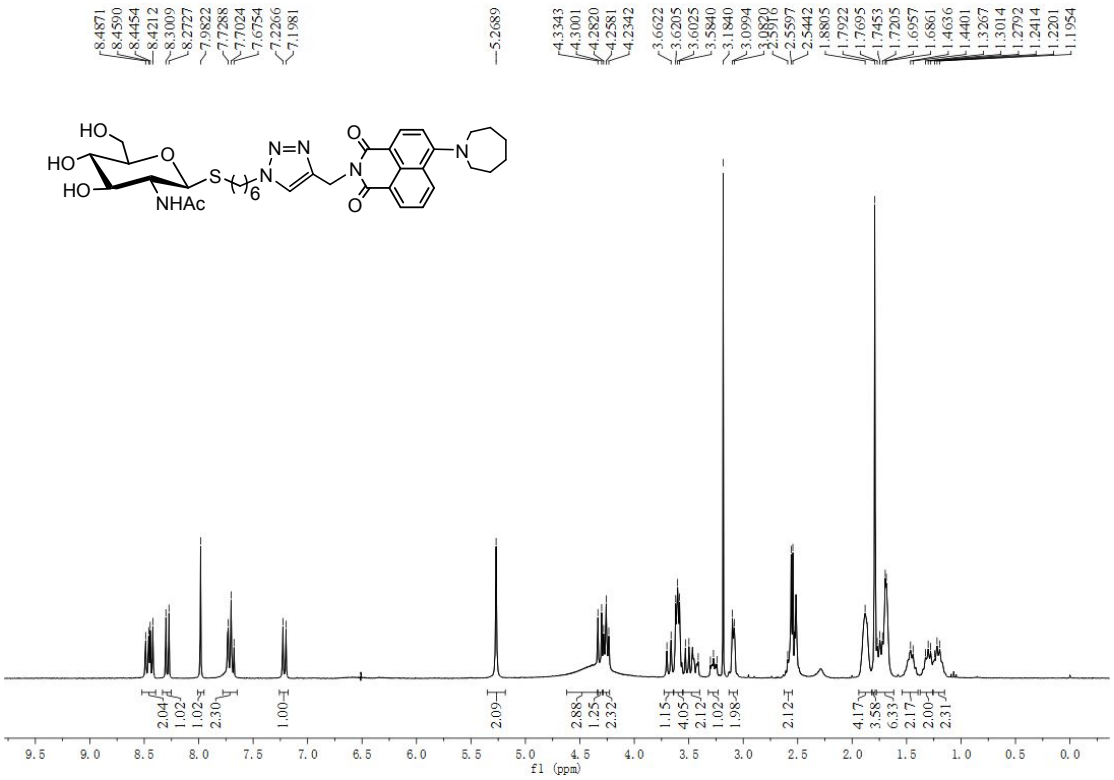
^{1}H NMR spectrum of 15x (300 MHz, DMSO-d_6)



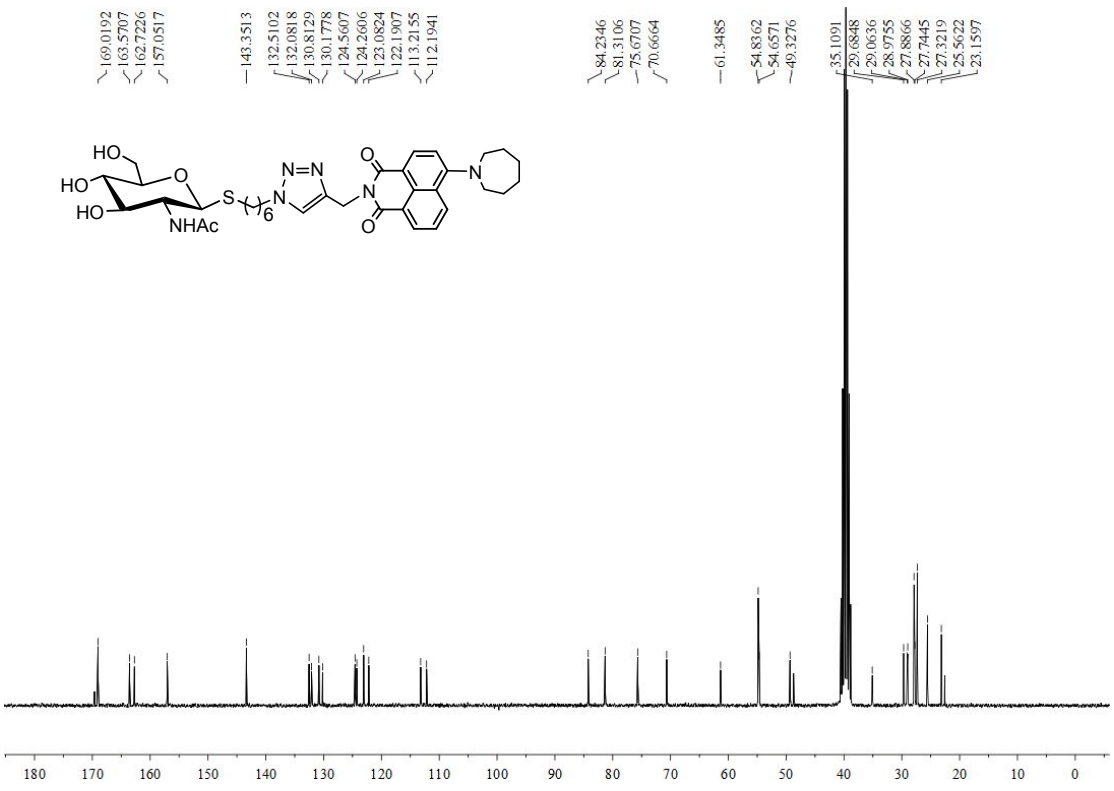
^{13}C NMR spectrum of 15x (75 MHz, DMSO-d_6)



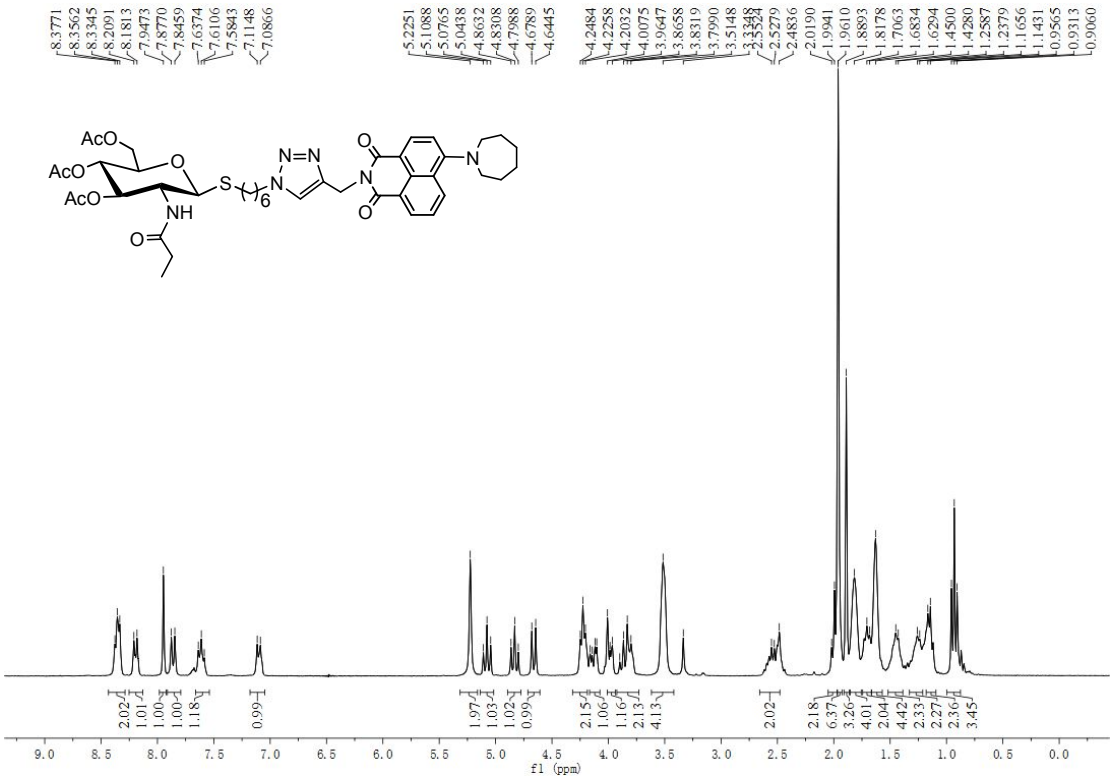
^{1}H NMR spectrum of 15y (300 MHz, DMSO-d_6)



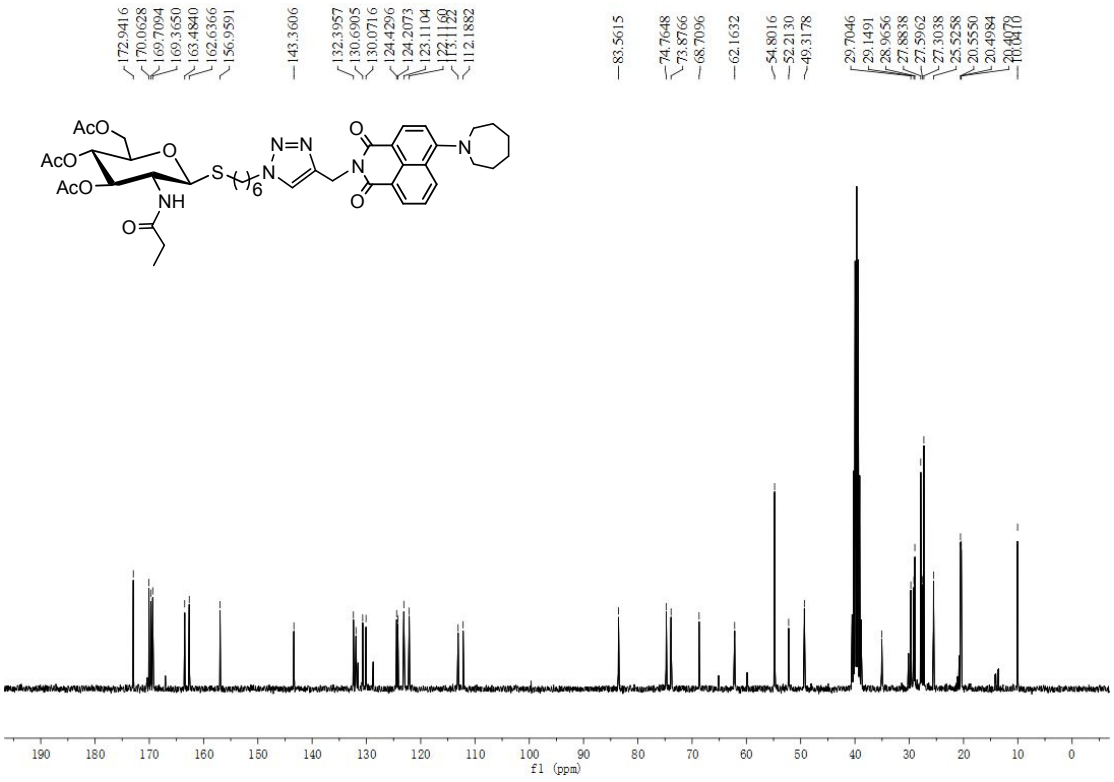
^{13}C NMR spectrum of 15y (75 MHz, DMSO-d_6)



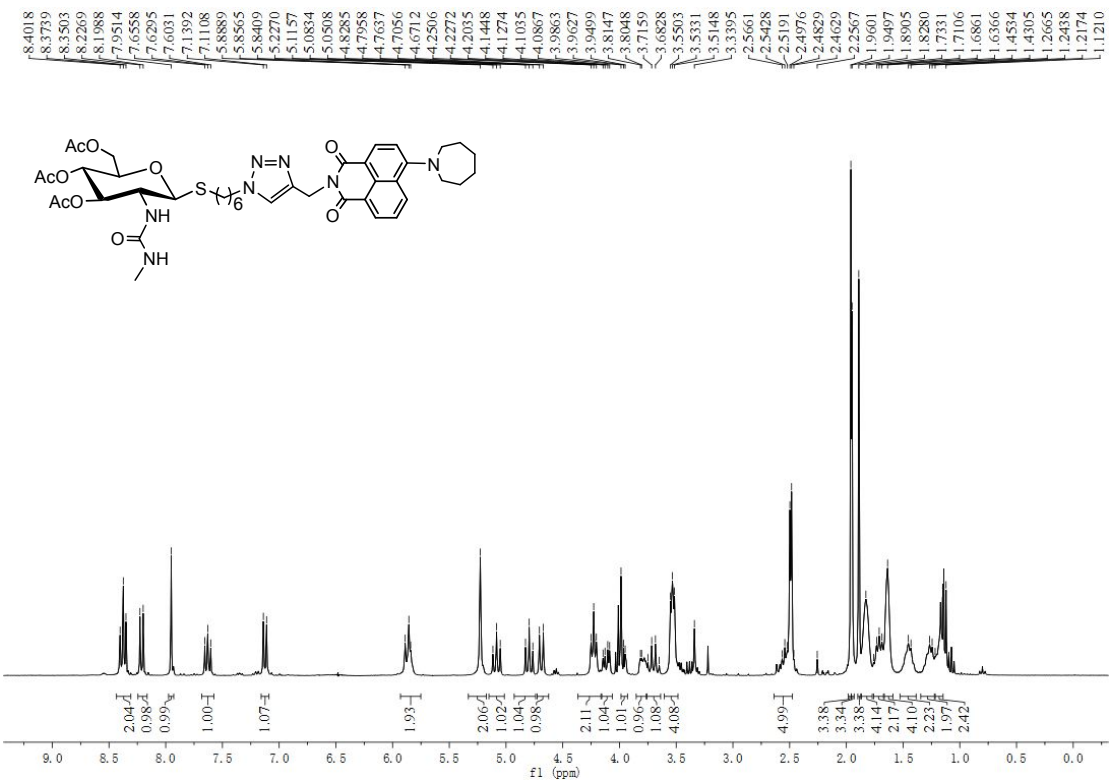
^{1}H NMR spectrum of 22a (300 MHz, DMSO-d_6)



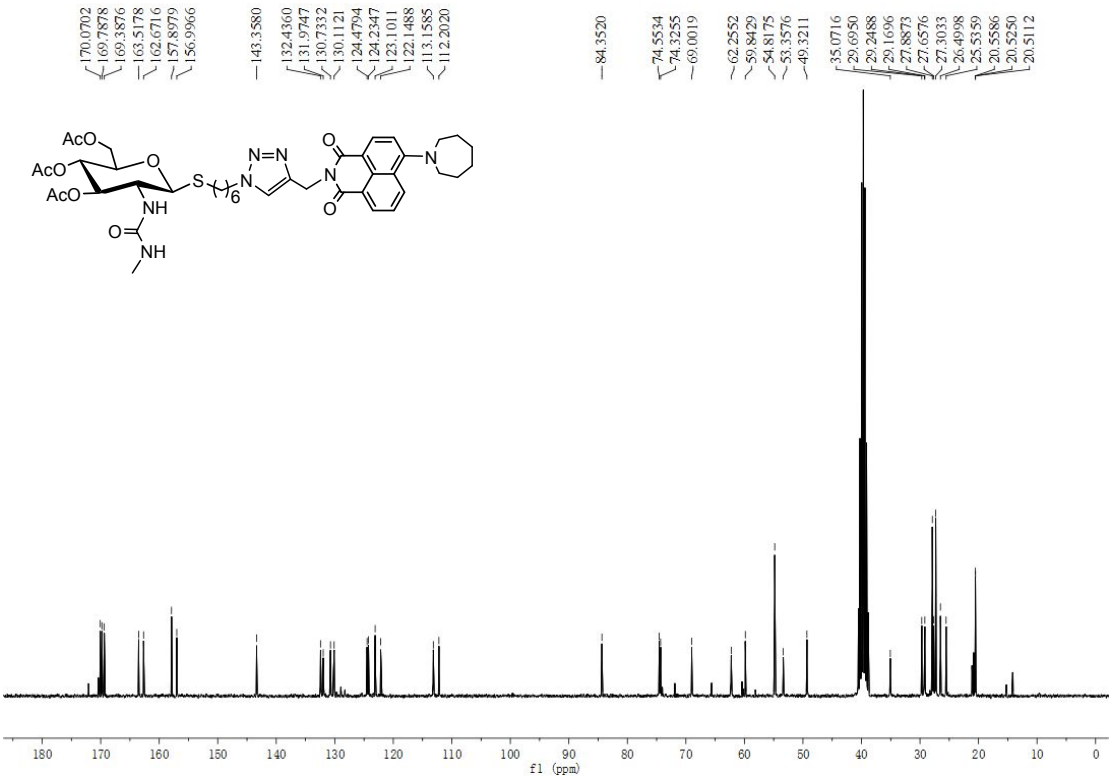
^{13}C NMR spectrum of 22a (75 MHz, DMSO-d_6)



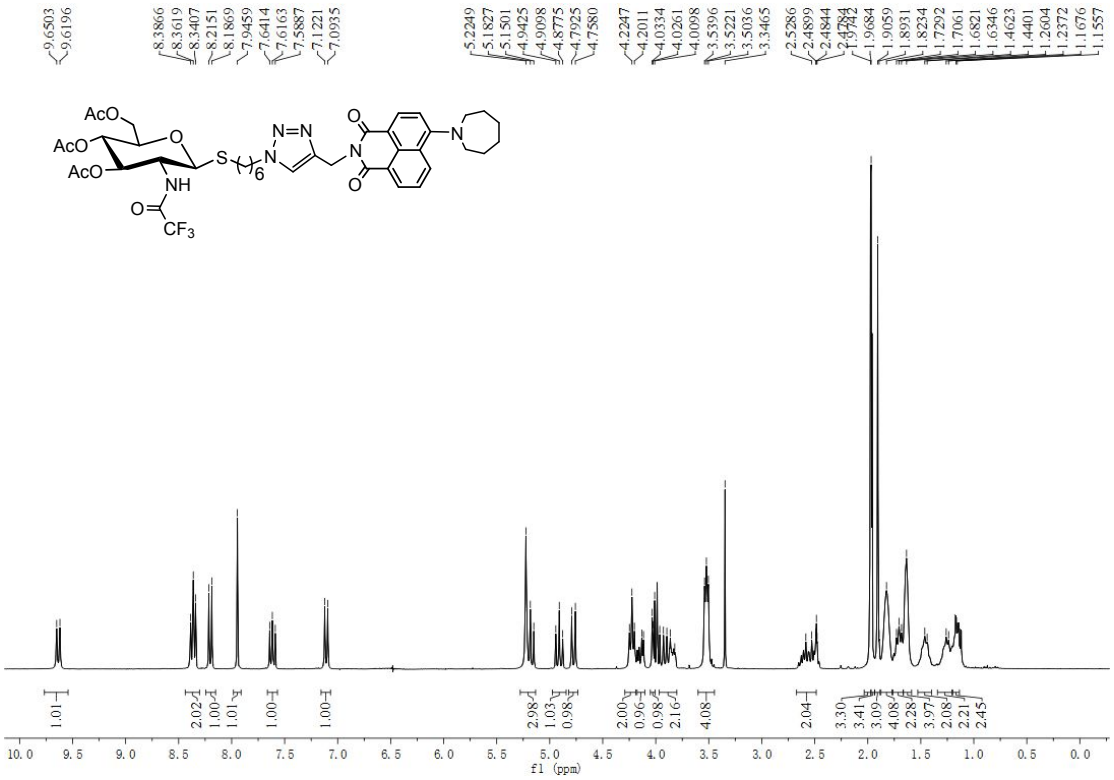
^{1}H NMR spectrum of 22b (300 MHz, DMSO-d_6)



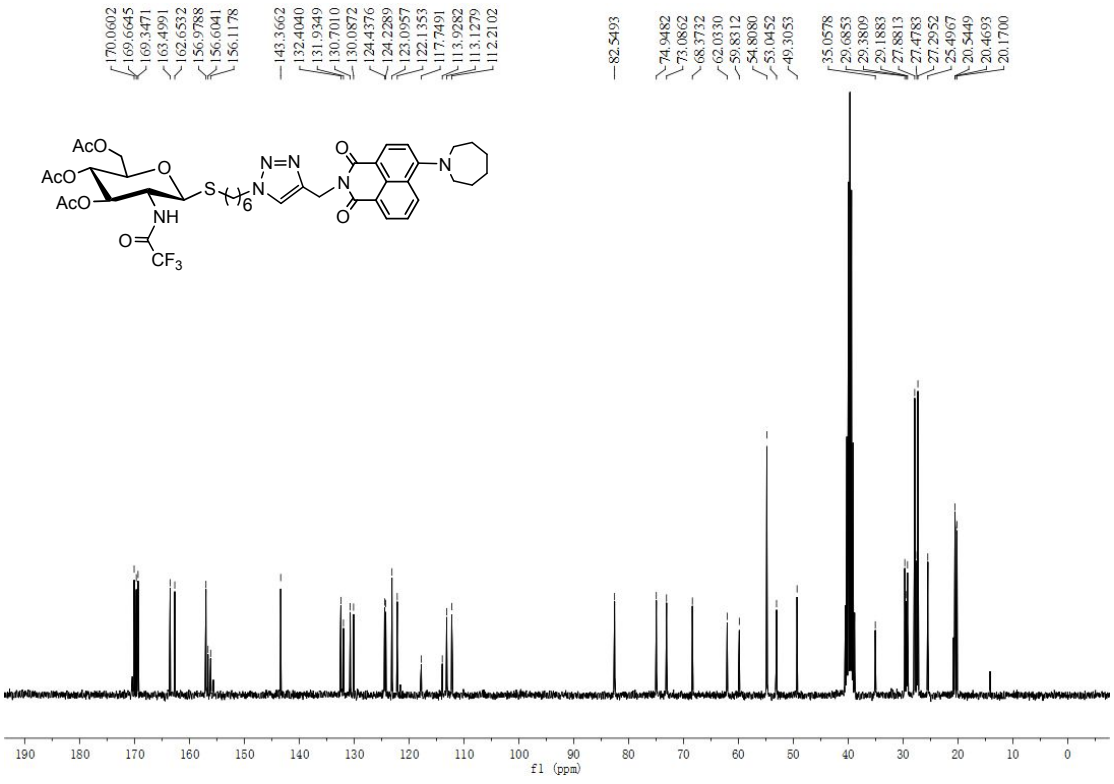
^{13}C NMR spectrum of 22b (75 MHz, DMSO-d_6)



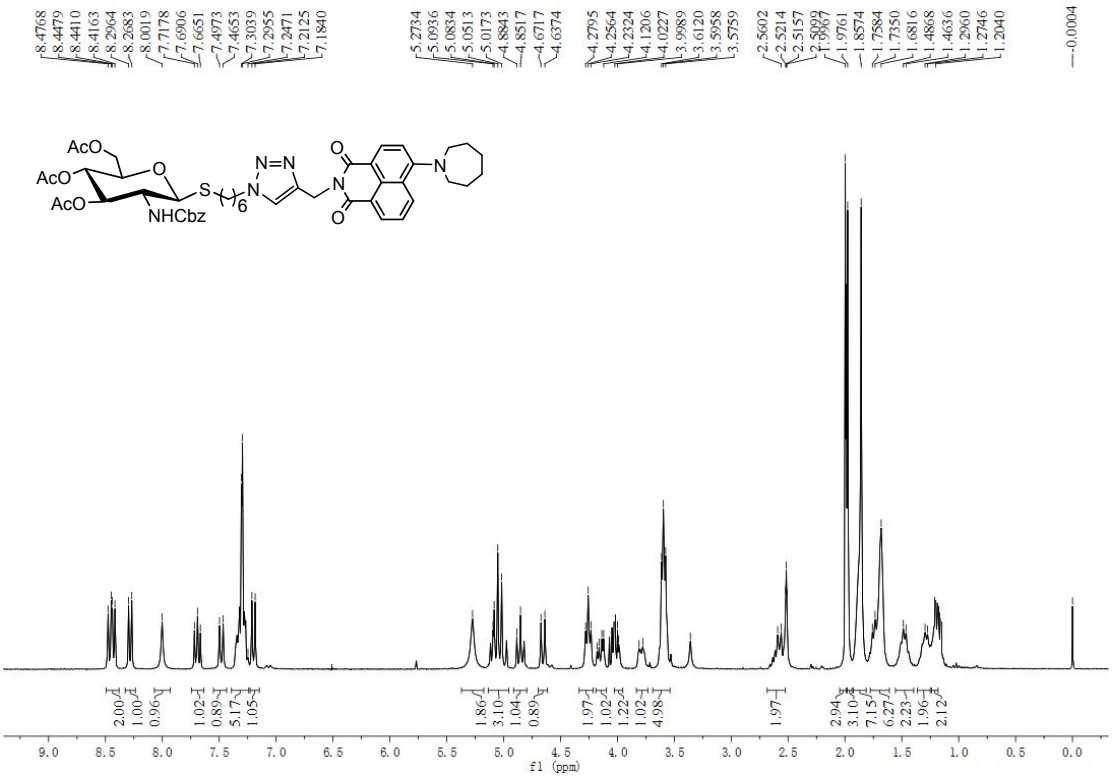
^{1}H NMR spectrum of 22c (300 MHz, DMSO-d_6)



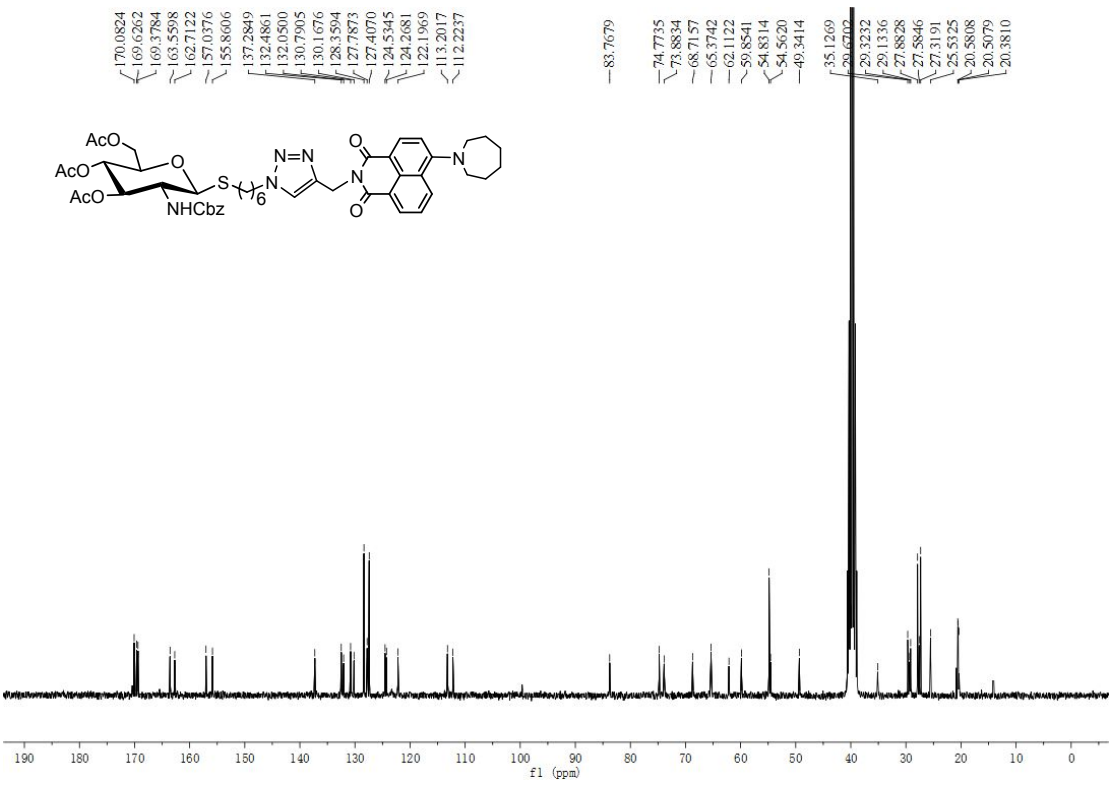
^{13}C NMR spectrum of 22c (75 MHz, DMSO-d_6)



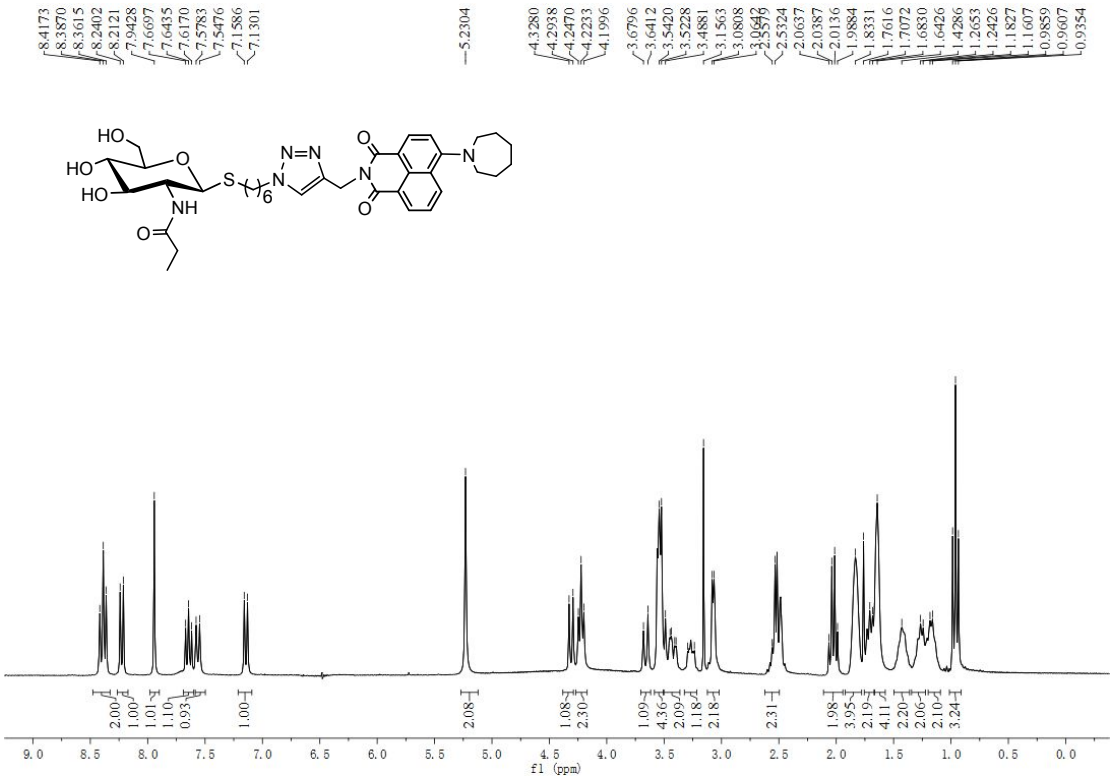
^{1}H NMR spectrum of 22d (300 MHz, DMSO-d_6)



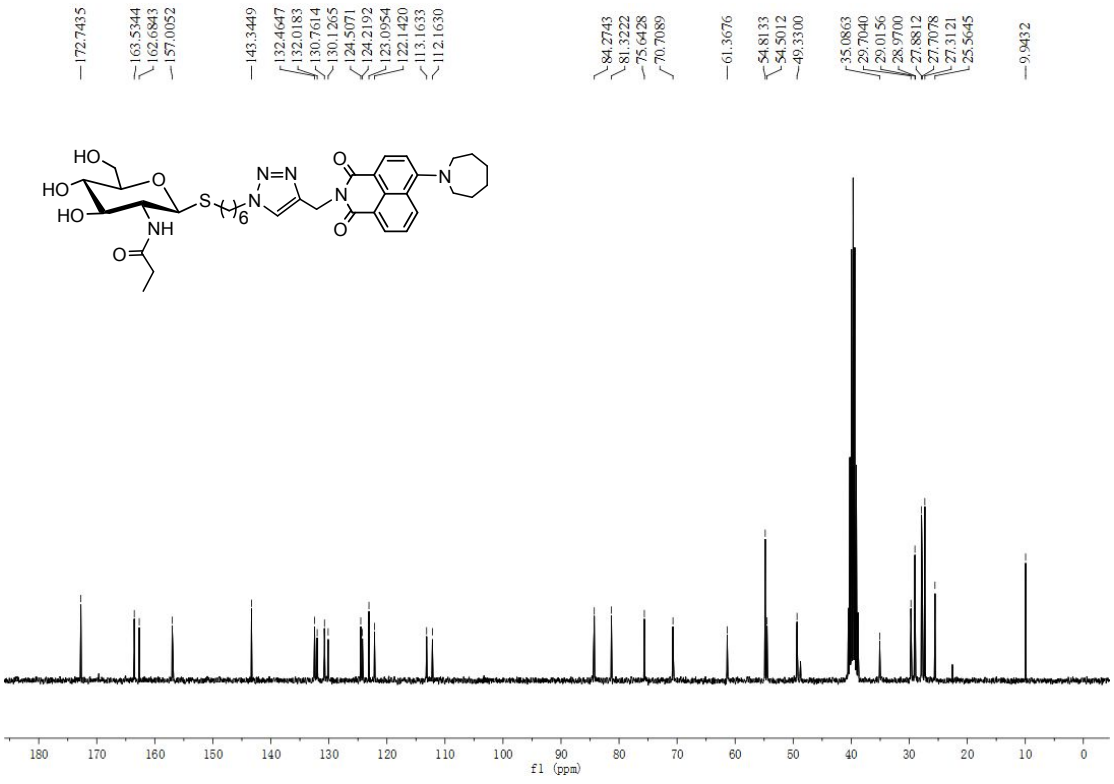
^{13}C NMR spectrum of 22d (75 MHz, DMSO-d_6)



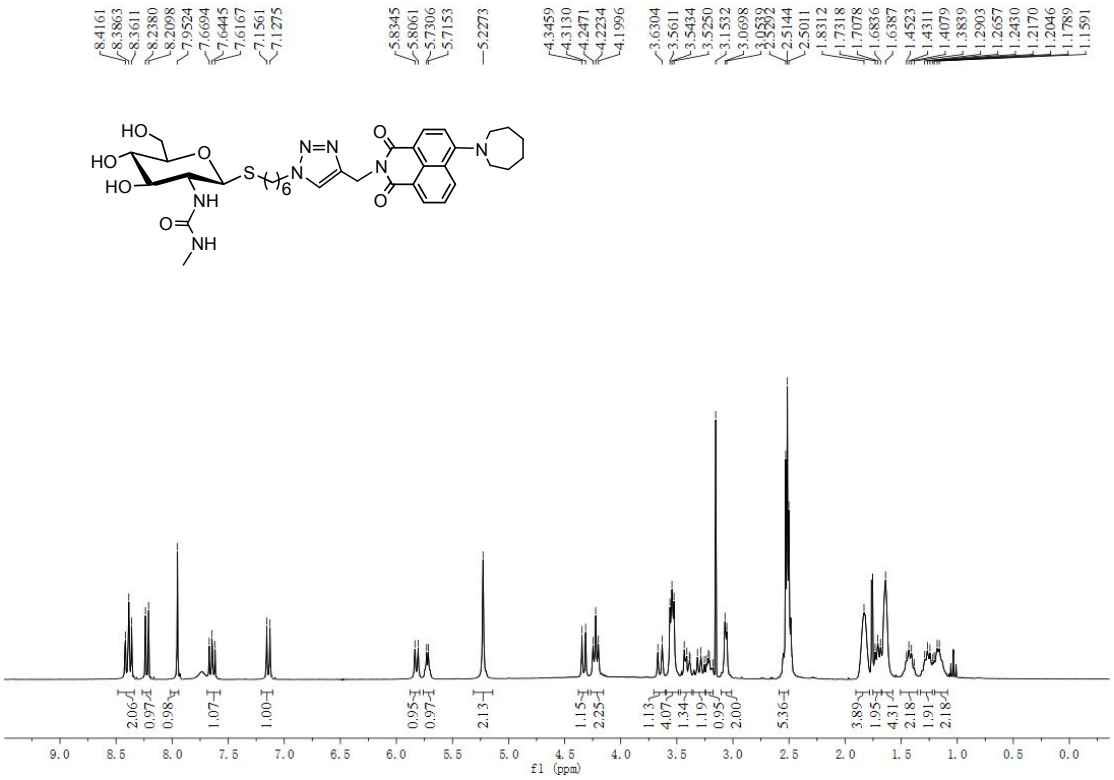
^{1}H NMR spectrum of 23a (300 MHz, DMSO-d_6)



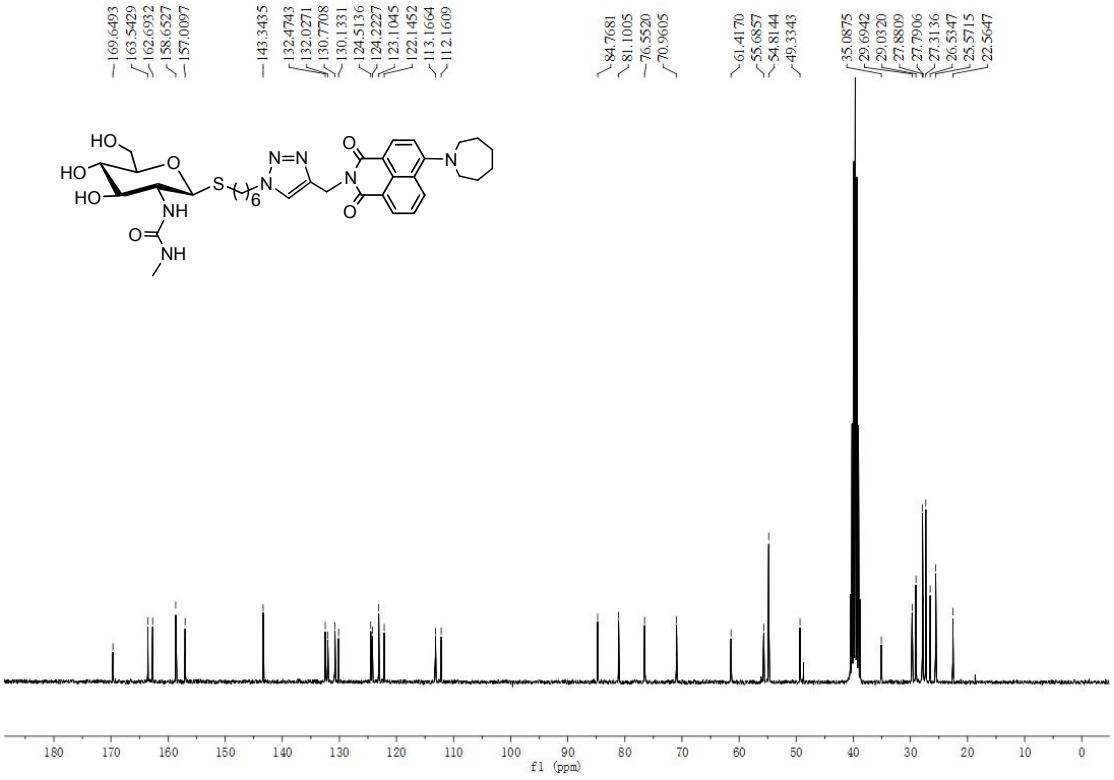
^{13}C NMR spectrum of 23a (75 MHz, DMSO-d_6)



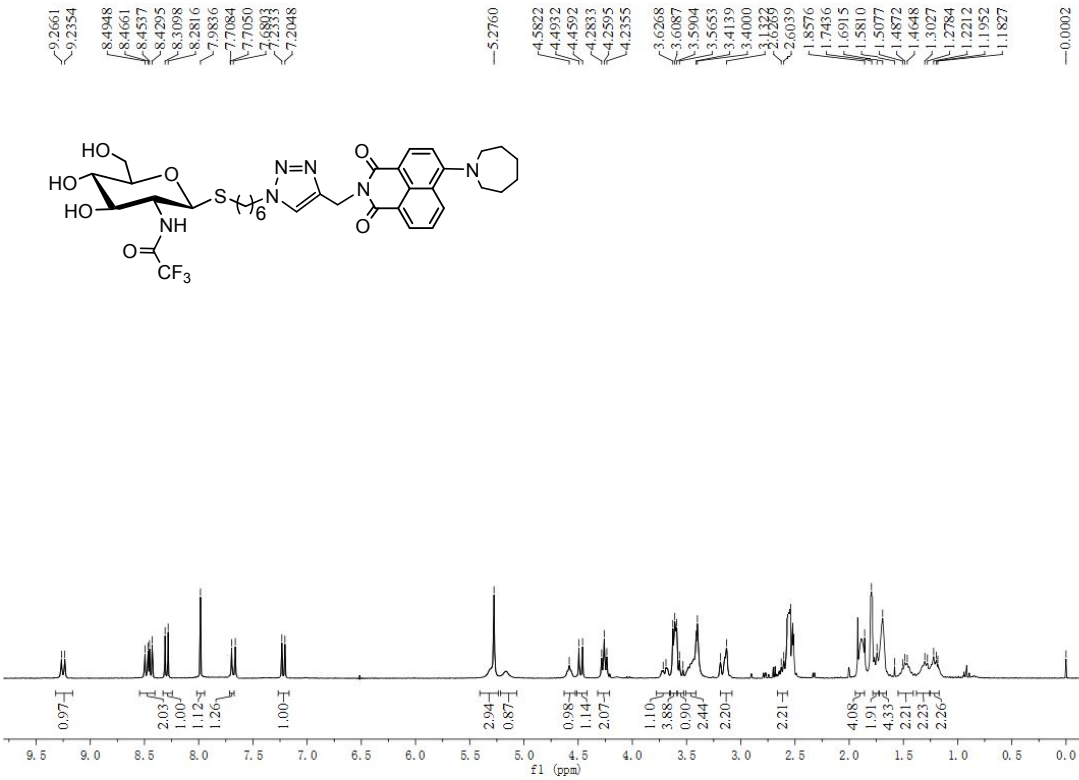
^{1}H NMR spectrum of 23b (300 MHz, DMSO-d_6)



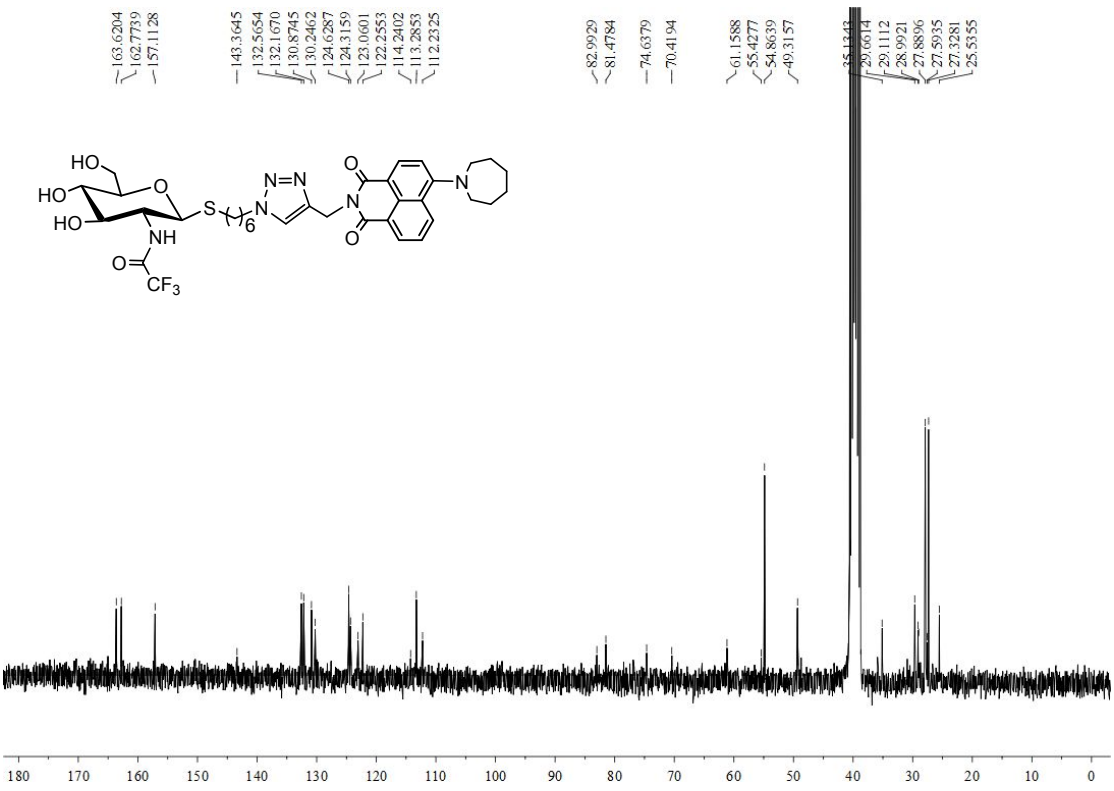
^{13}C NMR spectrum of 23b (75 MHz, DMSO-d_6)



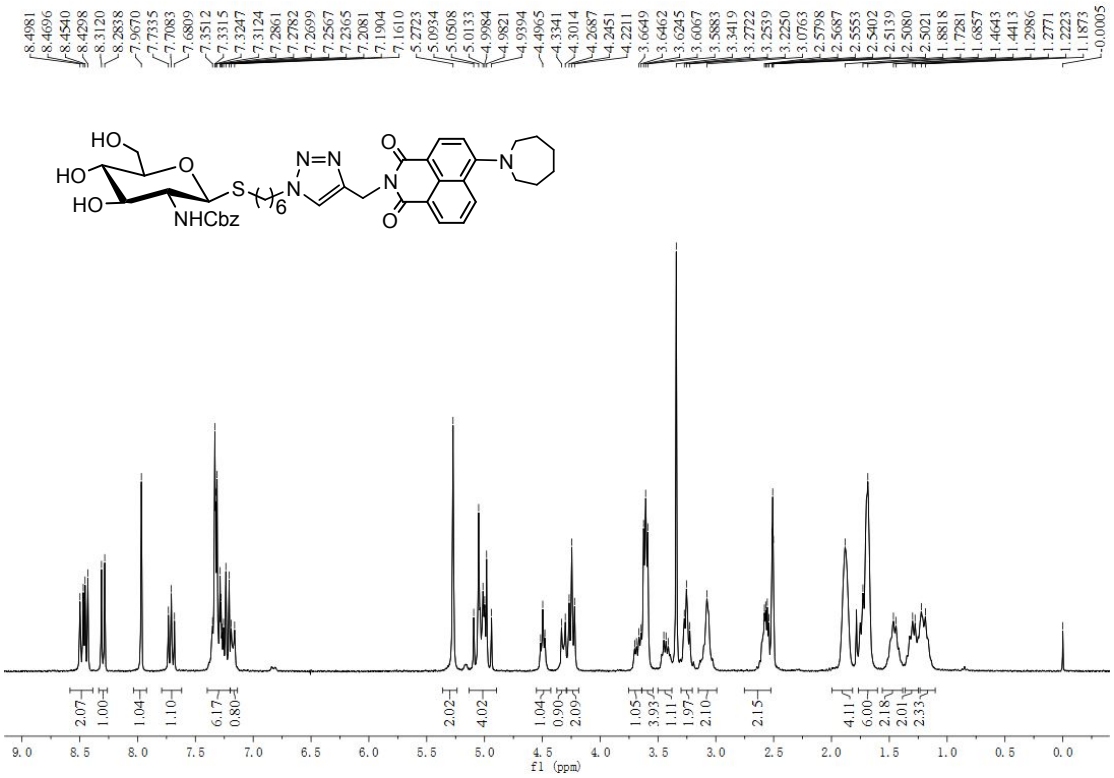
^{1}H NMR spectrum of 23c (300 MHz, DMSO-d_6)



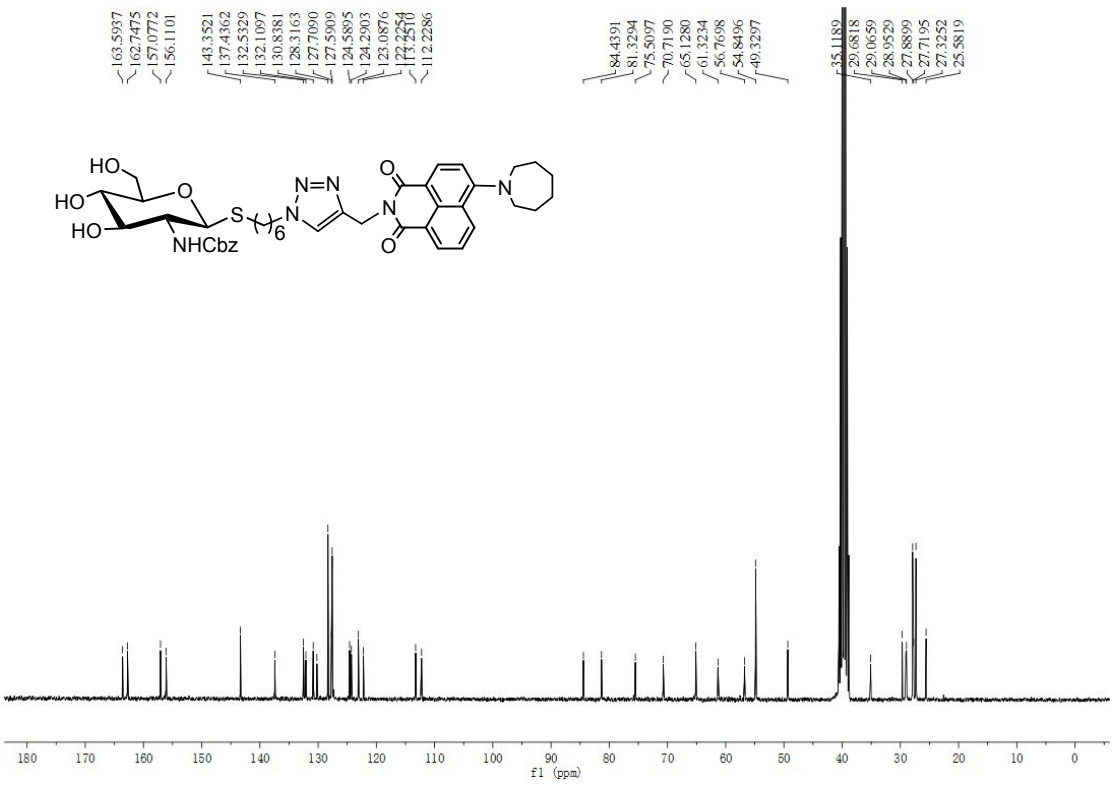
^{13}C NMR spectrum of 23c (75 MHz, DMSO-d_6)



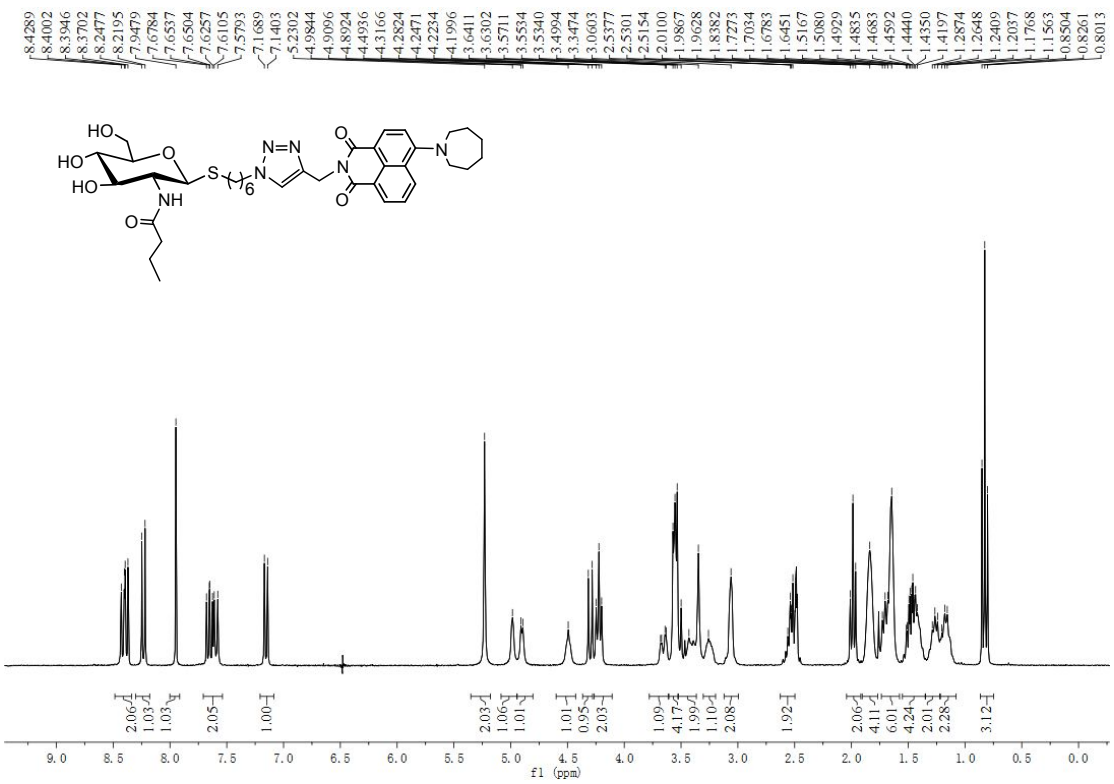
^{1}H NMR spectrum of 23d (300 MHz, DMSO-d_6)



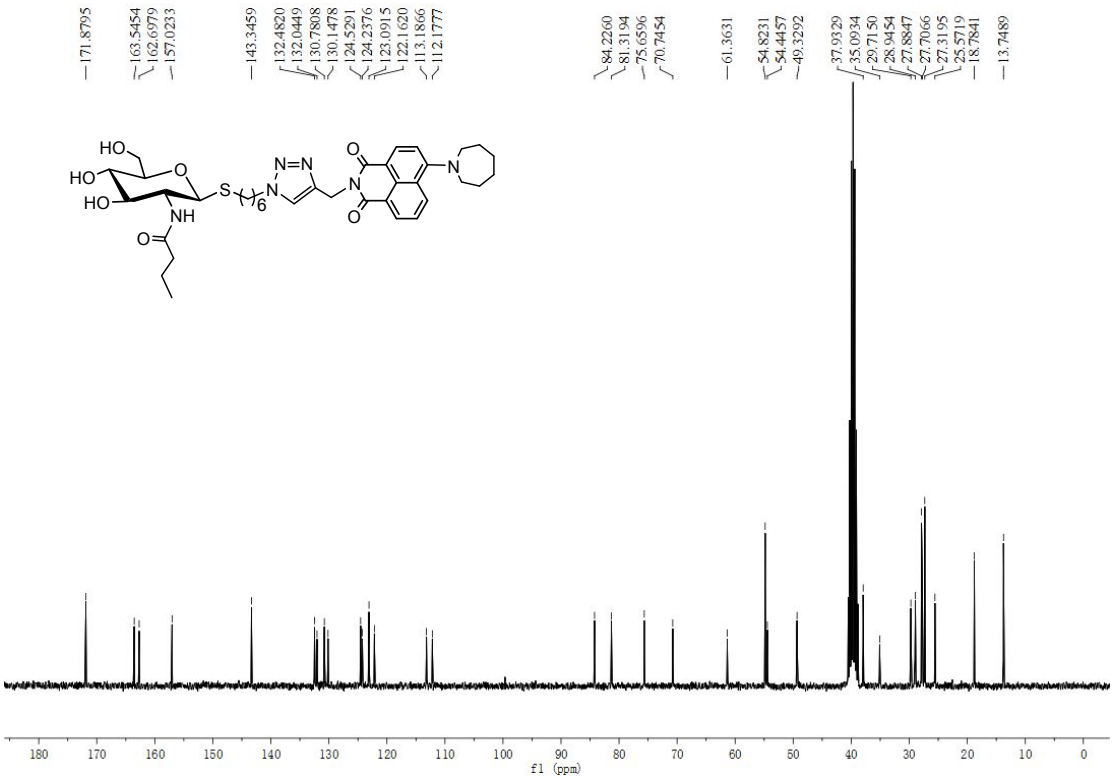
^{13}C NMR spectrum of 23d (75 MHz, DMSO-d_6)



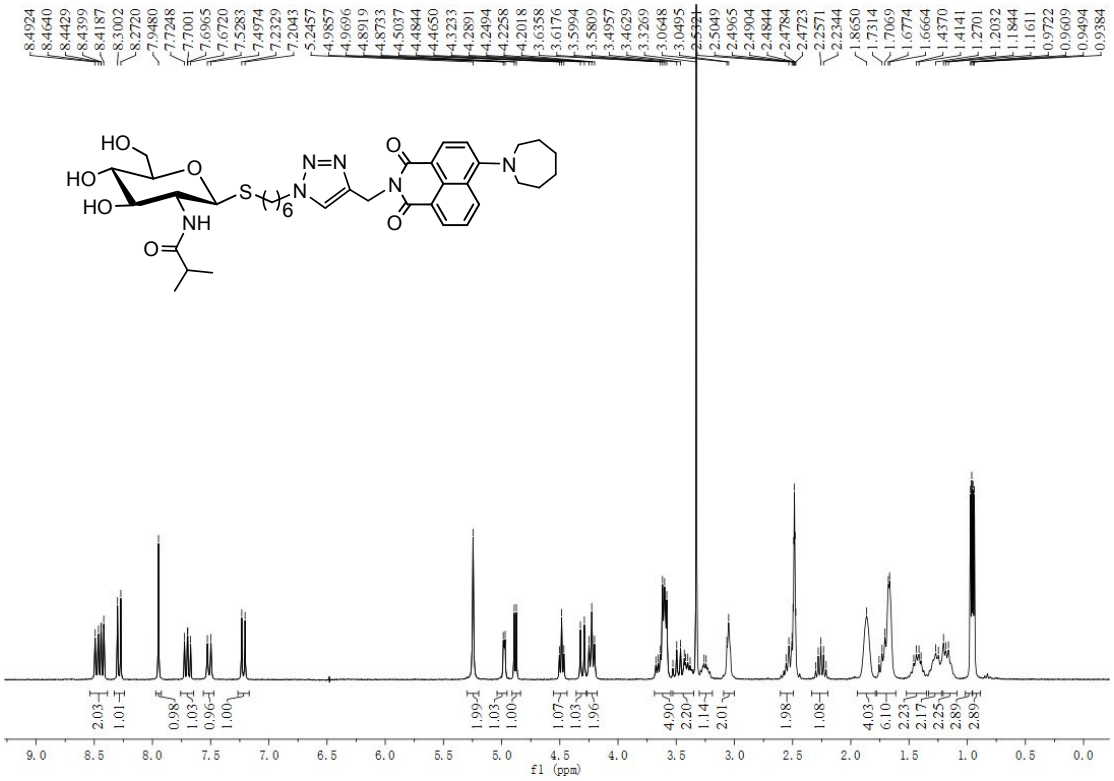
^{1}H NMR spectrum of 23e (300 MHz, DMSO-d_6)



^{13}C NMR spectrum of 23e (75 MHz, DMSO-d_6)



^{1}H NMR spectrum of 23f (300 MHz, DMSO-d_6)



^{13}C NMR spectrum of 23f (75 MHz, DMSO-d_6)