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Supporting information

Directed copper-Catalyzed Dehydrogenative C-H Amination of Unsaturated Sialic Acids

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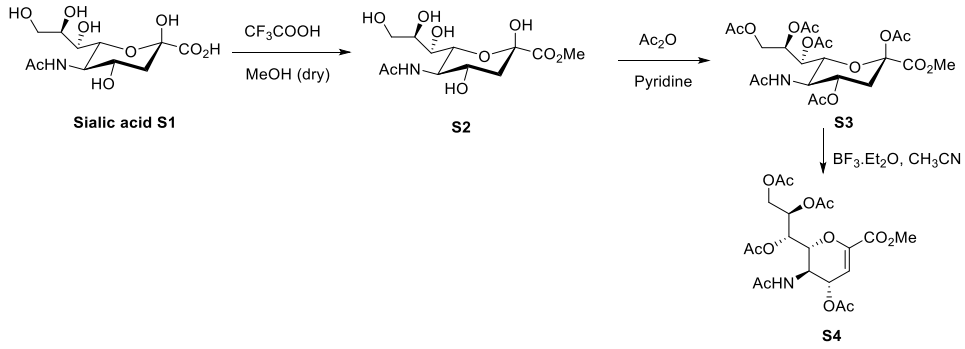
1. General information

All the solvents and reagents were obtained from commercial sources and were used without further purification. Unless otherwise noted, all reactions were carried out under argon atmosphere. Analytical TLC was performed using Merck TLC silica gel F254 plates and analyzed by UV light or by staining upon heating with vanillin solution (15 g of vanillin in 250 mL ethanol and 2.5 mL of concentrated sulfuric acid). Silica gel 60 (40-63 μm) were used for silica gel chromatography. The ^{1}H NMR and ^{13}C NMR J-MOD spectra were recorded in either $CDCl_3$ or d_6-actone or d_4-methanol on Bruker Avance 300, 400 spectrometers. The chemical shifts of ^{1}H, ^{13}C are reported in ppm relative to the solvent residual peaks. Melting points were recorded on a Büchi B-450 apparatus and are uncorrected. IR spectra were recorded on a IR-Affinity-1S. Optical rotations were obtained with a Polarimeter-MCP100. High resolution mass spectra (HR-MS) were recorded on a Micro Mass LCT Premier Spectrometer.

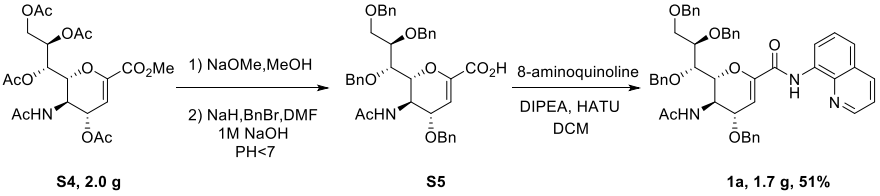
2. The synthesis of the Starting materials

2.1 The synthesis of S4 [1-3]



Compounds **S_2 S_3 S_4** were prepared according to the literature[1-3]

2.2 The synthesis of 1a [4-5]

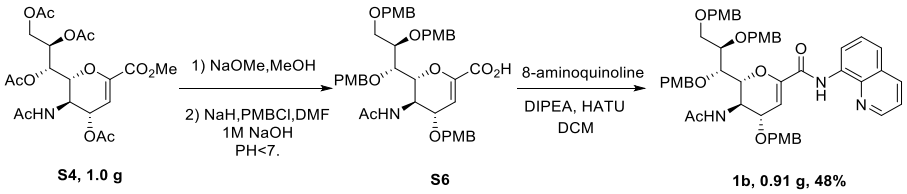


Step 1: To a solution of **S4** (2.0 g, 4.22 mmol) in MeOH (20 mL) was added fresh MeONa (0.5 M in MeOH, 1.0 mL) at room temperature. After stirring for 30 min, the mixture was concentrated in vacuo. To a solution of this crude material in DMF (30 mL) was added NaH (692 mg, 60% dispersion in mineral oil, 17.3 mmol, 4.1 eq.) at 0 °C. After stirring for 15 min, BnBr (2.52 mL, 21.1 mmol, 5.0 eq.) was added. After stirring for 1 h at 0 °C, additional NaH (169 mg, 60% dispersion in mineral oil, 4.22 mmol, 1.0 eq.) was added to the mixture. After further stirring for 30 min at room temperature, 1 M aqueous NaOH (6 mL) was added to the mixture at 0 °C. After stirring for 20 min, DCM (50 mL) was added and the mixture was acidified by adding 2 M aqueous HCl. The mixture was extracted with DCM (×3). The combined organic layer was washed by water and brine, dried (Na_2SO_4), and concentrated in vacuo. The residue was purified on a silica gel column (PE: EtOAc = 8:2 to 1:1 → CH_2Cl_2:MeOH = 10:1) to afford a crude material as a light yellow oil.

Step 2: The mixture of crude **S5** (4.22 mmol, 1.0 equiv.), 8-aminoquinoline (608 mg, 4.22

mmol, 1.0 equiv.), HATU (3.2 g, 8.44 mmol, 2.0 equiv.) and DIPEA (1.4 mL, 8.44 mmol, 2.0 equiv.) in anhydrous DCM (20 mL) was stirred at room temperature for 5 h. Then the mixture was extracted with NH_4Cl saturated solution (3 x 20 mL), and the organic layer was washed with water (20 mL) and brine (20 mL), dried over anhydrous Na_2SO_4 and concentrated in vacuo. The residue was purified on a silica gel column (PE: EtOAc = 3:1 to 2:1) to afford the title compound **1a** (1.7 g, 57%) as a light yellow foam. **mp**: 62 - 64 °C; **$[\alpha]_D^{20}$** = + 91.0 (c = 0.30, EtOH); **IR (neat, cm^{-1})**: 1654, 1525, 1487, 1454, 1327, 1087, 1028, 825, 734, 696; **^{1}H NMR (400 MHz, $CDCl_3$)** δ 10.86 (s, 1H), 8.71 (dd, *J* = 6.8, 2.0 Hz, 1H), 8.51 (dd, *J* = 4.1, 1.3 Hz, 1H), 8.03 (d, *J* = 8.2 Hz, 1H), 7.46 - 7.41, (m, 2H), 7.28 - 7.19 (m, 9H), 7.17 - 7.10 (m, 4H), 7.03 - 7.01 (m, 5H), 6.99 - 6.91(m, 3H), 6.24 (d, *J* = 3.6 Hz, 1H), 5.25 - 5.20 (m, 1H), 4.66 - 4.54 (m, 4H), 4.51 - 4.39 (m, 5H), 4.31 (m, 1H), 4.22 (m, 1H), 4.12 - 4.10 (m, 2H), 3.94 (dd, *J* = 9.9, 4.8 Hz, 1H), 3.69 (dd, *J* = 9.9, 4.6 Hz, 1H), 1.75 (s, 3H); **^{13}C NMR (J-MOD, 75 MHz, d_6-actone)** δ. 170.4 (C), 159.8 (C), 150.0 (CH), 147.4 (C), 140.1 (C), 140.0 (C), 139.9 (C), 139.5 (C), 137.5 (CH), 135.2 (C), 129.4 (CH), 129.3 (CH), 129.2 (CH), 129.0 (CH), 129.0 (CH), 128.8 (CH), 128.7 (CH), 128.5 (CH), 128.3 (CH), 128.2 (CH), 128.1 (CH), 123.1 (CH), 117.0 (CH), 106.8 (CH), 79.1 (CH), 78.8 (CH), 76.7 (CH), 75.4 (CH_2), 75.3 (CH), 74.3 (CH_2), 73.3 (CH_2), 71.1 (CH_2), 70.8 (CH_2), 48.6 (CH), 23.6 (CH_3); **HRMS** (ESI-TOF): m/z calculated for $C_{48}H_{48}N_3O_7$ $[M+H]^+$ 778.3487, found 778.3499.

2.3 The synthesis of 1b [4-5]



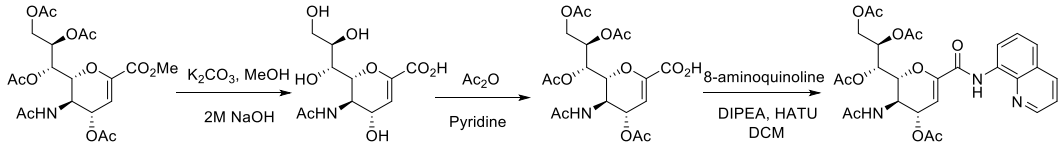
S4, 1.0 g **S6** **1b, 0.91 g, 48%**

Step 1: To a solution of **S4** (1.0 g, 2.11 mmol) in MeOH (10 mL) was added fresh MeONa (0.5 M in MeOH, 0.5 mL) at room temperature. After stirring for 30 min, the mixture was concentrated in vacuo. To a solution of this crude material in DMF (30 mL) was added NaH (346 mg, 60% dispersion in mineral oil, 8.65 mmol, 4.1 eq.) at 0 °C. After stirring for 15 min, PMBCl (1.43 mL, 10.55 mmol, 5.0 eq.) was added. After stirring for 1 h at 0 °C, additional NaH (85 mg, 60% dispersion in mineral oil, 2.11mmol, 1.0 eq.) was added to the mixture. After further stirring for 30 min at room temperature, 1 M aqueous NaOH (3 mL) was added to the mixture at 0 °C. After stirring for 20 min, DCM (50 mL) was added and the mixture was acidified by adding 2 M aqueous HCl. The mixture was extracted with DCM (×3). The combined organic layer was washed by water and brine, dried (Na_2SO_4), and concentrated in vacuo. The residue was purified on a silica gel column (PE: EtOAc = 2:1 to 0:1 → CH_2Cl_2:MeOH = 20:1) to afford a crude material as a yellow oil.

Step 2: The mixture of crude **S6** (2.11 mmol, 1.0 equiv.), 8-aminoquinoline (304 mg, 2.11 mmol, 1.0 equiv.), HATU (1.6 g, 4.22 mmol, 2.0 equiv.) and DIPEA (0.7 mL, 4.22 mmol, 2.0 equiv.) in anhydrous DCM (10 mL) was stirred at room temperature overnight. Then the mixture was extracted with NH_4Cl saturated solution (3 x 10 mL), and the organic layer was washed with water (10 mL) and brine (10 mL), dried over anhydrous Na_2SO_4 and concentrated in vacuo. The residue was purified on a silica gel column (PE: EtOAc = 2:1 to 1:1) to afford the title compound **1b** (0.91g, 48%) as a light yellow foam. **mp**: 66 - 67 °C; **$[\alpha]_D^{20}$** = + 76.0 (c = 0.20, EtOH); **IR (neat, cm^{-1})**: 1654, 1612, 1529, 1514, 1487, 1247, 1174, 1080, 1033, 823; **^{1}H NMR (400 MHz, $CDCl_3$)** δ 10.83 (s, 1H), 8.72 (d, *J* = 6.9 Hz, 1H), 8.54 (d, *J* = 3.0 Hz, 1H), 8.00 (d, *J* = 7.9 Hz, 1H), 7.45 - 7.38 (m, 2H), 7.27 - 7.19 (m, 5H), 7.01 (m, 4H), 6.77 (m, 4H), 6.58 (d, *J* = 8.4 Hz, 2H), 6.45 (d, *J* = 8.3 Hz,

2H), 6.22 (d, *J* = 3.3 Hz, 1H), 5.46 (d, *J* = 8.1 Hz, 1H), 4.63 - 4.56 (m, 2H), 4.53 - 4.31 (m, 9H), 4.20 - 4.18 (m, 1H), 4.11 - 4.07 (m, 2H), 3.90 (dd, *J* = 9.9, 4.4 Hz, 1H), 3.71 (s, 3H), 3.65 (s, 3H), 3.58 (s, 3H), 3.54 (s, 3H), 1.79 (s, 3H); **^{13}C NMR (J-MOD**, **101 MHz, CDCl$_3$)** δ. 169.6 (C), 159.4 (C), 159.4 (C), 159.3 (C), 159.1 (C), 159.0 (C), 148.5 (CH), 145.8 (C), 138.8 (C), 136.1 (CH), 133.9 (C), 130.7 (C), 130.6 (C), 130.5 (C), 130.1 (C), 129.9 (CH), 129.9 (CH), 129.5 (CH), 129.3 (CH) 127.9 (C), 127.3 (CH), 122.2 (CH), 121.6 (CH), 116.9 (CH), 113.9 (CH), 113.8 (CH), 113.6 (CH), 113.5 (CH), 105.6 (CH), 77.8 (CH), 77.7 (CH), 75.0 (CH), 74.3 (CH_2), 73.2 (CH_2), 72.0 (CH_2), 71.7 (CH), 70.2 (CH_2), 69.0 (CH_2), 55.3 (CH_3), 55.3 (CH_3), 55.2 (CH_3), 55.1 (CH_3), 47.8 (CH), 23.5 (CH_3); **HRMS** (ESI-TOF): m/z calculated for $C_{52}H_{56}N_3O_{11}$ $[M+H]^+$ 898.3909, found 898.3939.

2.4 The synthesis of 1c [5-6]



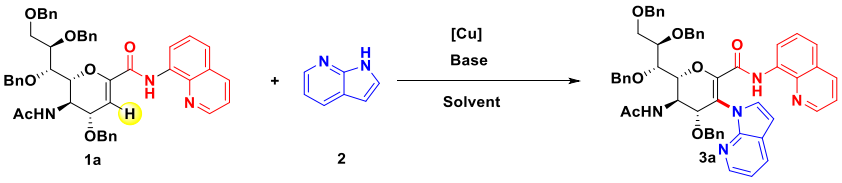
S4, 2.1 g **S7** **S8** **1c, 1.4 g, 54%**

Compounds **S$_7$ S$_8$** were prepared according to the literature[6] without purification.

Step 3: The mixture of crude **S8** (4.44 mmol, 1.0 equiv.), 8-aminoquinoline (638 mg, 4.44mmol, 1.0 equiv.), HATU (3.37 g, 8.88 mmol, 2.0 equiv.) and DIPEA (1.5 mL, 8.88 mmol, 2.0 equiv.) in anhydrous DCM (20 mL) was stirred at room temperature overnight. Then the mixture was extracted with NH_4Cl saturated solution (3 x 20 mL), and the organic layer was washed with water (20 mL) and brine (20 mL), dried over anhydrous Na_2SO_4 and concentrated in vacuo. The residue was purified on a silica gel column (PE : EtOAc = 3:1 to 0:1) to afford the title compound **1c** (1.4 g, 54%) as a white foam. **mp**: 116 - 118 °C; **[α]$_D$ ^{20}** = + 72.6 (c = 0.19, EtOH); **IR (neat, cm^{-1})**:1735, 1654, 1529, 1489, 1369, 1211, 1051, 1026, 842, 739; **^{1}H NMR (400 MHz, *d$_6$*-actone)** δ 10.81 (s, 1H), 8.86 (dd, *J* = 4.2, 1.6 Hz, 1H), 8.66 (dd, *J* = 7.6, 1.1 Hz, 1H), 8.27 (dd, *J* = 8.3, 1.5 Hz, 1H), 7.58 (dd, *J* = 8.3, 1.1 Hz, 1H), 7.54 - 7.46 (m, 2H), 7.32 (d, *J* =9.4, 1H), 5.96 (d, *J* = 3.2 Hz, 1H), 5.67 (td, *J* = 6.6, 3.7 Hz, 1H), 5.50 - 5.48 (m, 1H), 5.42 (dd, *J* = 7.0, 3.2 Hz, 1H), 4.63 (dd, *J* = 8.3, 4.1 Hz, 1H), 4.46 - 4.35 (m, 2H), 4.24 (dd, *J* = 12.1, 6.4 Hz, 1H), 1.95 (s, 3H), 1.93 (s, 3H), 1.90 (s, 3H), 1.85 (s, 3H), 1.76 (s, 3H); **^{13}C NMR (J-MOD**, **101 MHz, *d$_6$*-actone)** δ. 170.8 (C), 170.5 (C), 170.3 (C), 169.9 (C), 159.0 (C), 149.9 (CH), 148.1 (C), 139.3 (C), 137.2 (CH), 134.7 (C), 129.0 (C), 127.8 (CH), 123.2 (CH), 123.0 (CH), 117.0 (CH), 105.4 (CH), 77.5 (CH), 69.6 (CH), 68.9 (CH), 68.3 (CH), 62.5 (CH_2), 47.2 (CH), 22.9 (CH_3), 20.8 (CH_3), 20.8 (CH_3), 20.7 (CH_3), 20.6 (CH_3). **HRMS** (ESI-TOF): m/z calculated for $C_{28}H_{32}N_3O_{11}$ $[M+H]^+$ 586.2031, found 586.2042.

3. Optimization of the Reaction Conditions[a]

First set of optimizations



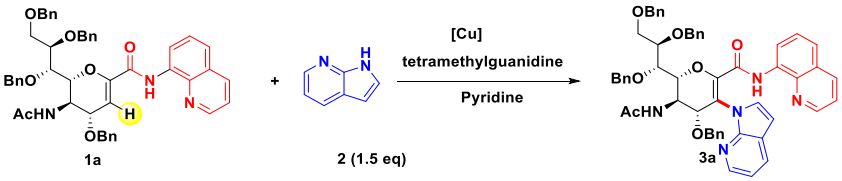
Entry	2	Oxidant	Catalyst (x mol%)	Base (x eq)	Solvent	Conv. (%)	Yield[b] (%)
1	1.5	air	$Cu(OAc)_2$ (15)	TMG (1.2)	Pyridine	52	25
2[c]	1.5	air	$Cu(OAc)_2$ (15)	TMG (1.2)	Pyridine	25	trace
3	2.5	air	$Cu(OAc)_2$ (15)	TMG (1.2)	Pyridine	45	12
4	3.5	air	$Cu(OAc)_2$ (15)	TMG (1.2)	Pyridine	35	trace
5	1.0	air	$Cu(OAc)_2$ (15)	TMG (1.2)	Pyridine	43	22
6	1.5	air	$Cu(OAc)_2$ (100)	TMG (1.2)	Pyridine	27	trace
7	1.5	air	$Cu(OAc)_2$ (30)	TMG (1.2)	Pyridine	67	22
8	1.5	air	$Cu(OAc)_2$ (30)	TMG (1.2)	Pyridine	30	19
9	1.5	O_2	$Cu(OAc)_2$ (15)	TMG (1.2)	Pyridine	61	33
10	1.5	NMO	$Cu(OAc)_2$ (15)	TMG (1.2)	Pyridine	63	24
11	1.5	O_2	$Cu(OAc)_2$ (15)	DMPI (1.2)	Pyridine	71	28
12	1.5	O_2	$Cu(OAc)_2$ (15)	K_2CO_3 (1.2)	Pyridine	42	trace
13	1.5	O_2	$Cu(OAc)_2$ (15)	DMAP (1.2)	Pyridine	31	trace
14	1.5	O_2	$Cu(OAc)_2$ (15)	^{t}BuONa (1.2)	Pyridine	37	trace
15	1.5	O_2	$Cu(OAc)_2$ (15)	TMG (1.2)	Toluene	69	32
16	1.5	O_2	$Cu(OAc)_2$ (15)	TMG (1.2)	DMF	69	22
17	1.5	O_2	$Cu(OAc)_2$ (15)	TMG (1.2)	DMSO	70	20
18	1.5	O_2	$Cu(OAc)_2$ (15)	TMG (1.2)	NMP	22	11
19	1.5	O_2	$Cu(OAc)_2$ (15)	TMG (2.4)	Pyridine	71	36
20	1.5	O_2	$Cu(OAc)_2$ (15)	TMG (3.6)	Pyridine	75	46
21	1.5	O_2	$Cu(OAc)_2$ (15)	TMG (4.8)	Pyridine	84	36

[a]Conditions: **1a** (50 mg), **2** (X eq), Catalyst (X mol%), Base (X eq), Solvent (0.15 mL), 130 ℃, 7.5 h; [b]Isolated Yield; [c]Microwave.

TMG: Tetramethylguanidine; DMPI: 2,4-dimethylpentan-3-imine

Second set of optimizations

(TMG and pyridine were fixed)



Entry	Catalyst (x mol%)	T (°C)	t	Yield[b]: **3a**/**1a**
1	$Cu(OAc)_2$ (15)	130	7.5 h	37% / 45%
2[c]	-	130	7.5 h	0% / 70%
3	$Cu(OAc)_2$ (15)	130	5 h	40% / 37%
4	$Cu(OAc)_2$ (15)	130	2.5 h	40% / 50%
5	$Cu(OAc)_2$ (15)	130	**45 m**	48% / 49%
6	$Cu(OAc)_2$ (15)	130	20 m	38% / 62%
7	$Cu(OAc)_2$ (15)	120	45 m	45% / 39%
8	$Cu(OAc)_2$ (15)	**140**	45 m	56% / 40%
9	$Cu(OAc)_2$ (15)	150	45 m	37% / 31%
10	$Cu(OAc)_2$ (15)	135	45 m	48% / 40%
11	$Cu(acac)_2$ (15)	140	45 m	37% / 60%
12	$CuSO_4$ (15)	140	45 m	23% / 76%
13	$Cu(CF_3SO_3)_2$ (15)	140	45 m	67% / 33%
14	$CuCl_2$ (15)	140	45 m	72% / 28%
15[d]	**$CuBr_2$** (15)	140	45 m	88% / 11%
16[e]	$Cu(NO_3)_2.3H_2O$ (15)	140	45 m	83% / 17%

[a]Conditions: **1a** (50 mg), **2** (1.5 eq), Catalyst (15 mol%), Tetramethylguanidine (3.6 eq), Pyridine (0.15 mL), O_2; [b]Yields were determined by ^{1}H-NMR using acetophenone as internal reference; [c]Isolated **1a**; [d]Isolated **3a**: 75%; [e]Isolated **3a**: 65%.

[b]The NMR yield of 3a was determined with acetophenone as internal reference: 7.52 μL of acetophenone (1 equiv. compared to compound **1a**) was added, and then the crude was concentrated. The NMR yield of **3a** on the ^{1}H NMR spectra could be determined by analytical signals: s at 2.52 ppm (CH_3 of acetophenone - calibrated for 3H) compared with the integrations of product signals:

□s at 1.92 ppm (AcNH of product **3a**)

Conversion of **1a** was determined in the same mixture by integration of:

□s at 1.80 ppm (AcNH of product **1a**)

4. General Procedures

4.1 General procedure for amination reaction

A sealable tube equipped with a cap was charged with sialic acid analogues (1.0 equiv.), $CuBr_2$ (15 mol%) and heterocyclic amine (1.5 equiv.). Pyridine (0.43 M) and 1,1,3,3-tetramethylguanidine (3.6 equiv.) were then added. The tube was flushed with Oxygen and the resulting mixture was stirred at 140 °C for 45 min. Then, the mixture was concentrated in vacuo. The residue was purified on a silica gel column to afford desired products.

4.2 General procedure of removing the directing group [7]

Step 1: To an ice-water cooled solution of compound **3a** (1 equiv, 0.40 mmol, 360 mg), DMAP (1.5 equiv, 0.6 mmol, 73.2 mg), Et_3N (3 equiv, 1.2 mmol, 122 mg) in anhydrous CH_3CN (3.0 mL), and Boc_2O (4 equiv, 1.6 mmol, 349 mg) were added. The reaction mixture was then stirred at room temperature for 2 h. The mixture was concentrated in vacuo. The residue was purified on a silica gel column (PE: EtOAc = 6:4) to afford crude product as light yellow oil.

Step 2: To a solution of the intermediate made above (1 equiv, 0.40 mmol) in THF (6 mL) and water (2 mL), 30% aq.solution of H_2O_2 (8.8 equiv, 3.52 mmol, 0.35 mL) and $LiOH.H_2O$ (1.5 equiv, 0.60 mmol, 25.2 mg) were added. The resulting mixture was stirred at room temperature overnight. After completion, the mixture was concentrated in vacuo. The residue was purified on a silica gel column (CH_2Cl_2: MeOH = 10:1) to afford the desired product **5** (228.9 mg, 74%) as yellow foam.

4.3 General procedure of removing the protecting groups[8]

To a solution of the compound **5** (1 equiv, 0.16 mmol, 124 mg) in dry DCM (3 mL) were added dropwise BCl_3 (20 equiv, 3.20 mmol, 3.2 mL, 1.0 M in methylene chloride) and the resulting mixture was stirred at rt for 1.5 h. The mixture was then concentrated in vacuo. The residue was purified on a silica gel column (CH_2Cl_2: MeOH = 2:1) to afford desired product **6** (35 mg, 53%) as white solid.

4.4 General procedure for the coupling reaction with cysteine [9]

A sealable tube purged with argon equipped with a cap was charged with the compound **3g** (1.0 equiv, 0.095 mmol, 97 mg), N-Acetyl-L-cysteine methyl ester (2.0 equiv, 0.19 mmol, 33.6 mg), PdG_3Xantphos (20 mmol%, 18 mg, 0.019 mmol) and the tube was flushed again with Argon. THF (0.9 mL) was then added. The mixture was stirred for 10 min and then Et_3N (3.0 equiv, 40.0 μL, 0.285 mmol) was added into the tube dropwise. The mixture allowed to stir vigorously at room temperature for 4 h and the mixture was then concentrated in vacuo. The residue was purified on a silica gel column (PE: EtOAc = 2:1 to 1:4) to afford desired product **7** (65 mg, 64%) as white foam.

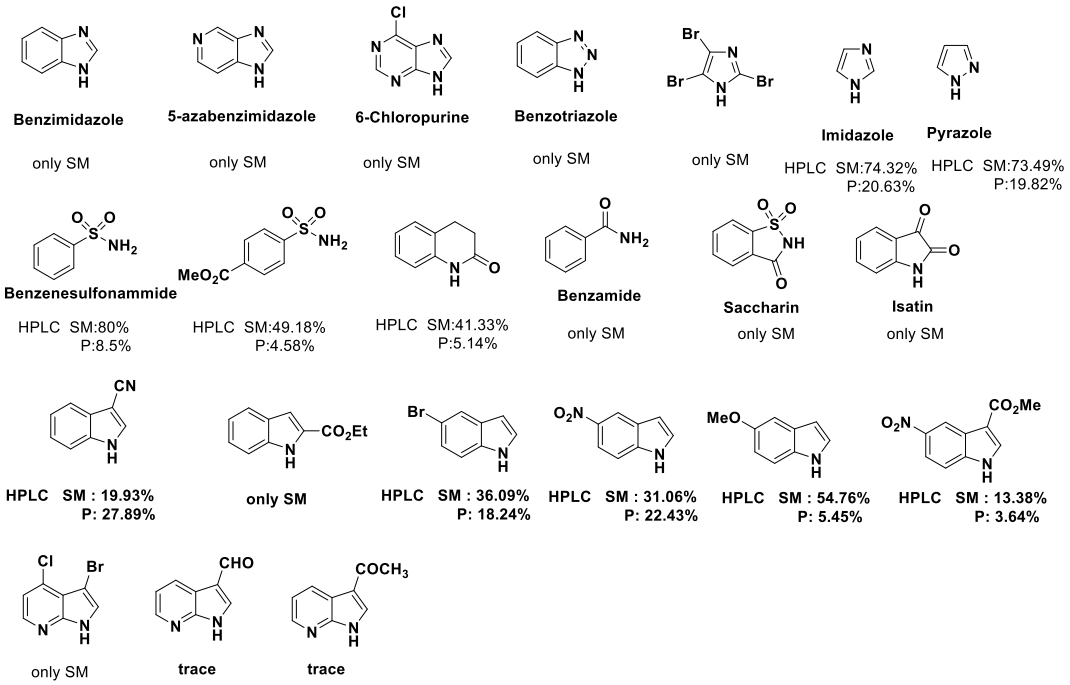
4.5 General procedure for the coupling reaction with thiosugar [9]

A sealable tube purged with argon equipped with a cap was charged with the compound **3g** (1.0 equiv, 0.084 mmol, 86 mg), peracetylated thioglucose (1.0 equiv, 0.084 mmol, 30.5 mg), PdG_3Xantphos (10 mmol%, 8.0 mg, 0.0084 mmol) and the tube was flushed again with Argon. THF (0.8 mL) was then added. The mixture was stirred for 10 min. Then Et_3N (1.5 equiv, 18 μL, 0.126 mmol) was added into the tube dropwise, and the mixture allowed to stir vigorously at room temperature for 1.5 h. The mixture was then concentrated in vacuo. The residue was purified on a silica gel column (PE: EtOAc = 3:1 to 1:3) to afford desired product **8** (79.8 mg, 75%) as yellow oil.

4.6 General procedure for the coupling reaction with phenylboronic acid [10]

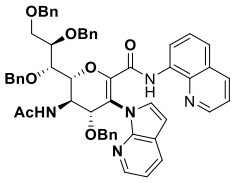
A sealable tube purged with argon equipped with a cap was charged with the compound **3g** (1.0 equiv, 0.069 mmol, 70 mg), phenylboronic acid (2.0 equiv, 0.138 mmol, 16.8 mg), PdG_3Xantphos (10 mmol%, 6.5 mg, 0.0069 mmol), K_2CO_3 (4.0 eq, 0.276 mmol, 38.0 mg) and the tube was flushed again with Argon. THF with water (0.35mL, 20 μL H_2O in 1.0 mL THF) was added. The mixture was stirred for 5 min. and the mixture allowed to stir vigorously for 5 h at 100 ℃. The mixture was then concentrated in vacuo. The residue was purified on a silica gel column (PE: EtOAc = 3:1 to 1:1) to afford desired product **9** (59.9 mg, 90%) as colorless oil.

5. Unsuccessful substrates



6. Characterization Data for desired products:

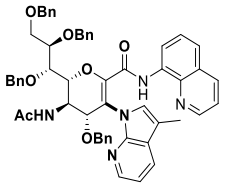
(2R,3R,4R)-3-acetamido-4-(benzyloxy)-5-(1H-pyrrolo[2,3-b]pyridin-1-yl)-N-(quinolin-8-yl)-2-((1S,2R)-1,2,3-tris(benzyloxy)propyl)-3,4-dihydro-2H-pyran-6-carboxamide (**3a**)



According to general procedure 4.1: **1a** (50 mg; 0.064 mmol; 1.0 equiv.), **7-azaindole** (11.4 mg; 0.096 mmol; 1.5 equiv.), $CuBr_2$ (2.2 mg; 0.0096 mmol; 15 mol%), Tetramethylguanidine (29 µL; 0.23 mmol; 3.6 equiv.), Pyridine (0.15 mL). The reaction mixture was stirred at 140 °C for 45 min. Product **3a** was isolated after purification on silica gel (PE: EtOAc = 3:1 to 1:1) as light yellow foam (43.0 mg, 75%). **mp**: 79 - 80 °C; **$[\alpha]_D^{20}$** = + 63.2 (c = 0.22, EtOH); **IR (neat, cm^{-1})**: 1689, 1525, 1427, 1454, 1325, 1091, 1072, 1028, 734, 698; **^{1}H NMR (300 MHz, d_6-actone)** δ 10.80 (s, 1H), 8.52 (bs, 1H), 8.29 (d, *J* = 7.5 Hz, 1H), 8.05 - 8.02 (m, 2H), 7.78 (d, *J* = 7.7 Hz, 1H), 7.69 (d, *J* = 7.6 Hz, 1H), 7.35 - 7.11 (m, 11H), 7.04 - 6.88 (m, 12H), 6.65 (bs, 2H), 6.39 (d, *J* = 3.5 Hz, 1H), 4.81 - 4.78 (m, 3H), 4.63 - 4.60 (m, 2H), 4.50 - 4.32 (m, 6H), 4.17 - 4.13 (m, 1H), 4.05 - 3.94 (m, 2H), 3.76 - 3.74 (m, 1H), 1.82 (s, 3H); **^{13}C NMR (J-MOD, 75 MHz, d_6-actone)** δ 170.2 (C), 158.4 (C), 149.6 (CH), 144.4 (C), 143.4 (CH), 139.8 (C), 139.7 (C), 139.6 (C), 139.2 (C), 138.7 (C), 137.2 (CH), 134.8 (C), 129.2 (CH), 129.0 (CH), 128.9 (CH), 128.8 (CH), 128.7 (CH), 128.5 (CH), 128.3 (CH) 128.2 (CH), 128.0 (CH), 127.8 (CH), 122.9 (CH), 122.8 (CH), 122.1(C), 116.8 (CH), 101.0 (CH), 79.2 (CH), 78.8 (CH), 77.1 (CH), 75.9 (CH), 75.5 (CH_2), 74.0 (CH_2), 73.1 (CH_2), 72.8 (CH_2), 70.3 (CH_2), 49.1 (CH), 23.4 (CH_3); **HRMS** (ESI-TOF): m/z calculated for $C_{55}H_{52}N_5O_7$ $[M+H]^+$

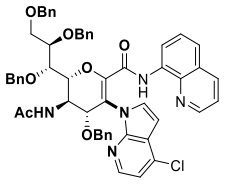
894.3861, found 894.3879.

(2R,3R,4R)-3-acetamido-4-(benzyloxy)-5-(3-methyl-1H-pyrrolo[2,3-b]pyridin-1-yl)-N-(quinolin-8-yl)-2-((1S,2R)-1,2,3-tris(benzyloxy)propyl)-3,4-dihydro-2H-pyran-6-carboxamide (**3b**)



According to general procedure 4.1: **1a** (100 mg; 0.129 mmol; 1.0 equiv.), **3-Methyl-7-azaindole** (25.6 mg; 0.194 mmol; 1.5 equiv.), $CuBr_2$ (4.4 mg; 0.0194 mmol; 15 mol%), Tetramethylguanidine (58 µL; 0.464 mmol; 3.6 equiv.), Pyridine (0.30 mL). The reaction mixture was stirred at 140 °C for 45 min. Product **3b** was isolated after purification on silica gel (PE: EtOAc = 2:1 to 1:1) as colorless oil (56.0 mg, 48%); **$[\alpha]_D^{20}$** = + 39.4 (c = 0.13, EtOH); **IR (neat, cm^{-1})**: 2922, 1658, 1525, 1487, 1440, 1373, 1327, 1089, 736, 698; **^{1}H NMR (300 MHz, *d*$_6$-actone)** δ 11.00 (s, 1H), 8.75 (bs, 1H), 8.51 (d, *J* = 7.6 Hz, 1H), 8.29 (d, *J* = 8.3 Hz, 1H), 8.20 - 8.19 (m, 1 H), 7.95 (d, *J* = 7.8 Hz, 1H), 7.87 (d, *J* = 7.0 Hz, 1H), 7.49 (d, *J* = 8.3 Hz, 1H), 7.49 - 7.44 (m, 4H), 7.41 - 7.33 (m, 6H), 7.26 - 7.24 (m, 2H), 7.21 - 7.16 (m, 3H), 7.12 - 7.07 (m, 7H), 6.86 (d, *J* = 3.4 Hz, 2H), 4.99 - 4.69 (m, 10H), 4.52 (bs, 1H), 4.40 (d, *J* = 11.2 Hz, 1H), 4.21 (t, *J* = 11.6 Hz, 2H), 3.96 - 3.94 (m, 1H), 2.35 (s, 3H), 2.04 (s, 3H); **^{13}C NMR (J-MOD**, **101 MHz, *d*$_6$-actone)** δ 170.3 (C), 158.8 (C), 149.7 (CH), 144.3 (C), 143.3 (CH), 140.1 (C), 140.0 (C), 139.8 (C), 139.4 (C), 138.9 (C), 137.4 (CH), 135.2 (C), 129.3 (CH), 129.2 (CH), 129.1 (CH), 129.0 (CH), 128.8 (CH), 128.6 (CH), 128.4 (CH), 128.3 (CH), 128.2 (CH), 128.2 (CH), 127.9 (CH), 127.6 (CH), 123.0 (CH), 123.0 (CH), 122.9 (C), 117.0 (CH), 116.3 (CH), 110.1 (C), 79.4 (CH), 79.1 (CH), 77.2 (CH), 76.2 (CH), 75.6 (CH_2), 74.2 (CH_2), 73.1 (CH_2), 72.9 (CH_2), 70.5 (CH_2), 49.4 (CH), 23.5 (CH_3), 10.0 (CH_3); **HRMS** (ESI-TOF): m/z calculated for $C_{56}H_{54}N_5O_7$ $[M+H]^+$ 908.4018, found 908.4050.

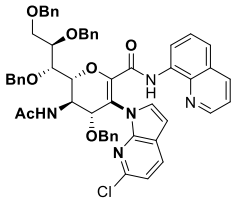
(2R,3R,4R)-3-acetamido-4-(benzyloxy)-5-(4-chloro-1H-pyrrolo[2,3-b]pyridin-1-yl)-N-(quinolin-8-yl)-2-((1S,2R)-1,2,3-tris(benzyloxy)propyl)-3,4-dihydro-2H-pyran-6-carboxamide (**3c**)



According to general procedure 4.1: **1a** (50 mg; 0.064 mmol; 1.0 equiv.), **4-Chloro-7-azaindole** (14.7 mg; 0.096 mmol; 1.5 equiv.), $CuBr_2$ (2.2 mg; 0.0096 mmol; 15 mol%), Tetramethylguanidine (29 µL; 0.23 mmol; 3.6 equiv.), Pyridine (0.15 mL). The reaction mixture was stirred at 140 °C for 45 min. Product **3c** was isolated after purification on silica gel (PE: EtOAc = 3:1 to 3:2) as colorless oil (43.5 mg, 73%); **$[\alpha]_D^{20}$** = + 25.7 (c = 0.14, EtOH); **IR (neat, cm^{-1})**: 1693, 1654, 1525, 1485, 1327, 1265, 1091, 827, 734, 698; **^{1}H NMR (300 MHz, *d*$_6$-actone)** δ 11.00 (s, 1H), 8.77 (bs, 1H), 8.48 - 8.42 (m, 1H), 8.32 - 8.26 (m, 1H), 8.14 - 8.09 (m, 1H), 7.88 - 7.85 (m, 1H), 7.61 - 7.58 (m, 1H), 7.52 - 7.38 (m, 10H), 7.24 - 7.10 (m, 12H), 6.87 (bs, 2H), 6.67 - 6.63 (m, 1H), 5.02 - 4.97 (m, 3H), 4.83 - 4.72 (m, 6H), 4.54 - 4.42 (m, 3H), 4.27 - 4.24 (m, 2H), 3.97 - 3.96 (m, 1H), 2.04 (s, 3H); **^{13}C NMR (J-MOD**, **101 MHz, *d*$_6$-actone)** δ 170.3 (C), 158.3 (C), 149.8 (CH), 144.0 (CH), 140.0

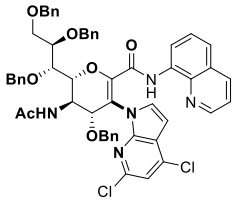
(C), 139.9 (C), 139.8 (C), 139.4 (C), 139.4 (C), 138.7 (C), 137.4 (CH), 135.9 (C), 134.9 (C), 134.8 (C), 129.3 (CH), 129.1 (CH), 129.1 (CH), 128.9 (CH), 128.9 (CH), 128.8 (CH), 128.6 (CH), 128.6 (CH), 128.4 (CH), 128.4 (CH), 128.2 (CH), 127.9 (CH), 123.2 (CH), 123.0 (CH), 121.2 (C), 117.1 (CH), 117.0 (CH), 116.9 (CH), 79.4 (CH), 79.0 (CH), 76.9 (CH), 76.1 (CH), 75.6 (CH_2), 74.2 (CH_2), 73.2 (CH_2), 72.9 (CH_2),70.4 (CH_2), 49.3 (CH), 23.4 (CH_3); **HRMS** (ESI-TOF): m/z calculated for $C_{55}H_{51}ClN_5O_7$ $[M+H]^+$928.3472, found 928.3492.

(2R,3R,4R)-3-acetamido-4-(benzyloxy)-5-(6-chloro-1H-pyrrolo[2,3-b]pyridin-1-yl)-N-(quinolin-8-yl)-2-((1S,2R)-1,2,3-tris(benzyloxy)propyl)-3,4-dihydro-2H-pyran-6-carboxamide (**3d**)



According to general procedure 4.1: **1a** (50 mg; 0.064 mmol; 1.0 equiv.), **6-Chloro-7-azaindole** (14.7 mg; 0.096 mmol; 1.5 equiv.), $CuBr_2$ (2.2 mg; 0.0096 mmol; 15 mol%), Tetramethylguanidine (29 µL; 0.23 mmol; 3.6 equiv.), Pyridine (0.15 mL). The reaction mixture was stirred at 140 °C for 45 min. Product **3d** was isolated after purification on silica gel (PE: EtOAc = 4:1 to 2:1) as colorless oil (42.0 mg, 70%); $[\alpha]_D^{20}$ = + 49.2 (c = 0.20, EtOH); **IR (neat, cm^{-1})**: 1691, 1654, 1525, 1485, 1454, 1423, 1327, 1103, 734, 698; **^{1}H NMR (300 MHz, *d*$_6$-actone)** δ 10.98 (s, 1H), 8.72 (bs, 1H), 8.47 - 8.42 (m, 1H), 8.30 - 8.27 (m, 1H), 8.01 - 7.95 (m, 1H), 7.85 - 7.83 (m, 1H), 7.59 - 7.53 (m, 1H), 7.50 - 7.30 (m, 10H), 7.20 - 7.05 (m, 12H), 6.85 (bs, 2H), 6.60 - 6.55 (m, 1H), 4.99 - 4.69 (m, 10H), 4.43 - 4.39 (m, 2H), 4.24 - 4.21 (m, 2H), 3.93 - 3.90 (m, 1H), 2.03 (s, 3H); **^{13}C NMR (101 MHz, *d*$_6$-actone)** δ 170.4, 158.4, 149.8, 144.9, 140.1, 139.9, 139.8, 139.4, 138.7, 137.4, 135.0, 132.1, 129.3, 129.1, 129.0, 128.9, 128.8, 128.6, 128.4, 128.4, 128.2, 128.1, 127.9, 123.2, 123.0, 120.9, 117.1, 116.8, 101.6, 79.3, 79.0, 76.6, 76.0, 74.2, 73.2, 72.8, 70.4, 49.2, 23.4; **HRMS** (ESI-TOF): m/z calculated for $C_{55}H_{51}ClN_5O_7$ $[M+H]^+$928.3472, found 928.3477.

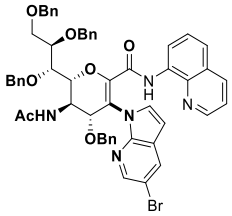
(2R,3R,4R)-3-acetamido-4-(benzyloxy)-5-(4,6-dichloro-1H-pyrrolo[2,3-b]pyridin-1-yl)-N-(quinolin-8-yl)-2-((1S,2R)-1,2,3-tris(benzyloxy)propyl)-3,4-dihydro-2H-pyran-6-carboxamide (**3e**)



According to general procedure 4.1: **1a** (100 mg; 0.129 mmol; 1.0 equiv.), **4,6-Dichloro- 7-azaindole** (35.8 mg; 0.194 mmol; 1.5 equiv.), $CuBr_2$ (4.4 mg; 0.0194 mmol; 15 mol%), Tetramethylguanidine (58 µL; 0.464 mmol; 3.6 equiv.), Pyridine (0.30 mL). The reaction mixture was stirred at 140 °C for 45 min. Product **3e** was isolated after purification on silica gel (PE: EtOAc = 4:1 to 3:1) as light yellow oil (68.0 mg, 55%); $[\alpha]_D^{20}$ = + 19.7 (c = 0.18, EtOH); **IR (neat, cm^{-1})**: 1691, 1658, 1527, 1487, 1454, 1242, 1099, 850, 734, 698; **^{1}H NMR (300 MHz, *d*$_6$-actone)** δ 10.99 (s, 1H), 8.73 (s, 1H), 8.45 (d, *J* = 7.5 Hz, 1H), 8.30 (d, *J* = 8.3 Hz, 1H), 7.86 (d, *J* = 9.0 Hz, 1H), 7.59 (d, *J* = 8.3 Hz, 1H), 7.52 - 7.44 (m, 5H), 7.40 - 7.24 (m, 7H), 7.20 - 7.03(m, 10H), 6.90 - 6.87 (m, 2H), 6.62 (d, *J* = 3.0 Hz 1H), 5.02 - 4.70 (m, 9H), 4.52 - 4.23 (m, 5H), 3.94 -3.92 (m, 1H), 2.03

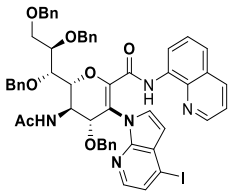
(s, 3H); **^{13}C NMR (J-MOD**, **101 MHz, d_6-actone)** δ 170.4 (C), 149.9 (CH), 140.0 (C), 139.9 (C), 139.7 (C), 139.4 (C), 138.5 (C), 137.4 (C), 137.4 (CH), 134.8 (C), 129.3 (CH), 129.2 (CH), 129.1 (CH), 129.1 (C), 129.1 (CH), 129.0 (CH), 128.7 (CH), 128.6 (CH), 128.4 (CH), 128.4 (CH), 128.3 (CH), 128.2 (CH), 128.1 (CH), 128.1 (CH), 127.9 (CH), 123.3 (CH), 123.0 (CH), 119.9 (C), 117.1 (CH), 116.3 (CH), 79.5 (CH), 78.9 (CH), 76.0 (CH), 74.2 (CH_2), 73.1 (CH_2), 72.8 (CH_2), 70.3 (CH_2), 23.4 (CH_3); **HRMS** (ESI-TOF): m/z calculated for $C_{55}H_{50}Cl_2N_5O_7$ $[M+H]^+$ 962.3082, found 962.3100.

(2R,3R,4R)-3-acetamido-4-(benzyloxy)-5-(4-bromo-1H-pyrrolo[2,3-b]pyridin-1-yl)-N-(quinolin-8-yl)-2-((1S,2R)-1,2,3-tris(benzyloxy)propyl)-3,4-dihydro-2H-pyran-6-carboxamide (**3f**)



According to general procedure 4.1: **1a** (50 mg; 0.064 mmol; 1.0 equiv.), **5-Bromo-7-azaindole** (19.0 mg; 0.096 mmol; 1.5 equiv.), $CuBr_2$ (2.2 mg; 0.0096 mmol; 15 mol%), Tetramethylguanidine (29 µL; 0.23 mmol; 3.6 equiv.), Pyridine (0.15 mL). The reaction mixture was stirred at 140 °C for 45 min. Product **3f** was isolated after purification on silica gel (PE: EtOAc = 4:1 to 3:1) as colorless oil (47.7 mg, 76%); **$[\alpha]_D^{20}$** = + 47.0 (c = 0.20, EtOH); **IR (neat, cm^{-1})**: 2924, 1654, 1525, 1485, 1454, 1325, 1261, 1074, 1026, 732, 696; **^{1}H NMR (400 MHz, $CDCl_3$)** δ 10.88 (s, 1H), 8.51 - 8.46 (s, 2H), 8.08 - 8.03 (m, 2H), 7.96 (s, 1H), 7.41 (d, *J* = 7.9 Hz, 1H), 7.34 - 7.23 (m, 7H), 7.19 - 7.08 (m, 10H), 7.04 - 6.93 (m, 5H), 6.80 - 6.79 (m, 2H), 6.46 (d, *J* = 3.5 Hz, 1H), 4.86 (t, *J* = 4.0 Hz, 1H), 4.74 - 4.73 (m, 3H), 4.62 - 4.38 (m, 6H), 4.23 - 4.13 (m, 3H), 4.01 (dd, *J* =10 Hz, 5.6 Hz, 1H), 3.78-3.75 (m, 1H), 1.89 (s, 3H); **^{13}C NMR (J-MOD**, **101 MHz, d_6-actone)** δ 170.3 (C), 158.3 (C), 149.8 (CH), 143.7(CH), 139.9 (C), 139.8 (C), 139.7 (C), 139.3 (C), 138.6 (C), 137.4 (CH), 134.9 (C), 131.2 (CH), 129.3 (CH), 129.0 (CH), 129.0 (C), 128.9 (CH), 128.8 (CH), 128.6 (CH), 128.5 (CH), 128.4 (CH), 128.3 (CH), 128.2 (CH), 127.9 (CH), 123.9 (C), 123.1(CH), 123.0 (CH), 116.9 (CH), 112.4 (C), 79.3 (CH), 78.8 (CH), 76.8 (CH), 75.9 (CH), 75.5 (CH_2), 74.1 (CH_2), 73.1 (CH_2), 72.6 (CH_2), 70.2 (CH_2), 49.1 (CH), 23.4 (CH_3); **HRMS** (ESI-TOF): m/z calculated for $C_{55}H_{51}BrN_5O_7$ $[M+H]^+$ 972.2966, found 972.2974.

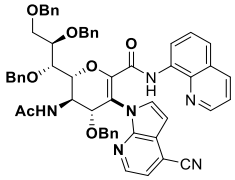
(2R,3R,4R)-3-acetamido-4-(benzyloxy)-5-(4-iodo-1H-pyrrolo[2,3-b]pyridin-1-yl)-N-(quinolin-8-yl)-2-((1S,2R)-1,2,3-tris(benzyloxy)propyl)-3,4-dihydro-2H-pyran-6-carboxamide (**3g**)



According to general procedure 4.1: **1a** (50 mg; 0.064 mmol; 1.0 equiv.), **4-Iodo -7-azaindole** (23.5 mg; 0.096 mmol; 1.5 equiv.), $CuBr_2$ (2.2 mg; 0.0096 mmol; 15 mol%), Tetramethylguanidine (29 µL; 0.23 mmol; 3.6 equiv.), Pyridine (0.15 mL). The reaction mixture was stirred at 140 °C for 45 min. Product **3g** was isolated after purification on silica gel (PE: EtOAc = 4:1 to 3:1) as white foam

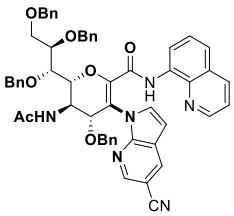
(45.9 mg, 70%); **mp**: 101 - 102 °C; **$[\alpha]_D^{20}$** = + 6.9 (c = 0.16, EtOH); **IR (neat, cm^{-1})**: 1654, 1525, 1485, 1454, 1327, 1261, 1087, 1026, 804, 732, 696; **^{1}H NMR (300 MHz, *d*$_6$-actone)** δ 11.01 (s, 1H), 8.75 (bs, 1H), 8.47 (d, *J* = 7.6 Hz, 1H), 8.31 - 8.28 (m, 1H), 7.87 - 7.82 (m, 2H), 7.58 (d, *J* = 8.3 Hz, 1H), 7.54 - 7.30 (m, 11H), 7.26 - 7.06 (m, 11H), 6.84 - 6.82 (m, 2H), 6.43 (d, *J* = 3.6 Hz, 1H), 5.05 - 4.93 (m, 3H), 4.85 - 4.71 (m, 6H), 4.52 - 4.41 (m, 3H), 4.26 - 4.23 (m, 2H), 3.96 (dd, *J* = 9.2, 3.4 Hz, 1H), 2.03 (s, 3H); **^{13}C NMR (J-MOD**, **101 MHz, *d*$_6$-actone)** δ 170.4 (C), 158.4 (C), 149.8 (CH), 144.7 (C), 143.7 (CH), 140.0 (C), 139.9 (C), 139.8 (C), 139.4 (C), 139.4 (C), 138.7 (C), 137.4 (CH),134.9 (C), 134.9 (C), 129.3 (CH), 129.1 (CH), 129.1(CH), 129.1(C), 128.9 (CH), 128.9 (CH), 128.8 (CH), 128.6 (CH), 128.6 (CH), 128.4 (CH), 128.4 (CH), 128.2 (CH), 127.9 (CH), 127.7 (C), 126.3 (CH), 123.2 (CH), 123.0 (CH), 117.1 (CH), 117.0 (CH), 98.8 (C) , 79.4 (CH), 79.0 (CH), 76.9 (CH), 76.1 (CH), 75.6 (CH_2), 74.2 (CH_2), 73.2 (CH_2), 72.8 (CH_2), 70.4 (CH_2), 49.4 (CH), 23.5 (CH_3); **HRMS** (ESI-TOF): m/z calculated for $C_{55}H_{51}IN_5O_7$ $[M+H]^+$ 1020.2828, found 1020.2852.

(2R,3R,4R)-3-acetamido-4-(benzyloxy)-5-(4-cyano-1H-pyrrolo[2,3-b]pyridin-1-yl)-N-(quinolin-8-yl)-2-((1S,2R)-1,2,3-tris(benzyloxy)propyl)-3,4-dihydro-2H-pyran-6-carboxamide (**3h**)



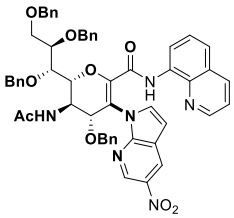
According to general procedure 4.1: **1a** (100 mg; 0.129 mmol; 1.0 equiv.), **4-Cyano-7-azaindole** (27.6 mg; 0.194 mmol; 1.5 equiv.), $CuBr_2$ (4.4 mg; 0.0194 mmol; 15 mol%), Tetramethylguanidine (58 µL; 0.464 mmol; 3.6 equiv.), Pyridine (0.30 mL). The reaction mixture was stirred at 140 °C for 45 min. Product **3h** was isolated after purification on silica gel (PE: EtOAc = 3:1 to 1:1) as light yellow foam (67.8 mg, 57%); **mp**: 84 - 85 °C; **$[\alpha]_D^{20}$** = + 17.2 (c = 0.16, EtOH); **IR (neat, cm^{-1})**: 2924, 1693, 1527, 1487, 1423, 1327, 1261, 1074, 740, 698; **^{1}H NMR (300 MHz, *d*$_6$-actone)** δ 11.03 (s, 1H), 8.76 (bs, 1H), 8.43 (d, *J* = 7.4 Hz, 1H), 8.33 - 8.27 (m, 2H), 7.85 (d, *J* = 8.0 Hz, 1H), 7.70 (d, *J* = 3.3 Hz, 1H), 7.58 (d, *J* = 8.2 Hz, 1H), 7.48 - 7.32 (m, 10H), 7.26 - 7.24 (m, 2H), 7.19 - 7.01 (m, 9H), 6.83 - 6.75 (m, 3H), 5.05 - 4.95 (m, 3H), 4.85 - 4.71 (m, 6H), 4.53 - 4.42 (m, 3H), 4.29 - 4.23 (m, 2H), 3.98 - 3.95 (m, 1H), 2.03 (s, 3H); **^{13}C NMR (J-MOD**, **101 MHz, *d*$_6$-actone)** δ 170.4 (C), 158.2 (C), 149.9 (CH), 144.8 (C), 143.5 (CH), 140.0 (C), 139.9 (C), 139.7 (C), 139.4 (C), 139.4 (C), 138.5 (C), 137.4 (CH), 134.8 (C), 134.7 (C), 129.3 (CH), 129.1 (CH), 129.1 (C), 128.9 (CH), 128.9 (CH), 128.8 (CH), 128.6 (CH), 128.6 (CH), 128.5 (CH), 128.4 (CH), 128.3 (CH), 127.9 (CH), 123.3 (CH), 123.1 (CH), 122.3 (C), 119.4 (CH), 117.4 (C), 117.1 (CH), 117.0 (CH), 111.1 (C), 79.5 (CH), 79.0 (CH), 76.6 (CH), 76.1 (CH), 75.5 (CH_2), 74.2 (CH_2), 73.2 (CH_2), 72.9 (CH_2), 70.4 (CH_2), 49.3 (CH), 23.5 (CH_3); **HRMS** (ESI-TOF): m/z calculated for $C_{56}H_{51}N_6O_7$ $[M+H]^+$ 919.3814, found 919.3850.

(2R,3R,4R)-3-acetamido-4-(benzyloxy)-5-(5-cyano-1H-pyrrolo[2,3-b]pyridin-1-yl)-N-(quinolin-8-yl)-2-((1S,2R)-1,2,3-tris(benzyloxy)propyl)-3,4-dihydro-2H-pyran-6-carboxamide (**3i**)



According to general procedure 4.1: **1a** (100 mg; 0.129 mmol; 1.0 equiv.), **5-Cyano-7-azaindole** (27.6 mg; 0.194 mmol; 1.5 equiv.), $CuBr_2$ (4.4 mg; 0.0194 mmol; 15 mol%), Tetramethylguanidine (58 µL; 0.464 mmol; 3.6 equiv.), Pyridine (0.30 mL). The reaction mixture was stirred at 140 °C for 45 min. Product **3i** was isolated after purification on silica gel (PE: EtOAc : CH_2Cl_2 = 6:2: 1) as colorless oil (54.6 mg, 46%); **$[\alpha]_D^{20}$** = + 39.9 (c = 0.15, EtOH); **IR (neat, cm^{-1})**: 2225, 1689, 1525, 1479, 1415, 1242, 1072, 1028, 732, 696; **^{1}H NMR (300 MHz, *d*$_6$-actone)** δ 11.05 (s, 1H), 8.77 (s, 1H), 8.47 - 8.37 (m, 3H), 8.30 (d, *J* = 7.3 Hz, 1H), 7.86 (d, *J* = 8.2 Hz, 1H), 7.61 - 7.58 (m, 2H), 7.52 - 7.33(m, 10H), 725 - 7.06 (m, 10H), 6.86 - 6.85 (m, 2H), 6.75 (d, *J* = 3.6 Hz, 1H), 5.09 - 4.96 (m, 3H), 4.86 - 4.43 (m, 9H), 4.31 - 4.25 (m, 2H), 3.99 - 3.96 (m, 1H), 2.05 (s, 3H); **^{13}C NMR (J-MOD**, **101 MHz, *d*$_6$-actone)** δ 170.4 (C), 158.2 (C), 149.8 (CH), 146.2 (CH), 144.7 (C), 139.9 (C), 139.9 (C), 139.7 (C), 139.4 (C), 139.3 (C), 138.5 (C), 137.4 (CH), 134.8 (C), 134.7 (C), 133.4 (CH), 129.3 (CH), 129.1(CH), 129.0 (C), 128.9 (CH), 128.9 (CH), 128.6 (CH), 128.6 (CH), 128.4 (CH), 128.4 (CH), 128. 3(CH), 127.9 (CH), 123.3 (CH), 123.0 (CH), 121.6 (C), 119.5 (C), 117.0 (CH), 117.0 (CH), 102.1(C), 79.4 (CH), 78.9 (CH), 76.6 (CH), 76.1 (CH), 75.6 (CH_2), 74.2 (CH_2), 73.1 (CH_2), 72.9 (CH_2), 70.4 (CH_2), 49.2 (CH), 23.5 (CH_3); **HRMS** (ESI-TOF): m/z calculated for $C_{56}H_{51}N_6O_7$ $[M+H]^+$ 919.3814, found 919.3845.

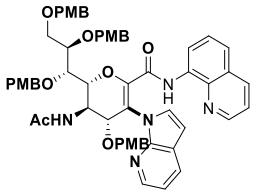
(2R,3R,4R)-3-acetamido-4-(benzyloxy)-5-(5-nitro-1H-pyrrolo[2,3-b]pyridin-1-yl)-N-(quinolin-8-yl)-2-((1S,2R)-1,2,3-tris(benzyloxy)propyl)-3,4-dihydro-2H-pyran-6-carboxamide (3j)



According to general procedure 4.1: **1a** (100 mg; 0.129 mmol; 1.0 equiv.), **5-Nitro-7-azaindole** (31.4 mg; 0.194 mmol; 1.5 equiv.), $CuBr_2$ (4.4 mg; 0.0194 mmol; 15 mol%), Tetramethylguanidine (58 µL; 0.464 mmol; 3.6 equiv.), Pyridine (0.30 mL). The reaction mixture was stirred at 140 °C for 45 min. Product **3j** was isolated after purification on silica gel (PE: EtOAc = 3:1) as light yellow foam (56.8 mg, 47%); **mp**: 85 - 86 °C; **$[\alpha]_D^{20}$** = + 34.5 (c = 0.11, EtOH); **IR (neat, cm^{-1})**: 1660, 1521, 1487, 1454, 1338, 1325, 1263, 1082, 732, 696; **^{1}H NMR (300 MHz, *d*$_6$-actone)** δ 11.07 (s, 1H), 9.03 (d, *J* = 2.4 Hz, 1H), 8.87 (d, *J* = 2.3 Hz, 1H), 8.80 (s, 1H), 8.47 (d, *J* = 7.6 Hz, 1H), 8.35 (dd, *J* = 8.3, 1.5 Hz, 1H), 7.89 (d, *J* = 8.4 Hz, 1H), 7.67 - 7.62 (m, 2H), 7.56 - 7.35 (m, 9H), 7.31 - 7.28 (m, 2H), 7.23 - 7.03 (m, 9H), 6.88 (d, *J* = 3.6 Hz, 3H), 5.11 - 4.97 (m, 3H), 4.88 - 4.69 (m, 6H), 4.55 - 4.48 (m, 3H), 4.36 - 4.26 (m, 2H), 4.02 - 3.98 (m, 1H), 2.07 (s, 3H); **^{13}C NMR (J-MOD**, **101 MHz, *d*$_6$-actone)** δ 170.5 (C), 149.9 (CH), 140.5 (C), 140.0 (C), 139.9 (C), 139.7 (C), 139.4 (C), 138.5 (C), 137.4 (CH), 134.8 (C), 129.3 (CH), 129.1 (CH), 129.0 (CH), 128.9 (CH), 128.6 (CH), 128.5 (CH), 128.3 (CH), 128.3 (CH), 127.9 (CH), 125.5 (CH), 123.3 (CH), 123.1 (CH), 121.3 (C),

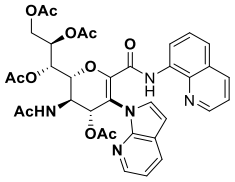
117.1 (CH), 79.5 (CH), 79.0 (CH), 76.4 (CH), 76.1 (CH), 75.6 (CH_2), 74.2 (CH_2), 73.1 (CH_2), 72.9 (CH_2), 70.3 (CH_2), 49.2 (CH), 23.4 (CH_3); **HRMS** (ESI-TOF): m/z calculated for $C_{55}H_{51}N_6O_9$ $[M+H]^+$ 939.3712, found 939.3733.

(2R,3R,4R)-3-acetamido-4-((4-methoxybenzyl)oxy)-5-(1H-pyrrolo[2,3-b]pyridin-1-yl)-N-(quinolin-8-yl)-2-((1S,2R)-1,2,3-tris((4-methoxybenzyl)oxy)propyl)-3,4-dihydro-2H-pyran-6-carboxamide (3k)



According to general procedure 4.1: **1b** (57.7 mg; 0.064 mmol; 1.0 equiv.), **7-azaindole** (11.4 mg; 0.096 mmol; 1.5 equiv.), $CuBr_2$ (2.2 mg; 0.0096 mmol; 15 mol%), Tetramethylguanidine (29 µL; 0.23 mmol; 3.6 equiv.), Pyridine (0.15 mL). The reaction mixture was stirred at 140 °C for 45 min. Product **3k** was isolated after purification on silica gel (PE: EtOAc = 2:1 to 2:3) as colorless oil (49.3 mg, 76%); **$[\alpha]_D^{20}$** = + 33.8 (c = 0.13, EtOH)**; IR (neat, cm^{-1})**: 1687, 1612, 1514, 1427, 1327, 1247, 1174, 1080, 1033, 821; **^{1}H NMR (400 MHz, *d*$_6$-actone)** δ 10.93 (s, 1H), 8.78 (d, *J* = 3.0 Hz, 1H), 8.48 (dd, *J* = 7.6, 0.8 Hz, 1H), 8.29 (dd, *J* = 8.3, 1.6 Hz, 1H), 8.21 (dd, *J* = 4.7, 1.5 Hz, 1H), 7.98 (dd, *J* = 7.8, 1.3 Hz, 1H), 7.74 (d, *J* = 7.9 Hz, 1H), 7.57 (dd, *J* = 8.3, 1.1 Hz, 1H), 7.50 (dd, *J* = 8.3, 4.2 Hz, 1H), 7.45 - 7.39 (m, 4H), 7.27 (d, *J* = 8.4 Hz, 2H), 7.14 - 7.07 (m, 3H), 6.97 - 6.93 (m, 2H), 6.77 (d, *J* = 7.3 Hz, 2H), 6.70 - 6.58 (m, 7H), 4.95 - 4.83 (m, 4H), 4.70 - 4.45 (m, 7H), 4.25 (d, *J* = 10.5 Hz, 1H), 4.16 (dd, *J* = 10.0, 3.3 Hz, 1H), 4.07 (d, *J* = 10.8 Hz, 1H), 3.90 - 3.86 (m, 1H), 3.81 (s, 3H), 3.69 (s, 3H), 3.66 (s, 3H), 3.60 (s, 3H), 2.03 (s, 3H); **^{13}C NMR (J-MOD**, **101 MHz, *d*$_6$-actone)** δ 170.2 (C), 160.5 (C), 160.3 (C), 160.2(C) , 160.2 (C), 158.6 (C), 149.8 (CH), 143.5 (CH), 139.5 (C), 137.4 (CH), 135.2 (C), 132.1 (C), 132.0 (C), 131.8 (C), 131.0 (CH), 130.9 (C), 130.7 (CH), 130.4 (CH), 130.2 (CH), 129.2 (CH), 129.1 (C), 128.0 (CH), 123.0 (CH), 123.0 (CH), 122.3 (C), 117.0 (CH), 117.0 (CH), 114.8 (CH), 114.5 (CH), 114.3 (CH), 114.2 (CH), 100.9 (CH), 79.4 (CH), 78.7 (CH), 76.8 (CH), 75.8 (CH), 75.4 (CH_2), 73.9 (CH_2), 73.0 (CH_2), 72.6 (CH_2), 70.3 (CH_2), 55.7 (CH_3), 55.6 (CH_3), 55.5 (CH_3), 55.5 (CH_3), 49.5 (CH), 23.6 (CH_3); **HRMS** (ESI-TOF): m/z calculated for $C_{59}H_{60}N_5O_{11}$ $[M+H]^+$1014.4284, found 1014.4334.

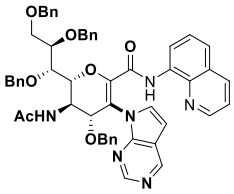
(1S,2R)-1-((2R,3R,4R)-3-acetamido-4-acetoxy-5-(1H-pyrrolo[2,3-b]pyridin-1-yl)-6-(quinolin-8-ylcarbamoyl)-3,4-dihydro-2H-pyran-2-yl)propane-1,2,3-triyl triacetate (3l)



According to general procedure 4.1: **1c** (58.5 mg; 0.1 mmol; 1.0 equiv.), **7-azaindole** (17.7 mg; 0.15 mmol; 1.5 equiv.), $CuBr_2$ (3.4 mg; 0.015 mmol; 15 mol%), Tetramethylguanidine (47 µL; 0.36 mmol; 3.6 equiv.), Pyridine (0.2 mL). The reaction mixture was stirred at 140 °C for 45 min. Product **3l** was isolated by prepared HPLC (Solvents used H_2O - 0.2% TFA/CAN, Conditions: 35-70 during 15 min) as colorless oil (10 mg, 14%); **$[\alpha]_D^{20}$** = + 73.7 (c = 0.17, EtOH); **IR (neat, cm^{-1})**: 1747, 1691, 1527, 1487, 1431, 1325, 1371, 1211, 1029, 844; **^{1}H NMR (400 MHz, *d*$_6$-actone)** δ 11.00 (s, 1H), 8.93 (dd, *J* = 4.2, 1.5 Hz, 1H), 8.44 - 8.36 (m, 4H), 7.70 - 7.62 (m, 3H), 7.54 (d, *J* = 2.9 Hz,

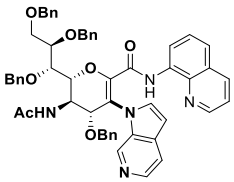
1H), 7.48 (t, *J* = 8.0 Hz, 1H), 7.40 - 7.35 (m, 1H), 6.77 (bs, 1H), 6.19 (d, *J* = 7.6 Hz, 1H), 5.88 - 5.84 (m, 1H), 5.77 (dd, *J* = 7.1, 3.3 Hz, 1H), 5.13 (dd, *J* = 9.1, 3.2 Hz, 1H), 4.82 - 4.75 (m, 1H), 4.58 (dd, *J* = 12.2, 3.3 Hz, 1H), 4.46 (dd, *J* = 12.2, 6.0 Hz, 1H), 2.14 (s, 3H), 2.01 (s, 3H), 1.99 (s, 3H), 1.89 (s, 3H), 1.69 (s, 3H); **^{13}C NMR (101 MHz, *d*$_6$-actone)** δ 170.8, 170.7, 170.5, 170.3, 170.1, 157.7, 150.0, 139.4, 137.4, 134.4, 133.0, 129.0, 127.8, 123.7, 123.1, 117.4, 117.4, 103.1, 78.2, 70.7, 70.2, 68.1, 62.7, 48.1, 23.0, 21.0, 20.8, 20.7, 20.3; **HRMS** (ESI-TOF): m/z calculated for $C_{35}H_{36}N_5O_{11}$ $[M+H]^+$ 702.2406, found 702.2421.

(2R,3R,4R)-3-acetamido-4-(benzyloxy)-5-(7H-pyrrolo[2,3-d]pyrimidin-7-yl)-N-(quinolin-8-yl)-2-((1S,2R)-1,2,3-tris(benzyloxy)propyl)-3,4-dihydro-2H-pyran-6-carboxamide (4a)



According to general procedure 4.1: **1a** (50 mg; 0.064 mmol; 1.0 equiv.), **7-Deazapurine** (11.5 mg; 0.096 mmol; 1.5 equiv.), $CuBr_2$ (2.2 mg; 0.0096 mmol; 15 mol%), Tetramethylguanidine (29 µL; 0.23 mmol; 3.6 equiv.), Pyridine (0.15 mL). The reaction mixture was stirred at 140 °C for 45 min. Product **4a** was isolated after purification on silica gel (PE: EtOAc = 6:4 to 1:2) as colorless oil (42.9 mg, 75%); **$[\alpha]_D^{20}$** = + 30.5 (c = 0.19, EtOH); **IR (neat, cm^{-1})**: 2924, 1691, 1525, 1485, 1454, 1327, 1226, 1074, 900, 732, 698; **^{1}H NMR (300 MHz, *d*$_6$-actone)** δ 11.03 (s, 1H), 9.00 (s, 1H), 8.77 (bs, 1H), 8.73 (s, 1H), 8.46 (d, *J* = 7.6 Hz, 1H), 8.30 (d, *J* = 8.3 Hz, 1H), 7.89 (d, *J* = 8.3 Hz, 1H), 7.59 (d, *J* = 8.3 Hz, 1H), 7.52 - 7.31 (m, 10H), 7.26 (d, *J* = 7.0 Hz, 2H), 7.20 - 7.11(m, 9H), 6.88 - 6.87 (m, 2H), 6.70 (d, *J* = 3.5 Hz, 1H), 5.08 - 4.95 (m, 3H), 4.86 - 4.72 (m, 6H), 4.54 - 4.44 (m, 3H), 4.30 - 4.23 (m, 2H), 3.97 (dd, *J* = 10.0, 3.5 Hz, 1H), 2.05 (s, 3H); **^{13}C NMR (J-MOD**, **75 MHz, *d*$_6$-actone)** δ 170.3 (C), 158.2 (C), 152.2 (CH), 149.8 (CH), 149.7 (CH), 144.6 (C), 139.9 (C), 139.8 (C), 139.6 (C), 139.3 (C), 138.5 (C), 137.3 (CH), 134.8 (C), 129.2 (CH), 129.0 (CH), 128.8 (CH), 128.5 (CH), 128.3 (CH), 128.3 (CH), 128.1 (CH), 128.0 (CH), 127.8 (CH), 123.1 (CH), 122.9 (CH), 120.5 (C), 117.0 (CH), 100.3 (CH), 79.4 (CH), 78.9 (CH), 76.7 (CH), 76.0 (CH), 75.5 (CH_2), 74.1 (CH_2), 73.1 (CH_2), 72.8 (CH_2), 70.3 (CH_2), 49.2 (CH), 23.3 (CH_3); **HRMS** (ESI-TOF): m/z calculated for $C_{54}H_{51}N_6O_7$ $[M+H]^+$ 895.3814, found 895.3830.

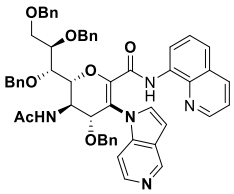
(2R,3R,4R)-3-acetamido-4-(benzyloxy)-5-(1H-pyrrolo[2,3-c]pyridin-1-yl)-N-(quinolin-8-yl)-2-((1S,2R)-1,2,3-tris(benzyloxy)propyl)-3,4-dihydro-2H-pyran-6-carboxamide (4b)



According to general procedure 4.1: **1a** (100 mg; 0.129 mmol; 1.0 equiv.), **6-azaindole** (22.8 mg; 0.194 mmol; 1.5 equiv.), $CuBr_2$ (4.4 mg; 0.0194 mmol; 15 mol%), Tetramethylguanidine (58 µL; 0.464 mmol; 3.6 equiv.), Pyridine (0.30 mL). The reaction mixture was stirred at 140 °C for 45 min. Product **4b** was isolated after purification on silica gel (CH_2Cl_2: EtOAc = 3:1) as colorless oil (45 mg, 39%); **$[\alpha]_D^{20}$** = + 22.3 (c = 0.13, EtOH); **IR (neat, cm^{-1})**: 2926, 1658, 1523, 1454, 1325, 1261, 1228, 1087, 1028, 732, 696; **^{1}H NMR (400 MHz, *d*$_6$-actone)** δ 11.01 (s, 1H), 8.79 - 8.74 (m, 2H), 8.45 (d, *J* = 7.6 Hz, 1H), 8.31 (dd, *J* = 8.3, 1.6 Hz, 1H), 8.20 (d, *J* = 5.4 Hz, 1H), 7.86 (d, *J* = 8.5

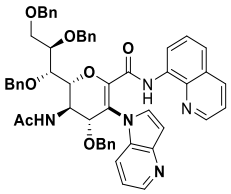
Hz, 1H), 7.60 - 7.56 (m, 2H), 7.51 - 7.45 (m, 4H), 7.43 - 7.31 (m, 6H), 7.27 - 7.25 (m, 2H), 7.21 - 6.98 (m, 11H), 6.63 (dd, *J* = 3.1, 0.6 Hz, 1H), 5.09 (dd, *J* = 7.3, 4.3 Hz, 1H), 4.94 - 4.92 (m, 2H), 4.80 - 4.71 (m, 5H), 4.60 - 4.42 (m, 3H), 4.31 - 4.24 (m, 2H), 4.13 - 4.11 (m, 1H), 3.98 - 3.97 (m, 1H), 2.00 (s, 3H); **^{13}C NMR (J-MOD**, **101 MHz, *d*$_6$-actone)** δ 170.4 (C), 158.0 (C), 149.9 (CH), 140.0 (C), 139.9 (C), 139.8 (C), 139.7 (CH), 139.4 (C), 138.5 (C), 137.5 (CH), 134.8 (C), 129.4 (CH), 129.1 (CH), 129.1(CH), 129.0 (CH), 128.7 (CH), 128.7 (CH), 128.5 (CH), 128.4 (CH), 128.3 (CH), 128.0 (CH), 123.3 (CH), 123.1 (CH), 120.5 (C), 117.1 (CH), 116.0 (CH), 102.1 (CH), 79.7 (CH), 79.0 (CH), 77.1 (CH), 76.4 (CH), 75.5 (CH_2), 74.3 (CH_2), 73.8 (CH_2), 73.0 (CH_2), 70.4 (CH_2), 49.4 (CH), 23.5 (CH_3); **HRMS** (ESI-TOF): m/z calculated for $C_{55}H_{52}N_5O_7$ $[M+H]^+$ 894.3861, found 894.3879.

(2R,3R,4R)-3-acetamido-4-(benzyloxy)-5-(1H-pyrrolo[3,2-c]pyridin-1-yl)-N-(quinolin-8-yl)-2-((1S,2R)-1,2,3-tris(benzyloxy)propyl)-3,4-dihydro-2H-pyran-6-carboxamide (4c)



According to general procedure 4.1: **1a** (100 mg; 0.129 mmol; 1.0 equiv.), **5-azaindole** (22.8 mg; 0.194 mmol; 1.5 equiv.), $CuBr_2$ (4.4 mg; 0.0194 mmol; 15 mol%), Tetramethylguanidine (58 μL; 0.464 mmol; 3.6 equiv.), Pyridine (0.30 mL). The reaction mixture was stirred at 140 °C for 45 min. Product **4c** was isolated after purification on silica gel (CH_2Cl_2: MeOH= 50:1 to 40:1) as colorless oil (47.2 mg, 41%); **$[\alpha]_D^{20}$** = + 6.9 (c = 0.16, EtOH); **IR (neat, cm^{-1})**: 1612, 1525, 1355, 1327, 1263, 1087, 1026, 898, 810, 729, 696; **^{1}H NMR (300 MHz, *d*$_6$-actone)** δ 11.00 (s, 1H), 8.93 - 8.78 (m, 2H), 8.45 (d, *J* = 2.9 Hz, 1H), 8.32 - 8.18 (m, 2H), 7.88 (d, *J* = 7.6 Hz, 1H), 7.59 (d, *J* = 8.3 Hz, 1H), 7.52 - 7.37 (m, 11H), 7.24 - 6.98 (m, 13H), 6.71 (d, *J* = 3.2 Hz, 1H), 5.07 - 5.06 (m, 1H), 4.92 - 4.71 (m, 7H), 4.55 - 4.44 (m, 3H), 4.33 - 4.22, (m, 2H), 4.12 (d, *J* = 7.7 Hz, 1H), 3.98 - 3.95 (m, 1H), 2.00 (s, 3H); **^{13}C NMR (J-MOD**, **101 MHz, *d*$_6$-actone)** δ 170.4 (C), 158.0 (C), 149.9 (CH), 144.2 (CH), 141.8 (CH), 139.9 (C), 139.8 (C), 139.7 (C), 139.4 (C), 138.5 (C), 137.5 (CH), 134.8 (C), 133.5 (CH), 129.3 (CH), 129.1 (CH), 129.0 (CH), 128.7 (CH), 128.6 (CH), 128.5 (CH), 128.3 (CH), 128.0 (CH), 123.3 (CH), 123.1 (CH), 120.3 (C), 117.1 (CH), 101.9 (CH), 79.6 (CH), 79.0 (CH), 76.6 (CH), 76.3 (CH), 75.5 (CH_2), 74.2 (CH_2), 73.8 (CH_2), 73.0 (CH_2), 70.4 (CH_2), 49.5 (CH), 23.5 (CH_3); **HRMS** (ESI-TOF): m/z calculated for $C_{55}H_{52}N_5O_7$ $[M+H]^+$ 894.3861, found 894.3888.

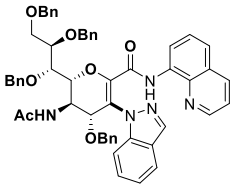
(2R,3R,4R)-3-acetamido-4-(benzyloxy)-5-(1H-pyrrolo[3,2-b]pyridin-1-yl)-N-(quinolin-8-yl)-2-((1S,2R)-1,2,3-tris(benzyloxy)propyl)-3,4-dihydro-2H-pyran-6-carboxamide (4d)



According to general procedure 4.1: **1a** (100 mg; 0.129 mmol; 1.0 equiv.), **4-azaindole** (22.8 mg; 0.194 mmol; 1.5 equiv.), $CuBr_2$ (4.4 mg; 0.0194 mmol; 15 mol%), Tetramethylguanidine (58 μL; 0.464 mmol; 3.6 equiv.), Pyridine (0.30 mL). The reaction mixture was stirred at 140 °C for 45 min. Product **4d** was isolated after purification on silica gel (PE: EtOAc = 2:1 to 1:2) as colorless oil (34.4 mg, 30%); **$[\alpha]_D^{20}$** = + 5.8 (c = 0.12, EtOH); **IR (neat, cm^{-1})**: 2924, 1693, 1523, 1483, 1421,

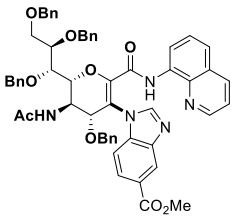
1325, 1265, 1072, 732, 696; **^{1}H NMR (400 MHz, d_6-actone)** δ 10.98 (s, 1H), 8.77 (dd, *J* = 4.2, 1.5 Hz, 1H), 8.44 (d, *J* = 7.3 Hz, 1H), 8.37 - 8.36 (m, 1H), 8.29 (dd, *J* = 8.3, 1.4 Hz, 1H), 7.80 (d, *J* = 8.4 Hz, 1H), 7.59 - 7.56 (m, 2H), 7.50 - 7.03 (m, 24H), 6.69 (d, *J* = 3.2 Hz, 1H), 5.04 (bs, 1H), 4.92 (d, *J* = 10.3 Hz, 1H), 4.87 - 4.85 (m, 1H), 4.83 - 4.69 (m, 5H), 4.53 - 4.45 (m, 3H), 4.30 (d, *J* = 11.3 Hz, 1H), 4.23 - 4.04 (m, 2H), 3.95 (dd, *J* = 10.1, 4.6 Hz, 1H), 1.97 (s, 3H); **^{13}C NMR (J-MOD**, **101 MHz, d_6-actone)** δ 170.4 (C), 158.1 (C), 149.9 (CH), 143.9 (CH), 140.0 (C), 139.9 (C), 139.8 (C), 139.4 (C), 138.5 (C), 137.5 (CH), 134.9 (C), 129.3 (CH), 129.1 (CH), 129.1 (CH), 129.0 (CH), 128.7 (CH), 128.6 (CH), 128.5 (CH), 128.3 (CH), 128.0 (CH), 123.3 (CH), 123.1 (CH), 120.6 (C), 117.1 (CH), 79.6 (CH), 79.1 (CH), 78.4 (CH), 76.4 (CH), 75.5 (CH_2), 74.2 (CH_2), 73.7 (CH_2), 73.0 (CH_2), 70.4 (CH_2), 49.6 (CH), 23.4 (CH_3); **HRMS** (ESI-TOF): m/z calculated for $C_{55}H_{52}N_5O_7$ $[M+H]^+$ 894.3861, found 894.3898.

(2R,3R,4R)-3-acetamido-4-(benzyloxy)-5-(1H-indazol-1-yl)-N-(quinolin-8-yl)-2-((1S,2R)-1,2,3-tris(benzyloxy)propyl)-3,4-dihydro-2H-pyran-6-carboxamide (4e)



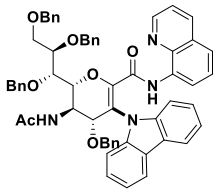
According to general procedure 4.1: **1a** (100 mg; 0.129 mmol; 1.0 equiv.), **Indazole** (22.8 mg; 0.194 mmol; 1.5 equiv.), $CuBr_2$ (4.4 mg; 0.0194 mmol; 15 mol%), Tetramethylguanidine (58 µL; 0.464 mmol; 3.6 equiv.), Pyridine (0.30 mL). The reaction mixture was stirred at 140 °C for 45 min. Product **4e** was isolated after purification on silica gel (PE: EtOAc = 3:1 to 1:1) as white foam (55 mg, 48%); **mp**: 83 - 84 °C; **$[\alpha]_D^{20}$** = - 39.3 (c = 0.29, EtOH); **IR (neat, cm^{-1})**: 2924, 1654, 1525, 1485, 1454, 1425, 1327, 1263, 1072, 734, 696; **^{1}H NMR (400 MHz, $CDCl_3$)** δ 11.00 (s, 1H), 8.60 (d, *J* = 3.0 Hz, 1H), 8.56 (d, *J* = 7.6 Hz, 1H), 8.15 (s, 1H), 8.12 (d, *J* = 8.1 Hz, 1H), 7.77 (d, *J* = 8.0 Hz, 1H), 7.48 (d, *J* = 8.0 Hz, 1H), 7.40 - 7.26 (m, 12H), 7.19 (q, *J* = 7.1 Hz, 4H), 7.12 - 7.08 (m, 3H), 7.07 - 6.99 (m, 4H), 6.67 (d, *J* = 7.3 Hz, 2H), 5.80 (d, *J* = 7.3 Hz, 1H), 4.99 - 4.75 (m, 1H), 4.89 (s, 2H), 4.79 - 4.75 (m, 1H), 4.62 - 4.56 (m, 4H), 4.39 (s, 2H), 4.29 - 4.20 (m, 2H), 4.11 - 4.03 (m, 2H), 3.83 (dd, *J* = 9.6, 4.5 Hz, 1H), 1.89 (s, 3H); **^{13}C NMR (J-MOD**, **101 MHz, $CDCl_3$)** δ 169.7 (C), 157.2 (C), 148.5 (CH), 142.8 (C), 142.2 (C), 138.7 (C), 138.5 (C), 138.4 (C), 138.2 (C), 137.1 (C), 136.3 (CH), 135.5 (CH), 133.6 (C), 128.5 (CH), 128.4 (CH), 128.4 (CH), 128.3 (CH), 128.2 (CH), 127.9 (C), 127.8 (CH), 127.8 (CH), 127.7 (CH), 127.6 (CH), 127.5 (CH), 127.5 (CH), 127.3 (CH), 127.1 (CH), 124.3 (C), 122.4 (CH), 121.7 (CH), 121.2 (CH), 121.2 (CH), 120.8 (C), 117.4 (CH), 110.5 (CH), 78.8 (CH), 78.2 (CH), 75.1 (CH),74.9 (CH), 74.8 (CH_2), 73.7(CH_2), 73.0 (CH_2), 72.2 (CH_2), 68.9 (CH_2), 48.9 (CH), 23.5 (CH_3); **HRMS** (ESI-TOF): m/z calculated for $C_{55}H_{52}N_5O_7$ $[M+H]^+$ 894.3861, found 894.3867.

methyl 1-((2R,3R,4R)-3-acetamido-4-(benzyloxy)-6-(quinolin-8-ylcarbamoyl)-2-((1S,2R)-1,2,3-tris(benzyloxy)propyl)-3,4-dihydro-2H-pyran-5-yl)-1H-benzo[d]imidazole-5-carboxylate (4f)



According to general procedure 4.1: **1a** (100 mg; 0.129 mmol; 1.0 equiv.), **Methyl Benzimidazole-5-carboxylate** (34.0 mg; 0.194 mmol; 1.5 equiv.), $CuBr_2$ (4.4 mg; 0.0194 mmol; 15 mol%), Tetramethylguanidine (58 µL; 0.464 mmol; 3.6 equiv.), Pyridine (0.30 mL). The reaction mixture was stirred at 140 °C for 45 min. Product **4f** was isolated after purification on silica gel (CH_2Cl_2: EtOAc = 5:1 to 3:1) as colorless oil (45.2 mg, 37%). In the NMR solvent, **4f** looks like as a mixture of two rotamers, although by LCMS, the purity of **4f** is 100% (see LCMS, pS44); **$[\alpha]_D^{20}$** = + 11.8 (c = 0.11, EtOH); **IR (neat, cm^{-1})**: 2924, 1714, 1689, 1525, 1483, 1325, 1080, 827, 732, 698; **^{1}H NMR (300 MHz, *d*$_6$-actone)** δ 11.07 (s, 1H), 8.82 (s, 1H), 8.42 (bs, 1H), 8.34 (d, *J* = 8.0 Hz, 1H), 8.12 (bs, 1H), 8.01 - 7.82 (m, 3H), 7.63 (d, *J* = 8.4 Hz, 1H), 7.54 - 7.28 (m, 12H), 7.20 - 6.96 (m, 11H), 5.14 - 5.11 (m, 1H), 4.95 - 4.91 (m, 2H), 4.84 - 4.73 (m, 5H), 4.60 - 4.42 (m, 4H), 4.28 - 4.22 (m, 2H), 4.01 - 3.86 (m, 4H), 2.06 (s, 3H); **^{13}C NMR (J-MOD**, **101 MHz, *d*$_6$-actone)** δ 170.4 (C), 170.3 (C), 167.8 (C), 167.7 (C), 157.7 (C), 149.8 (CH), 139.8 (C), 139.7 (C), 139.7 (C), 139.6 (C), 139.3 (C), 138.0 (C), 138.0 (C), 137.4 (CH), 134.5 (C), 129.2 (CH), 129.0 (CH), 129.0 (CH), 128.8 (CH), 128.8(CH) , 128.8 (CH), 128.6 (CH), 128.5 (CH), 128.5 (CH), 128.4 (CH), 128.4 (CH), 128.4 (CH), 128.2 (CH), 128.2 (CH), 128.1 (CH), 127.9 (CH), 125.6 (C), 124.9 (CH), 123.8 (CH), 123.4 (CH), 123.0 (CH), 122.8 (CH), 117.8 (C), 117.1 (CH), 79.6 (CH), 79.5 (CH), 78.8 (CH), 78.7 (CH), 76.2 (CH), 76.1 (CH), 75.3 (CH_2), 74.1 (CH_2), 73.5 (CH_2), 73.4 (CH_2), 72.8 (CH_2), 72.8 (CH_2), 70.2 (CH_2), 70.1 (CH_2), 52.2 (CH_3), 49.1 (CH), 48.6 (CH), 23.3 (CH_3), 23.3 (CH_3); **HRMS** (ESI-TOF): m/z calculated for $C_{57}H_{54}N_5O_9$ $[M+H]^+$ 952.3916, found 952.3924.

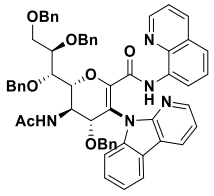
(2R,3R,4R)-3-acetamido-4-(benzyloxy)-5-(9H-carbazol-9-yl)-N-(quinolin-8-yl)-2-((1S,2R)-1,2,3-tris(benzyloxy)propyl)-3,4-dihydro-2H-pyran-6-carboxamide (4g)



According to general procedure 4.1: **1a** (100 mg; 0.129 mmol; 1.0 equiv.), **Carbazole** (32.2 mg; 0.194 mmol; 1.5 equiv.), $CuBr_2$ (4.4 mg; 0.0194 mmol; 15 mol%), Tetramethylguanidine (58 µL; 0.464 mmol; 3.6 equiv.), Pyridine (0.30 mL). The reaction mixture was stirred at 140 °C for 45 min. Product **4g** was isolated after purification on silica gel (PE: EtOAc = 5:1 to 3:1) as colorless oil (54.6 mg, 45%); **$[\alpha]_D^{20}$** = - 25.5 (c = 0.16, EtOH); **IR (neat, cm^{-1})**: 1660, 1525, 1485, 1452, 1373, 1313, 1163, 1097, 750, 698; **^{1}H NMR (400 MHz, *d*$_6$-actone)** δ 11.03 (s, 1H), 8.70 (dd, *J* = 4.3, 1.6 Hz, 1H), 8.38 (dd, *J* = 7.8, 1.1 Hz, 1H), 8.27 (dd, *J* = 8.3, 1.6 Hz, 1H), 8.17 (dd, *J* = 7.7, 3.2 Hz, 2H), 7.87 (d, *J* = 8.3 Hz, 1H), 7.55 - 7.46 (m, 5H), 7.42 - 7.33 (m, 9H), 7.28 - 7.11 (m, 10H), 6.99-6.95 (m, 1H), 6.89 (t, *J* = 7.4 Hz, 2H), 6.52 - 6.50 (m, 2H), 5.15 (t, *J* = 4.0 Hz, 1H), 5.03 (d, *J* = 10.8 Hz, 1H), 4.94 - 4.87 (m, 2H), 4.71 (s, 2H), 4.67 - 4.61 (m, 4H), 4.54 (q, *J* = 10.4, 4.8 Hz, 1H), 4.24 (dd, *J* =10.8, 4.4 Hz, 1H), 4.11 (d, *J* = 11.3 Hz, 1H), 3.96 (dd, *J* = 10.0, 4.7 Hz, 1H), 3.84 (d, *J* = 11.2 Hz, 1H), 2.02 (s, 3H); **^{13}C NMR (J-MOD**, **101 MHz, *d*$_6$-actone)** δ 170.4 (C), 158.1 (C), 149.8 (CH), 146.9 (C), 143.8 (C), 141.6 (C), 140.1 (C), 140.0 (C), 139.8 (C), 139.4 (C), 138.3 (C), 137.4 (CH), 135.0 (C), 129.4 (CH), 129.2 (CH), 129.1 (C), 129.0 (CH), 129.0 (CH), 128.7 (CH), 128.7 (CH), 128.6 (CH), 128.5 (CH), 128.3 (CH), 128.3 (CH), 128.3 (CH), 128.0 (CH), 126.7 (CH), 126.6 (CH), 125.0 (C), 124.5 (C), 123.2 (CH), 123.0 (CH), 121.3 (CH), 120.8 (CH), 120.5 (CH), 120.3 (CH), 118.8 (C), 117.1 (CH), 112.5 (CH), 110.5 (CH), 80.0 (CH), 79.2 (CH), 76.6 (CH), 76.2 (CH),

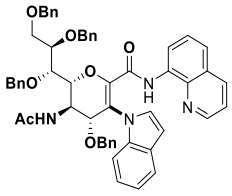
75.7 (CH_2), 74.3 (CH_2), 73.9 (CH_2), 73.0 (CH_2), 70.3 (CH_2), 49.7 (CH), 23.4 (CH_3); **HRMS** (ESI-TOF): m/z calculated for $C_{60}H_{55}N_4O_7$ $[M+H]^+$ 943.4065, found 943.4086.

(2R,3R,4R)-3-acetamido-4-(benzyloxy)-5-(9H-pyrido[2,3-b]indol-9-yl)-N-(quinolin-8-yl)-2-((1S,2R)-1,2,3-tris(benzyloxy)propyl)-3,4-dihydro-2H-pyran-6-carboxamide (4h)



According to general procedure 4.1: **1a** (100 mg; 0.129 mmol; 1.0 equiv.), **Norharmane** (32.4 mg; 0.194 mmol; 1.5 equiv.), $CuBr_2$ (4.4 mg; 0.0194 mmol; 15 mol%), Tetramethylguanidine (58 µL; 0.464 mmol; 3.6 equiv.), Pyridine (0.30 mL). The reaction mixture was stirred at 140 °C for 45 min. Product **4h** was isolated after purification on silica gel (PE: EtOAc = 3:1 to 1:1) as colorless oil (36.4 mg, 30%); **$[\alpha]_D^{20}$** = - 16.7 (c = 0.18, EtOH); **IR (neat, cm^{-1})**: 2924, 1660, 1525, 1487, 1454, 1371, 1327, 1089, 1028, 732, 698; **^{1}H NMR (300 MHz, *d*$_6$-actone)** δ 11.01 (s, 1H), 8.93 - 8.91 (m, 1H), 8.71 - 8.70 (m, 1H), 8.40 (d, *J* = 5.2 Hz, 1H), 8.28 - 8.20 (m, 3H), 8.05 - 8.01 (m, 1H), 7.91 (d, *J* = 8.2 Hz, 1H), 7.51 - 7.44 (m, 3H), 7.42 - 7.38 (m, 3H), 7.35 - 7.29 (m, 5H), 7.28 - 7.22 (m, 4H), 7.20 - 7.15 (m, 2H), 7.13 - 7.09 (m, 1H), 7.07 - 7.02 (m, 3H), 6.93 - 6.87 (m, 1H), 6.83 - 6.78 (m, 2H), 6.45 (d, *J* = 8.2 Hz, 2H), 5.17 (t, *J* = 5.8 Hz, 1H), 4.98 - 4.91 (m, 1H), 4.89 - 4.83 (m, 2H), 4.71 - 4.64 (m, 4H), 4.60 - 4.50 (m, 3H), 4.22 (dd, *J* = 10.0, 4.7 Hz, 1H), 4.11 (d, *J* = 11.5 Hz, 1H), 3.96 - 3.89 (m, 2H), 1.97 (s, 3H); **^{13}C NMR (J-MOD**, **101 MHz, *d*$_6$-actone)** δ 170.5 (C), 157.9 (C), 149.9 (CH), 147.0 (C), 142.2 (C), 140.1 (CH), 140.0 (C), 139.8 (C), 139.8 (C), 139.7 (C), 139.3 (C), 138.0 (C), 137.5 (CH), 135.9 (CH), 134.7 (C), 129.4 (C), 129.4 (CH), 129.2 (CH), 129.1 (CH), 129.1 (C), 129.0 (CH), 129.0 (CH), 129.0 (CH), 128.7 (CH), 128.7 (CH), 128.6 (CH), 128.5 (CH), 128.3 (CH), 128.3 (CH), 128.3 (CH), 128.0 (CH), 123.3 (CH), 123.1 (C), 123.1 (CH), 122.8 (CH), 121.0 (CH), 118.2 (C), 117.1 (CH), 115.1 (CH), 111.1 (CH), 80.2 (CH), 79.2 (CH), 76.7 (CH), 75.9 (CH), 75.8 (CH_2), 74.3 (CH_2), 73.7 (CH_2), 73.0 (CH_2), 70.3 (CH_2), 49.7 (CH), 23.4 (CH_3); **HRMS** (ESI-TOF): m/z calculated for $C_{59}H_{54}N_5O_7$ $[M+H]^+$ 944.4018, found 944.4054.

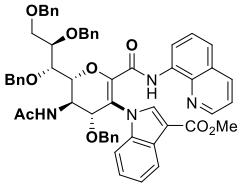
(2R,3R,4R)-3-acetamido-4-(benzyloxy)-5-(1H-indol-1-yl)-N-(quinolin-8-yl)-2-((1S,2R)-1,2,3-tris(benzyloxy)propyl)-3,4-dihydro-2H-pyran-6-carboxamide (4i)



According to general procedure 4.1: **1a** (100 mg; 0.129 mmol; 1.0 equiv.), **Indole** (22.6 mg; 0.194 mmol; 1.5 equiv.), $CuBr_2$ (4.4 mg; 0.0194 mmol; 15 mol%), Tetramethylguanidine (58 µL; 0.464 mmol; 3.6 equiv.), Pyridine (0.30 mL). The reaction mixture was stirred at 140 °C for 45 min. Product **4i** was isolated after purification on silica gel (PE: EtOAc: CH_2Cl_2 = 7:2:1) as colorless oil (18 mg, 16%); **$[\alpha]_D^{20}$** = + 33.0 (c = 0.1, EtOH); **IR (neat, cm^{-1})**: 2924, 1658, 1525, 1487, 1456, 1369,1087, 1028, 738, 696; **^{1}H NMR (300 MHz, *d*$_6$-actone)** δ 11.00 (s, 1H), 8.80 (bs, 1H), 8.54 - 8.52 (m, 1H), 8.35 - 8.30 (m, 1H), 7.79 - 7.77 (m, 1H), 7.64 - 7.58 (m, 2H), 7.50 - 7.04 (m, 26H), 6.71 - 6.63 (m, 1H), 5.10 - 4.42 (m, 11H), 4.28 - 4.18 (m, 2H), 4.06 - 3.96 (m, 2H), 2.02 (s, 3H); **^{13}C NMR (J-MOD**, **101 MHz, *d*$_6$-actone)** δ 170.3 (C), 158.2 (C), 149.8 (CH), 140.0 (C), 139.9 (C),

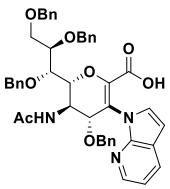
139.8 (C), 139.3 (C), 138.8 (C), 137.4 (CH), 135.0 (C), 134.9 (C), 129.3 (CH), 129.2 (CH), 129.1 (CH), 129.1 (CH), 129.0 (CH), 128.9 (CH), 128.7 (CH), 128.6 (CH), 128.5 (CH), 128.5 (CH), 128.4 (CH), 128.3 (CH), 128.0 (CH), 123.1 (CH), 123.0 (CH), 122.4 (CH), 121.7 (CH), 120.5 (CH), 117.0 (CH), 117.0 (CH), 110.9 (CH), 102.7 (CH), 79.5 (CH), 79.0 (CH), 76.8 (CH), 76.2 (CH), 75.5 (CH_2), 74.2 (CH_2), 73.9 (CH_2), 73.0 (CH_2), 70.4 (CH_2), 49.7 (CH), 23.5 (CH_3); **HRMS** (ESI-TOF): m/z calculated for $C_{56}H_{53}N_4O_7$ $[M+H]^+$ 893.3909, found 893.3928.

methyl 1-((2R,3R,4R)-3-acetamido-4-(benzyloxy)-6-(quinolin-8-ylcarbamoyl)-2-((1S,2R)-1,2,3-tris(benzyloxy)propyl)-3,4-dihydro-2H-pyran-5-yl)-1H-indole-3-carboxylate (4j)



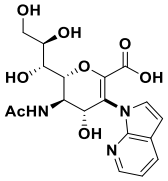
According to general procedure 4.1: **1a** (100 mg; 0.129 mmol; 1.0 equiv.), **Methyl indole-3-carboxylate** (33.8 mg; 0.194 mmol; 1.5 equiv.), $CuBr_2$ (4.4 mg; 0.0194 mmol; 15 mol%), Tetramethylguanidine (58 µL; 0.464 mmol; 3.6 equiv.), Pyridine (0.30 mL). The reaction mixture was stirred at 140 °C for 45 min. Product **4j** was isolated after purification on silica gel (PE: EtOAc = 3:1) as colorless oil (48.8 mg, 40%); in the NMR solvent, **4j** looks like as a mixture of two rotamers, although by LCMS, the purity of **4j** is 100% (see LCMS, pS48); $[\alpha]_D^{20} = 0$ (c = 0.18, EtOH); **IR (neat, cm^{-1})**: 1695, 1525, 1485, 1456, 1327, 1261, 1107, 827, 748, 698; **^{1}H NMR (300 MHz, *d*$_6$-actone)** δ 11.05 (s, 1H), 8.83 - 8.77 (m, 1H), 8.48 - 8.40 (m, 1H), 8.33 (d, *J* = 8.1 Hz, 1H), 8.22 - 8.19 (m, 1H), 8.00 - 7.99 (m, 1H), 7.86 - 7.77 (m, 1H), 7.61 (d, *J* = 8.1 Hz, 1H), 7.55 - 7.35 (m, 10H), 7.31 - 7.06 (m, 12H), 7.04 - 6.99 (m, 2H), 6.65 (d, *J* = 6.6 Hz, 1H), 5.16 - 5.07 (m, 1H), 5.02 - 4.86 (m, 2H), 4.83 - 4.79 (m, 2H), 4.74 - 4.65 (m, 3H), 4.59 - 4.47 (m, 3H), 4.37 (d, *J* = 11.2 Hz, 1H), 4.30 - 4.15 (m, 2H), 4.02 - 3.95 (m, 1H), 3.91 - 3.88 (m, 3H), 2.02 (s, 3H); **^{13}C NMR (J-MOD**, **101 MHz, *d*$_6$-actone)** δ 170.5 (C), 170.4 (C), 165.7 (C), 165.7 (C), 157.9 (C), 157.8 (C), 149.9 (CH), 146.0 (C), 145.0 (C), 140.5 (C), 140.0 (C), 139.8 (C), 139.8 (C), 139.7 (C), 139.4 (C), 139.3 (C), 138.9 (CH), 138.3 (C), 138.2 (C), 138.2 (C), 137.5 (CH), 137.5 (CH), 135.3 (CH), 134.7 (C), 134.7 (C), 129.3 (CH), 129.3 (CH), 129.2 (CH), 129.1 (CH), 129.1 (CH), 129.1 (C), 129.1 (CH), 128.9 (CH), 128.9 (CH), 128.9 (CH), 128.7 (CH), 128.6 (CH), 128.6 (CH), 128.5 (CH), 128.4 (CH), 128.3 (CH), 128.2 (CH), 128.0 (CH), 127.5 (C), 123.7 (CH), 123.7 (CH), 123.3 (CH), 123.1 (CH), 122.6 (CH), 122.5 (CH), 122.3 (CH), 121.8 (CH), 120.1 (C), 119.7 (C), 117.2 (CH), 113.1 (CH), 111.4 (CH), 109.5 (C), 108.6 (C), 79.8 (CH), 79.7 (CH), 79.3 (CH), 79.0 (CH), 77.8 (CH), 76.5 (CH), 76.2 (CH), 76.1 (CH), 75.6 (CH_2), 75.4 (CH_2),74.2 (CH_2), 74.2 (CH_2), 73.9 (CH_2), 73.6 (CH_2), 73.0 (CH_2), 72.9 (CH_2), 70.3 (CH_2), 70.2 (CH_2), 51.1 (CH_3), 51.0 (CH_3), 49.4 (CH), 49.4 (CH), 23.4 (CH_3), 23.3 (CH_3); **HRMS** (ESI-TOF): m/z calculated for $C_{58}H_{55}N_4O_9$ $[M+H]^+$ 951.3964, found 951.3984.

(2R,3R,4R)-3-acetamido-4-(benzyloxy)-5-(1H-pyrrolo[2,3-b]pyridin-1-yl)-2-((1S,2R)-1,2,3-tris(benzyloxy)propyl)-3,4-dihydro-2H-pyran-6-carboxylic acid (5)



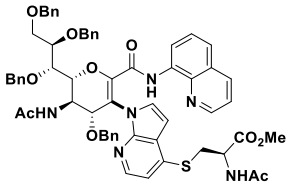
According to general procedure 4.2: Product **5** was isolated after purification as yellow foam (228.9 mg, 74%); **mp**: 107 - 108 °C; **$[\alpha]_D^{20}$** = - 25.8 (c = 0.12, EtOH); **IR (neat, cm^{-1})**: 2926, 1672, 1512, 1354, 1261, 1072, 1028, 800, 734, 696; **^{1}H NMR (400 MHz, *d*$_6$-actone)** δ 8.10 (br, 1H), 7.86 (bs, 1H), 7.41 - 7.27 (m, 16H), 7.08 - 7.04 (m, 5H), 6.81 (bs, 2H), 6.45 (bs, 1H), 4.90 (bs, 1H), 4.79 - 4.73 (m, 3H), 4.52 - 4.48 (m, 6H), 4.29 (bs, 1H), 4.10 - 3.90 (m, 3H), 3.70 (bs, 1H), 1.86 (s, 3H); **^{13}C NMR (101 MHz, *d*$_6$-actone)** δ 170.4, 149.2, 143.1, 140.0, 139.7, 138.8, 132.8, 129.7, 129.5, 129.1, 129.0, 129.0, 128.7, 128.6, 128.4, 128.2, 128.1, 128.0, 122.2, 116.8, 100.9, 79.4, 76.3, 75.5, 73.8, 72.7, 72.6, 69.9, 48.8, 23.3; **HRMS** (ESI-TOF): m/z calculated for $C_{46}H_{46}N_3O_8$ $[M+H]^+$ 768.3279, found 768.3286.

(2R,3R,4R)-3-acetamido-4-hydroxy-5-(1H-pyrrolo[2,3-b]pyridin-1-yl)-2-((1R,2R)-1,2,3-trihydroxypropyl)-3,4-dihydro-2H-pyran-6-carboxylic acid (6)



According to general procedure 4.3: Product **6** was isolated after purification as white solid (35 mg, 53%); **mp**: 220 - 221 °C; **$[\alpha]_D^{20}$** = - 25.4 (c = 0.18, EtOH); **IR (neat, cm^{-1})**: 3265, 1595, 1565, 1406, 1325, 1199, 1074, 802, 773; **^{1}H NMR (400 MHz, *d*$_4$-methanol)** δ 8.15 (dd, *J* = 4.8, 1.5 Hz, 1H), 7.93 (dd, *J* = 7.8, 1.5 Hz, 1H), 7.35 (d, *J* = 3.6 Hz, 1H), 7.07 (dd, *J* = 7.8, 4.8 Hz, 1H), 6.46 (d, *J* = 3.6 Hz, 1H), 4.61 (d, *J* = 7.4 Hz, 1H), 4.55 (dd, *J* = 9.5, 1.5 Hz, 1H), 4.40 (dd, *J* = 9.3, 7.6 Hz, 1H), 3.91 (m, 1H), 3.88 - 3.83 (m, 1H), 3.78 - 3.68 (m, 2H), 2.03 (s, 3H); **^{13}C NMR (101 MHz, *d*$_4$-methanol)** δ 174.4 (C), 168.7 (C), 152.7 (C), 149.5 (C), 142.6 (CH), 133.8 (CH), 130.2 (CH), 123.2 (C), 116.7 (CH), 113.8 (C), 100.5 (CH), 77.9 (CH), 71.2 (CH), 70.9 (CH), 69.6 (CH), 64.8 (CH_2), 52.4 (CH), 22.7 (CH_3); **HRMS** (ESI-TOF): m/z calculated for $C_{18}H_{22}N_3O_8$ $[M+H]^+$ 408.1401, found 408.1415.

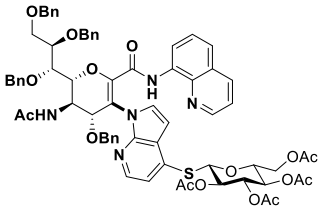
methyl S-(1-((2R,3R,4R)-3-acetamido-4-(benzyloxy)-6-(quinolin-8-ylcarbamoyl)-2-((1S,2R)-1,2,3-tris(benzyloxy)propyl)-3,4-dihydro-2H-pyran-5-yl)-1H-pyrrolo[2,3-b]pyridin-4-yl)-N-acetyl-L-cysteinate (7)



According to general procedure 4.4: Product **7** was isolated after purification on silica gel (PE: EtOAc = 2:1 to 1:4) as white foam (65 mg, 64%); **mp**: 87 - 88 °C; **$[\alpha]_D^{20}$** = + 23.1 (c = 0.17, EtOH); **IR (neat, cm^{-1})**: 2926, 1745, 1654, 1525, 1485, 1213, 1089, 825, 736, 698; **^{1}H NMR (300 MHz, *d*$_6$-actone)** δ 10.99 (s, 1H), 8.76 - 8.75 (m, 1H), 8.49 (d, *J* = 7.6 Hz, 1H), 8.29 (dd, *J* = 8.3, 1.5 Hz, 1H), 8.11 (d, *J* = 5.1 Hz, 1H), 7.84 (d, *J* = 8.1 Hz, 1H), 7.66 (d, *J* = 7.6 Hz, 1H), 7.60 - 7.57 (m, 1H), 7.51 - 7.33 (m, 10H), 7.25 - 7.23 (m, 2H), 7.20 - 7.08 (m, 9H), 6.88 - 6.87 (m, 2H), 6.60 - 6.56 (m, 1H), 5.03 - 4.93 (m, 3H), 4.91 - 4.71 (m, 7H), 4.52 (bs, 1H), 4.42 - 4.37 (m, 1H), 4.26 - 4.19 (m, 2H), 3.98 - 3.93(m, 1H), 3.72 - 3.65 (m, 5H), 3.61 - 3.54 (m, 1H), 3.26 - 3.08 (m, 1H), 2.03 (s, 3H), 1.94 (s, 3H); **^{13}C NMR (J-MOD**, **101 MHz, *d*$_6$-actone)** δ 171.7 (C), 170.5 (C), 170.3 (C), 158.5 (C), 149.8 (CH), 144.6 (C), 143.7 (CH), 140.0 (C), 139.9 (C), 139.8 (C), 139.7 (C), 139.4 (C), 138.8

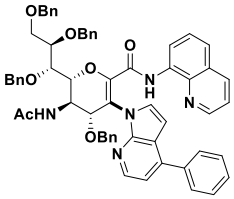
(C), 137.3 (CH), 135.0 (C), 129.3 (CH), 129.1 (CH), 129.1 (CH), 129.0 (C), 128.9 (CH), 128.9 (CH), 128.6 (CH), 128.6 (CH), 128.4 (CH), 128.3 (CH), 128.2 (CH), 127.9 (CH), 123.1 (CH), 123.0 (CH), 120.6 (C), 117.0 (CH), 113.6 (CH), 79.4 (CH), 79.0 (CH), 77.1 (CH), 76.1 (CH), 75.5 (CH_2), 74.2 (CH_2), 73.3 (CH_2), 72.9 (CH_2), 70.5 (CH_2), 53.2 (CH), 52.7 (CH_3), 49.3 (CH), 41.2 (CH_2), 23.5 (CH_3), 22.8 (CH_3); **HRMS** (ESI-TOF): m/z calculated for $C_{61}H_{61}N_6O_{10}S$ $[M+H]^+$ 1069.4164, found 1069.4164.

(2S,3R,4S,5R,6R)-2-((1-((2R,3R,4R)-3-acetamido-4-(benzyloxy)-6-(quinolin-8-ylcarbamoyl)-2-((1S,2R)-1,2,3-tris(benzyloxy)propyl)-3,4-dihydro-2H-pyran-5-yl)-1H-pyrrolo[2,3-b]pyridin-4-yl)thio)-6-(acetoxymethyl)tetrahydro-2H-pyran-3,4,5-triyl triacetate (8)



According to general procedure 4.5: Product **8** was isolated after purification on silica gel (PE: EtOAc = 3:1 to 1:3) as yellow oil (79.8 mg, 75%); **$[\alpha]_D^{20}$** = + 2.7 (c = 0.15, EtOH); **IR (neat, cm^{-1})**: 2926, 1751, 1691, 1525, 1485, 1367, 1215, 1039, 912, 827, 734, 698;**^{1}H NMR (400 MHz, *d*$_6$-actone)** δ 10.98 (s, 1H), 8.74 - 8.73 (m, 1H), 8.47 (d, *J* = 7.6 Hz, 1H), 8.29 (dd, *J* = 8.3, 1.6 Hz, 1H), 8.13 (d, *J* = 5.2 Hz, 1H), 7.89 (bs, 1H), 7.58 (dd, *J* = 8.3, 1.1 Hz, 1H), 7.50 - 7.44 (m, 5H), 7.42 - 7.29 (m, 7H), 7.24 - 7.23 (m, 2H), 7.17 (t, *J* = 7.3 Hz, 2H), 7.12 - 7.07 (m, 6H), 6.86 (bs, 2H), 6.64 (d, *J* = 3.6 Hz, 1H), 5.55 (d, *J* = 10.1 Hz, 1H), 5.46 (t, *J* = 9.4 Hz, 1H), 5.17 (m, 2H), 5.03 - 4.93 (m, 3H), 4.83 - 4.41 (m, 9H), 4.30 - 4.16 (m, 5H), 3.95 - 3.93 (m, 1H), 2.07 (s, 3H), 2.03 (m, 6H), 2.01 (s, 3H), 1.98 (s, 3H); **^{13}C NMR (J-MOD**, **101 MHz, *d*$_6$-actone)** δ 170.8 (C), 170.4 (C), 170.4 (C), 170.2 (C), 170.0 (C), 158.5 (C), 149.8 (CH), 140.1 (C), 140.0 (C), 139.8 (C), 139.4 (C), 138.8 (C), 137.4 (CH), 135.0 (C), 129.3 (CH), 129.1 (CH), 129.1 (CH), 129.0 (CH), 128.9 (CH), 128.9 (CH), 128.6 (CH), 128.6 (CH), 128.4 (CH), 128.4 (CH), 128.2 (CH), 128.0 (CH), 123.1 (CH), 123.0 (CH), 121.6 (C), 117.1 (CH), 115.8 (CH), 84.2 (CH), 79.5 (CH), 79.1 (CH), 76.9 (CH), 76.6 (CH), 76.1 (CH), 75.6 (CH_2), 74.5 (CH), 74.2 (CH_2), 73.3 (CH_2), 72.9 (CH_2), 71.1 (CH), 70.4 (CH_2), 69.5 (CH), 63.2 (CH_2), 49.4 (CH), 23.5 (CH_3), 20.9 (CH_3), 20.8 (CH_3), 20.8 (CH_3), 20.7 (CH_3); **HRMS** (ESI-TOF): m/z calculated for $C_{69}H_{70}N_5O_{16}S$ $[M+H]^+$ 1256.4533, found 1256.4574.

(2R,3R,4R)-3-acetamido-4-(benzyloxy)-5-(4-phenyl-1H-pyrrolo[2,3-b]pyridin-1-yl)-N-(quinolin-8-yl)-2-((1S,2R)-1,2,3-tris(benzyloxy)propyl)-3,4-dihydro-2H-pyran-6-carboxamide (9)



According to general procedure 4.6: Product **9** was isolated after purification on silica gel (PE: EtOAc = 3:1 to 1:1) as colorless oil (59.9 mg, 90%); **$[\alpha]_D^{20}$** = + 2.6 (c = 0.15, EtOH); **IR (neat, cm^{-1})**: 2926, 1689, 1525, 1485, 1454, 1423, 1327, 1089, 734, 698; **^{1}H NMR (300 MHz, *d*$_6$-actone)** δ 11.02 (s, 1H), 8.75 (bs, 1H), 8.52 (d, *J* = 7.7 Hz, 1H), 8.30 – 8.27 (m, 2H), 7.86 (d, *J* = 7.9 Hz, 3H), 7.63 – 7.56 (m, 3H), 7.52 – 7.46 (m, 5H), 7.44 – 7.33 (m, 6H), 7.27 – 7.05 (m, 12H), 6.86 – 6.78

(m, 3H), 5.03 – 4.82 (m, 5H), 4.72 (s, 4H), 4.55 – 4.41 (m, 3H), 4.25 (d, J = 6.6 Hz, 2H), 3.97 (dd, J = 9.2, 3.8 Hz, 1H), 2.05 (s, 3H); **^{13}C NMR (J-MOD, 101 MHz, d_6-actone)** δ 170.4 (C), 158.7 (C), 149.8 (CH), 144.5 (C), 144.1 (CH), 142.3 (C), 140.1 (C), 140.0 (C), 139.8 (C), 139.4 (C), 138.9 (C), 137.4 (CH), 135.1 (C), 130.0 (CH), 129.5 (CH), 129.4 (CH), 129.3 (CH), 129.2 (CH), 129.1 (CH), 129.1 (C), 129.0 (CH), 128.9 (CH), 128.8 (CH), 128.7 (CH), 128.5 (CH), 128.3 (CH), 128.2 (CH), 128.0 (CH), 123.1 (CH), 123.0 (CH), 119.9 (C), 117.1 (CH), 116.0 (CH), 79.4 (CH), 79.1 (CH), 77.2 (CH), 76.2 (CH), 75.6 (CH_2), 74.2 (CH_2), 73.3 (CH_2), 73.0 (CH_2), 70.5 (CH_2), 49.4 (CH), 23.5 (CH_3); **HRMS** (ESI-TOF): m/z calculated for $C_{61}H_{56}N_5O_7$ $[M+H]^+$ 970.4174, found 970.4193.

7. References

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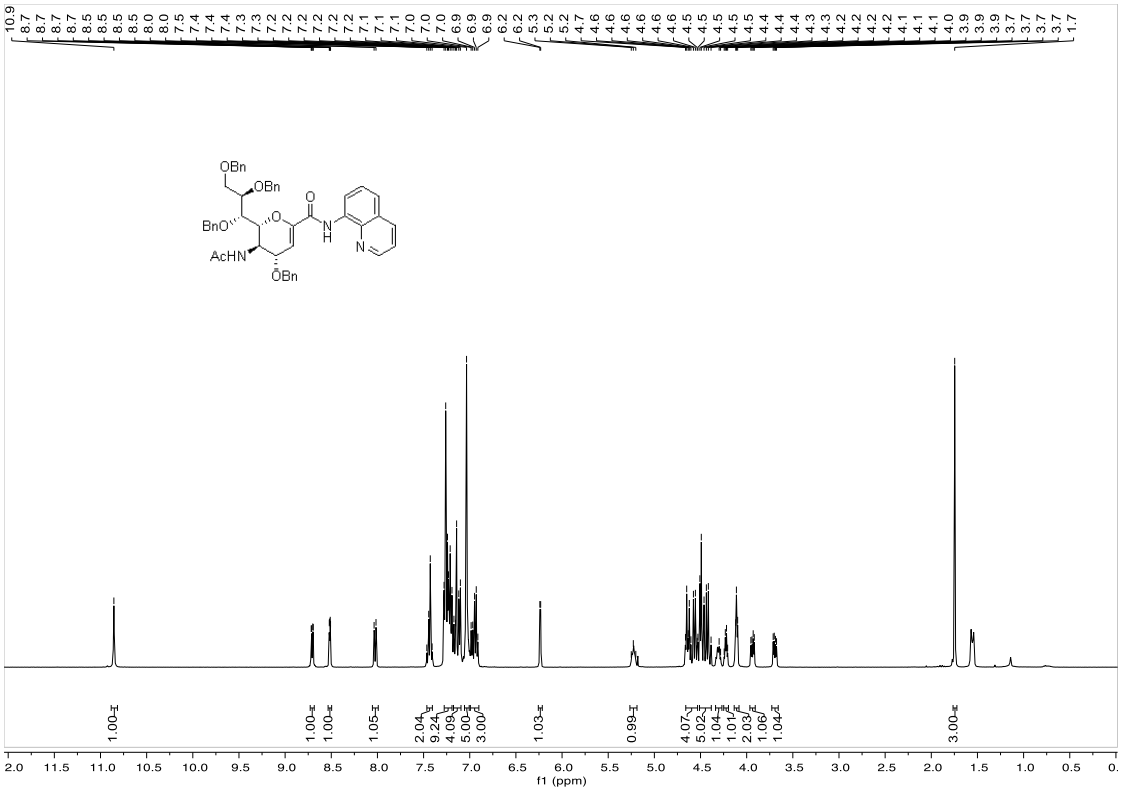
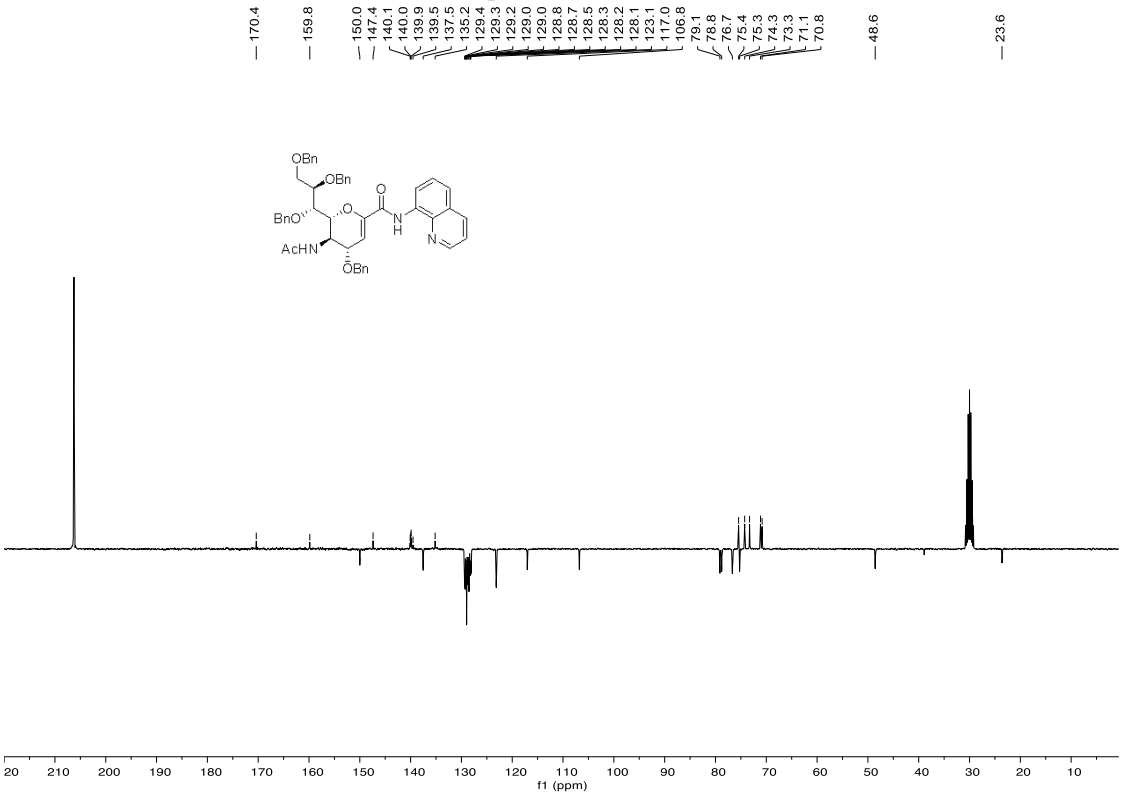
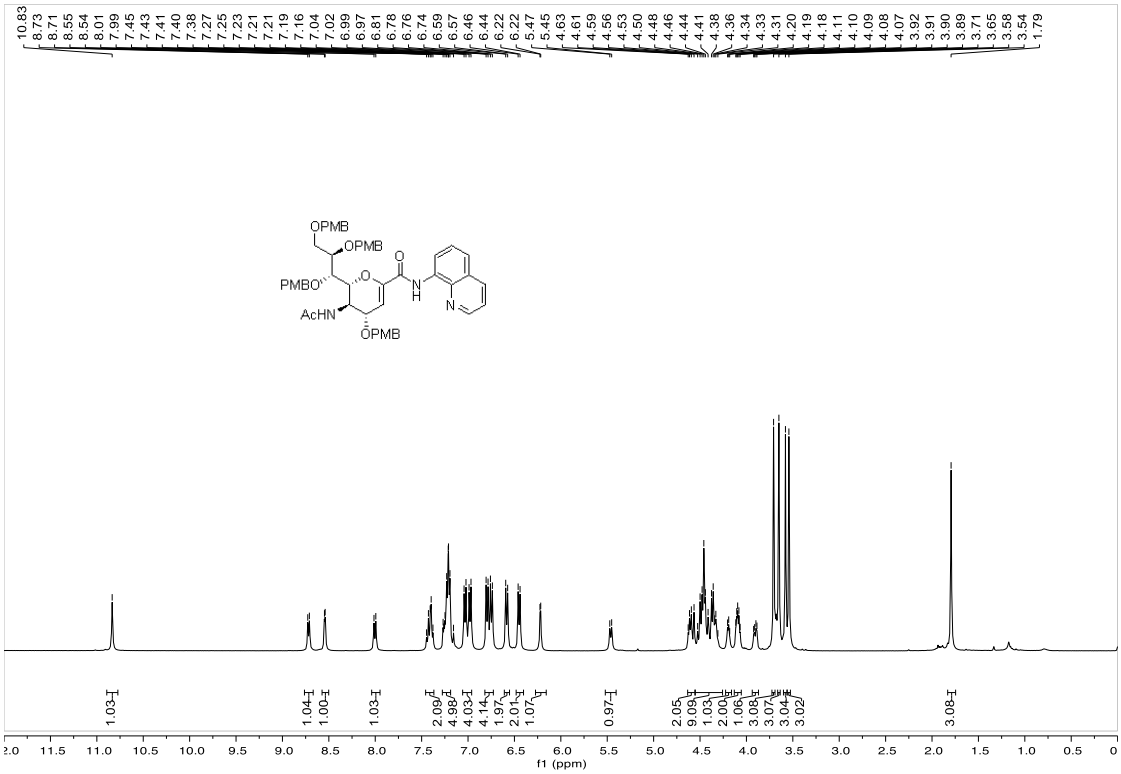
8. NMR Spectras



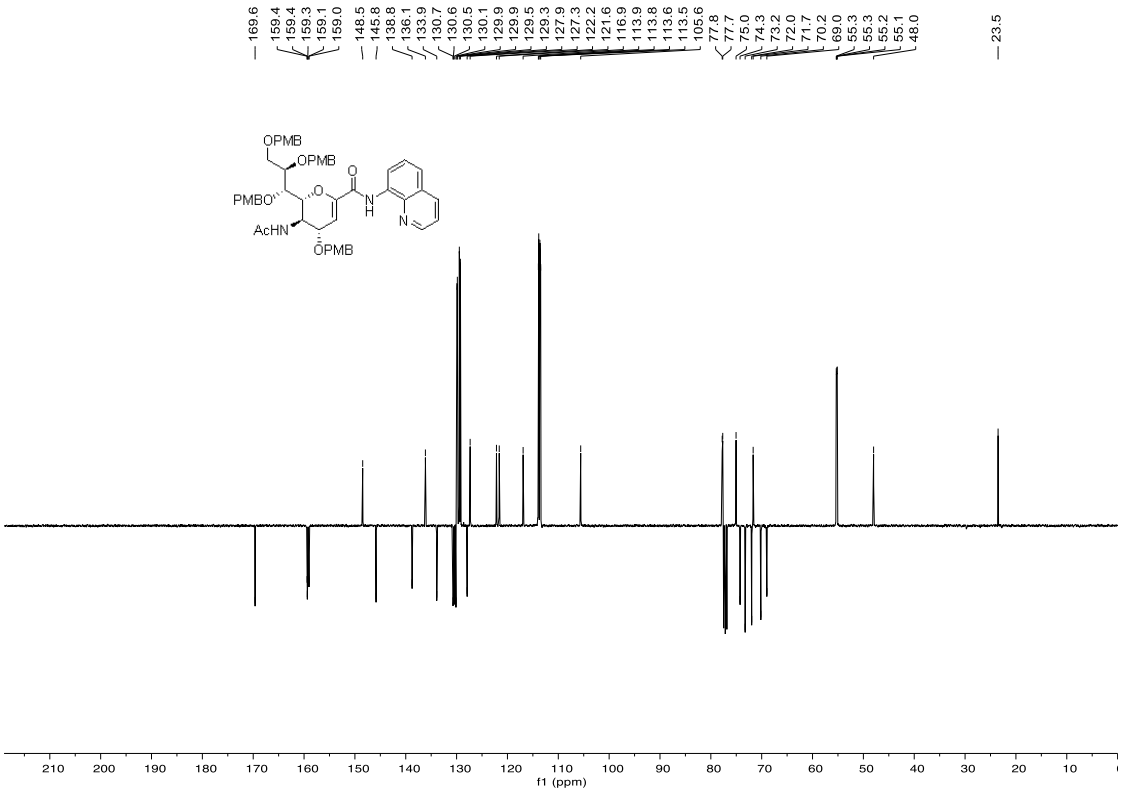
^{1}H NMR spectrum of **1a** ($CDCl_3$)



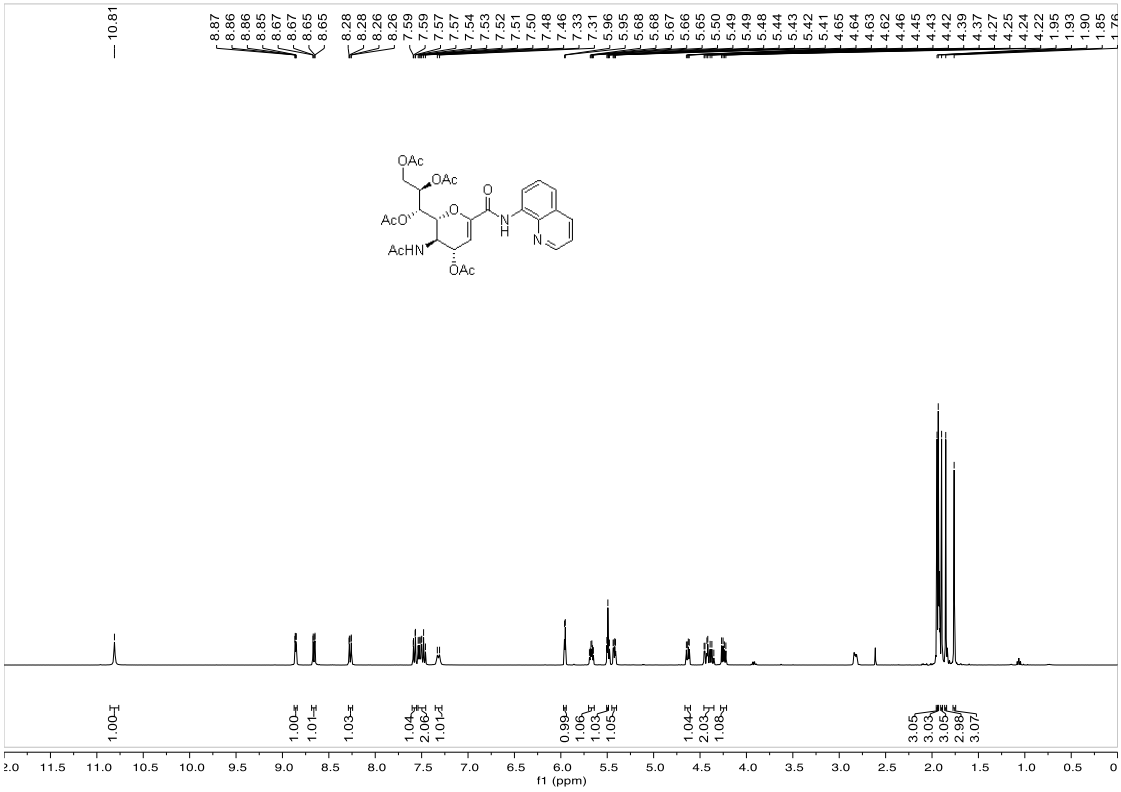
^{13}C NMR spectrum of **1a** (d_6-actone)



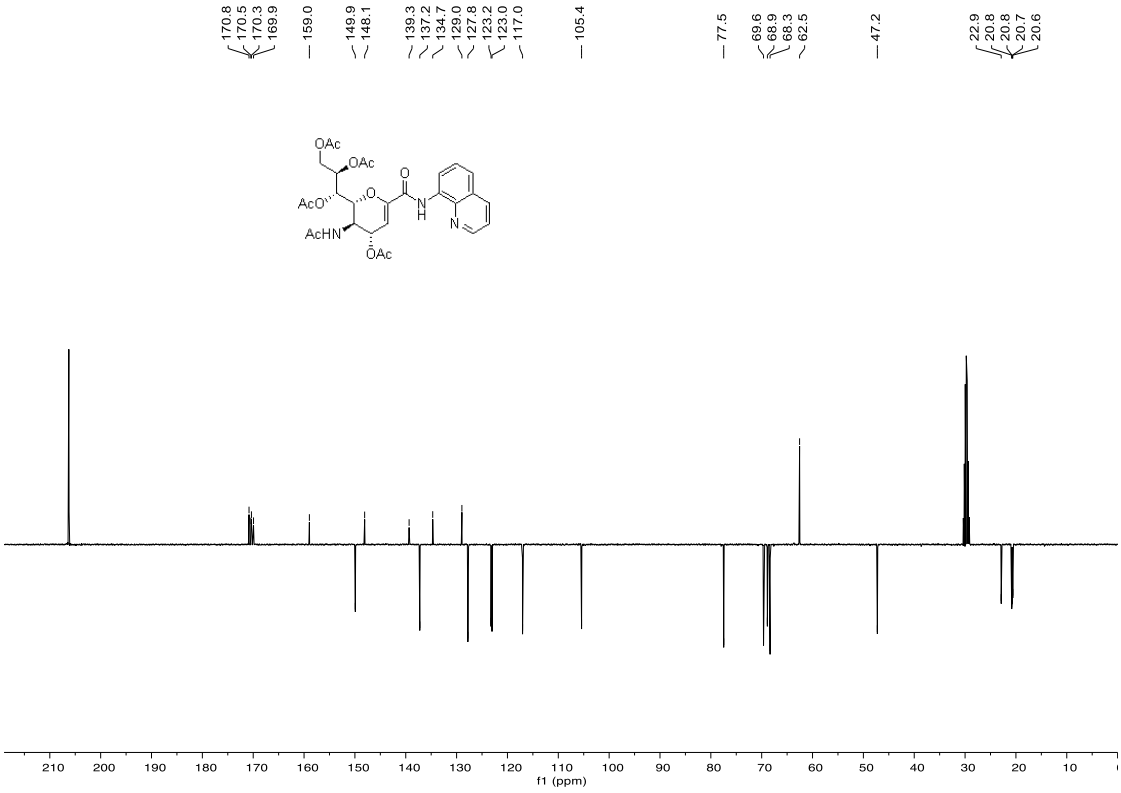
^{1}H NMR spectrum of **1b** ($CDCl_3$)



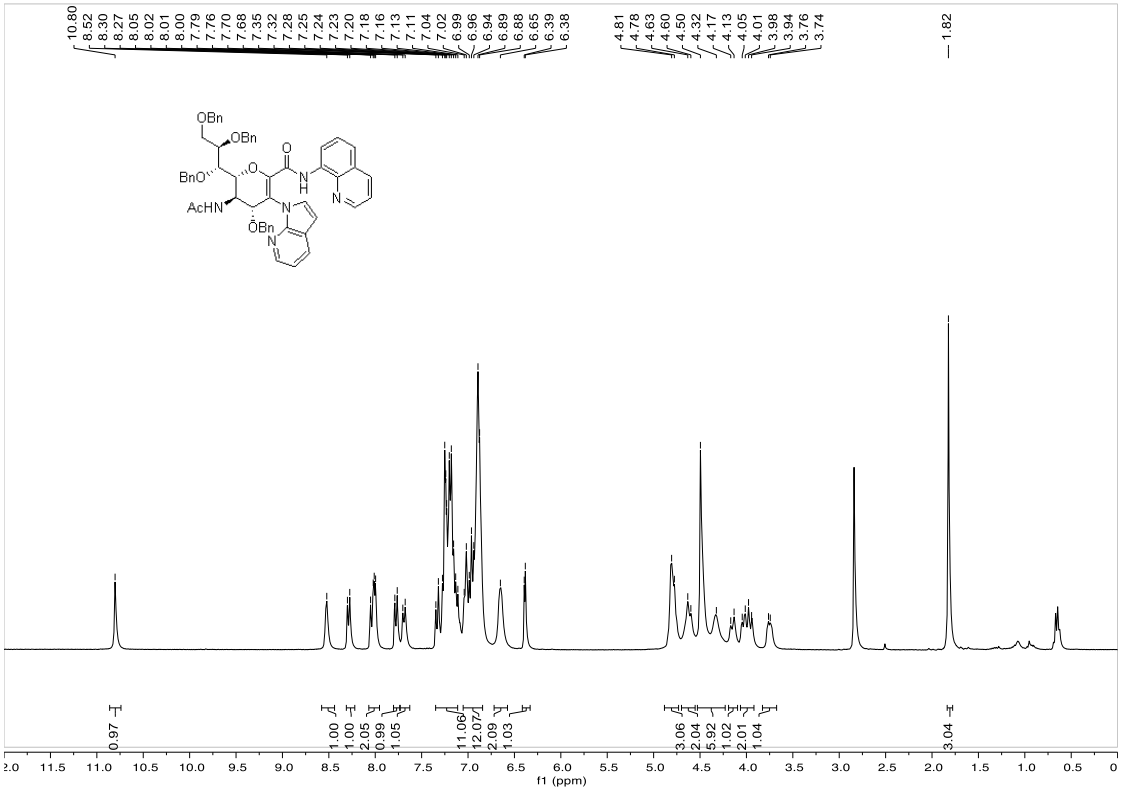
^{13}C NMR spectrum of **1b** ($CDCl_3$)



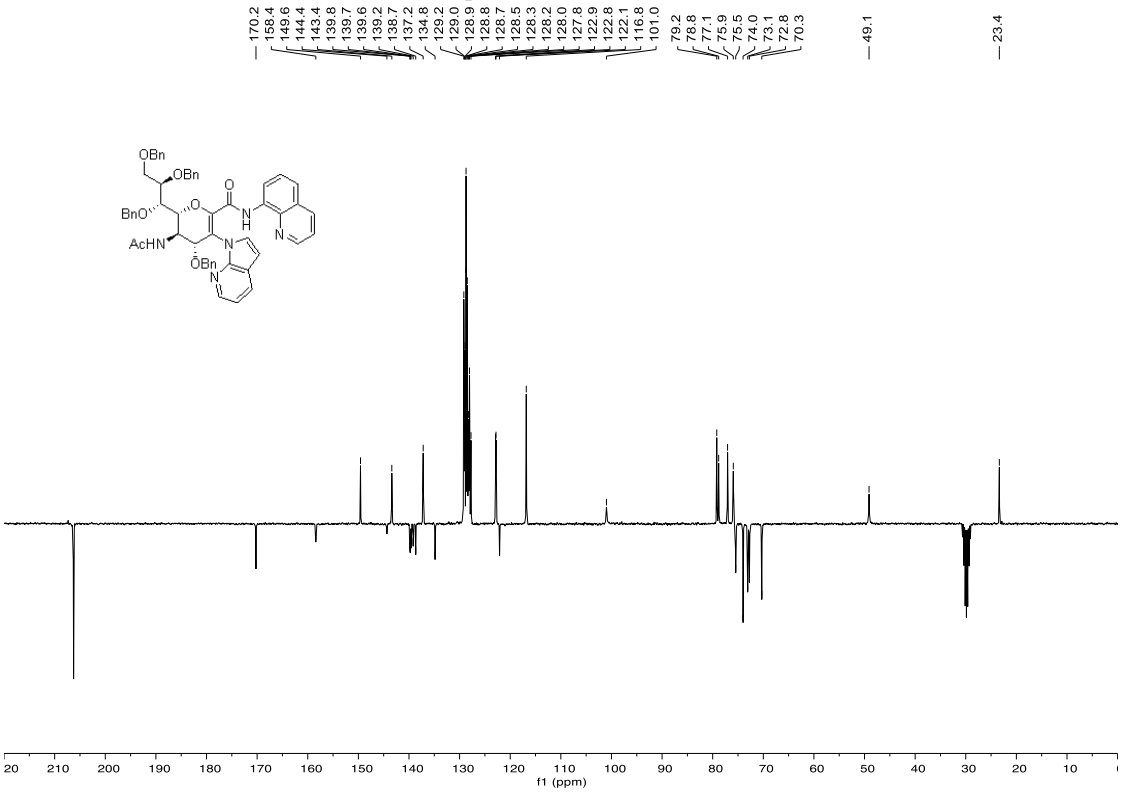
^{1}H NMR spectrum of **1c** (d_6-actone)



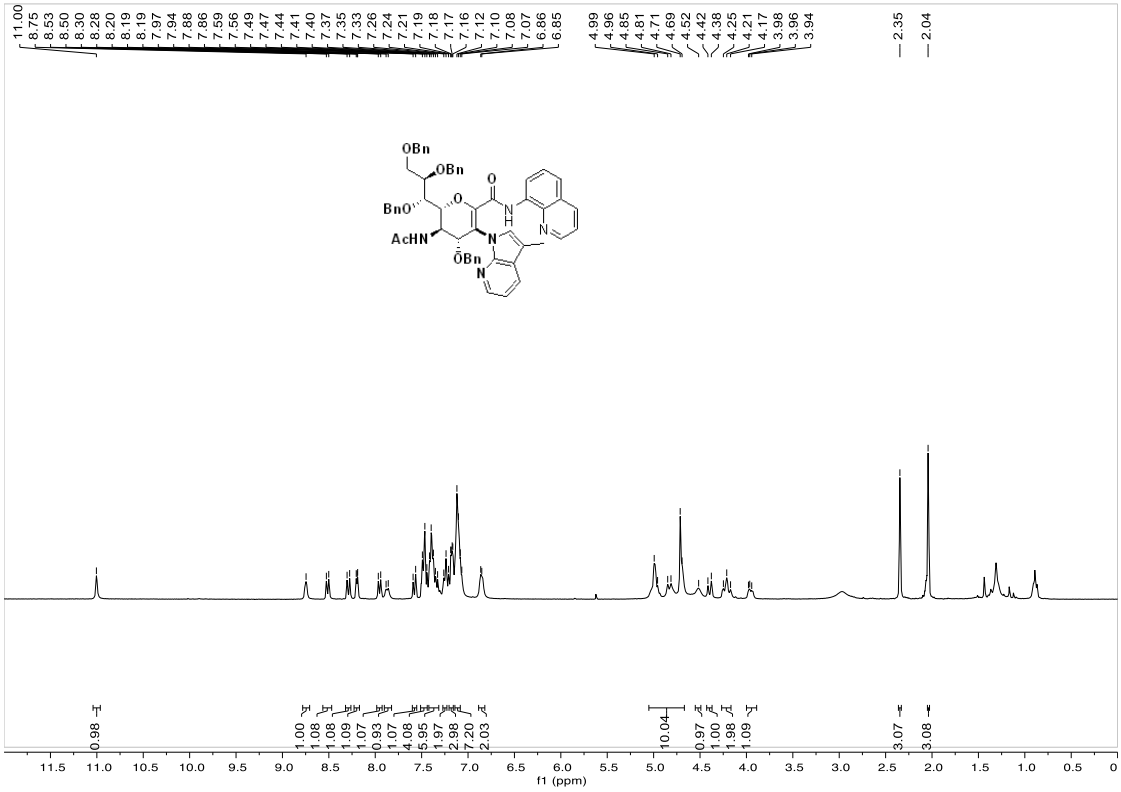
^{13}C NMR spectrum of **1c** (d_6-actone)



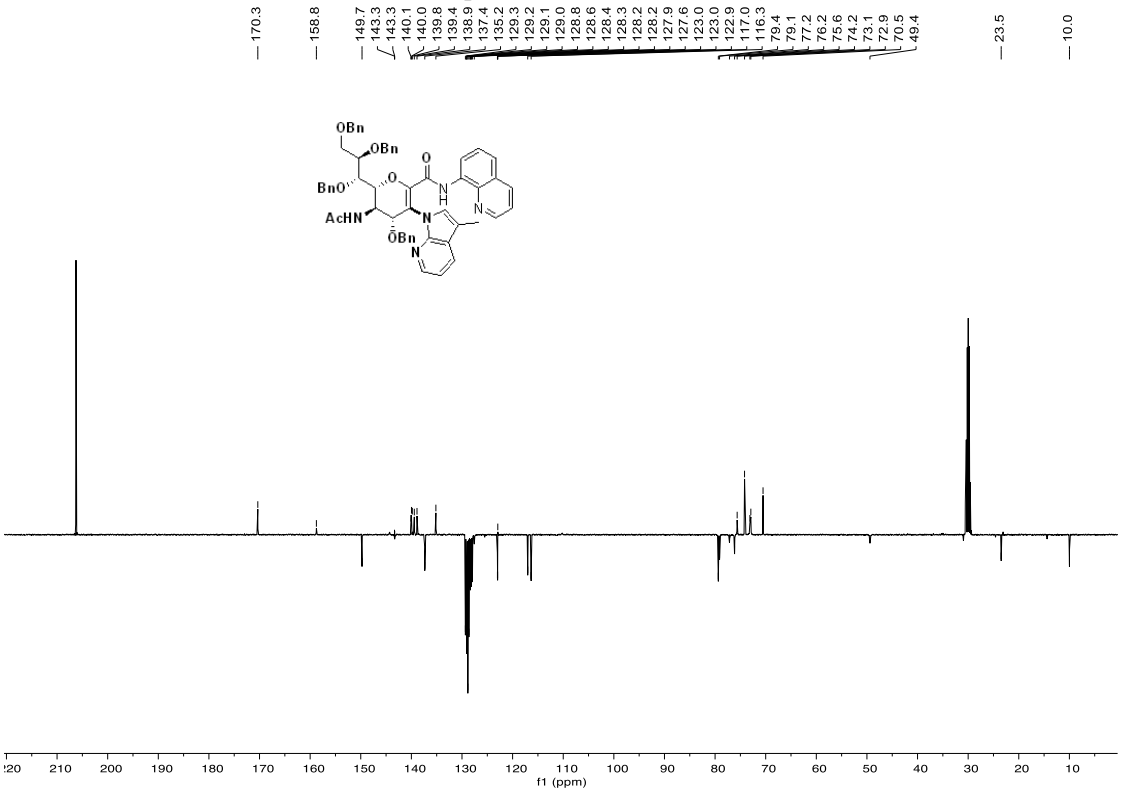
^{1}H NMR spectrum of **3a** (d_6-actone)



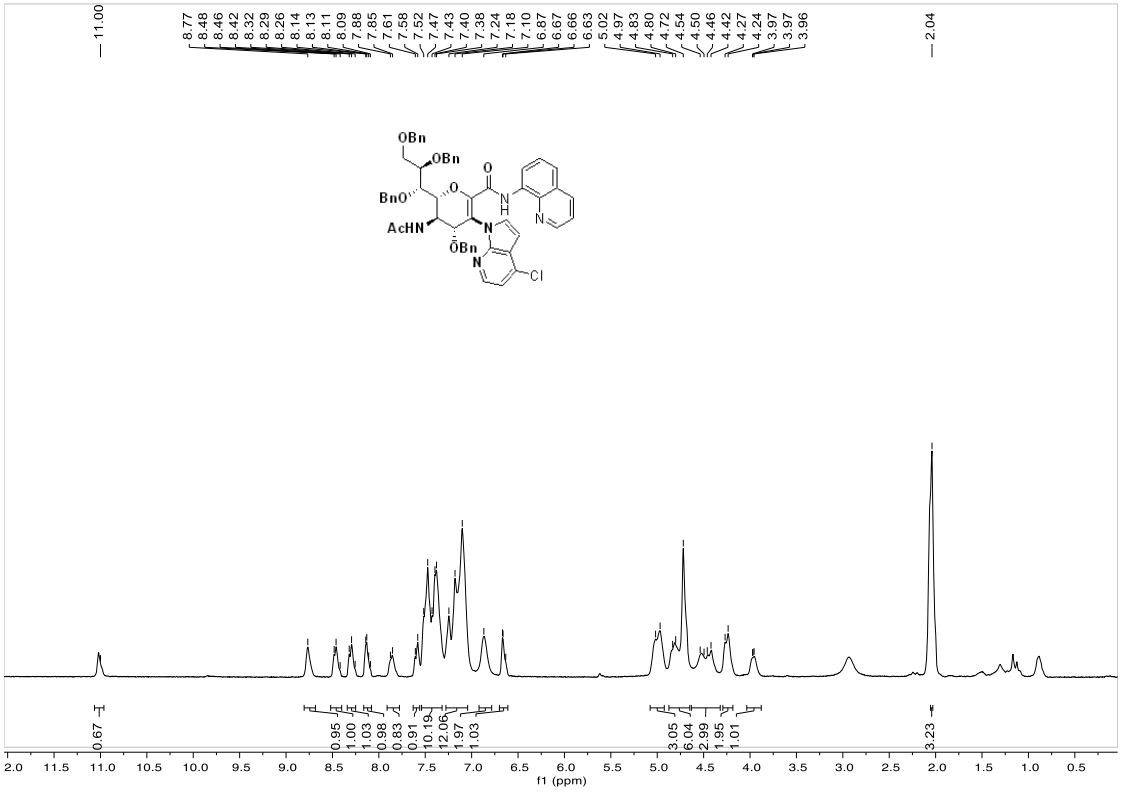
^{13}C NMR spectrum of **3a** (d_6-actone)



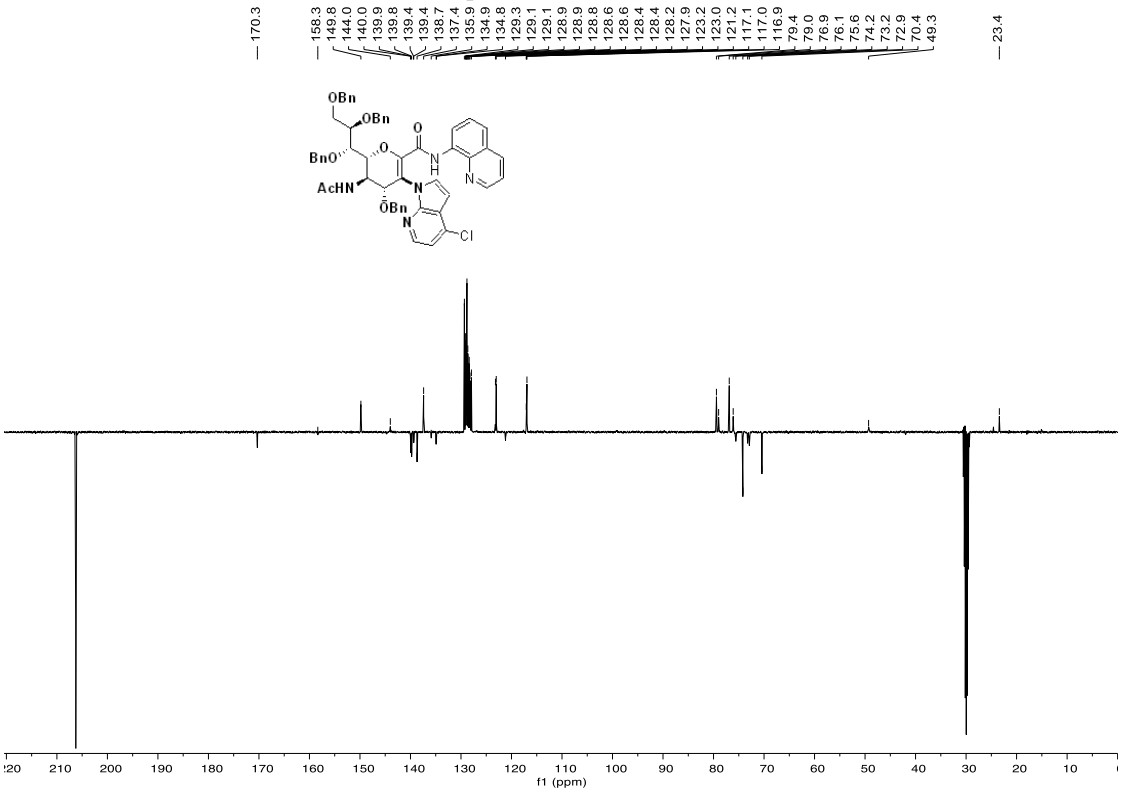
^{1}H NMR spectrum of **3b** (d_6-actone)



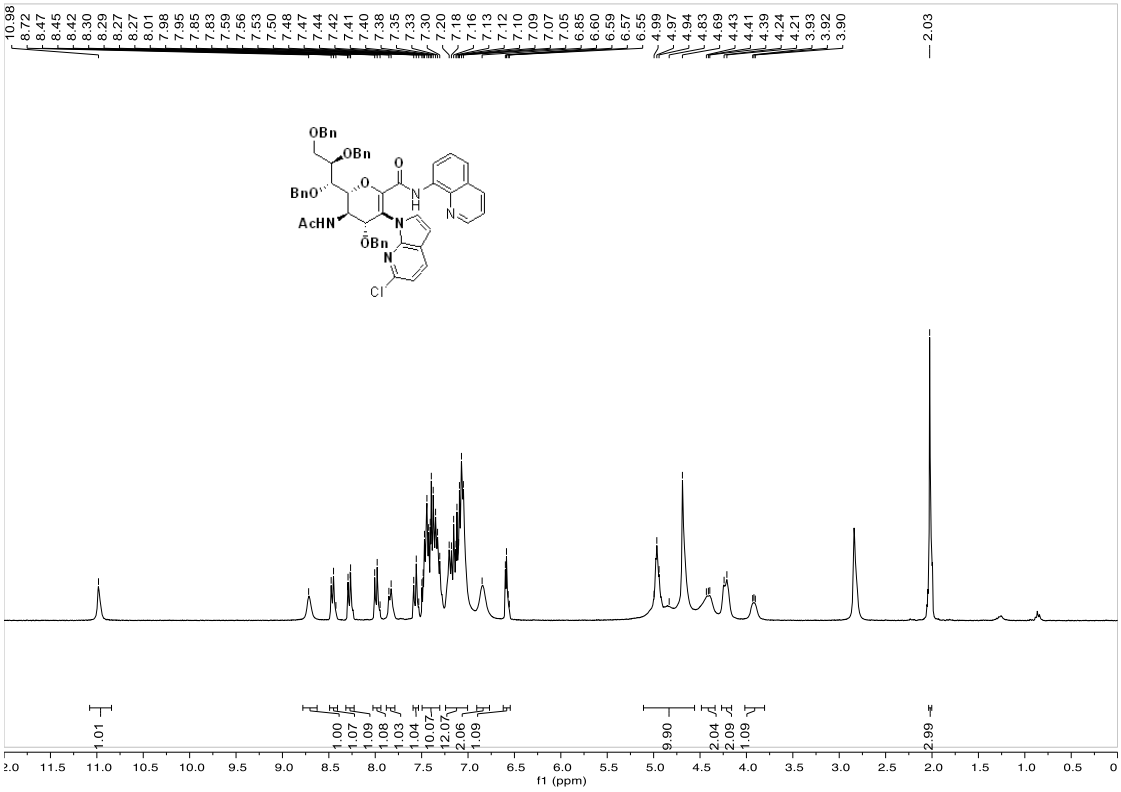
^{13}C NMR spectrum of **3b** (d_6-actone)



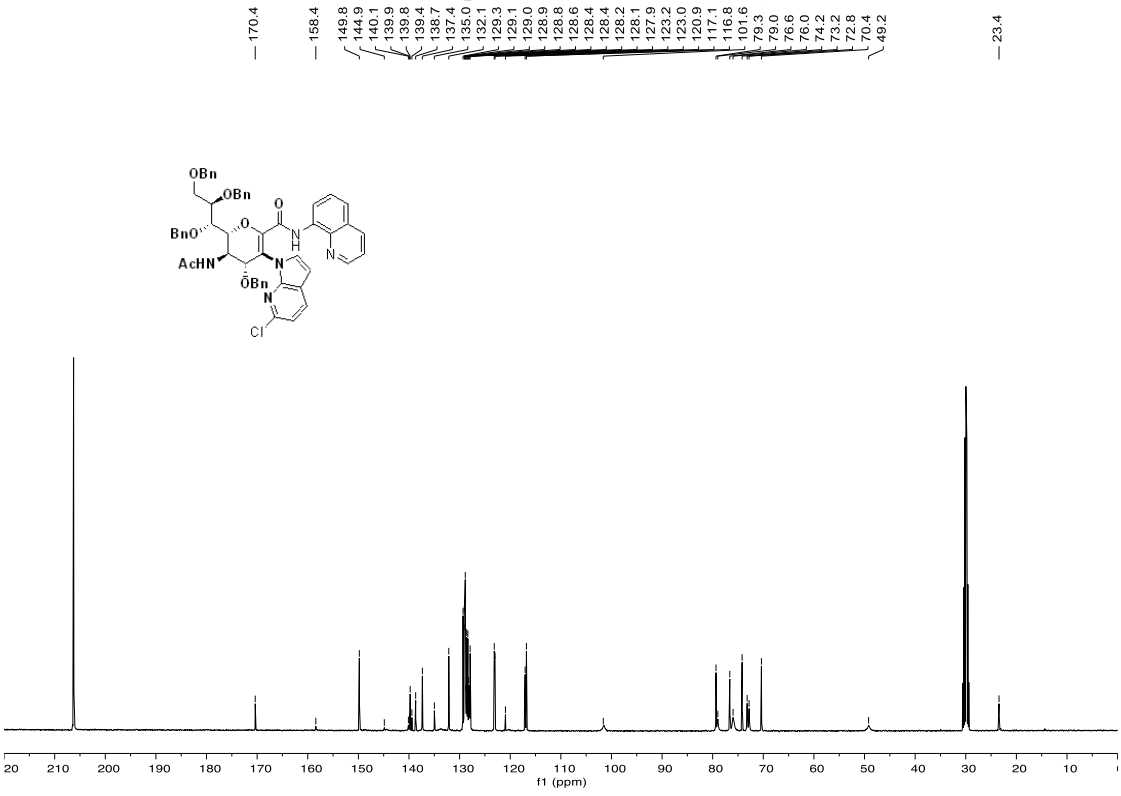
^{1}H NMR spectrum of **3c** (d_6-actone)



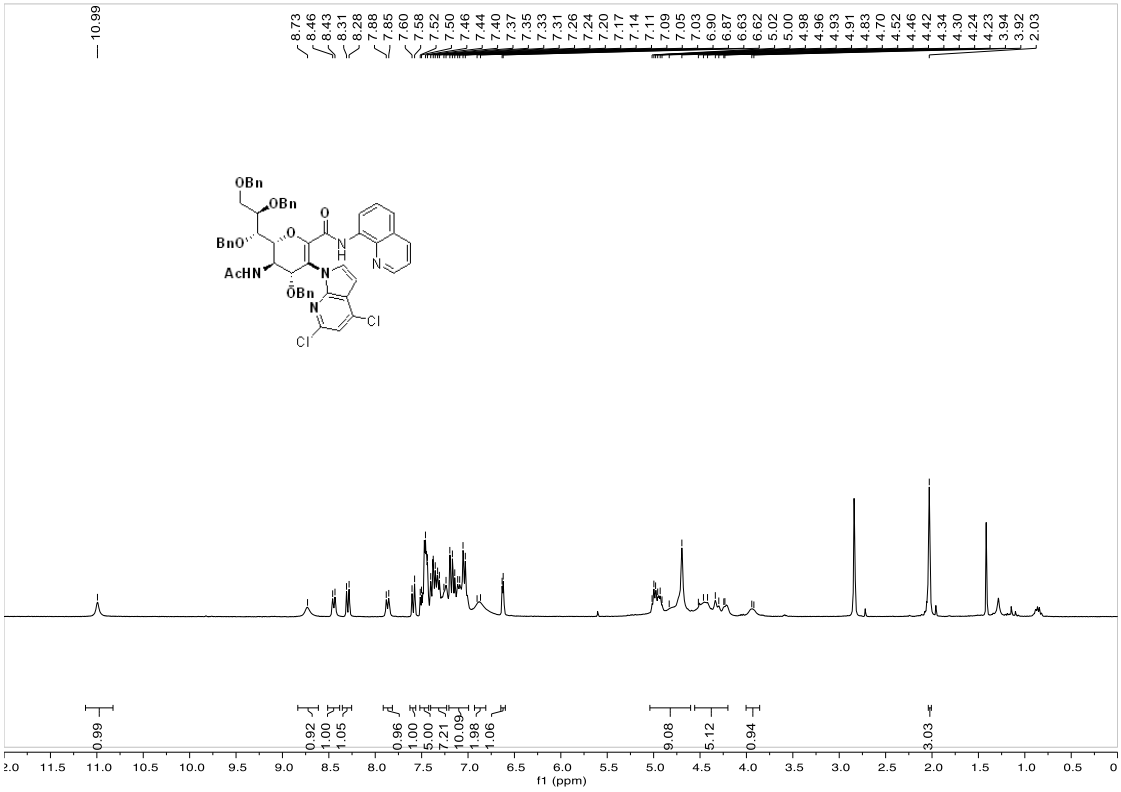
^{13}C NMR spectrum of **3c** (d_6-actone)



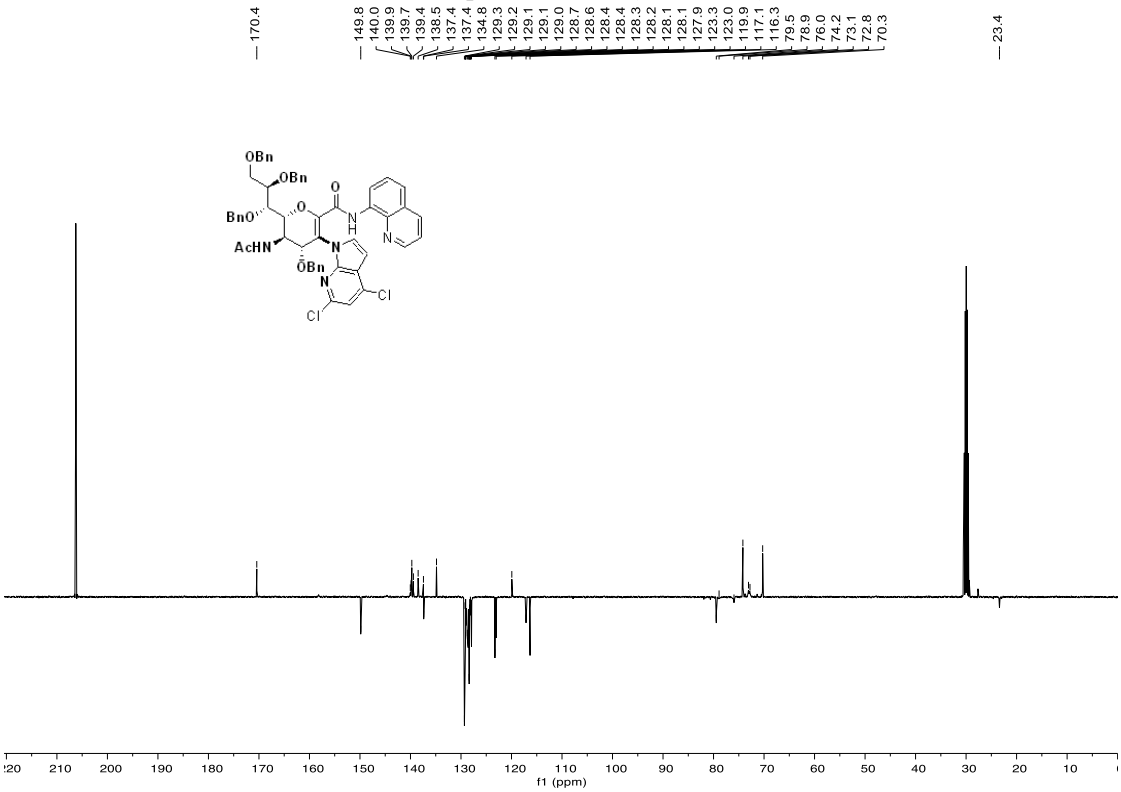
^{1}H NMR spectrum of **3d** (d_6-actone)



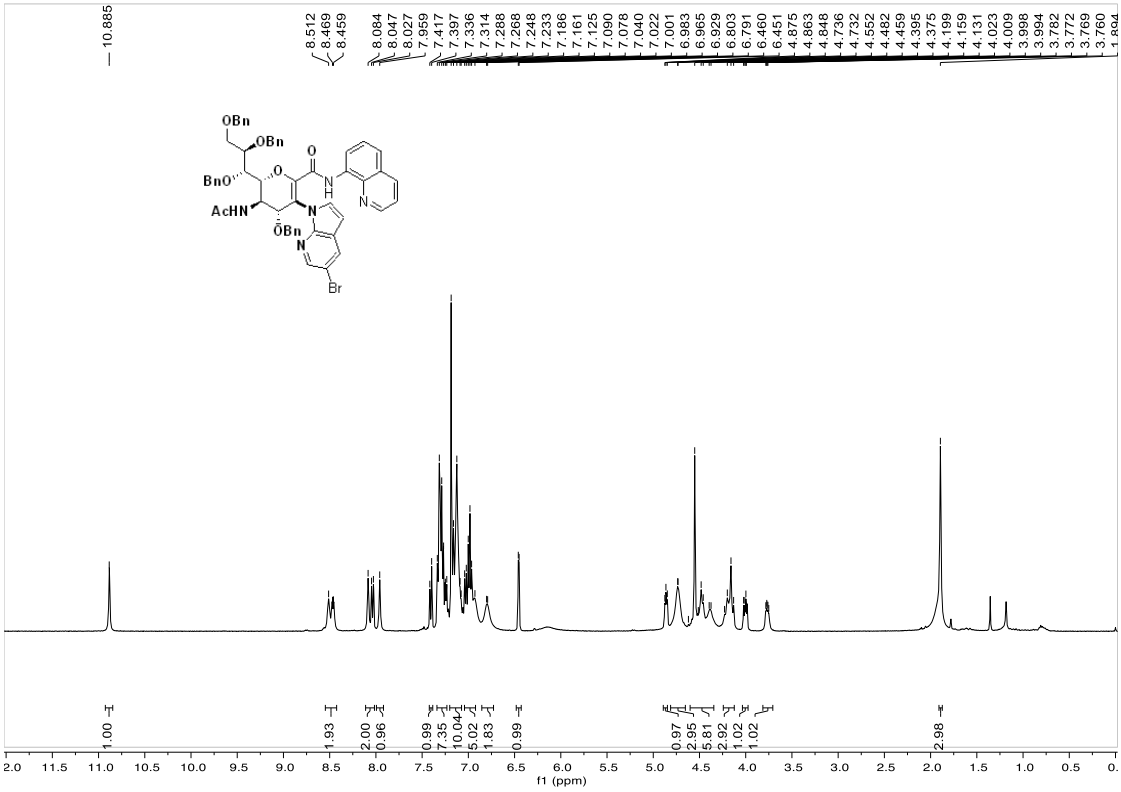
^{13}C NMR spectrum of **3d** (d_6-actone)



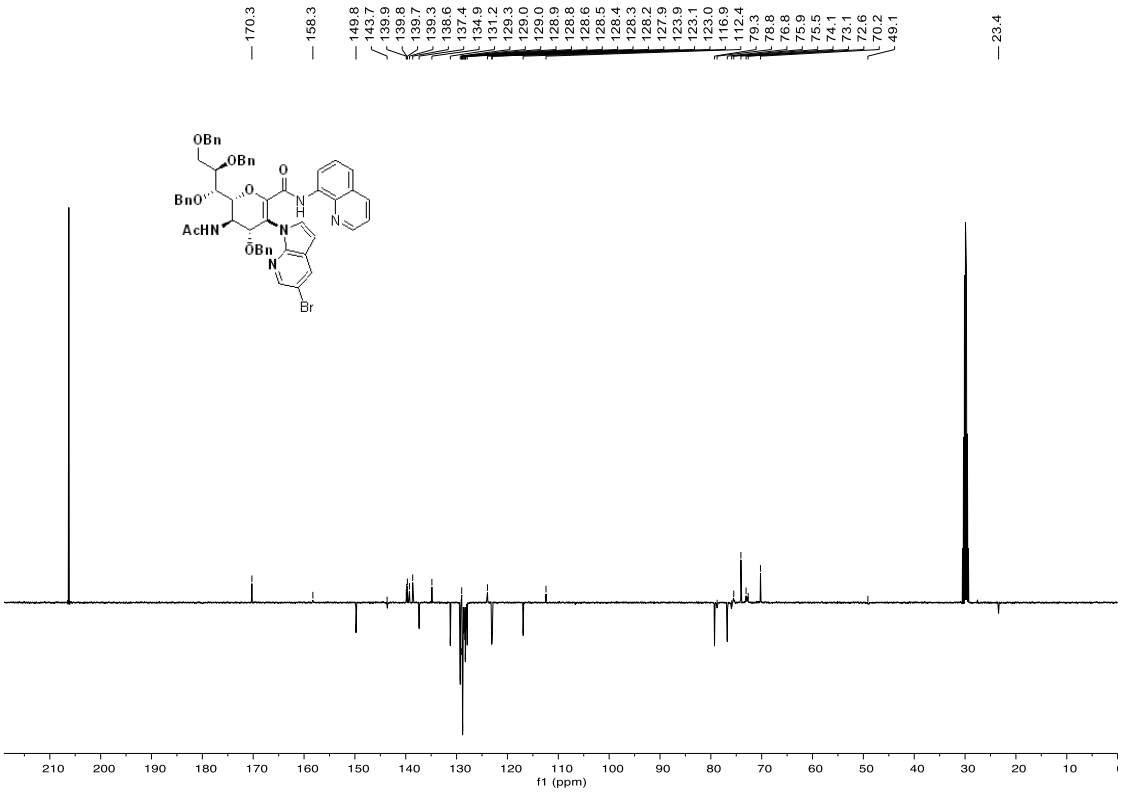
^{1}H NMR spectrum of **3e** (d_6-actone)



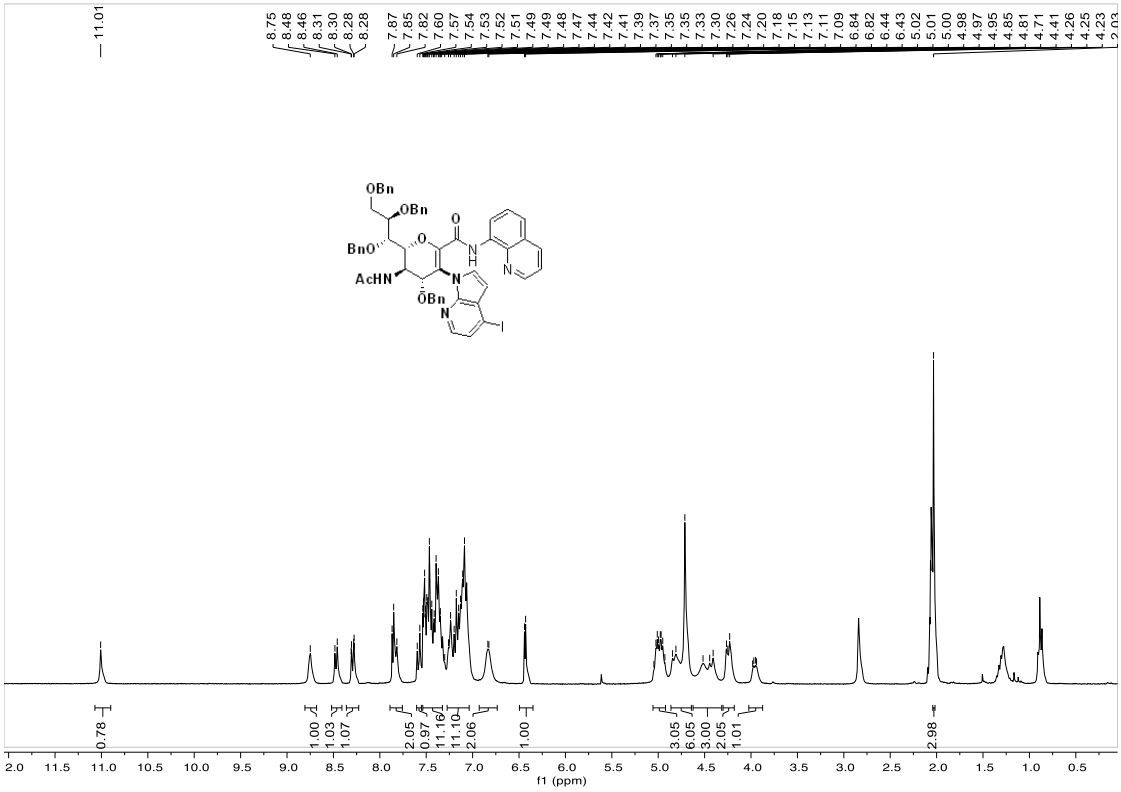
^{13}C NMR spectrum of **3e** (d_6-actone)



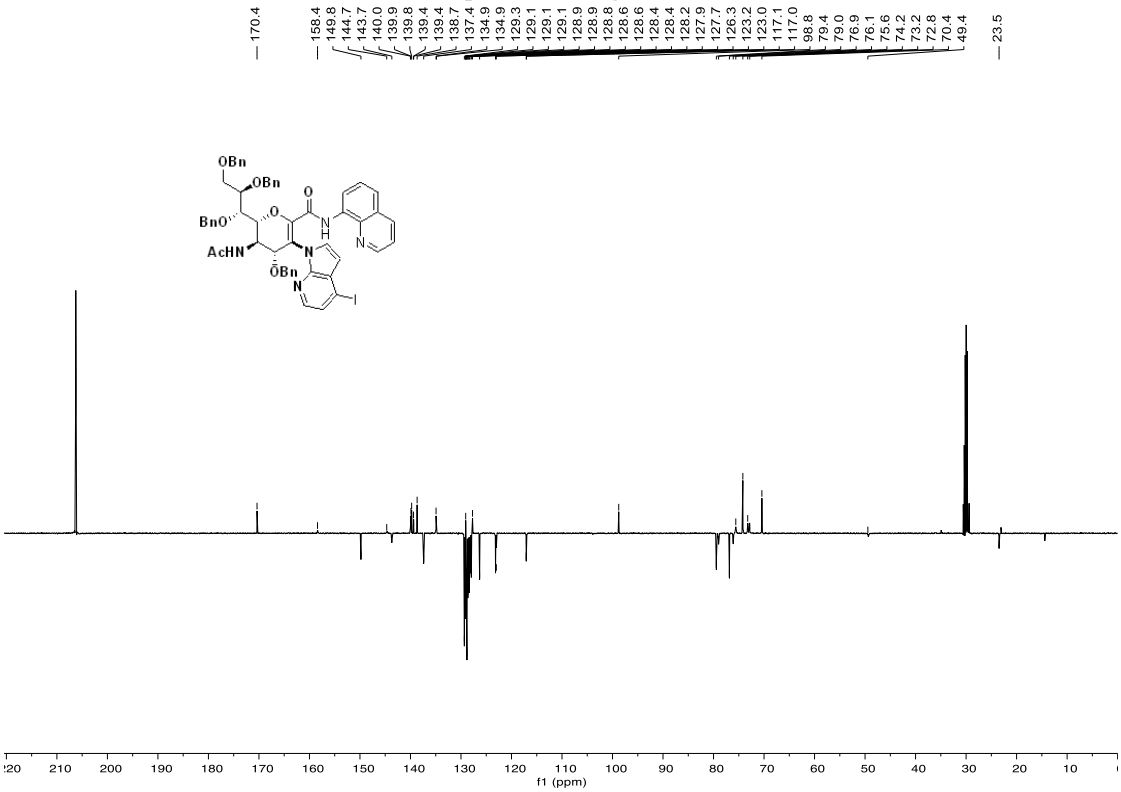
^{1}H NMR spectrum of **3f** ($CDCl_3$)



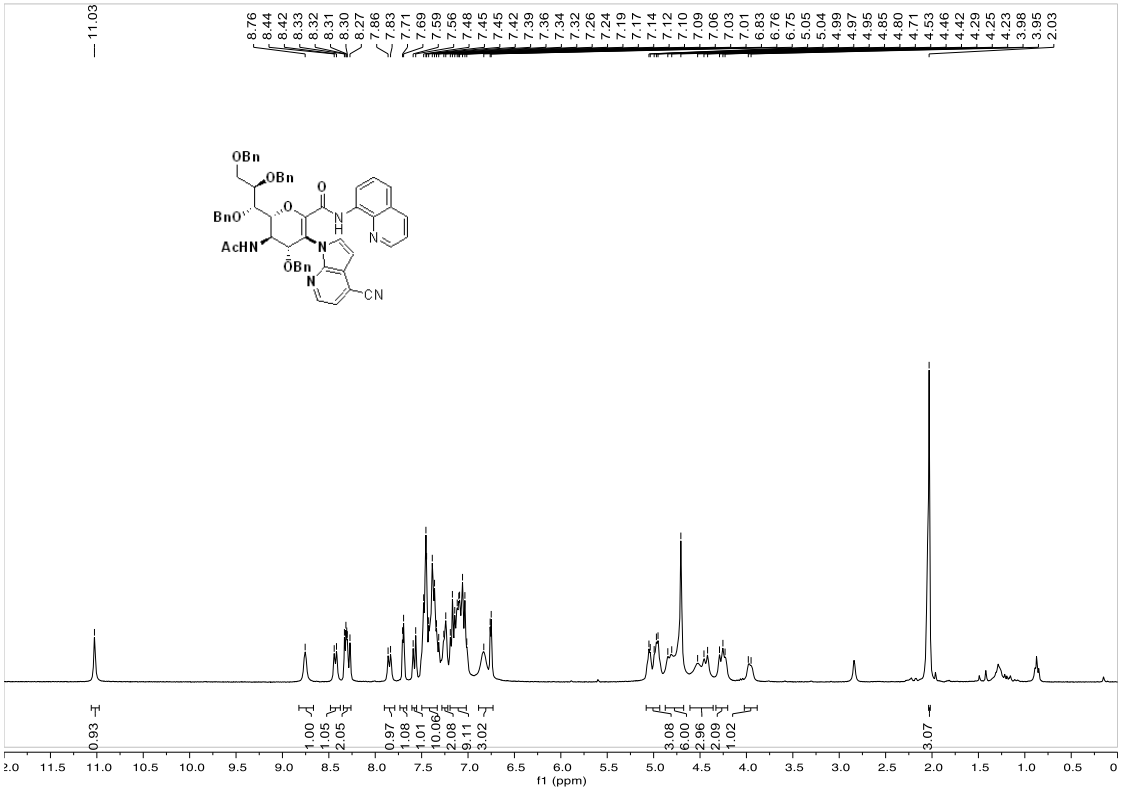
^{13}C NMR spectrum of **3f** (d_6-actone)



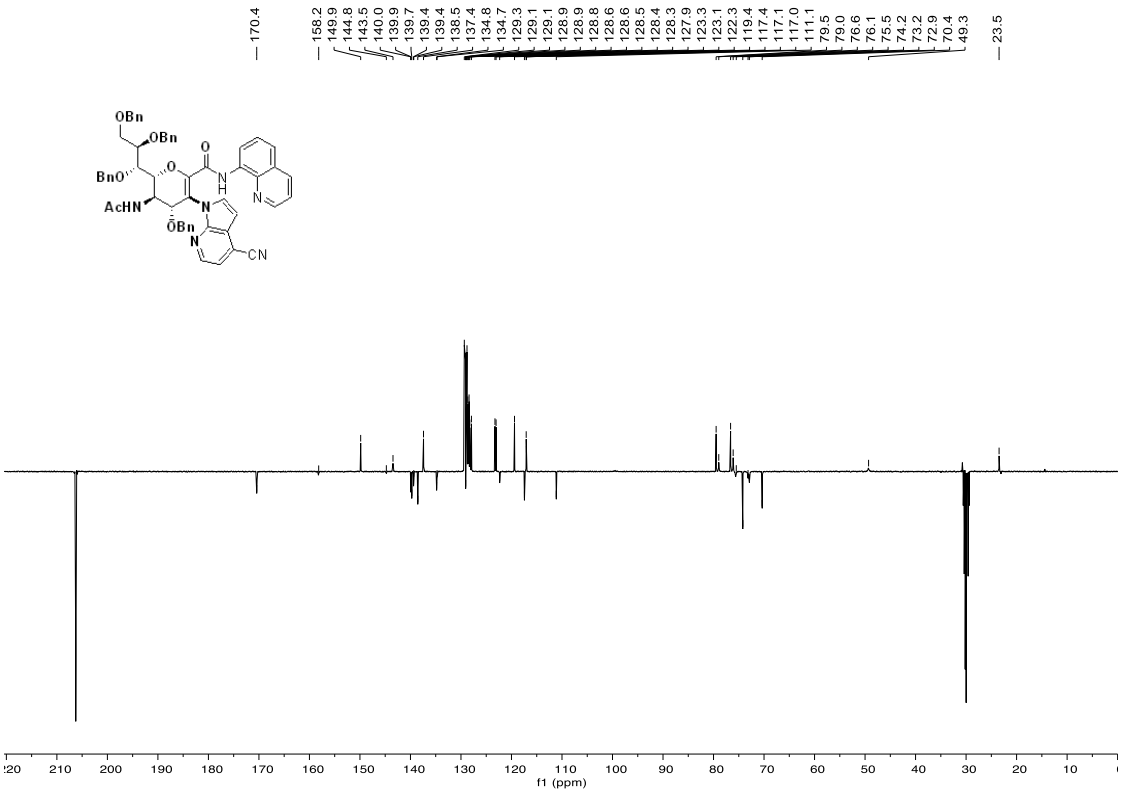
^{1}H NMR spectrum of **3g** (d_6-actone)



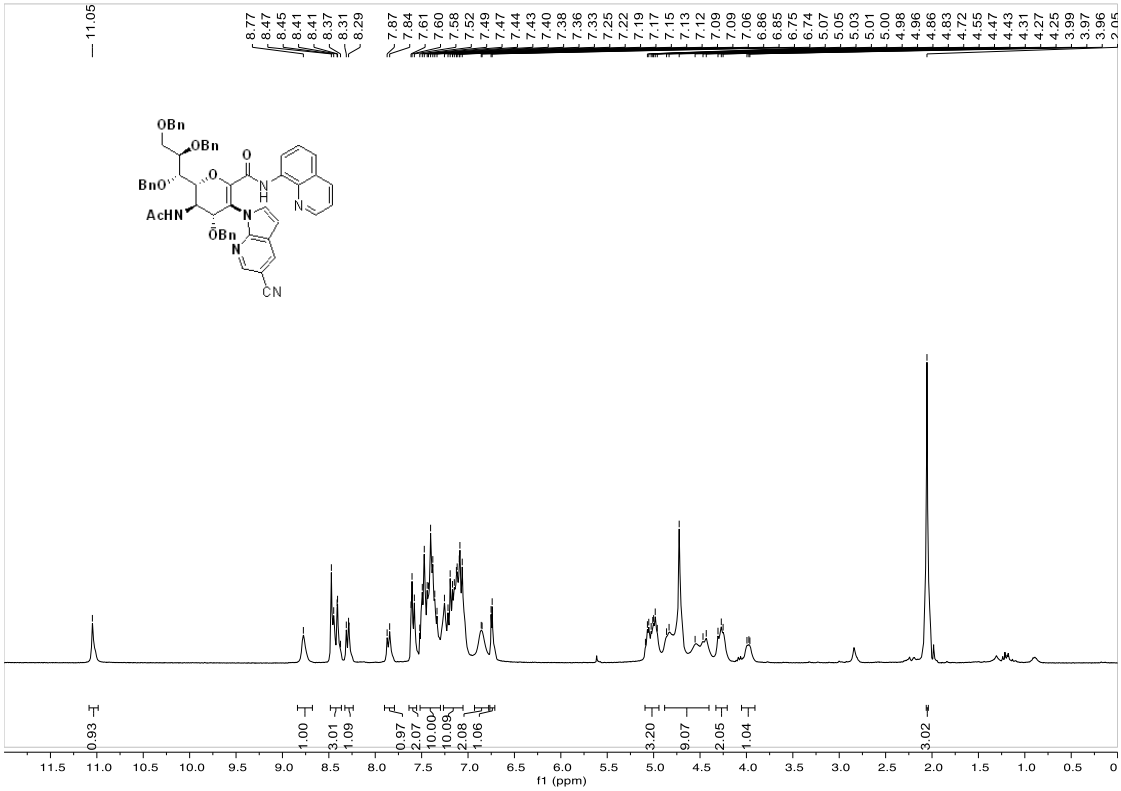
^{13}C NMR spectrum of **3g** (d_6-actone)



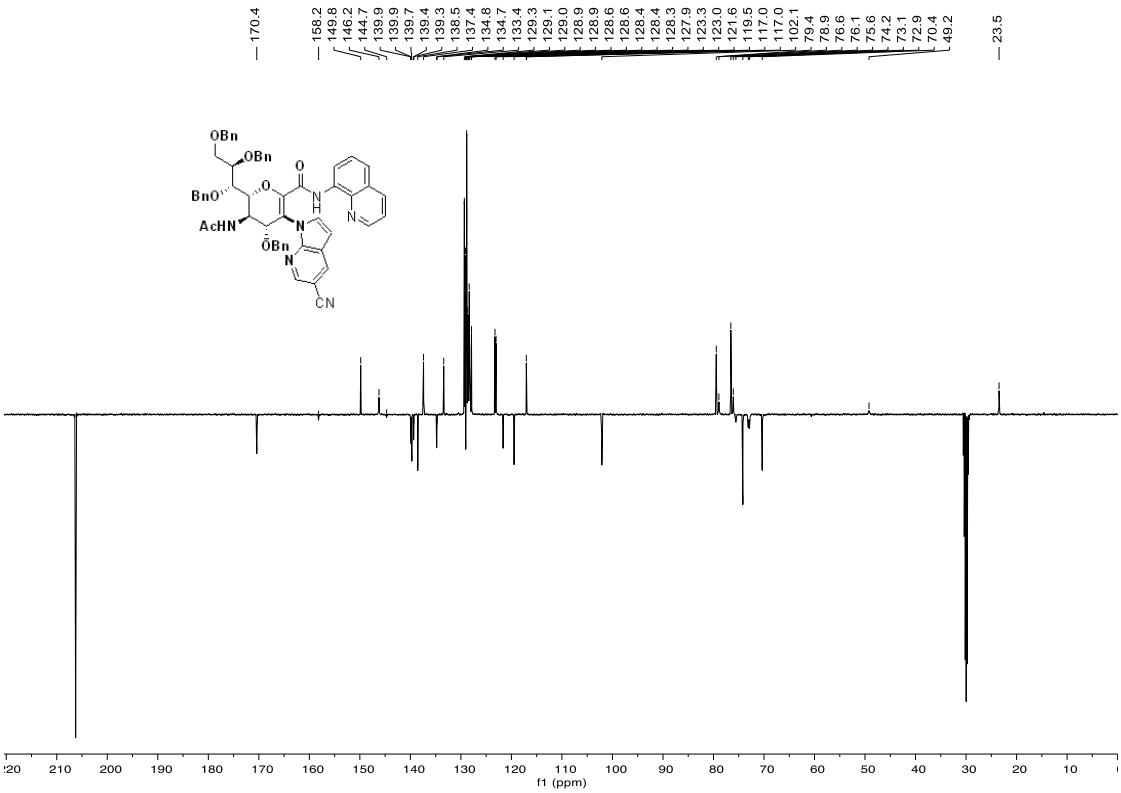
^{1}H NMR spectrum of **3h** (d_6-actone)



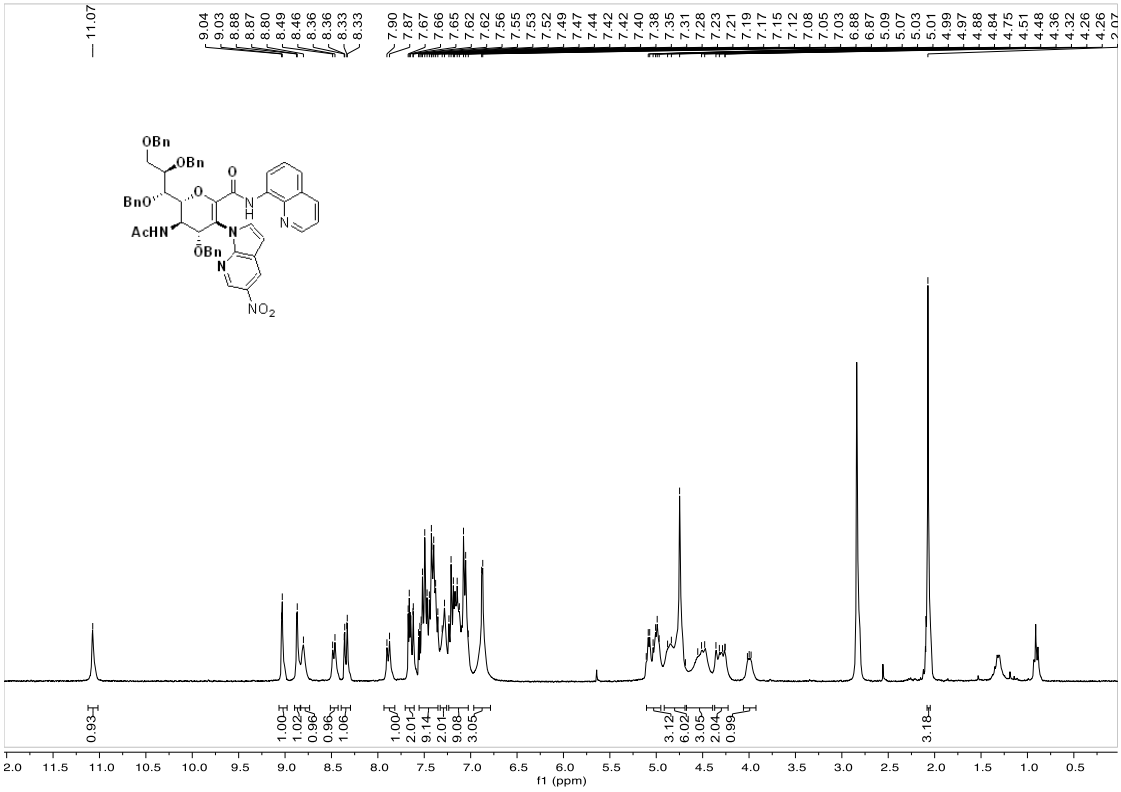
^{13}C NMR spectrum of **3h** (d_6-actone)



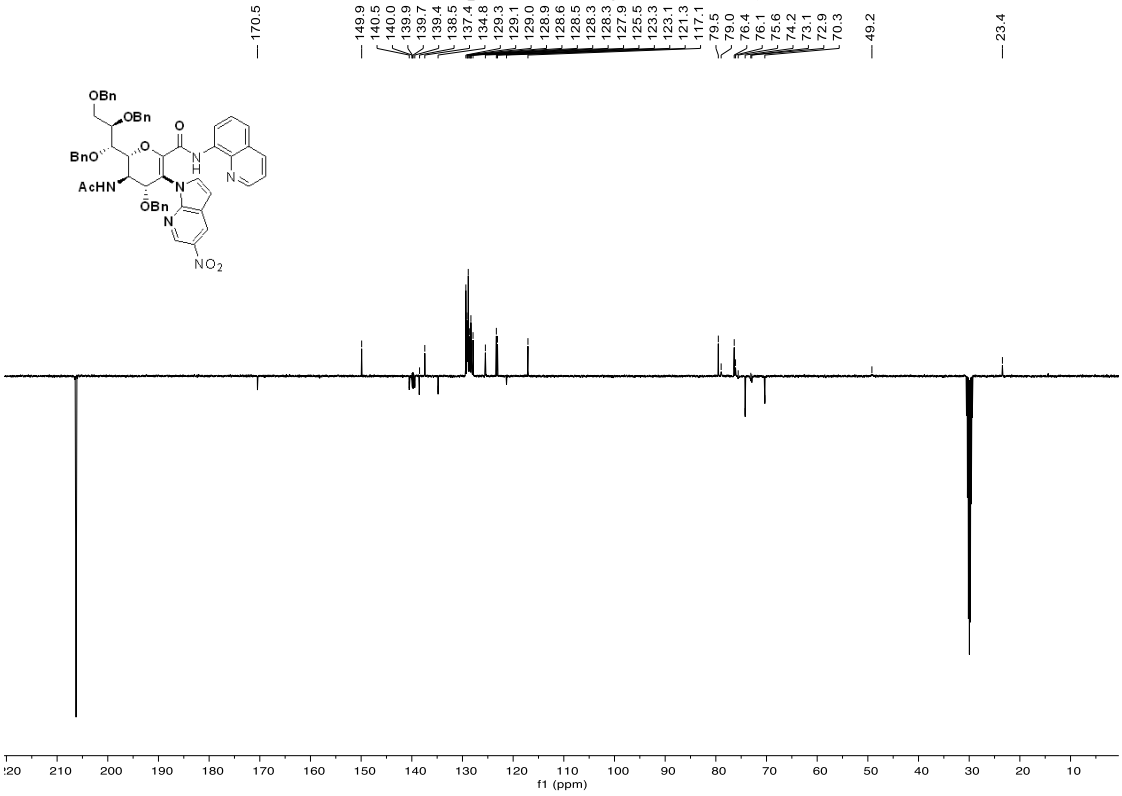
^{1}H NMR spectrum of **3i** (d_6-actone)



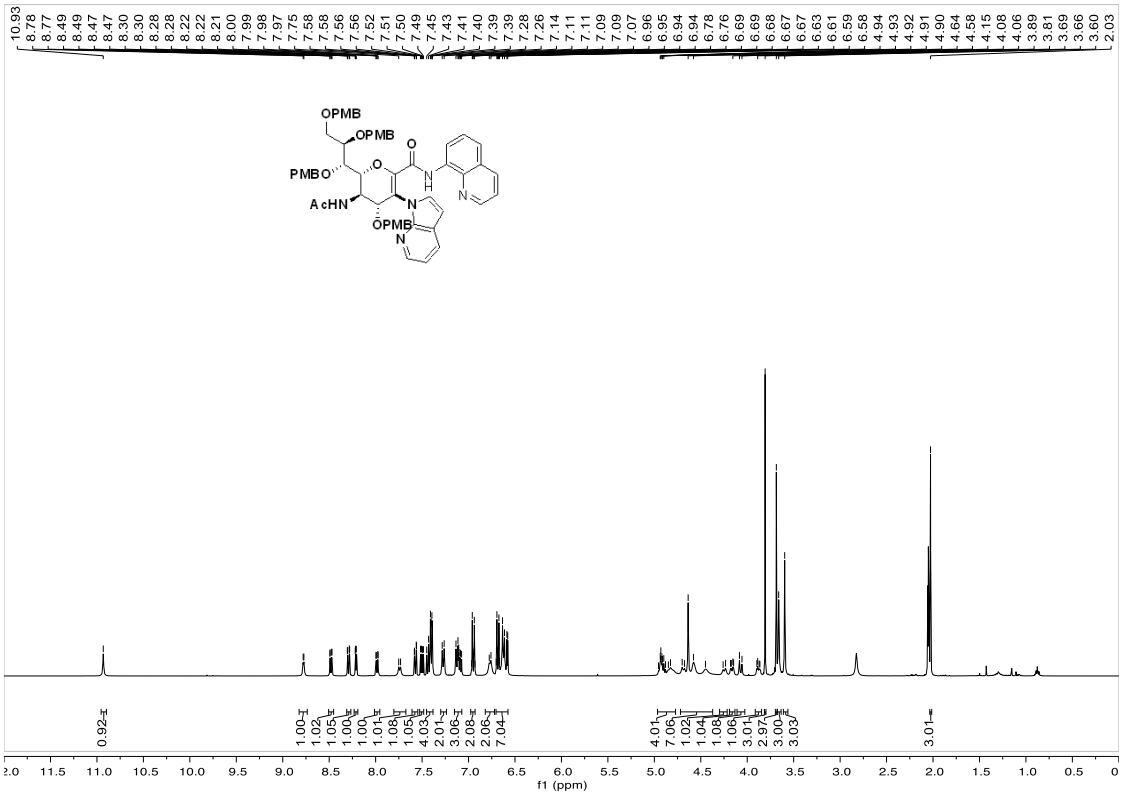
^{13}C NMR spectrum of **3i** (d_6-actone)



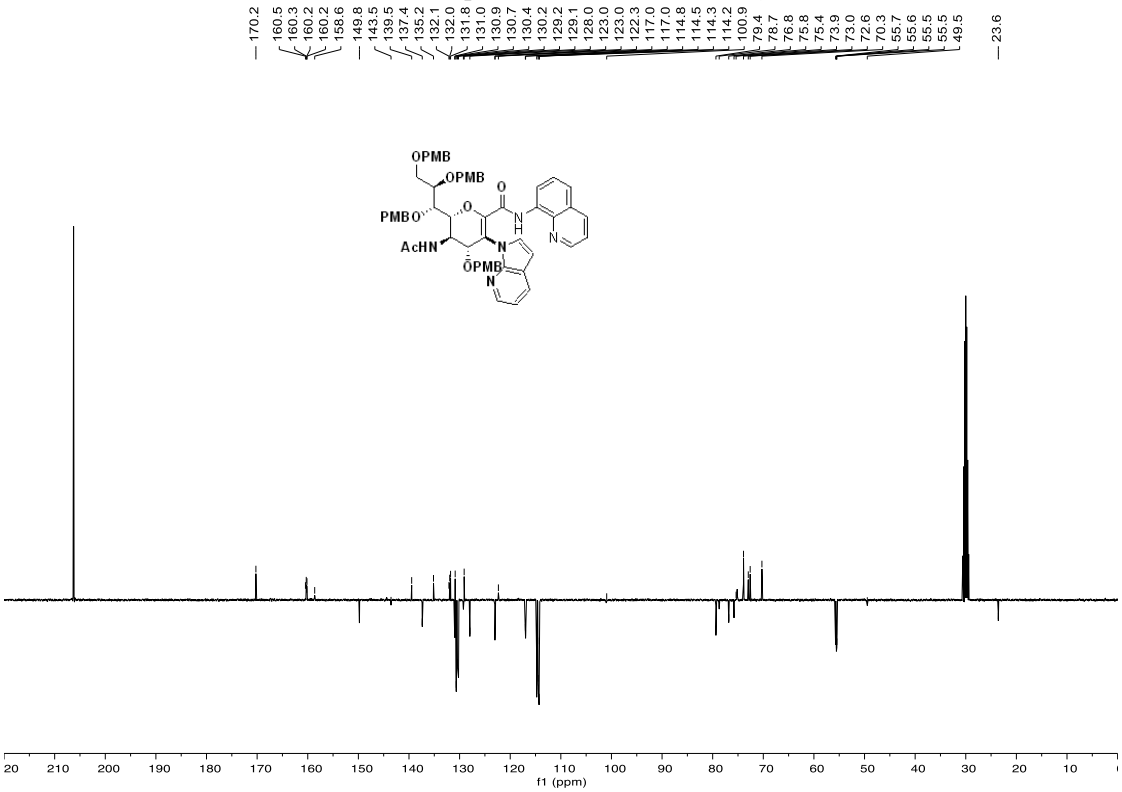
^{1}H NMR spectrum of **3j** (d_6-actone)



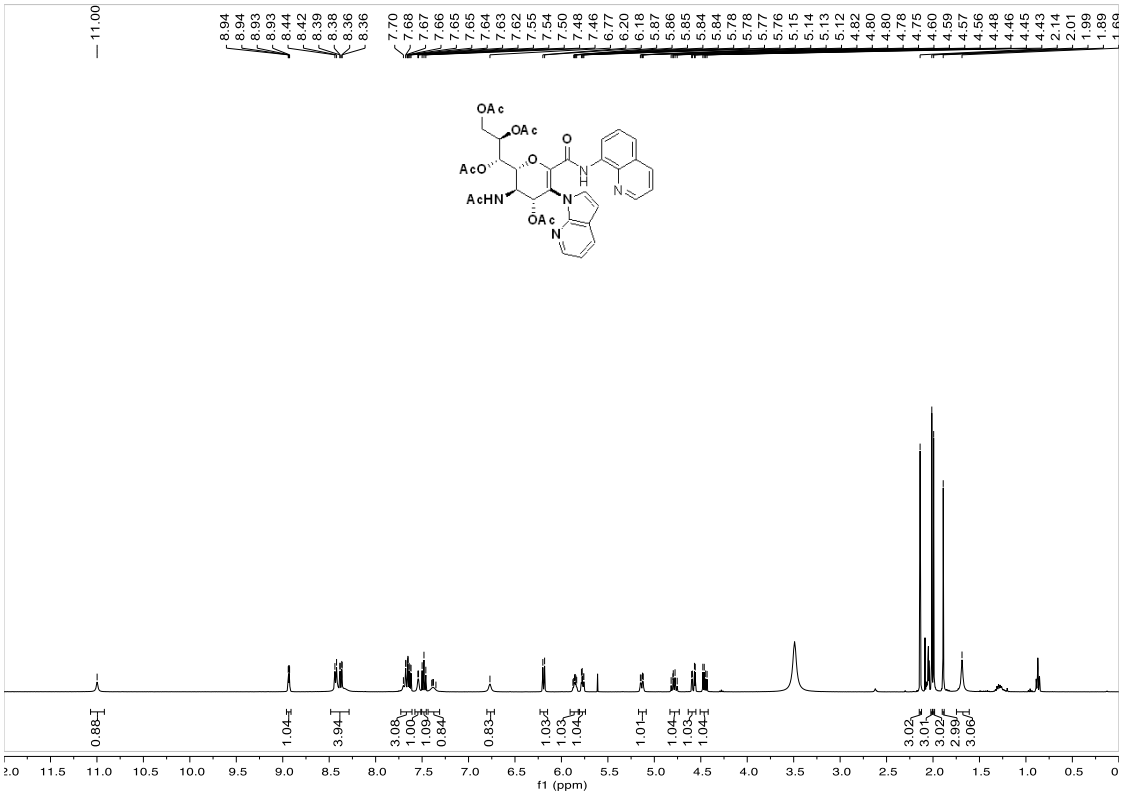
^{13}C NMR spectrum of **3j** (d_6-actone)



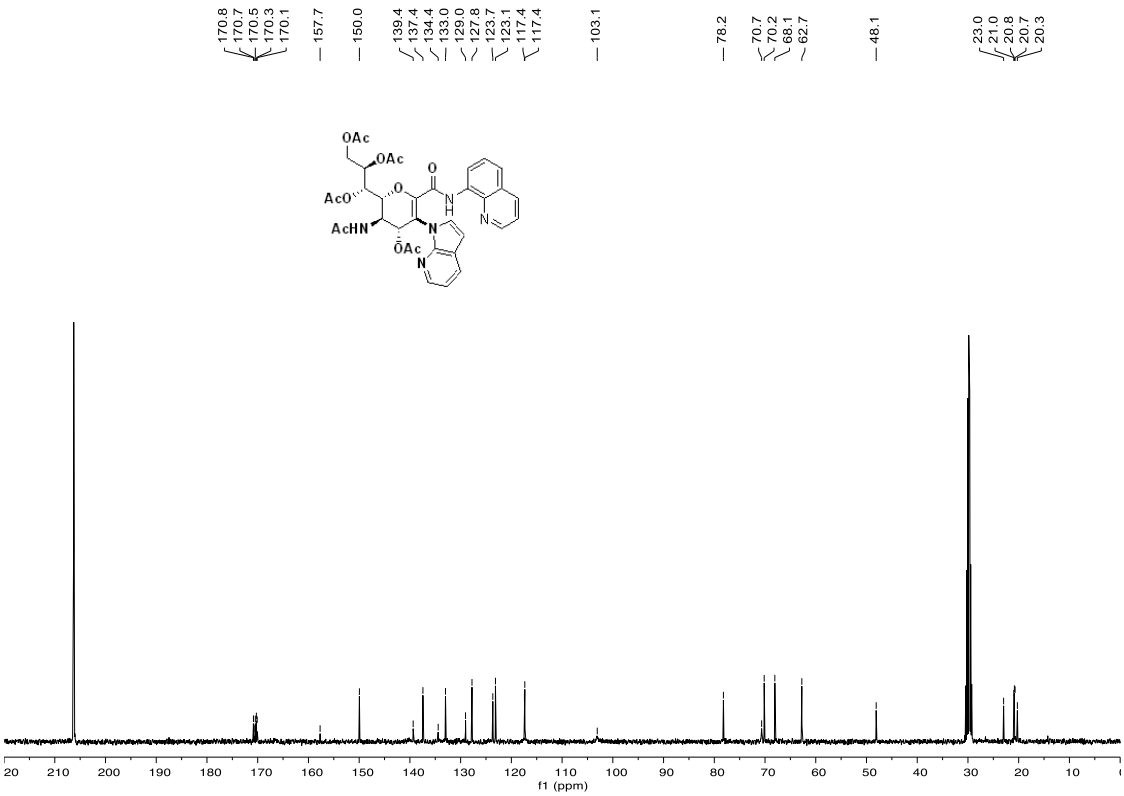
^{1}H NMR spectrum of **3k** (d_6-actone)



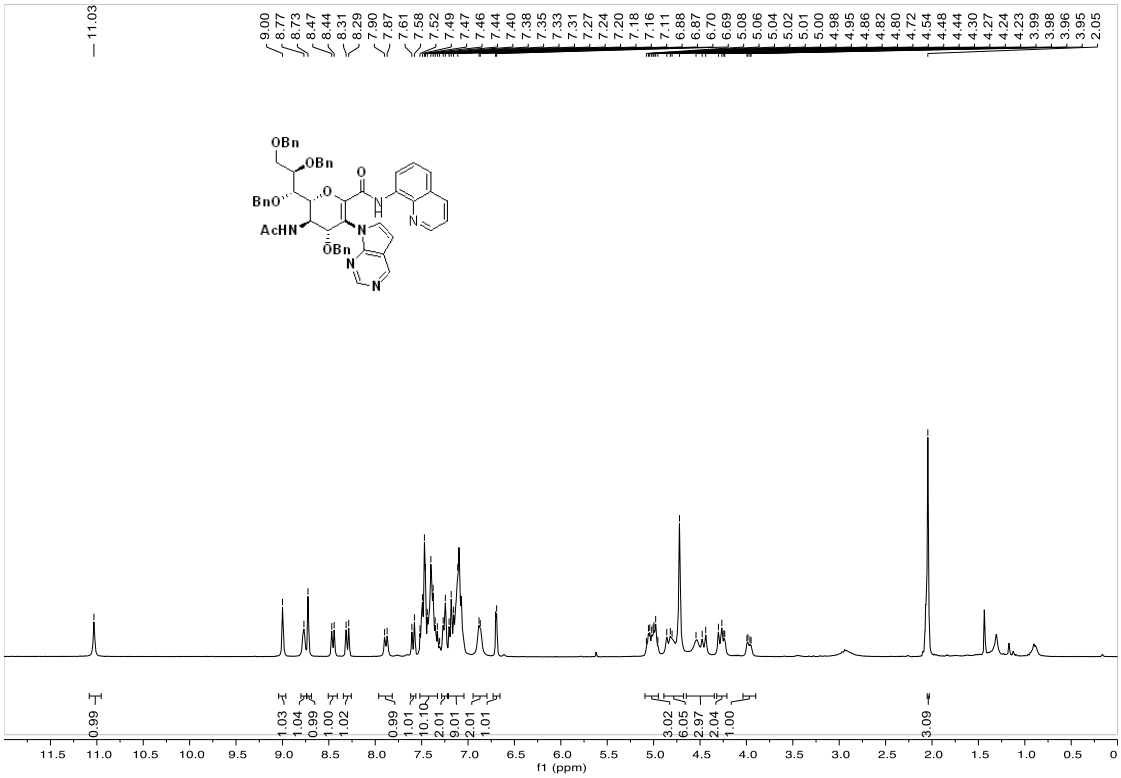
^{13}C NMR spectrum of **3k** (d_6-actone)



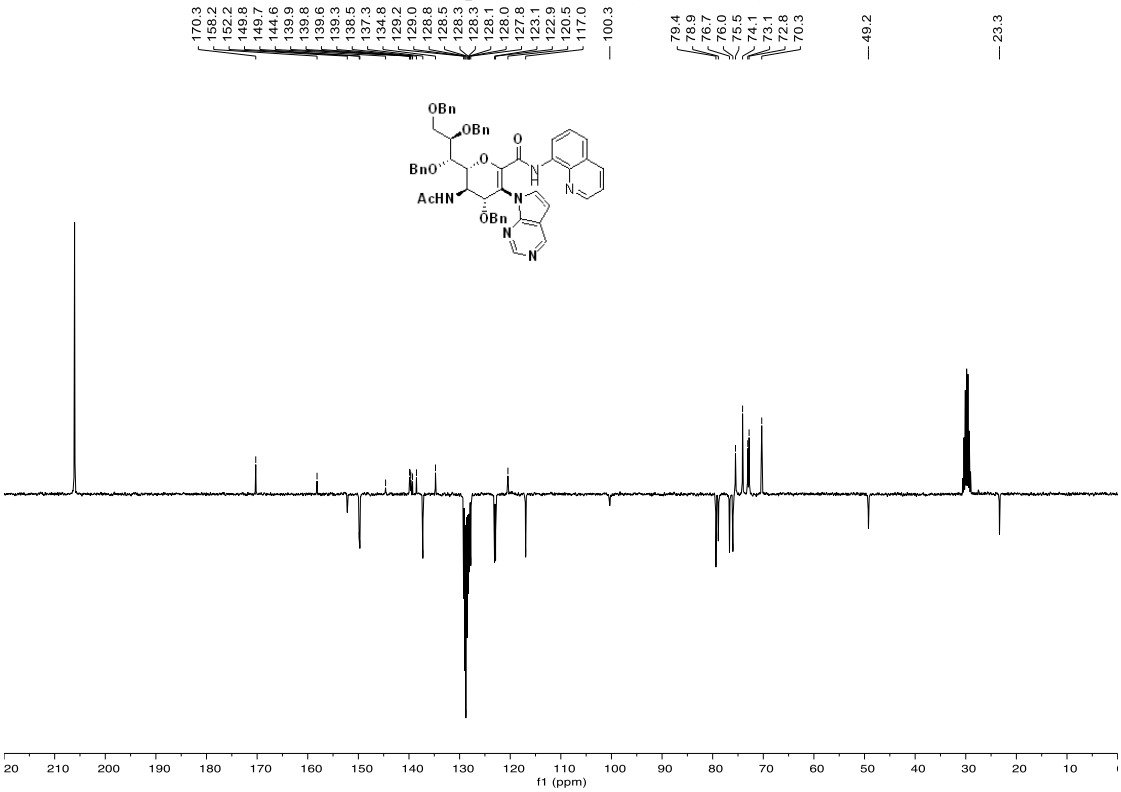
^{1}H NMR spectrum of **3l** (d_6-actone)



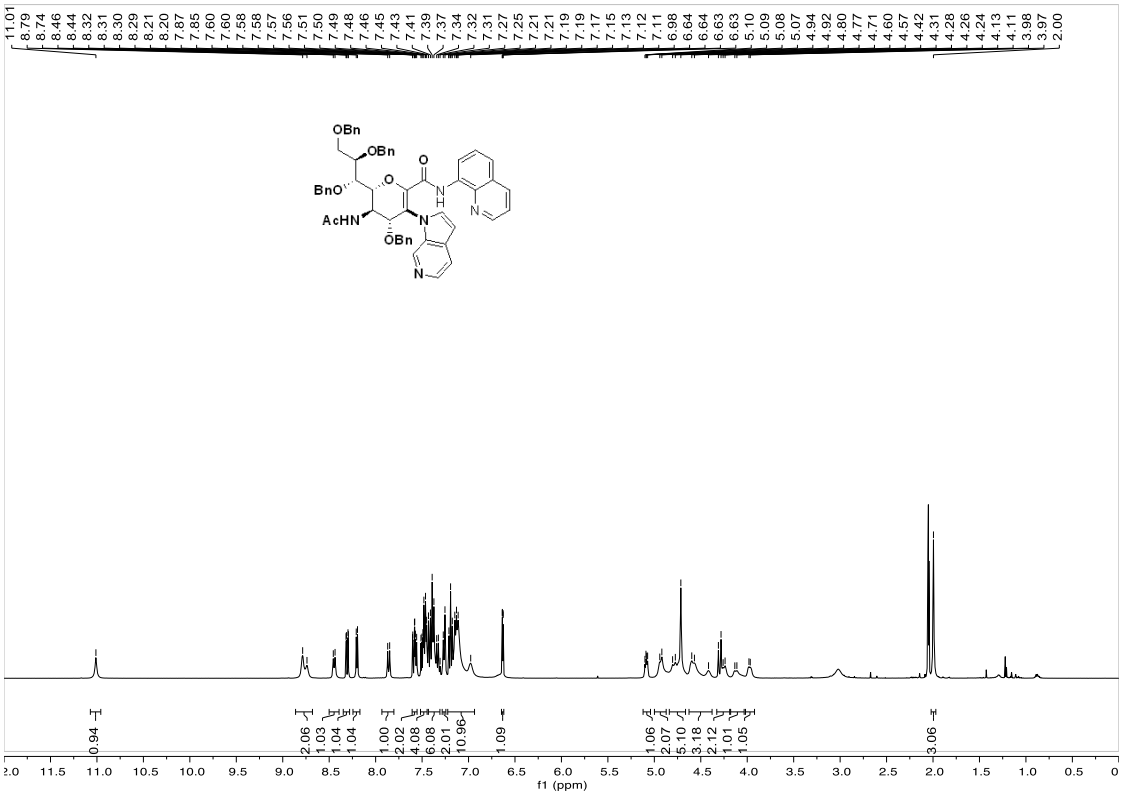
^{13}C NMR spectrum of **3l** (d_6-actone)



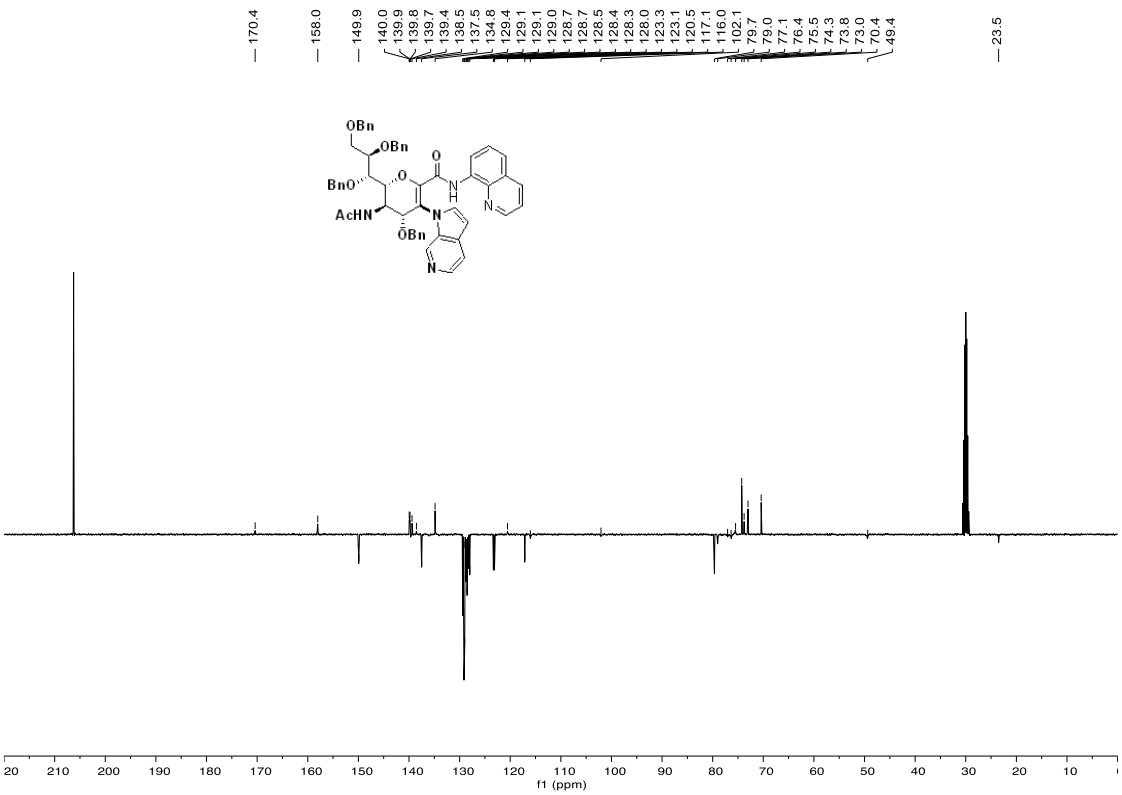
^{1}H NMR spectrum of **4a** (d_6-actone)



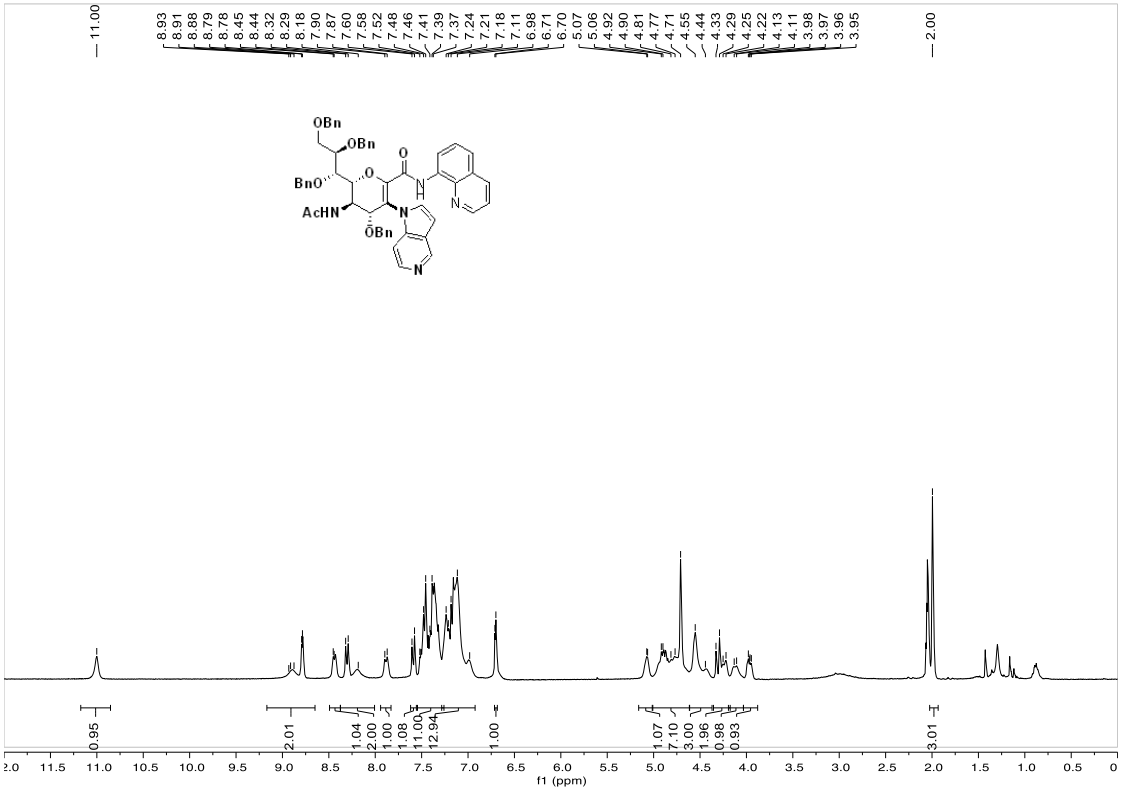
^{13}C NMR spectrum of **4a** (d_6-actone)



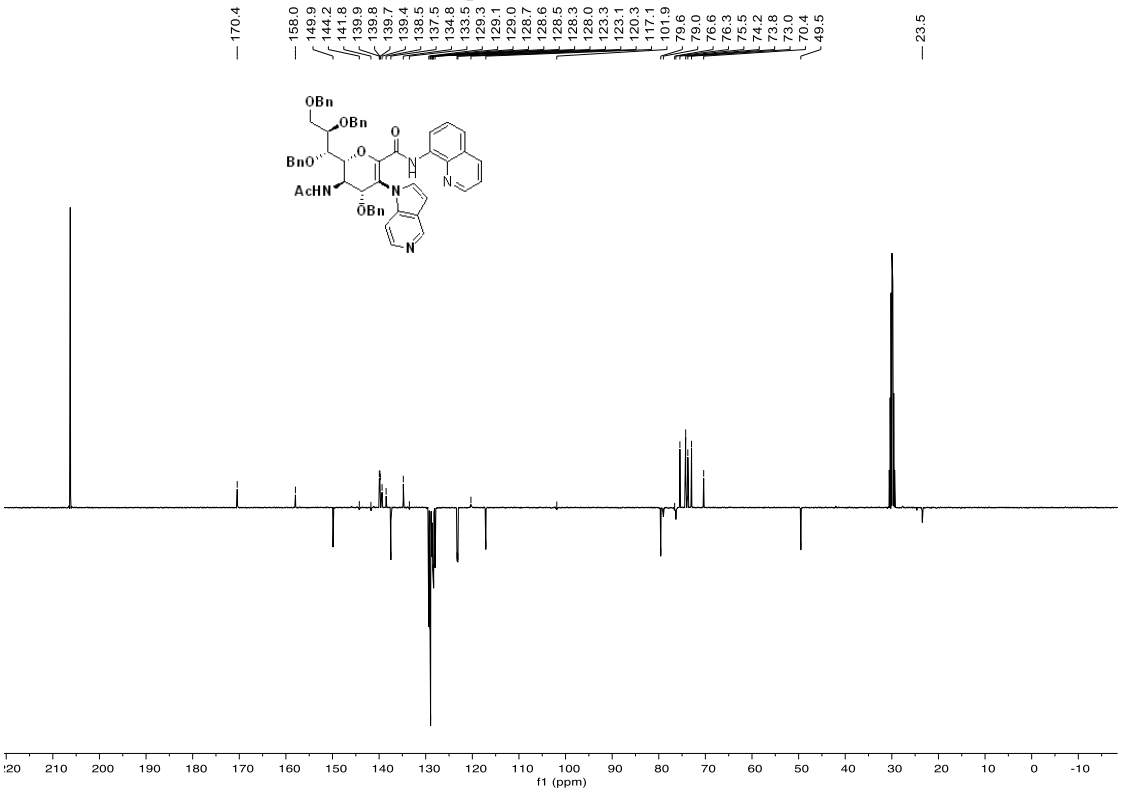
^{1}H NMR spectrum of **4b** (d_6-actone)



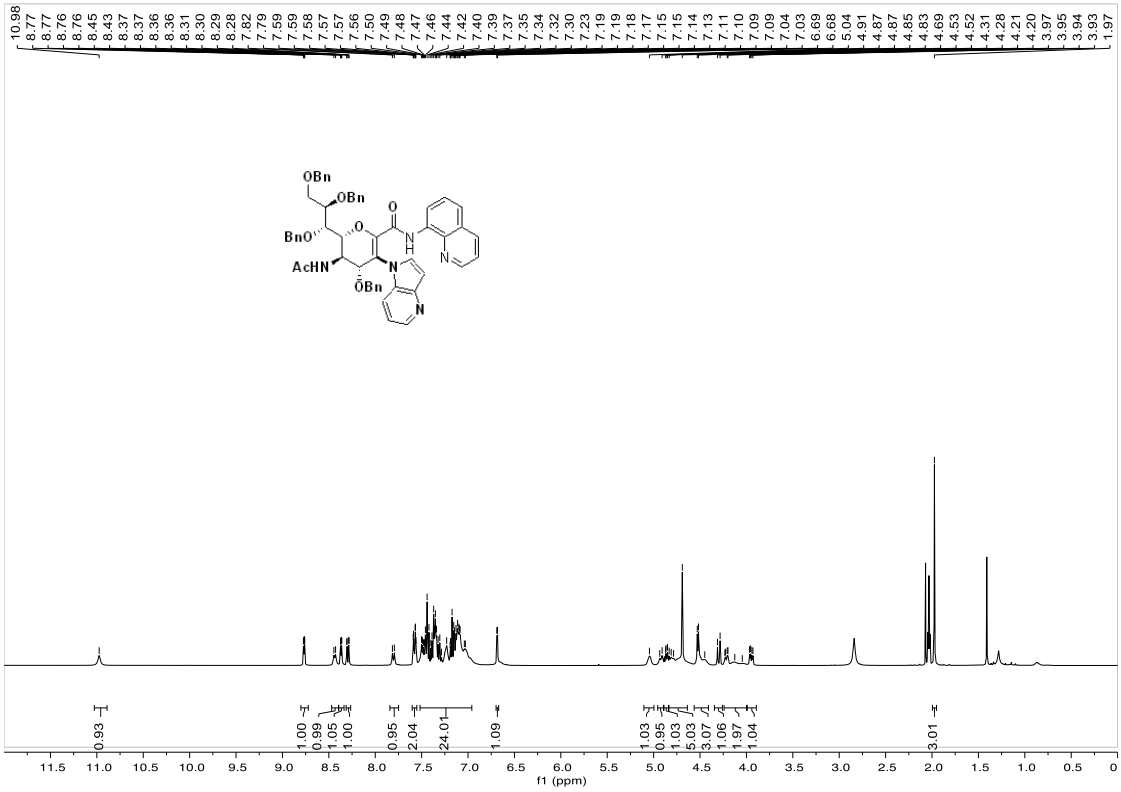
^{13}C NMR spectrum of **4b** (d_6-actone)



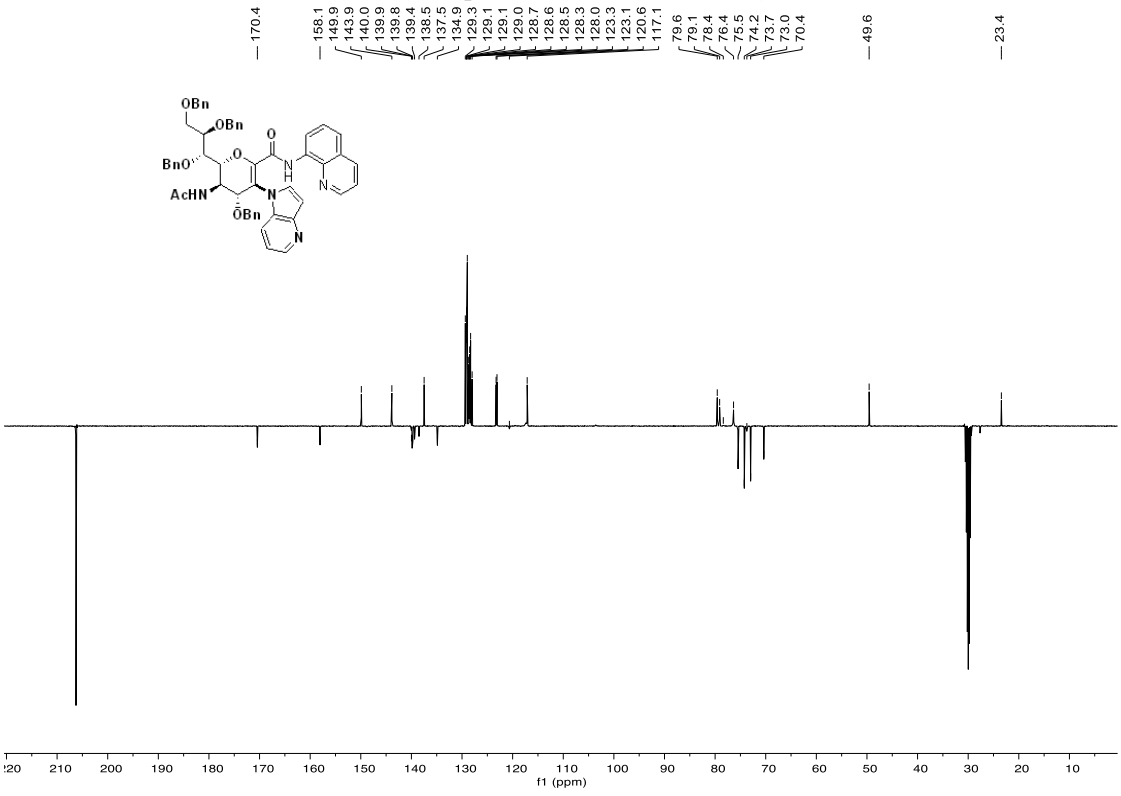
^{1}H NMR spectrum of **4c** (d_6-actone)



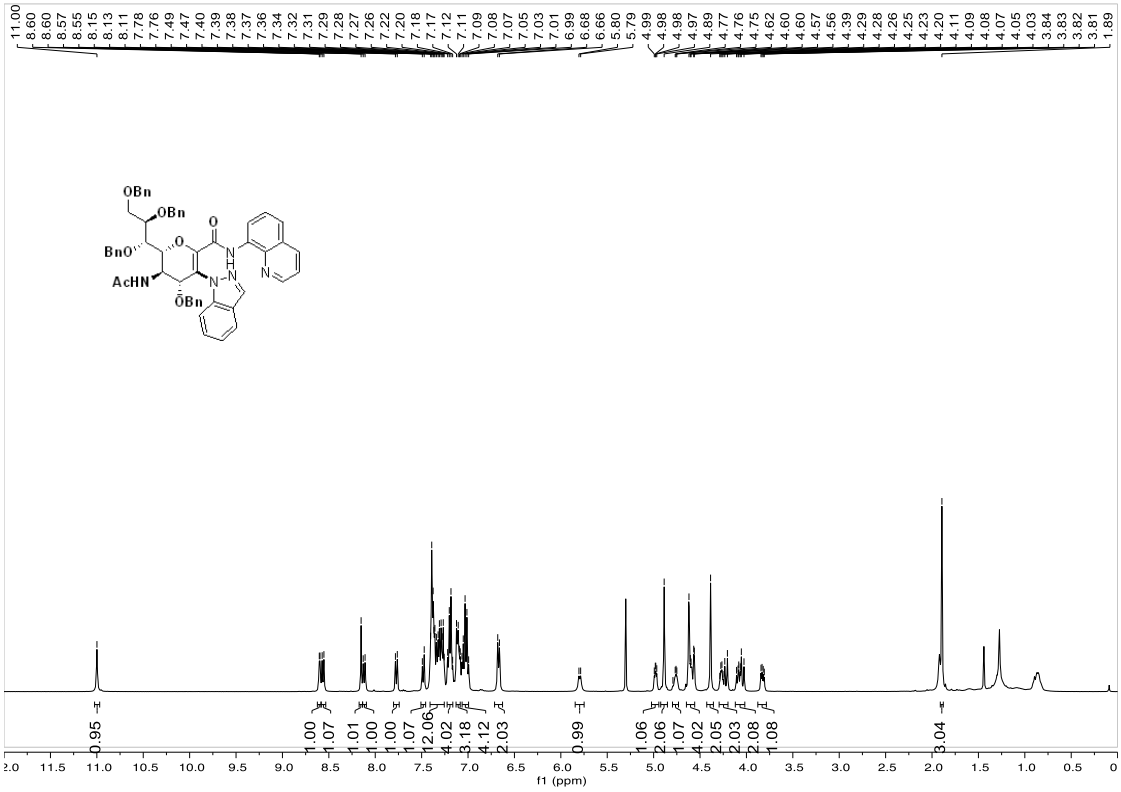
^{13}C NMR spectrum of **4c** (d_6-actone)



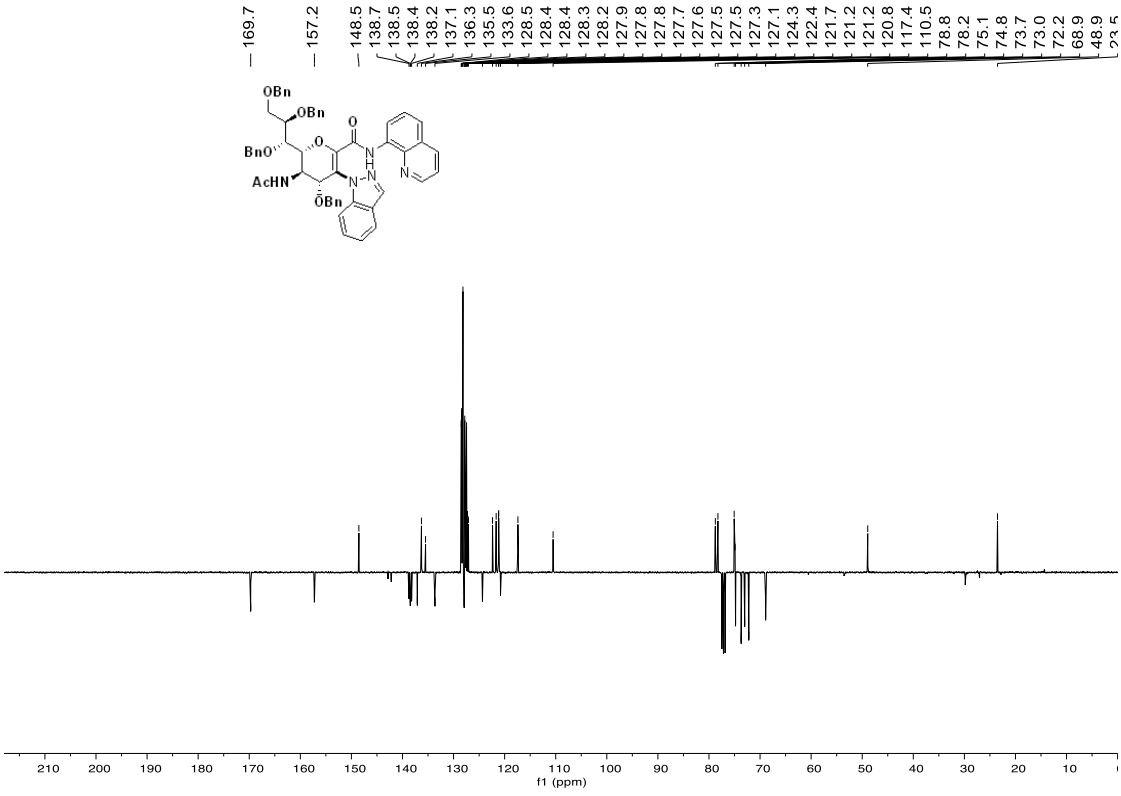
^{1}H NMR spectrum of **4d** (d_6-actone)



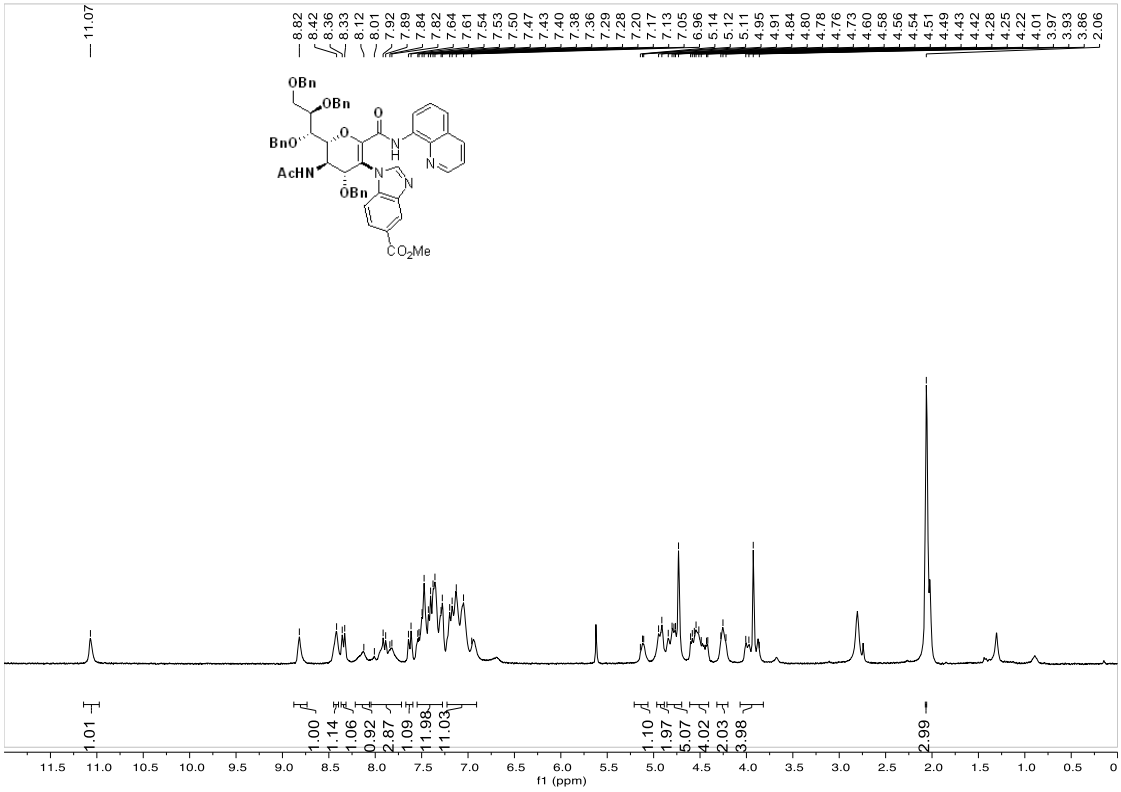
^{13}C NMR spectrum of **4d** (d_6-actone)



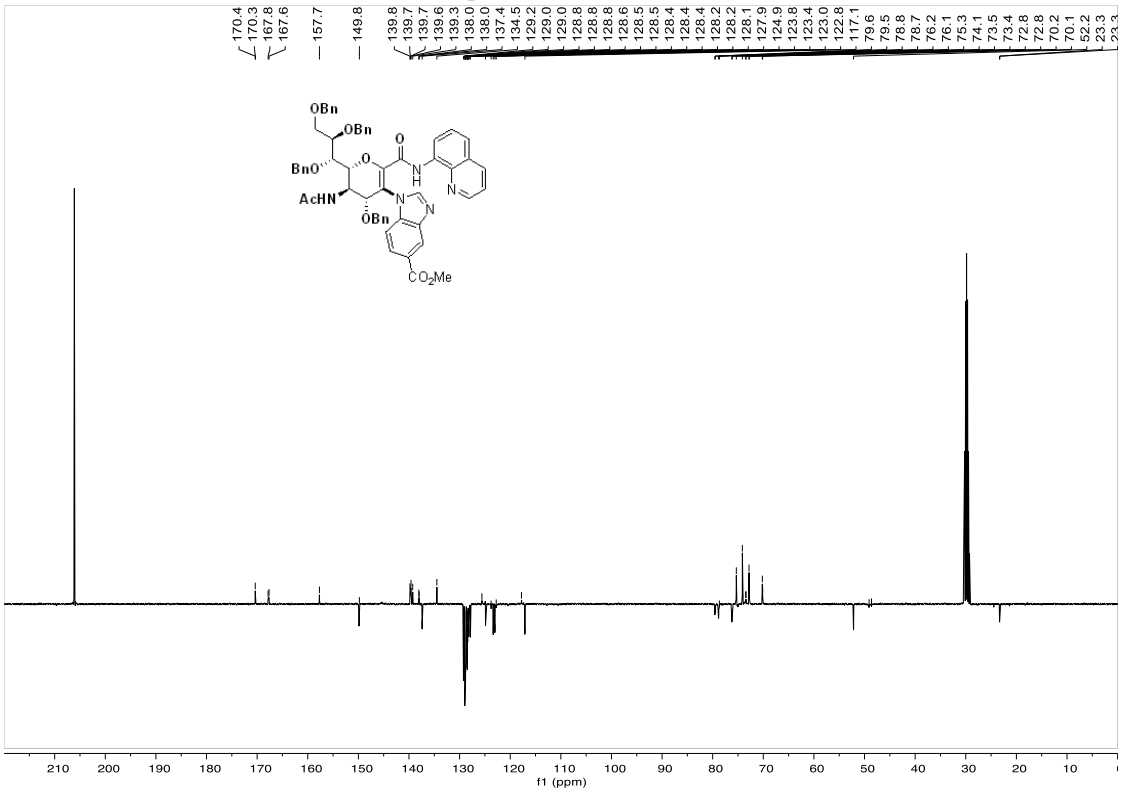
^{1}H NMR spectrum of **4e** ($CDCl_3$)



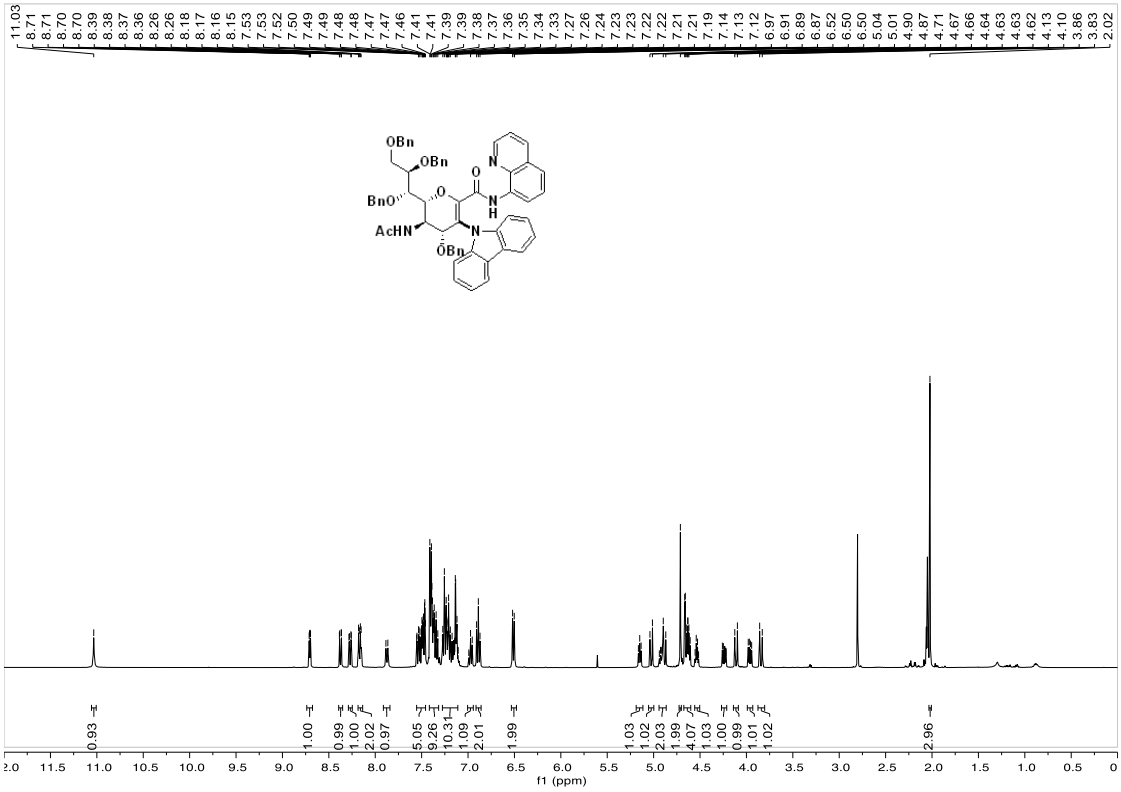
^{13}C NMR spectrum of **4e** ($CDCl_3$)



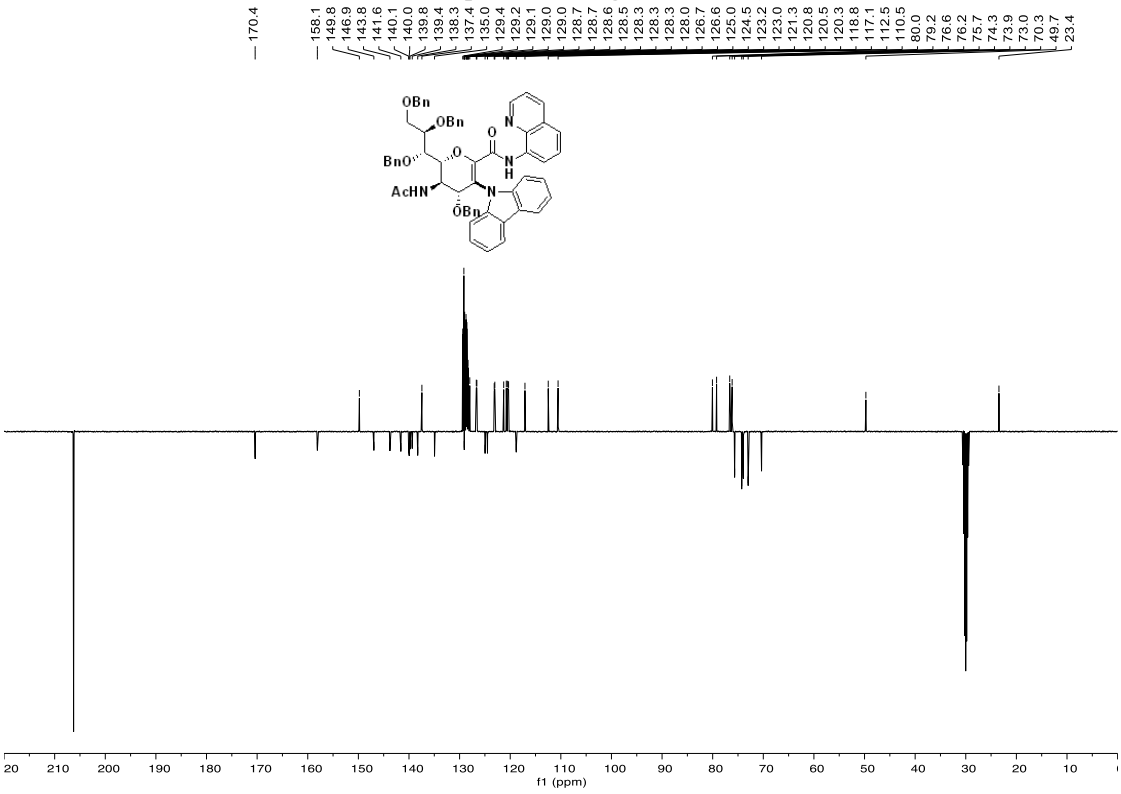
^{1}H NMR spectrum of **4f** (d_6-actone)



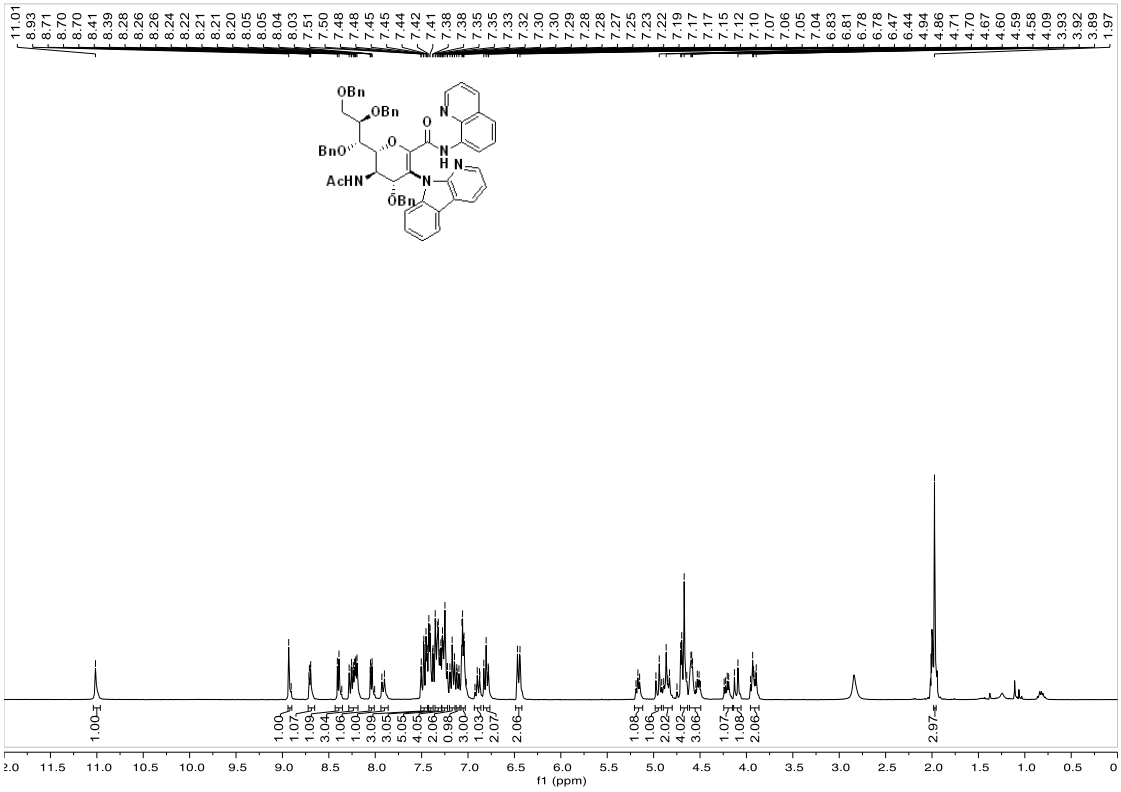
^{13}C NMR spectrum of **4f** (d_6-actone)



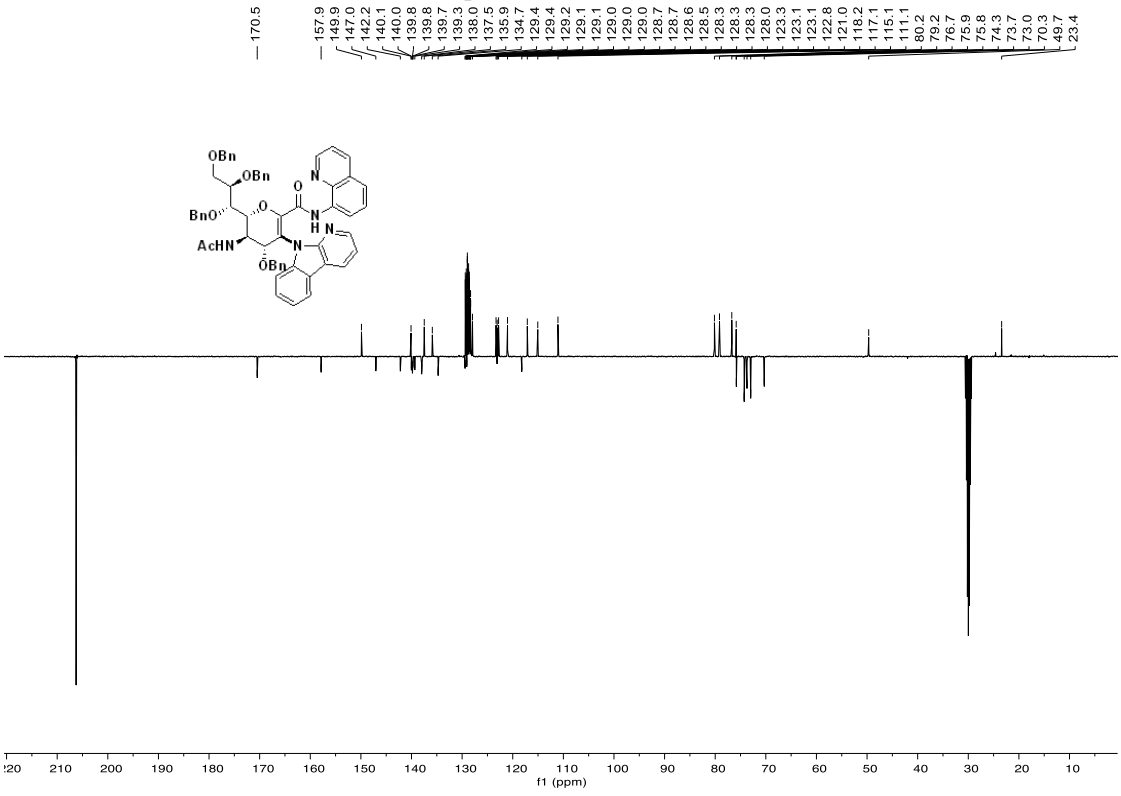
^{1}H NMR spectrum of **4g** (d_6-actone)



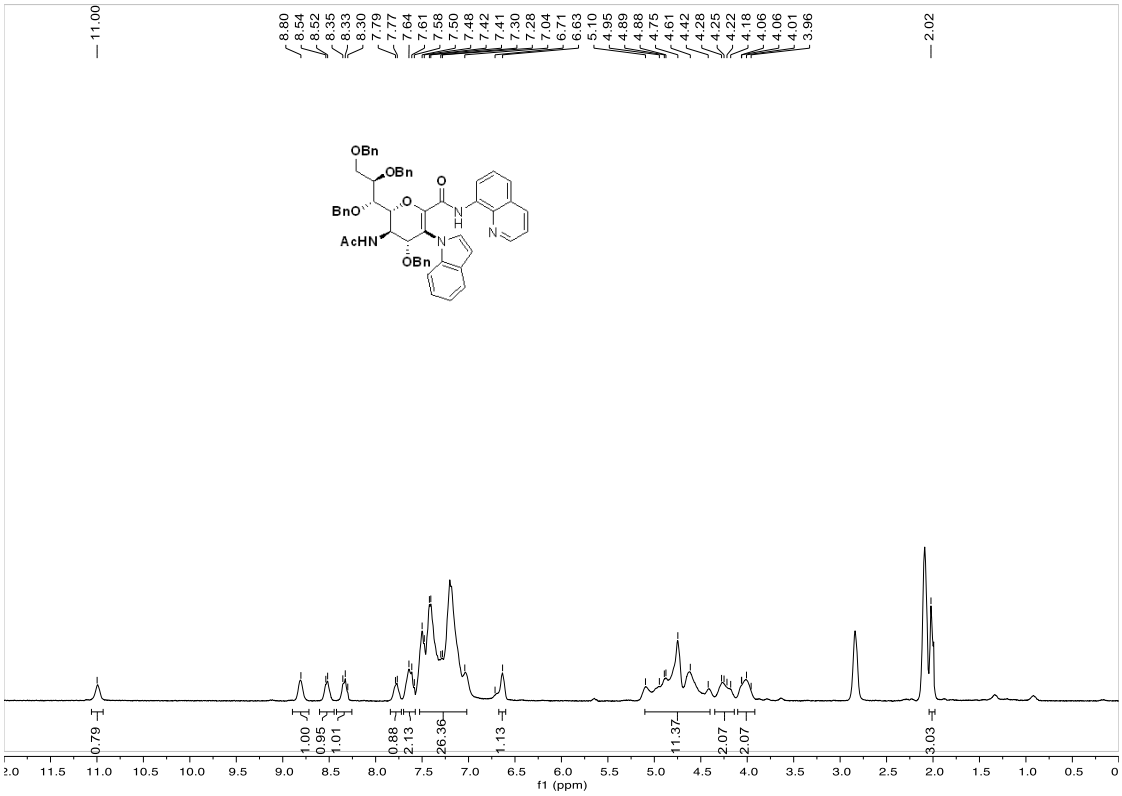
^{13}C NMR spectrum of **4g** (d_6-actone)



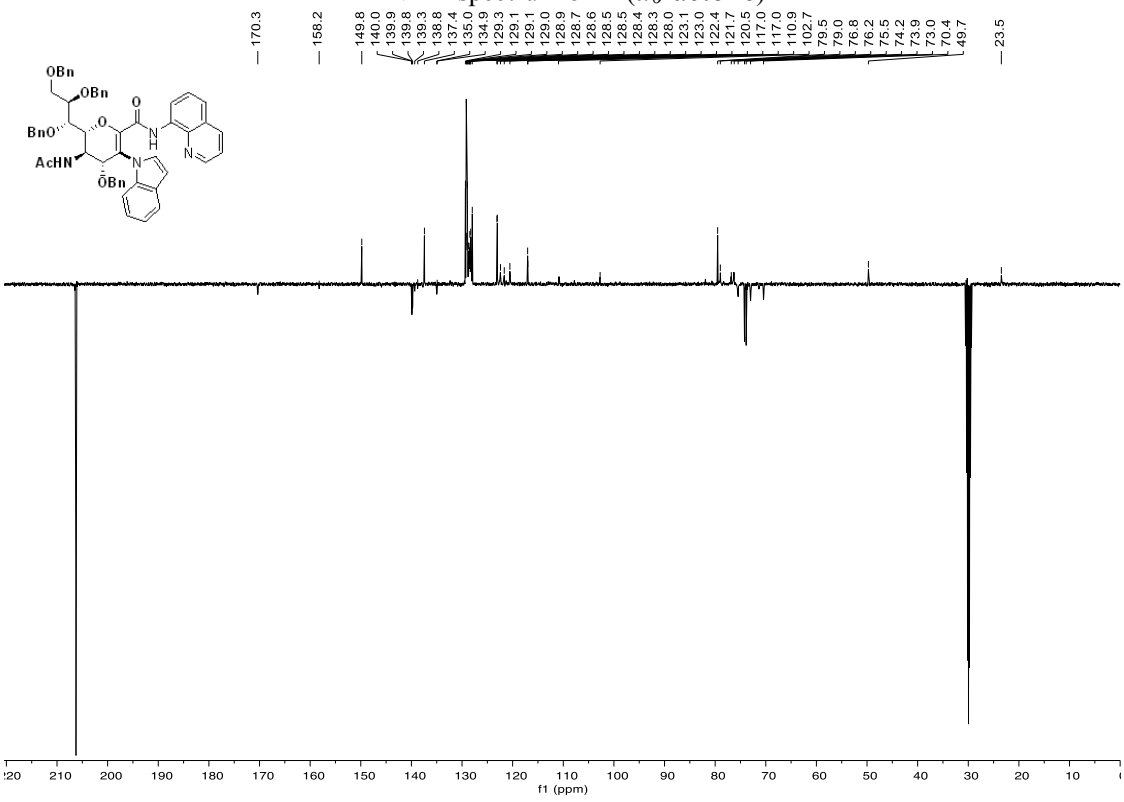
^{1}H NMR spectrum of **4h** (d_6-actone)



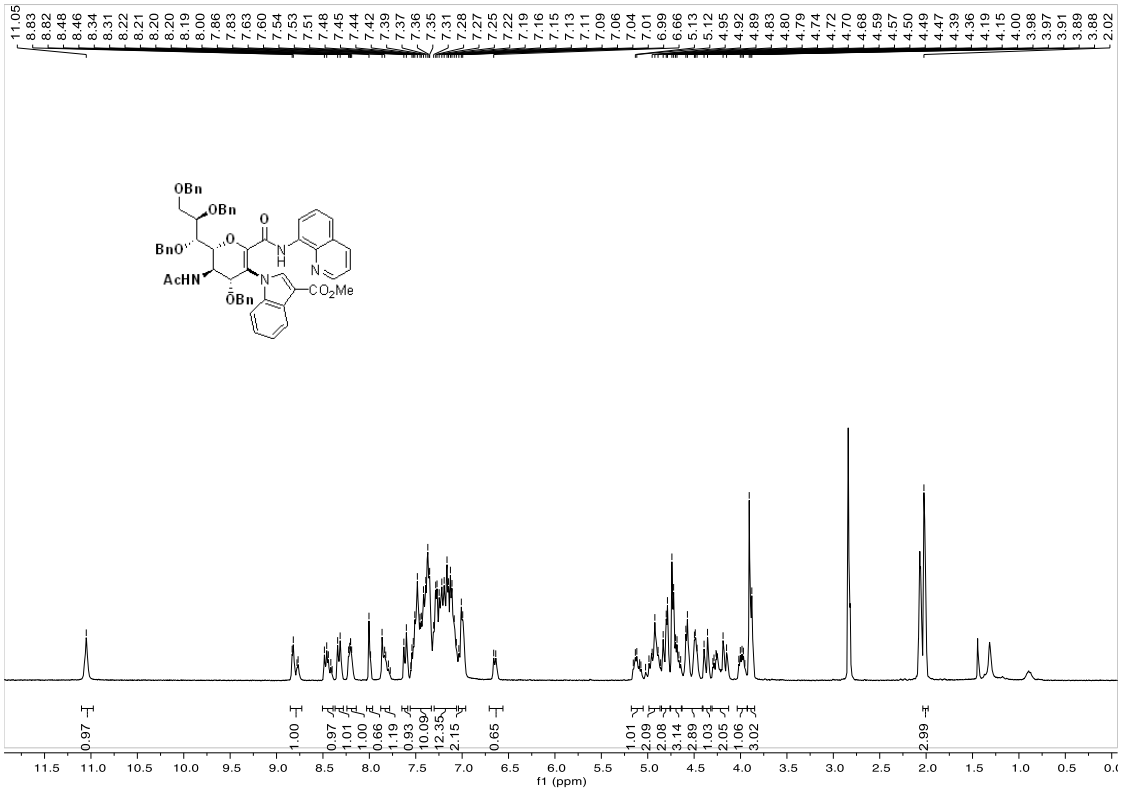
^{13}C NMR spectrum of **4h** (d_6-actone)



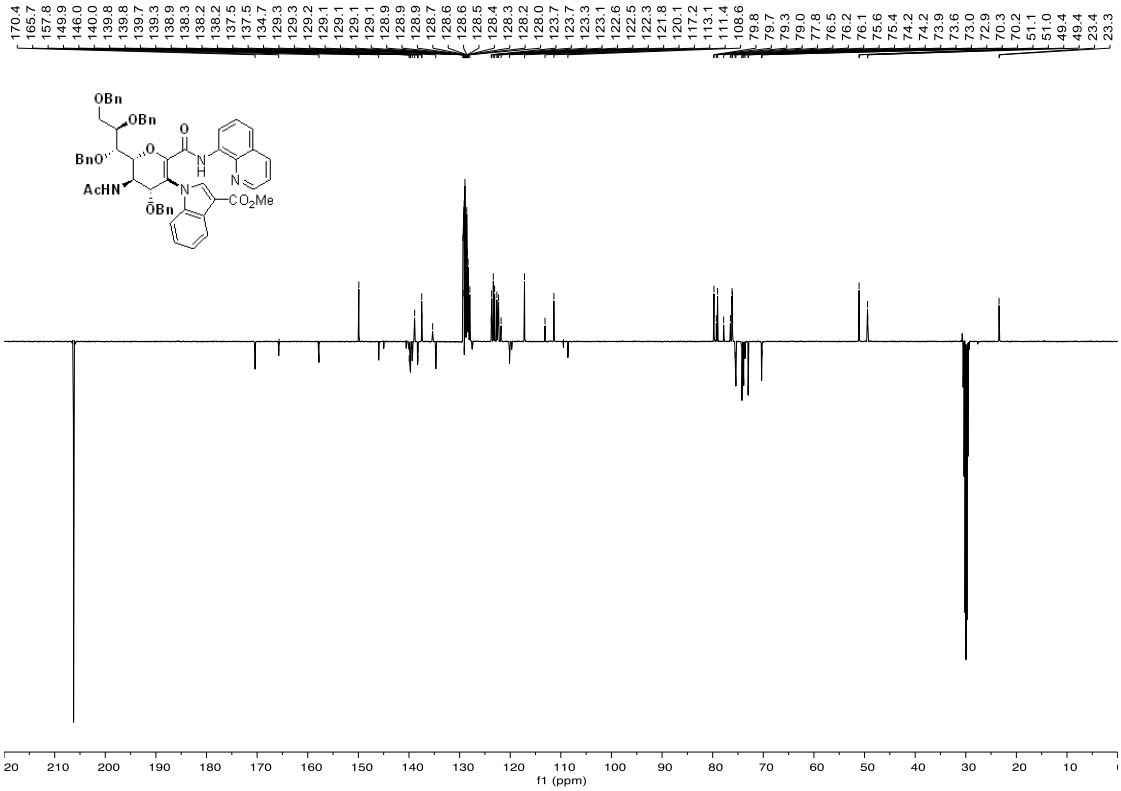
^{1}H NMR spectrum of **4i** (d_6-actone)



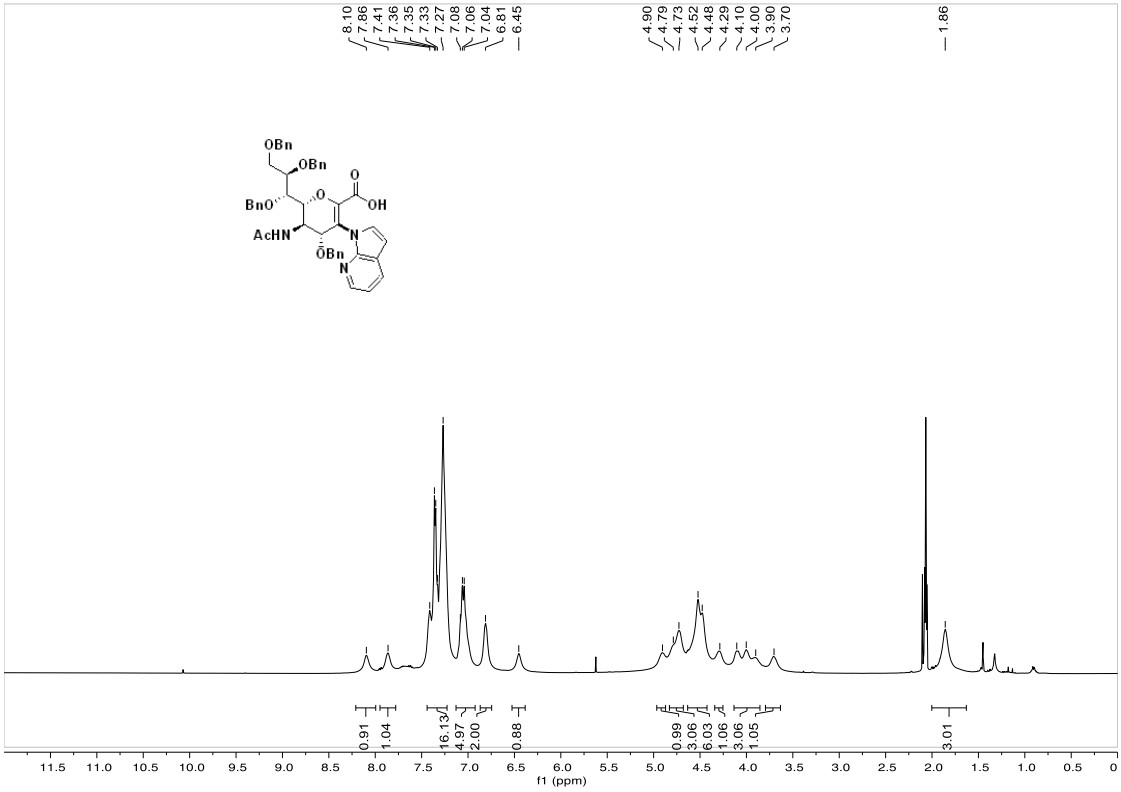
^{13}C NMR spectrum of **4i** (d_6-actone)



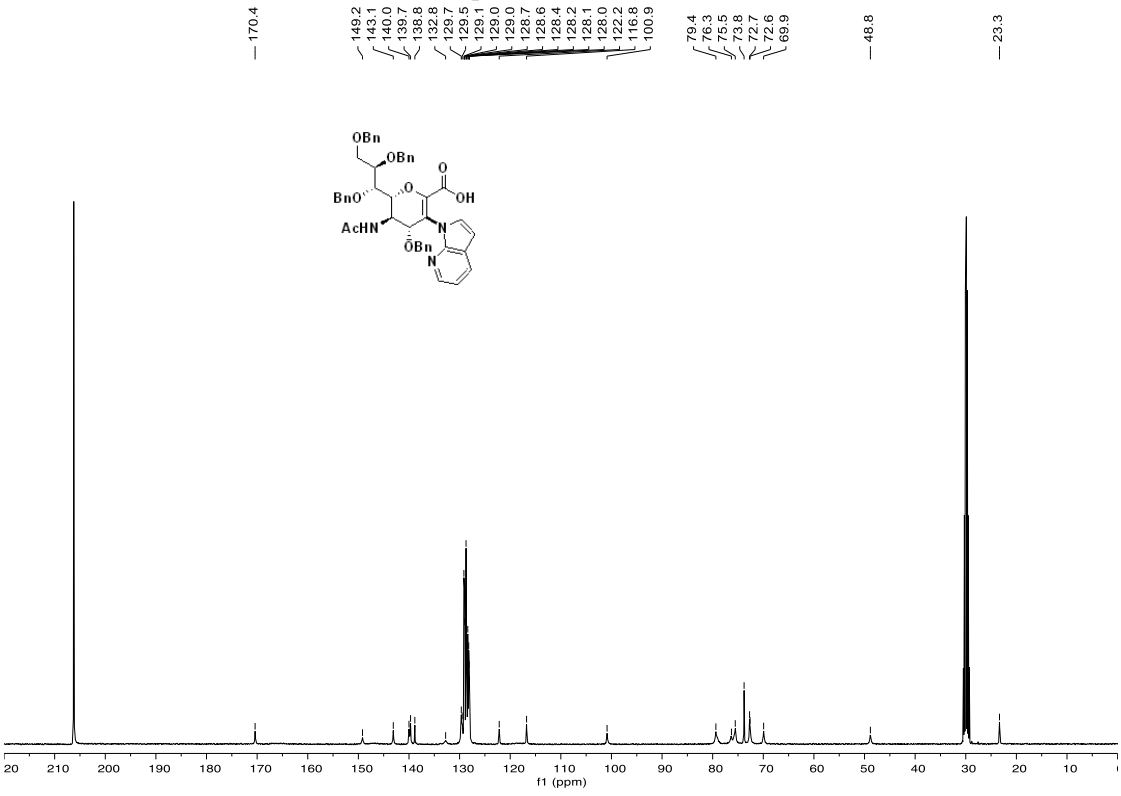
^{1}H NMR spectrum of **4j** (d_6-actone)



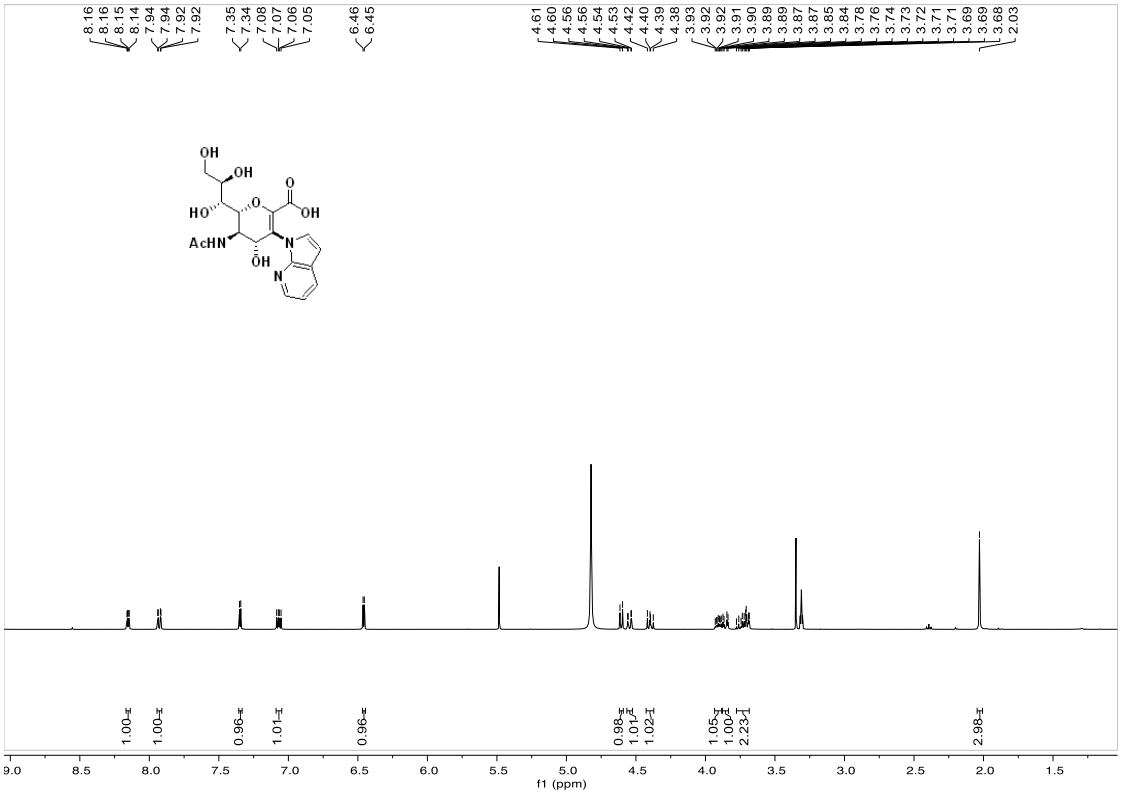
^{13}C NMR spectrum of **4j** (d_6-actone)



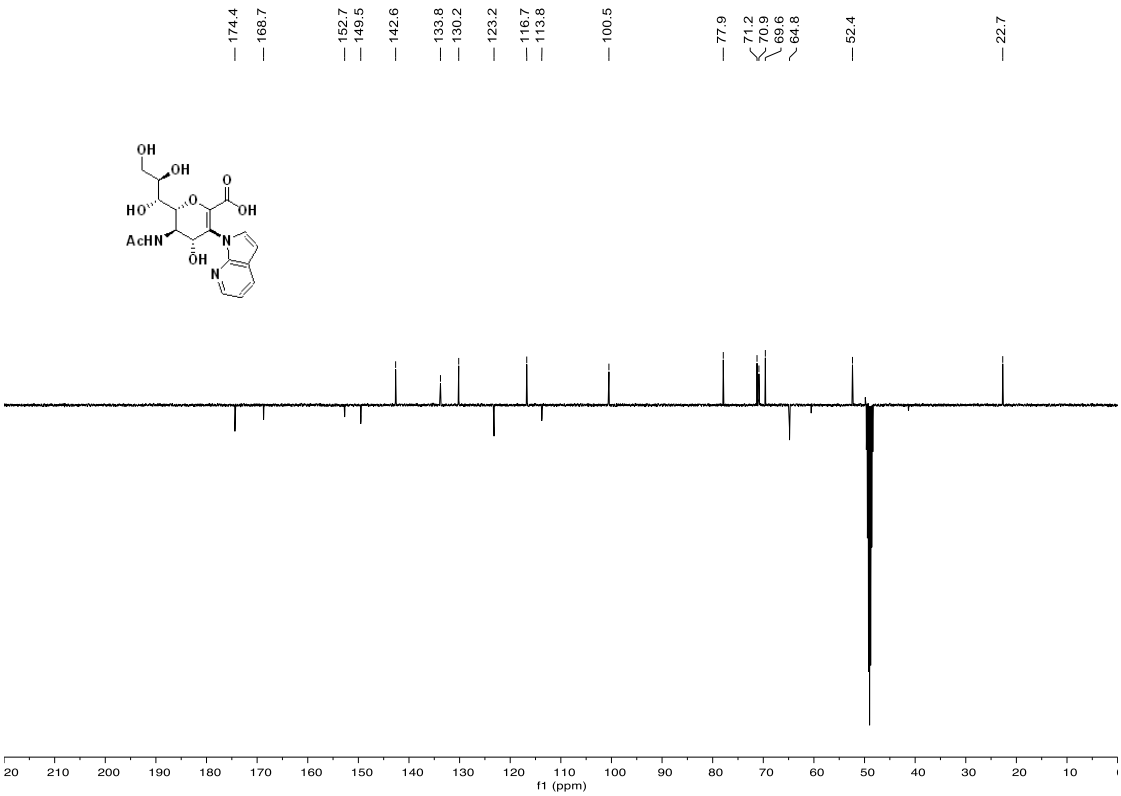
^{1}H NMR spectrum of **5** (d_6-actone)



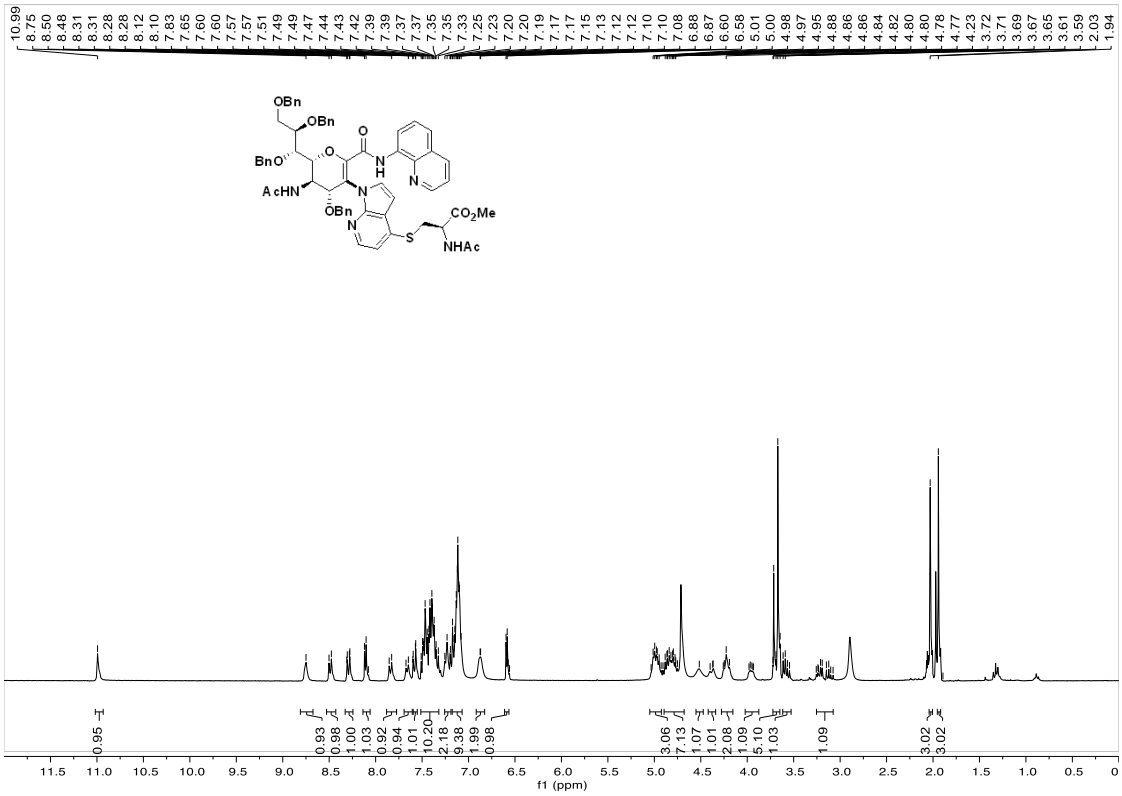
^{13}C NMR spectrum of **5** (d_6-actone)



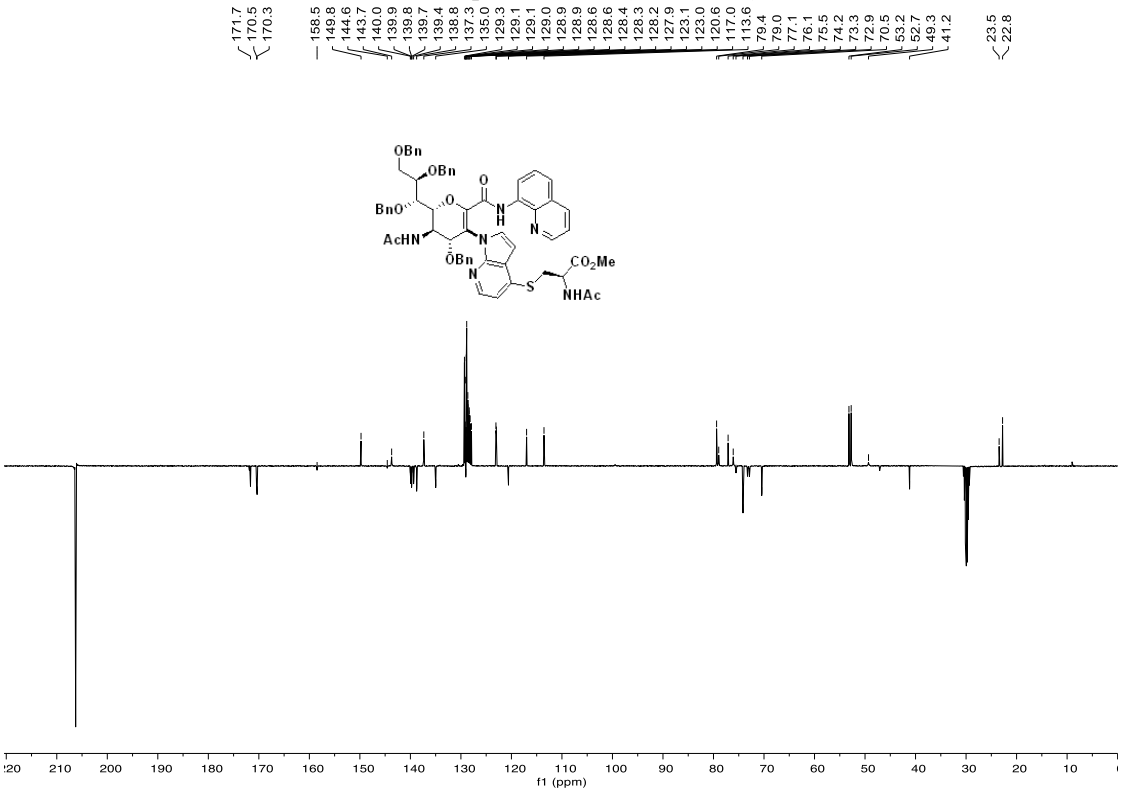
^{1}H NMR spectrum of **6** (d_4-methanol)



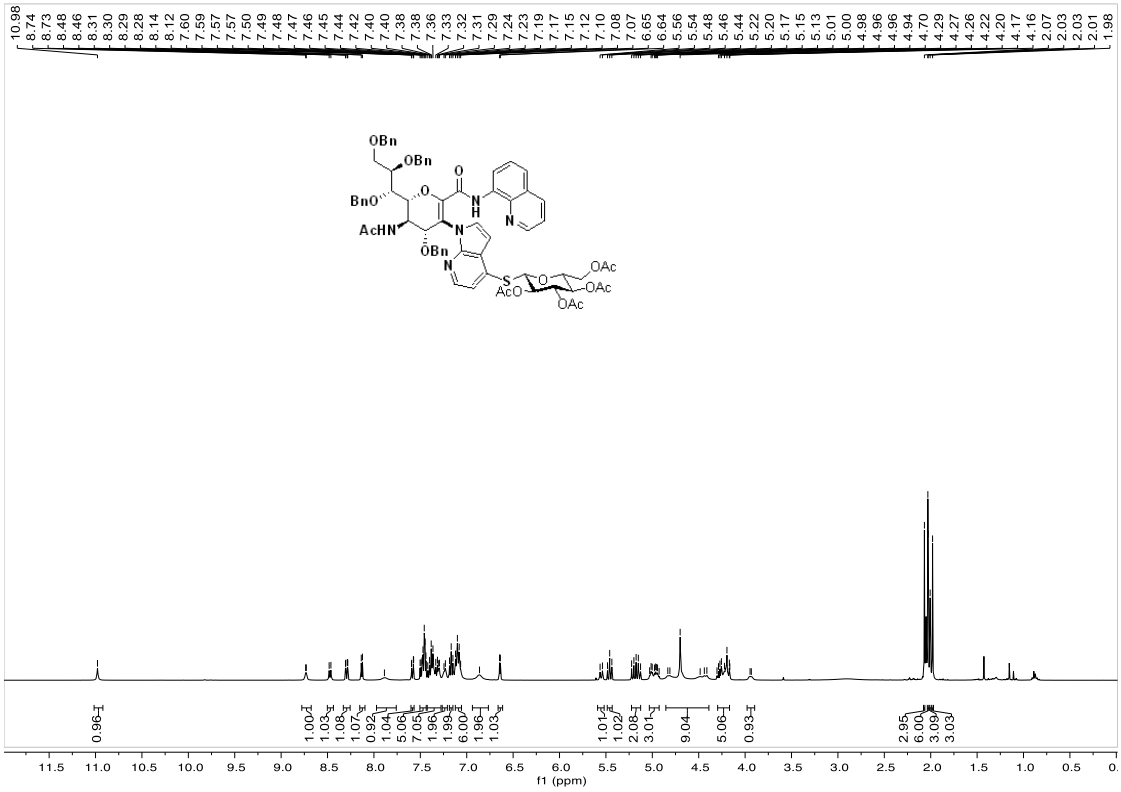
^{13}C NMR spectrum of **6** (d_4-methanol)



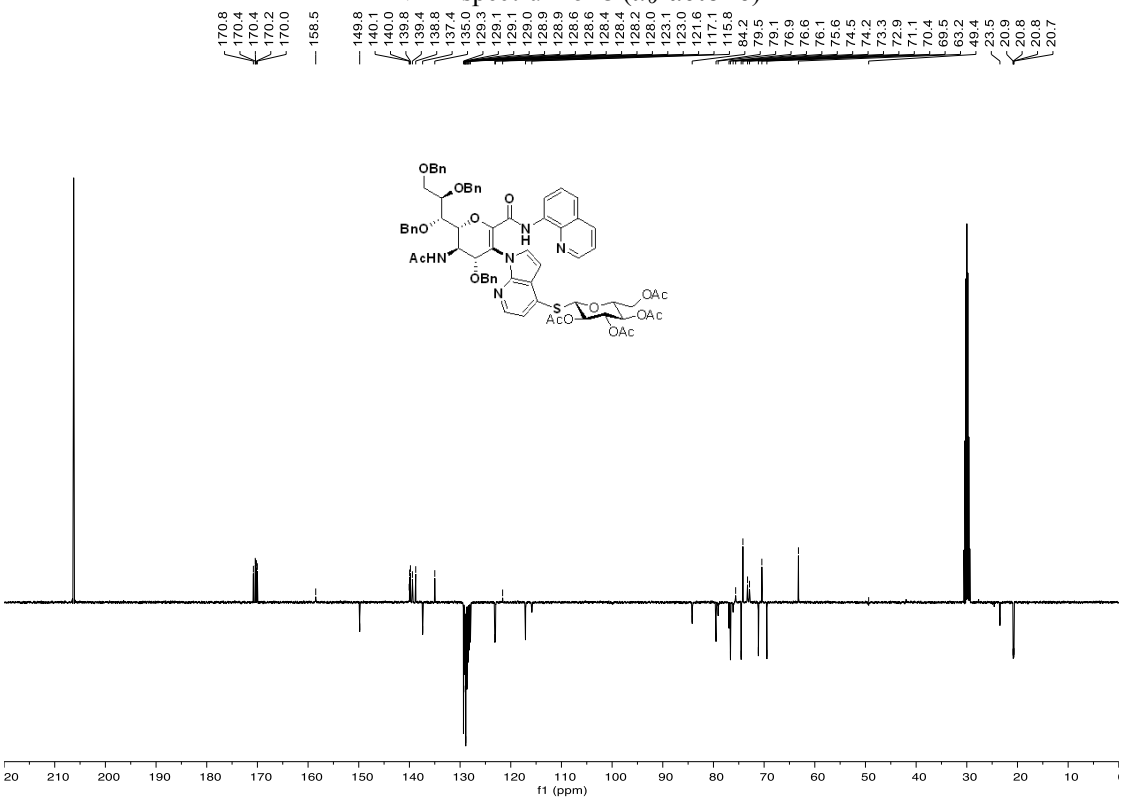
^{1}H NMR spectrum of **7** (d_6-actone)



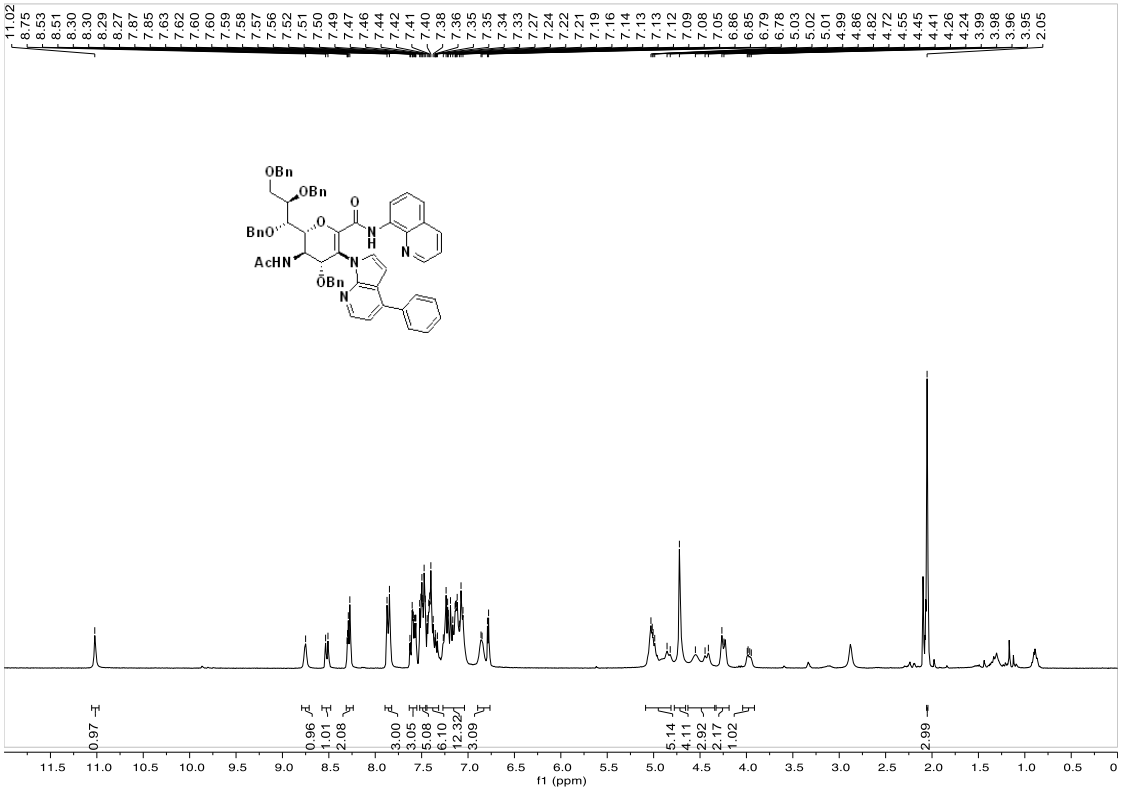
^{13}C NMR spectrum of **7** (d_6-actone)



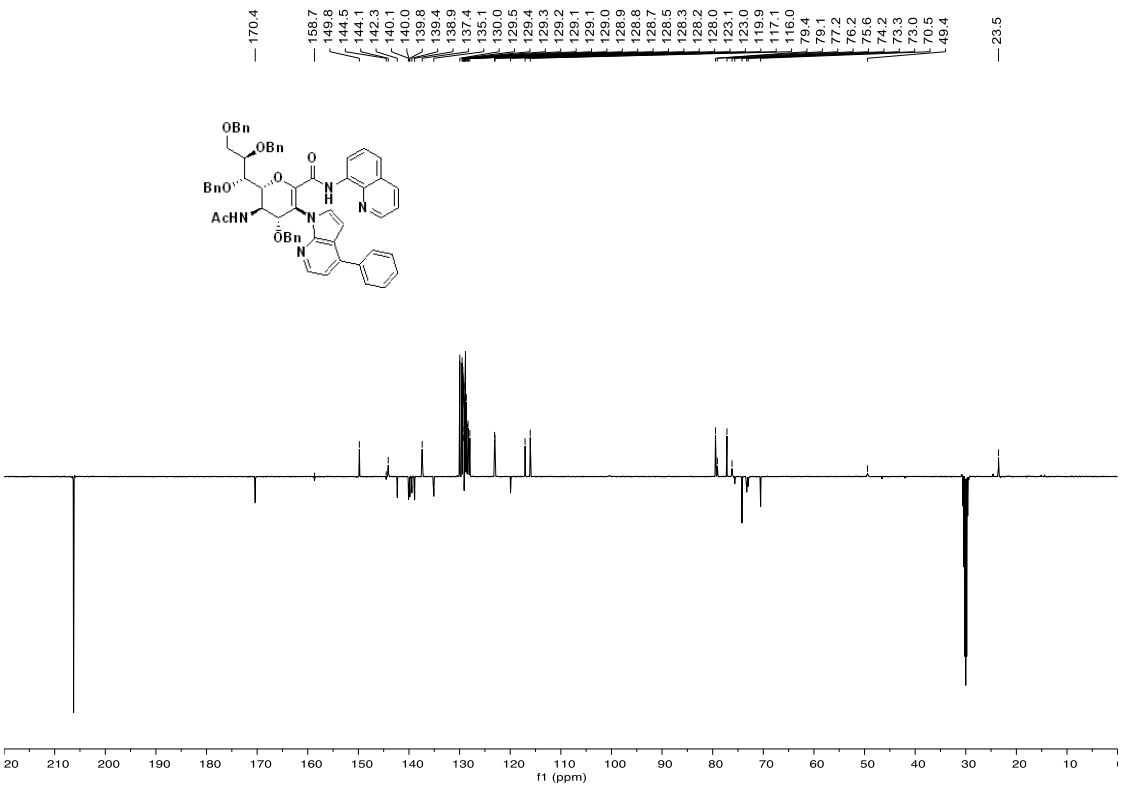
^{1}H NMR spectrum of **8** (d_6-actone)



^{13}C NMR spectrum of **8** (d_6-actone)



^{1}H NMR spectrum of **9** (d_6-actone)



^{13}C NMR spectrum of **9** (d_6-actone)