Electronic Supplementary Material (ESI) for ChemComm.

Supporting Information

Highly regioselective and stereoselective synthesis of C-Aryl glycosides via Nickel-catalyzed ortho-C-H glycosylation of 8-aminoquinoline amides

Wei-Yu Shi, Ya-Nan Ding, Nian Zheng, Xue-Ya Gou, Zhe Zhang, Xi Chen, Yu-Yong Luan, Zhi-Jie Niu and Yong-Min Liang *

State Key Laboratory of Applied Organic Chemistry, Lanzhou University, Lanzhou 730000, China
E-mail: liangym@lzu.edu.cn

Table of Contents

1. General Remarks

Unless otherwise noted, all of these reactions were carried out under an argon atmosphere. Solvent was freshly distilled prior to use unless otherwise noted. For column chromatography, silica gel (200-300 mesh) was employed. Analytical TLC was performed with silica gel GF254 plates. Organic solutions were concentrated under reduced pressure using a rotary evaporator. Room temperature (r.t.) is 15-23°C.

Materials. Unless otherwise noted below, all other compounds have been reported in the literature or are commercially available. Commercial reagents were used without further purification. 1,4-Dioxane were dried with CaH_2 and freshly distilled, and the Ni(dppf)Cl_2 was purchased from Boka.

Instrumentation. Deuterated solvents were purchased from Cambridge Isotope Laboratories. ^{1}H NMR spectra were recorded on Bruker AVANCE III 400, 600 and INOVA instruments with 400, 300 and 600 MHz frequencies, and ^{13}C NMR spectra were recorded on Bruker AVANCE III 400 and 600 with 101 and 75 MHz frequencies. ^{19}F NMR spectra were recorded on a Bruker AVANCE III 400 spectrometer with a ^{19}F operating frequency of 376 MHz. Chemical shifts (δ) were reported in ppm relative to the residual solvent signal ($CDCl_3$ δ = 7.26 for ^{1}H NMR and δ = 77.0 for ^{13}C NMR). Chemical shifts (ppm) were recorded with tetramethylsilane (TMS) as the internal reference standard. Multiplicities are given as s (singlet), d (doublet), t (triplet), q (quartet), dd (doublet of doublets), dt (doublet od triplet), dq (double of quartet) td (triplet of doublets) or m (multiplet). HRMS was obtained using a Q-TOF instrument equipped with an ESI source. Data collection for crystal structure was performed at room temperature using Mo Kα radiation on a Bruker APEXII diffractometer.

2. Optimization of reaction conditions

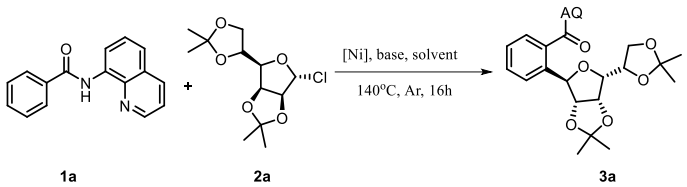
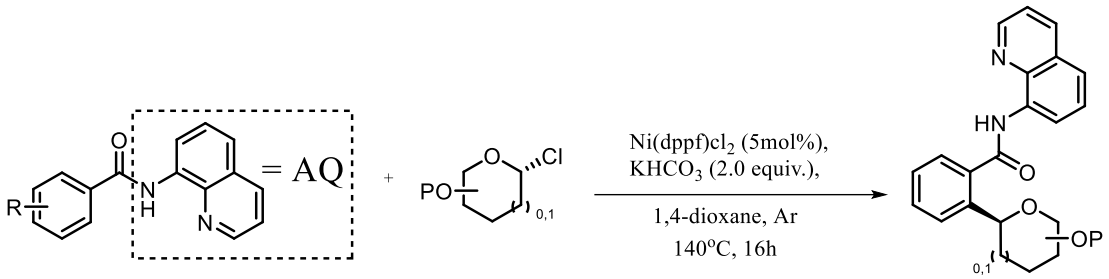


Table S1 Optimization of reaction conditions[a]

Entry	1a:2a	Catalyst	Solvent	Base	Yield[b] (%)
1	1:2	Ni_2CO_3	Dioxane	$KHCO_3$	n.r.[c]
2	1:2	$Ni(OTf)_2$	Dioxane	$KHCO_3$	trace
3	1:2	$Ni(OAc)_2$	Dioxane	$KHCO_3$	trace
4	1:2	$Ni(DME)Cl_2$	Dioxane	$KHCO_3$	27
5	1:2	$Ni(dppf)Cl_2$	Dioxane	$KHCO_3$	38
6	1:2	-	Dioxane	$KHCO_3$	n.r.
7	1:2	$Ni(dppf)Cl_2$	PhMe	$KHCO_3$	31
8	1:2	$Ni(dppf)Cl_2$	DMF	$KHCO_3$	n.r.
9	1:2	$Ni(dppf)Cl_2$	DCE	$KHCO_3$	21
10	1:2	$Ni(dppf)Cl_2$	PhCl	$KHCO_3$	20
11	**2:1[d]**	**$Ni(dppf)Cl_2$**	**Dioxane**	**$KHCO_3$**	**61**
12	2:1	$Ni(dppf)Cl_2$	Dioxane	K_2CO_3	48
13	2:1	$Ni(dppf)Cl_2$	Dioxane	K_3PO_4	trace
14	2:1	$Ni(dppf)Cl_2$	Dioxane	KOAc	52
15	2:1	$Ni(dppf)Cl_2$	Dioxane	NEt_3	n.r.
16	2:1	$Ni(dppf)Cl_2$	Dioxane	$NaHCO_3$	47
17	2:1	$Ni(dppf)Cl_2$	Dioxane	$CsHCO_3$	53
18	2:1	$Ni(dppf)Cl_2$	Dioxane	-	n.r.

[a]Reaction conditions: **1a** (0.1mmol), 2a (0.2 mmol, 2.0 equiv.), catalyst (5mol%), base (0.2mmol, 2.0 equiv.), solvent (0.5mL), 140°C, 16h and Ar. [b]Isolated yield. [c]n.r.: no reaction. [d]Reaction conditions: **1a** (0.2mmol, 2.0 equiv.), **2a** (0.1 mmol).

3. General Procedure



1 **2** **3-4**

In an oven-dried 10 ml tube, starting amide 1 (0.2 mmol), 2 (0.1 mmol), $KHCO_3$ (0.4 mmol, 20mg) and Ni(dppf)Cl_2 (5 mol%, 3.4 mg) were added and charged with argon more than five times (The tube was sealed with tipping plug). Dioxane (0.5 mL) was injected into the tube. The resulting suspension was stirred vigorously at 140 ℃ for 16 h. After the reaction was completed, the resulting mixture was filtered through a celite pad and concentrated under reduced pressure. The residue was purified with chromatography column on silica gel or preparative TLC (Petroleum ether/EtOAc = 8:1 - 3:1).

4. General Procedure for the Preparation of Starting amides

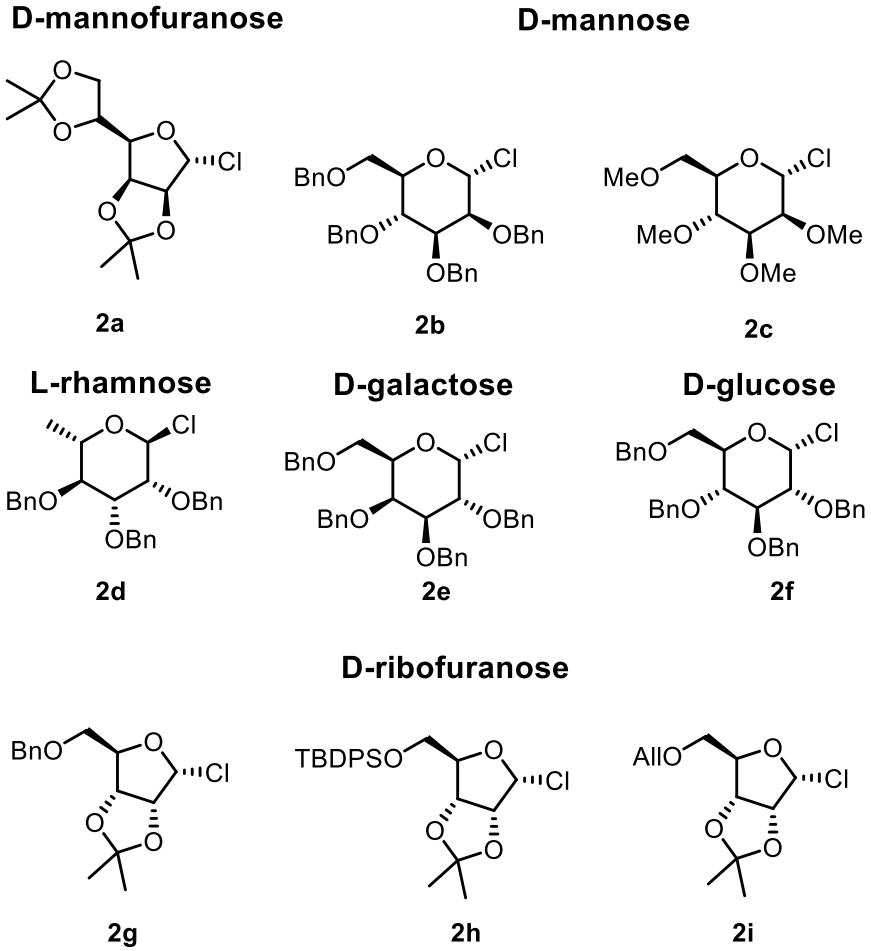
All aromatic amides bearing an 8-aminoquinoline moiety were prepared by reacting the corresponding acid or the corresponding acid chlorides with 8-aminoquinoline.[1]

Method 1: 8-Aminoquinoline (4.0 mmol) and triethylamine (6.0 mmol) were dissolved in anhydrous dichloromethane (20 mL), and the mixture was cooled to 0 oC. After the dropwise addition of the corresponding acid chloride in 5 mL of dichloromethane (4.4 mmol) via syringe pump, the reaction mixture was warmed to room temperature and stirred overnight. Dichloromethane (20 mL) was added and the mixture was washed with saturated aqueous sodium bicarbonate (20 mL), 1N HCl (20 mL), and brine (30 mL), dried over MgSO4 and the solvent was removed in vacuo. The crude product was purified by flash column chromatography (silica gel, EtOAc/hexanes, 1:20 to 1:4) to give the corresponding quinoline amide product.

Method 2: To an oven-dried 100 mL three-necked flask, acid (15 mmol), DMF (5 drops) and DCM (30 mL) were added under a N_2 atmosphere. Oxalyl chloride (1.5 mL, 18 mmol, 1.2 equiv.) was added dropwise at 0 °C resulting in vigorous bubbling. The mixture was stirred for 5 h at room temperature, and the solvent was then removed in vacuo. The resulting acid chloride was used immediately without further purification.

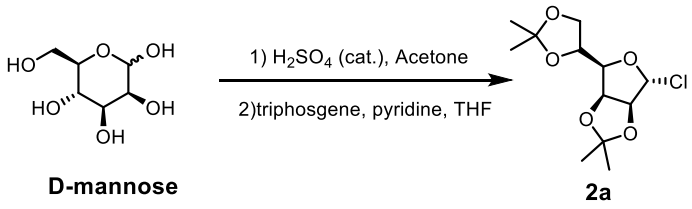
To another oven-dried 100 mL three-necked flask, 8-aminoquinoline (2.9 g, 20 mmol, 1.3 equiv.), Et_3N (4.1 mL, 30 mmol, 2 equiv.) and DCM (30 mL) were added. A solution of the acid chloride in DCM (10 mL) was added dropwise to the solution at 0 °C, and the solution was then warmed to room temperature. After stirring overnight, the reaction system was quenched with sat. aq. NaHCO3 (30 mL) and the organic layer was separated. The aqueous layer was extracted with DCM (2 x 15mL). The combined organic layers were washed with 1 M HCl aq. (30 mL) and brine (30 mL), dried over MgSO4, filtered and evaporated in vacuo. The obtained crude amide was purified by column chromatography on silica gel (hexane/EtOAc = 10/1) to afford the desired amide.

5. General Procedure for the Preparation of Glycosyl chlorides



The synthesis of sugars was based on the pervious literatures, and the spectra data are consistent with those reported in literatures.

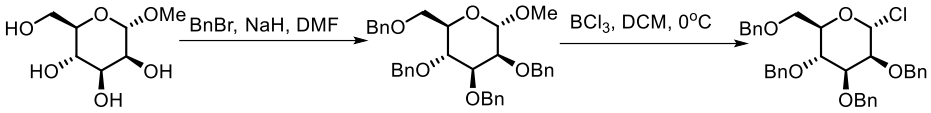
a) Synthesis of (3aS,4R,6R,6aS)-4-chloro-6-((R)-2,2-dimethyl-1,3-dioxolan-4-yl)-2,2-dimethyltetrahydrofuro[3,4-d][1,3]dioxole (**2a**)[2]



Step 1: To an ice-water cooled solution of D-mannose (7.2 g, 40 mmol) in acetone (100 mL) was added H_2SO_4 (0.5ml), and the mixture was left to stir at 0 ºC for 30 minutes. The mixture was diluted with EtOAc (200 ml) and washed thoroughly with saturated aqueous $NaHCO_3$ solution water and brine. The organic layer was dried over anhydrous Na_2SO_4 and the resulting solution was concentrated under reduced pressure. The crude product was used for next step without further purification.

Step 2: The relevant crude product (10 mmol) was dissolved in dry THF (50 ml), triphosgene (1.2 g, 4 mmol) was added, and the mixture was stirred at room temperature with exclusion of moisture. Pyridine (1ml) was added slowly and the mixture was allowed to stir at room temperature for 2h while being monitored by TLC. After the reaction was completed, pyridinium hydrochloride was filtered. The solid was washed with THF, and the filtrate was concentrated under reduced pressure. The residue was purified with chromatography column on silica gel to give desired product **2a** in 95% yield.

b) Synthesis of (2R,3R,4S,5S,6R)-3,4,5-tris(benzyloxy)-2-((benzyloxy)methyl)-6-chlorotetrahydro-2H-pyran (**2b**)[2-3]

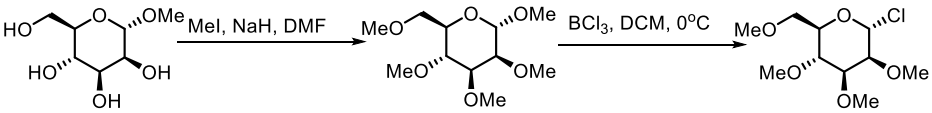


2b-1 **2b-2** **2b**

Step 1: To a 0 °C cooled solution of **2b-1** (10mmol) in DMF (80 mL), was carefully added NaH (64.40 mmol). Then, BnBr (64.40 mmol) was slowly added about 30 min. After 16 h at room temperature, the reaction mixture was carefully quenched with water. Then, the crude was diluted with water (50 mL) and extracted with CH_2Cl_2 (3 × 100 mL). The combined organic layers were washed with brine, dried over Na_2SO_4, filtered, and concentrated *in vacuo* to give compound **2b-2**.

Step 2: To a −78 °C cooled solution of **2b-2** in DCM, was added dropwise BCl_3 (1.5 equiv, 1M in DCM). The reaction was stirred at -78 °C overnight. The reaction mixture was extracted with CH_2Cl_2 and washed with brine. The organic layer was dried over Na_2SO_4, filtered, and concentrated *in vacuo*. The resulting residue was purified by silica gel flash chromatography to give compound **2b**.

c) Synthesis of (2R,3R,4S,5S,6R)-2-(acetoxymethyl)-6-chlorotetrahydro-2H-pyran-3,4,5-triyl triacetate (**2c**)[3]

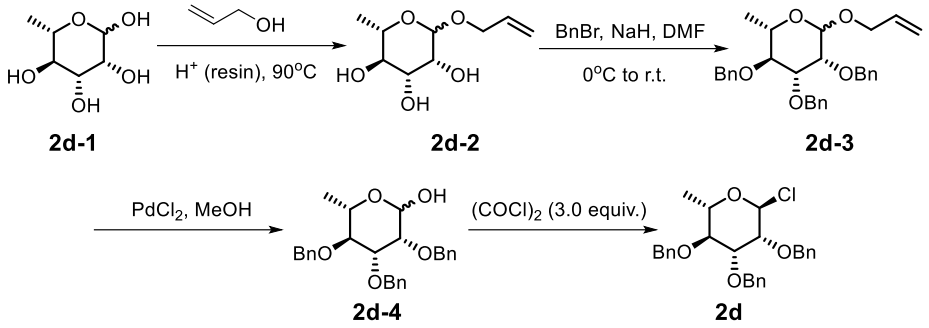


2c-1 **2c-2** **2c**

Step 1: To a 0 °C cooled solution of **2c-1** (10mmol) in DMF (80 mL), was carefully added NaH (64.40 mmol). Then, MeI (64.40 mmol) was slowly added about 30 min. After 16 h at room temperature, the reaction mixture was carefully quenched with water. Then, the crude was diluted with water (50 mL) and extracted with CH_2Cl_2 (3 × 100 mL). The combined organic layers were washed with brine, dried over Na_2SO_4, filtered, and concentrated *in vacuo* to give compound **2c-2**.

Step 2: To a −78 °C cooled solution of **2c-2** in DCM, was added dropwise BCl_3 (1.5 equiv, 1M in DCM). The reaction was stirred at -78 °C overnight. The reaction mixture was extracted with CH_2Cl_2 and washed with brine. The organic layer was dried over Na_2SO_4, filtered, and concentrated *in vacuo*. The resulting residue was purified by silica gel flash chromatography to give compound **2c**.

d) Synthesis of (2S,3R,4R,5S,6S)-3,4,5-tris(benzyloxy)-2-chloro-6-methyltetrahydro-2H-pyran (**2d**)[3-4]



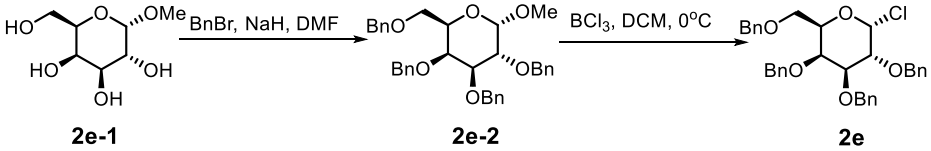
Step 1: To a solution of **2d-1** (6.7 mmol) in allyl alcohol (8 mL), Amberlite IR 120 (H^+) (0.6 g) was added, and the suspension was stirred at 90 °C for 4 h. The ion exchanger was filtered off, and the excess of allyl alcohol was removed by vacuum distillation. The crude product was purified by flash column chromatography (CH_2Cl_2/MeOH = 20:1) to give **2d-2**.

Step 2: To a 0 °C cooled solution of **2d-2** (10mmol) in DMF (80 mL), was carefully added NaH (40 mmol). Then, BnBr (40 mmol) was slowly added about 30 min. After 16 h at room temperature, the reaction mixture was carefully quenched with water. Then, the crude was diluted with water (50 mL) and extracted with CH_2Cl_2 (3 × 100 mL). The combined organic layers were washed with brine, dried over Na_2SO_4, filtered, and concentrated *in vacuo* to give compound **2d-3**.

Step 3: To a solution of compound **2d-3** (5 mmol) in anhydrous MeOH (35 mL) at room temperature, $PdCl_2$ (1 mmol) was added. The mixture was was allowed to stir at room temperature. Then, the reaction was diluted with Et_2O (30 mL), filtered through Celite pad, and concentrated under reduced pressure. The crude residue was purified by flash column chromatography on silica gel to afford **2d-4**.

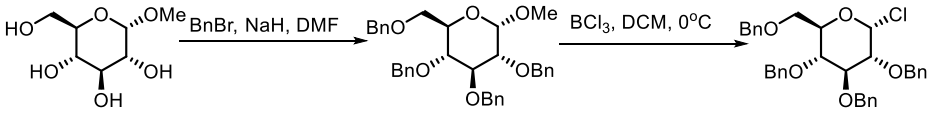
Step 4: To a solution of compound **2d-4** (5.0 mmol) in DMF, $(COCl)_2$ (15 mmol, 3.0 equiv.) was slowly added at 0 °C. The mixture was stirred at 0 °C. After the complete consumption of compound **2d-4** monitored by TLC analysis, the reaction mixture was diluted with CH_2Cl_2. The organic layer was washed with brine, dried over anhydrous Na_2SO_4, the solvent was removed under reduced pressure. The resulting residue was purified by silica gel flash chromatography to give compound **2d**.

e) Synthesis of (2R,3S,4S,5R,6R)-3,4,5-tris(benzyloxy)-2-((benzyloxy)methyl)-6-chlorotetrahydro-2H-pyran (**2e**)[2-3]



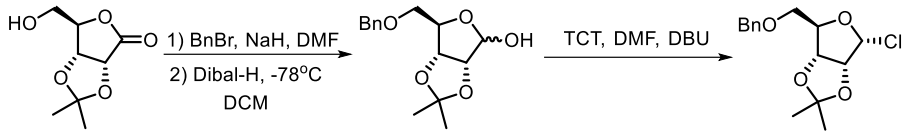
The compound **2e** was synthesized following the same procedure as compound **2b**.

f) Synthesis of (2R,3R,4S,5R,6R)-3,4,5-tris(benzyloxy)-2-((benzyloxy)methyl)-6-chlorotetrahydro-2H-pyran (**2f**)[2-3]



The compound **2f** was synthesized following the same procedure as compound **2b**.

g) Synthesis of (3aR,4R,6R,6aR)-4-((benzyloxy)methyl)-6-chloro-2,2-dimethyltetrahydrofuro[3,4-d][1,3]dioxole (**2g**)[2, 5]

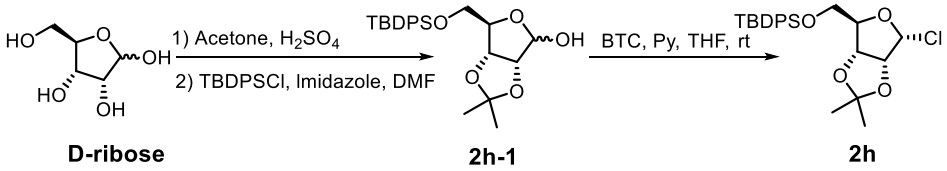


Step 1: To a 0 °C cooled solution of **2g-1** (10mmol) in DMF (80 mL), was carefully added NaH (15 mmol). Then, BnBr (15 mmol) was slowly added about 30 min. After 16 h at room temperature, the reaction mixture was carefully quenched with water. Then, the crude was diluted with water (50 mL) and extracted with CH_2Cl_2 (3 × 100 mL). The combined organic layers were washed with brine, dried over Na_2SO_4, filtered, and concentrated *in vacuo* to give a benzyl protected compound.

Step 2: 2,3,5-Tri-O-benzyl-D-lyxofuranolactone (2.1 g, 5 mmol) was dissolved in DCM (25 ml) and cooled to -78 °C. Diisobutylaluminum hydride (7 ml, 7 mmol, 1M in hexanes) was added slowly over 10-15 minutes and the reaction mixture kept at -78 °C for 1h. Methanol (2 ml) was added dropwise to quench the reaction and the solution allowed to warm to room temperature. The solution was diluted with DCM and washed with brine. The solution was dried over anhydrous $MgSO_4$, filtered and concentrated under reduced pressure. The product was purified by flash chromatography to give compound **2g-2**.

Step 3: DMF (1.55ml, 20.0mmol) was added to 2,4,6-trichloro-[1,3,5]-triazine (TCT) (1.0g, 5.5mmol) and the solution was stirred at room temperature for 15 minutes under N_2. Compound **2g-2** (5.0 mmol) in DCE was added to the TCT-DMF suspension, the followed by addition of DBU (0.8ml, 5.5mmol). The mixture was stirred at 60 ºC and monitored by TLC. The temperature was brought to room temperature and Et_2O was added to the mixture for the precipitation of cyanuric salt. Cyanuric salt was removed by filtration and the filtrate was concentrated *in vacuo*. The resulting residue was purified by silica gel flash chromatography to give compound **2g**.

h) Synthesis of tert-butyl(((3aR,4R,6R,6aR)-6-chloro-2,2-dimethyltetrahydrofuro[3,4-d][1,3]dioxol-4-yl)methoxy)diphenylsilane (**2h**)[2, 6]



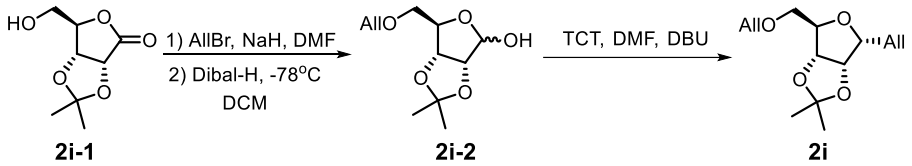
Step 1: To a stirred suspension of D-ribose (7.5 g, 50 mmol) in acetone (75 mL) was added dropwise

H_2SO_4 (conc., 0.25 mL) at room temperature and the reaction mixture was stirred at rt for 1h. Then, excess solid $NaHCO_3$ was carefully added to the reaction mixture. The resulting mixture was stirred until quenching of the reaction was complete. The mixture was filtered, and the filter cake was washed with acetone (150 mL). The combined filtrates were concentrated under reduced pressure to give a colorless oil, which was purified by flash column chromatography to give an anomeric mixture of acetonide protected D-ribose.

Step 2: To a mixture of acetonide-protected D-ribose (12.0 g, 63.0 mmol, 1.0 equiv) were sequentially added at 0 °C to a solution of imidazole (12.9 g, 189 mmol, 3.0 equiv) in DMF (65 mL) and tertbutyl(chloro)diphenylsilane (18.0 mL, 69.3 mmol, 1.1 equiv). The mixture was stirred at 0 °C for 3 h and then poured into cold water (400 mL). The resulting mixture was extracted with ethyl acetate (750 mL). The combined organic layers were washed with brine (200 mL), dried over Na_2SO_4, and concentrated under reduced pressure to give a colorless oil, which was purified by flash column chromatography to give **2h-1**.

The compound **2h** was synthesized following the same procedure as compound **2a** (**Step 2**).

i) Synthesis of (3aR,4R,6R,6aR)-4-chloro-2,2-dimethyl-6-((((E)-prop-1-en-1-yl)oxy)methyl)tetrahydrofuro[3,4-d][1,3]dioxole (**2i**)[2, 5]

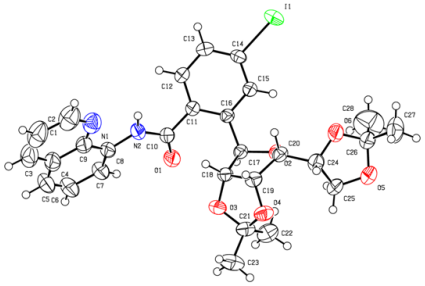


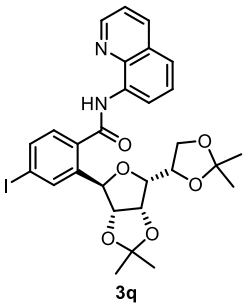
2i-1 **2i-2** **2i**

Step 1: To a 0 °C cooled solution of **2g-1** (10mmol) in DMF (80 mL), was carefully added NaH (12 mmol). Then, allyl bromide (12 mmol) was slowly added about 30 min. After 16 h at room temperature, the reaction mixture was carefully quenched with water. Then, the crude was diluted with water (50 mL) and extracted with CH_2Cl_2 (3 × 100 mL). The combined organic layers were washed with brine, dried over Na_2SO_4, filtered, and concentrated *in vacuo* to give a allyl protected compound.

The compound **2f** was synthesized following the same procedure as compound **2b** (**Step 2 and 3**).

6. X-ray Single Crystal Diffraction Data of 3q





3q

Bond precision:	C-C = 0.0055 A		Wavelength=1.54184
Cell:	a=11.6830(1)	b=11.6830(1)	c=39.0801(3)
	alpha=90	beta=90	gamma=90
Temperature:	301 K		

	Calculated	Reported
Volume	5334.14(10)	5334.14(10)
Space group	P 43 21 2	P 43 21 2
Hall group	P 4nw 2abw	P 4nw 2abw
Moiety formula	C28 H29 I N2 O6	C28 H29 I N2 O6
Sum formula	C28 H29 I N2 O6	C28 H29 I N2 O6
Mr	616.43	616.43
Dx,g cm^{-3}	1.535	1.535
Z	8	8
Mu (mm-1)	9.809	9.809
F000	2496.0	2496.0
F000’	2500.69	
h,k,lmax	14, 14, 49	14, 14, 49
Nref	5611 [3314]	5511
Tmin,Tmax	0.583, 0.675	0.388, 1.000
Tmin’	0.435	

Correction method= # Reported T Limits: Tmin=0.388 Tmax=1.000
AbsCorr = MULTI-SCAN

Data completeness= 1.66 / 0.98 Theta(max)= 76.564

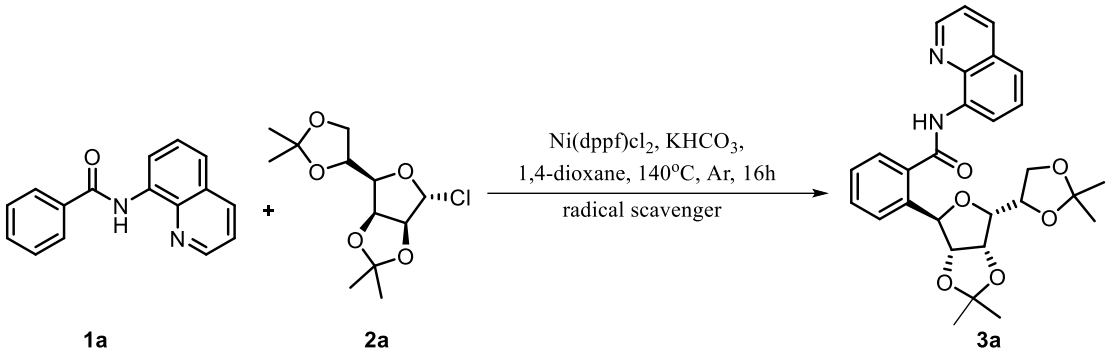
R(reflections)= 0.0248 (5145) wR2(reflections)= 0.0627 (5511)

S = 1.047 Npar= 338

Thermal ellipsoids are shown at 30% probability

7. Preliminary Mechanism Research and Hydrolysis experiment

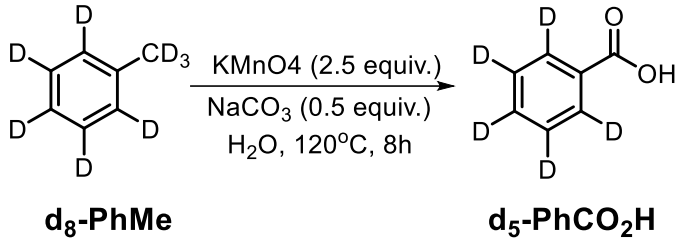
a) Radical scavenger Experiments

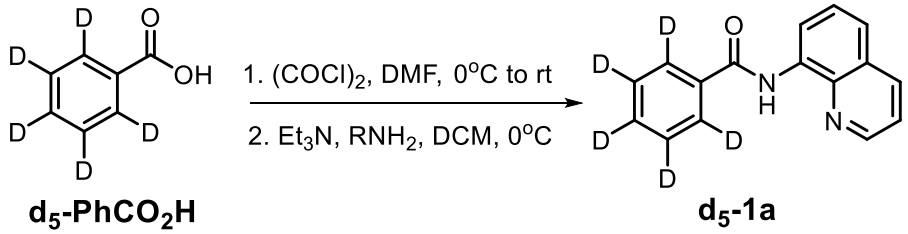


Radical scavenger (2.0 equiv.)	Yield of 3a
TEMPO	41%
BHT	49%
DPE	48%

In an oven-dried 10 ml tube, starting amide **1a** (0.2 mmol), glycosyl chloride **2a** (0.1 mmol), $KHCO_3$ (0.4 mmol, 20mg), $Ni(dppf)Cl_2$ (5 mol%, 3.4 mg) and radical scavenger (0.2mmol) were added and charged with argon more than five times (The tube was sealed with tipping plug). Dioxane (0.5 mL) was injected into the tube. The resulting suspension was stirred vigorously at 140 ℃ for 16 h. After the reaction was completed, the resulting mixture was filtered through a celite pad and concentrated under reduced pressure. The residue was purified with chromatography column on silica gel (Petroleum ether/EtOAc = 8:1 - 3:1).

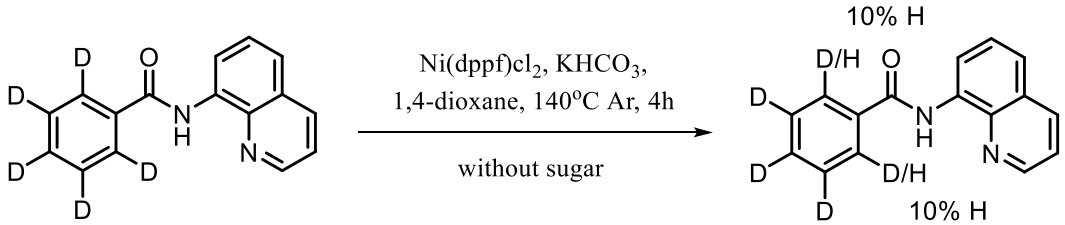
b) Deuterium-Labeling Experiments[7]





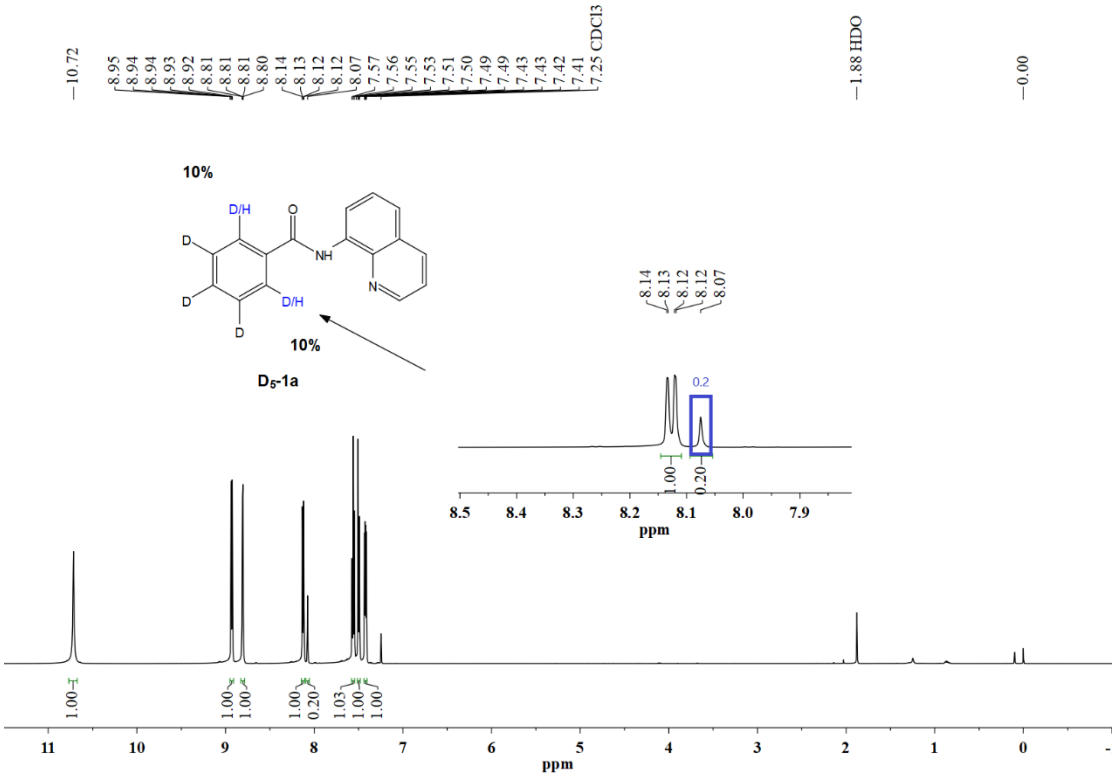
A round-bottom flask equipped with a stir bar and a condenser was charged with d8-toluene (99.9% atom D) (5 g, 50 mmol), $KMnO_4$ (20g, 125 mmol), Na_2CO_3 (2.64g, 25 mmol), and water (150 mL). The reaction mixture was refluxed for 8 h and then cooled to room temperature. The mixture was filtered through a pad of Celite, and the filtrate was acidified with 12 M HCl and extracted with DCM (3 × 30 mL). The organic

layer was washed with water and concentrated under vacuum. The crude product was recrystallized from water to give $C_6D_5CO_2H$ as white needles (4g, 64%). Synthesis of the amide **[D5]-1a** from $C_6D_5CO_2H$ was performed using the general procedure given for the synthesis of aromatic amides.

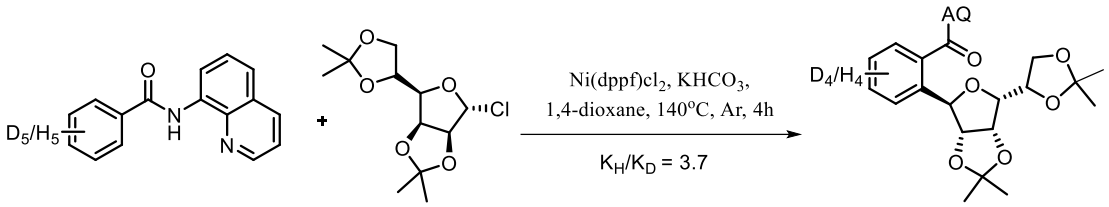


D_5-1a (> 99% D) **D_n-1b, 97%**

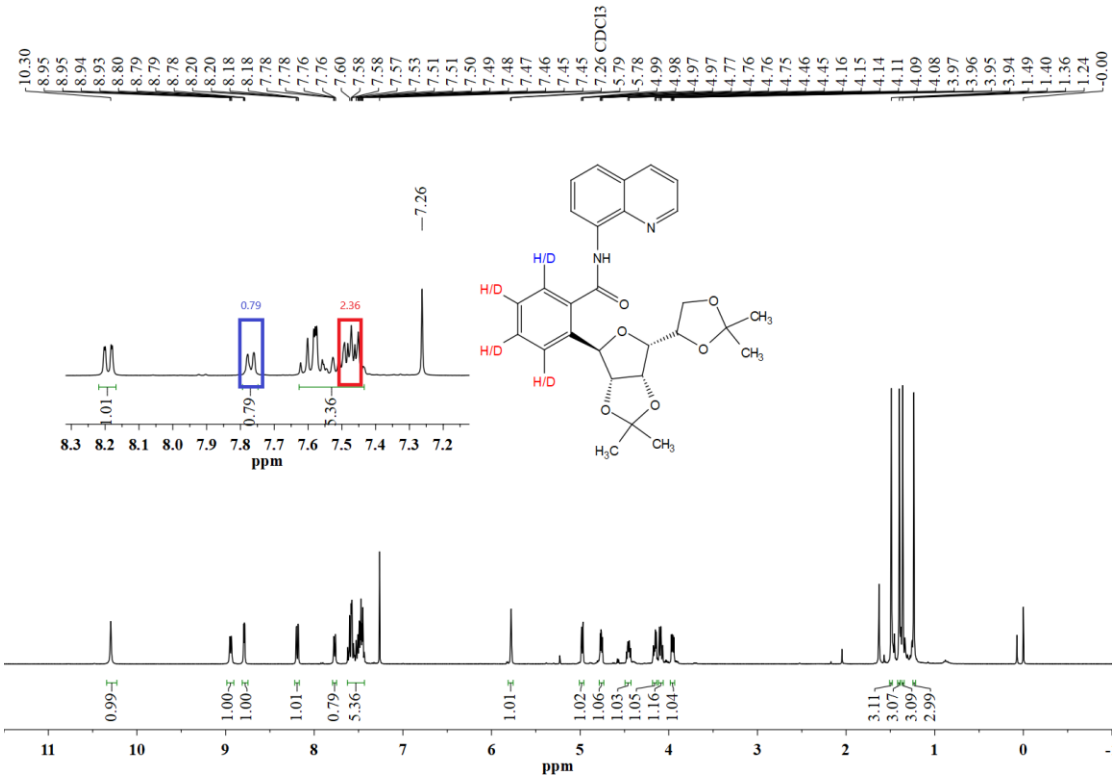
In an oven-dried 10 ml tube, isotopically labeled compound **D_5-1a** (0.2 mmol), $KHCO_3$ (0.4 mmol, 20mg) and $Ni(dppf)Cl_2$ (5 mol%, 3.4 mg) were added and charged with argon more than five times (The tube was sealed with tipping plug). Dioxane (0.5 mL) was injected into the tube. The resulting suspension was stirred vigorously at 140 ℃ for 4 h. After the reaction was completed, the resulting mixture was filtered through a celite pad and concentrated under reduced pressure. The residue was purified with chromatography column on silica gel to give the product **[Dn]-1b** (48.3mg, 97%) (Petroleum ether/EtOAc = 8:1).



c) Kinetic Isotope Effect (KIE)

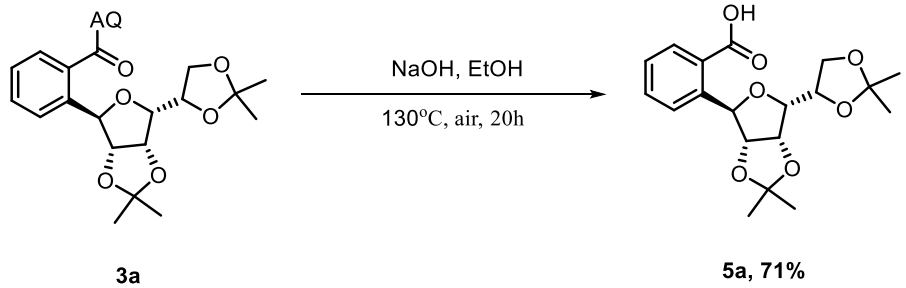


In an oven-dried 10 ml tube, isotopically labeled compound **D5-1a** (0.1 mmol), amide 1a (0.1 mmol), $KHCO_3$ (0.4 mmol, 20mg), glycosyl chloride **2a (0.1 mmol)** and $Ni(dppf)Cl_2$ (5 mol%, 3.4 mg) were added and charged with argon more than five times (The tube was sealed with tipping plug). Dioxane (0.5 mL) was injected into the tube. The resulting suspension was stirred vigorously at 140 ℃ for 4 h. After the reaction was completed, the resulting mixture was filtered through a celite pad and concentrated under reduced pressure. The residue was purified with chromatography column on silica gel to give the product **3a** and **[D4]-3a** (10.9mg, 12%) (Petroleum ether/EtOAc = 3:1).



KIE=K_H/K_D=2.36/0.64=3.7

d) Hydrolysis reaction



In an oven-dried 10 ml tube, **3a** (0.1 mmol, 49 mg) and NaOH (2.25mmol, 90 mg) were added under air. Then EtOH (1 mL) was added with a syringe. The reaction mixture was allowed to stir at 130 ℃ for 20 h. After completion of the reaction (TLC monitored), the resulting mixture was filtered through a celite pad and concentrated under reduced pressure. The residue was purified with chromatography column on silica gel to give the product **5a** (25.7 mg, 71%) as a white solid.

8. References

Y. Aihara, N. Chatani, *J. Am. Chem. Soc.* **2013**, *135*, 5308-11; W. Y. Shi, Y. N. Ding, C. Liu, N. Zheng, X. Y. Gou, M. Li, Z. Zhang, H. C. Liu, Z. J. Niu, Y. M. Liang, *Chem Commun (Camb)* **2020**, *56*, 12729-12732; N. Rajesh, B. Sundararaju, *Asian J. Org. Chem.* **2018**, *7*, 1368-1371.

Q. Wang, S. An, Z. Deng, W. Zhu, Z. Huang, G. He, G. Chen, *Nat. Catal.* **2019**, *2*, 793-800.

Y. N. Ding, W. Y. Shi, C. Liu, N. Zheng, M. Li, Y. An, Z. Zhang, C. T. Wang, B. S. Zhang, Y. M. Liang, *J. Org. Chem.* **2020**, *85*, 11280-11296.

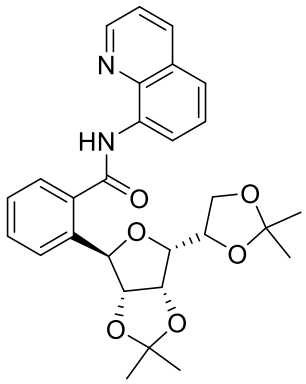
H. Ye, C. Xiao, Q. Q. Zhou, P. G. Wang, W. J. Xiao, *J. Org. Chem.* **2018**, *83*, 13325-13334.

C.-W. Chang, S.-S. Chang, C.-S. Chao, K.-K. T. Mong, *Tetrahedron Lett.* **2009**, *50*, 4536-4540; E. R. van Rijssel, P. van Delft, G. Lodder, H. S. Overkleeft, G. A. van der Marel, D. V. Filippov, J. D. Codee, *Angew. Chem. Int. Ed.* **2014**, *53*, 10381-5; J. Zeng, S. Vedachalam, S. Xiang, X.-W. Liu, *Org. Lett.* **2011**, *13*, 42-45.

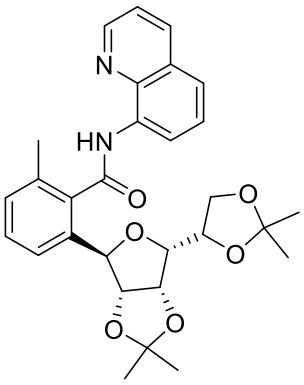
K. C. Nicolaou, S. R. Rekula, S. M. Kumar, A. R. Podilapu, R. P. Matuszak, P. M. Jung, L. T. Lam, A. C. Phillips, J. Lyssikatos, S. Munneke, C. Gu, H. Sarvaiya, J. Sandoval, M. Hammond, M. Aujay, J. W. Purcell, R. M. Reilly, J. Gavrilyuk, *J. Org. Chem.* **2021**, *86*, 2499-2521.

Q. L. Yang, X. Y. Wang, T. L. Wang, X. Yang, D. Liu, X. Tong, X. Y. Wu, T. S. Mei, *Org. Lett.* **2019**, *21*, 2645-2649.

9. Characterization Data



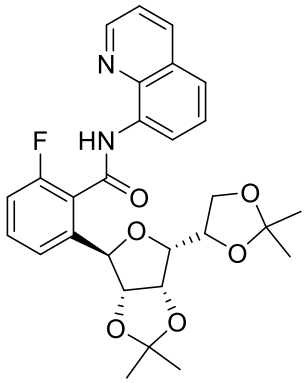
2-((3a*R*,4*R*,6*R*,6a*S*)-6-((*R*)-2,2-dimethyl-1,3-dioxolan-4-yl)-2,2-dimethyltetrahydrofuro[3,4-*d*][1,3]dioxol-4-yl)-*N*-(quinolin-8-yl)benzamide **(3a)**
Colorless oil, 60% (29.5mg)
^{1}H NMR (400 MHz, Chloroform-d) δ 10.30 (s, 1H), 8.94 (d, J = 6.8 Hz, 1H), 8.78 (dd, J = 4.2, 1.8 Hz, 1H), 8.18 (d, J = 8.0 Hz, 1H), 7.77 (d, J = 7.4 Hz, 1H), 7.61 – 7.43 (m, 6H), 5.79 (s, 1H), 4.98 (d, J = 5.6 Hz, 1H), 4.77 (dd, J = 6.0, 3.9 Hz, 1H), 4.46 (q, J = 6.4 Hz, 1H), 4.20 – 4.14 (m, 1H), 4.12 – 4.07 (m, 1H), 3.96 (dd, J = 7.7, 3.9 Hz, 1H), 1.50 (s, 3H), 1.40 (s, 3H), 1.36 (s, 3H), 1.24 (s, 3H).
^{13}C NMR (101 MHz, Chloroform-*d*) δ 167.4, 148.2, 138.6, 137.3, 136.3, 135.6, 134.4, 130.5, 128.0, 128.0, 127.9, 127.3, 126.5, 121.9, 121.6, 116.8, 112.7, 109.1, 87.1, 84.0, 81.4, 80.8, 73.5, 66.9, 26.8, 26.2, 25.2, 24.6.
HRMS (ESI-TOF) m/z: $[M + Na]^+$ Calcd for $C_{28}H_{30}N_2O_6Na$ 513.1996.1438; Found 513.1993.



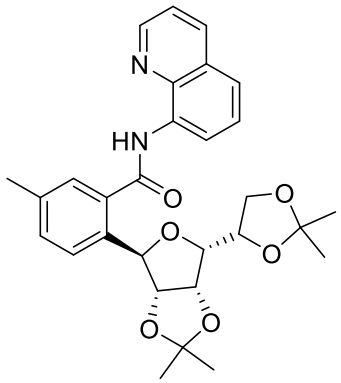
.

2-((3a*R*,4*R*,6*R*,6a*S*)-6-((*R*)-2,2-dimethyl-1,3-dioxolan-4-yl)-2,2-dimethyltetrahydrofuro[3,4-*d*][1,3]dioxol-4-yl)-6-methyl-*N*-(quinolin-8-yl)benzamide **(3b)**
Colorless oil, 56% (28.2mg)
^{1}H NMR (400 MHz, Chloroform-*d*) δ 9.98 (s, 1H), 8.97 (dd, *J* = 7.3, 1.7 Hz, 1H), 8.75 (dd, *J* = 4.2, 1.7 Hz, 1H), 8.18 (dd, *J* = 8.3, 1.7 Hz, 1H), 7.63 – 7.55 (m, 2H), 7.44 (dd, *J* = 8.3, 4.2 Hz, 1H), 7.35 (t, *J* = 7.7 Hz, 1H), 7.24 (d, *J* = 8.3, 1H), 7.15 (d, *J*

= 7.8 Hz, 1H), 5.38 (d, *J* = 1.8 Hz, 1H), 5.09 (dd, *J* = 6.0, 1.8 Hz, 1H), 4.84 (dd, *J* = 6.0, 4.0 Hz, 1H), 4.39 – 4.32 (m, 1H), 4.07 – 4.03 (m, 1H), 3.97 – 3.92 (m, 2H), 2.46 (s, 3H), 1.37 (s, 3H), 1.35 (s, 3H), 1.32 (s, 3H), 1.21 (s, 3H).
^{13}C NMR (101 MHz, Chloroform-*d*) δ 167.9, 148.2, 138.5, 136.8, 136.3, 135.9, 135.6, 134.3, 130.2, 129.0, 127.9, 127.3, 123.5, 122.0, 121.6, 116.9, 112.8, 109.1, 86.3, 84.1, 81.3, 81.1, 73.4, 66.9, 26.9, 26.2, 25.2, 24.6, 19.5.
HRMS (ESI-TOF) m/z: $[M + Na]^+$ Calcd for $C_{29}H_{32}N_2O_6Na$ 527.2153; Found 527.2148.



2-((3a*R*,4*R*,6*R*,6a*S*)-6-((*R*)-2,2-dimethyl-1,3-dioxolan-4-yl)-2,2-dimethyltetrahydrofuro[3,4-*d*][1,3]dioxol-4-yl)-6-fluoro-*N*-(quinolin-8-yl)benzamide **(3c)**
Yellow oil, 26% (13.2mg)
^{1}H NMR (400 MHz, Chloroform-*d*) δ 10.23 (s, 1H), 8.95 (dd, *J* = 6.7, 2.2 Hz, 1H), 8.79 (dd, *J* = 4.2, 1.7 Hz, 1H), 8.19 (dd, *J* = 8.3, 1.7 Hz, 1H), 7.63 – 7.57 (m, 2H), 7.46 (dd, *J* = 8.3, 4.5 Hz, 2H), 7.23 (d, *J* = 7.8 Hz, 1H), 7.17 (t, *J* = 8.8 Hz, 1H), 5.56 (d, *J* = 1.8 Hz, 1H), 5.02 (dd, *J* = 5.9, 2.0 Hz, 1H), 4.78 (dd, *J* = 6.0, 4.0 Hz, 1H), 4.43 – 4.38 (m, 1H), 4.02 (t, *J* = 5.3 Hz, 2H), 3.96 (dd, *J* = 7.8, 4.0 Hz, 1H), 1.46 (s, 3H), 1.34 (s, 3H), 1.33 (s, 3H), 1.21 (s, 3H).
^{13}C NMR (101 MHz, Chloroform-*d*) δ 162.4, 159.5 (d, *J* = 248.5 Hz), 148.0, 139.5 (d, *J* = 2.3 Hz), 138.1, 136.0, 133.8, 130.9 (d, *J* = 8.7 Hz), 127.6, 127.0, 123.5 (d, *J* = 17.7 Hz), 121.9, 121.7 (d, *J* = 3.0 Hz), 121.4, 116.7, 115.3 (d, *J* = 22.4 Hz), 112.7, 108.8, 86.4, 83.9 (d, *J* = 2.1 Hz), 81.4, 80.6, 73.1, 66.5, 26.5, 26.1, 24.9, 24.4.
^{19}F NMR (376 MHz, Chloroform-*d*) δ -114.5.
HRMS (ESI-TOF) m/z: $[M + Na]^+$ Calcd for $C_{28}H_{29}FN_2O_6Na$ 531.1902; Found 531.1896.



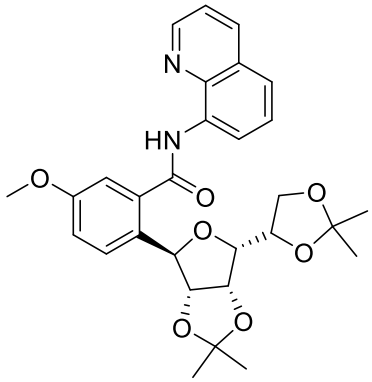
2-((3a*R*,4*R*,6*R*,6a*S*)-6-((*R*)-2,2-dimethyl-1,3-dioxolan-4-yl)-2,2-dimethyltetrahydrofuro[3,4-*d*][1,3]dioxol-4-yl)-5-methyl-*N*-(quinolin-8-yl)benzamide **(3d)**

Light yellow oil, 42% (21.3mg)

^{1}H NMR (400 MHz, Chloroform-*d*) δ 10.25 (s, 1H), 8.93 (dd, *J* = 7.2, 1.8 Hz, 1H), 8.79 (dd, *J* = 4.2, 1.7 Hz, 1H), 8.18 (dd, *J* = 8.3, 1.7 Hz, 1H), 7.62 – 7.54 (m, 3H), 7.46 (dd, *J* = 8.3, 4.2 Hz, 1H), 7.35 – 7.29 (m, 2H), 5.71 (s, 1H), 4.98 (dd, *J* = 6.0, 1.4 Hz, 1H), 4.77 (dd, *J* = 6.0, 4.0 Hz, 1H), 4.47 – 4.40 (m, 1H), 4.15 (dd, *J* = 8.7, 4.5 Hz, 1H), 4.07 (dd, *J* = 8.7, 6.3 Hz, 1H), 3.92 (dd, *J* = 7.8, 3.9 Hz, 1H), 2.43 (s, 3H), 1.47 (s, 3H), 1.39 (s, 3H), 1.35 (s, 3H), 1.24 (s, 3H).

^{13}C NMR (101 MHz, Chloroform-*d*) δ 167.7, 148.2, 138.7, 138.0, 136.3, 135.9, 134.5, 134.0, 131.1, 128.8, 127.9, 127.4, 126.5, 121.9, 121.6, 116.9, 112.6, 109.1, 86.9, 83.8, 81.3, 80.9, 73.5, 67.0, 26.9, 26.2, 25.2, 24.7, 21.0.

HRMS (ESI-TOF) m/z: $[M + Na]^+$ Calcd for $C_{29}H_{32}N_2O_6Na$ 527.2153; Found 527.2148.

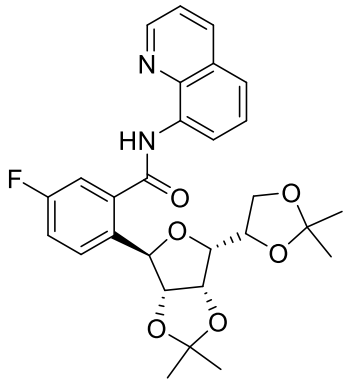


2-((3a*R*,4*R*,6*R*,6a*S*)-6-((*R*)-2,2-dimethyl-1,3-dioxolan-4-yl)-2,2-dimethyltetrahydrofuro[3,4-*d*][1,3]dioxol-4-yl)-5-methoxy-*N*-(quinolin-8-yl)benzamide **(3e)**

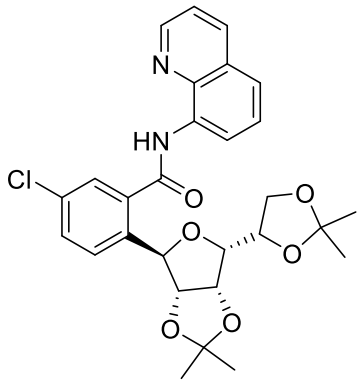
Colorless oil, 53% (27.3mg)

^{1}H NMR (400 MHz, Chloroform-*d*) δ 10.27 (s, 1H), 8.92 (dd, *J* = 7.1, 1.9 Hz, 1H), 8.78 (dd, *J* = 4.2, 1.7 Hz, 1H), 8.18 (dd, *J* = 8.3, 1.7 Hz, 1H), 7.61 – 7.55 (m, 2H), 7.46 (dd, *J* = 8.3, 4.2 Hz, 1H), 7.34 (d, *J* = 8.6 Hz, 1H), 7.28 (d, *J* = 2.7 Hz, 1H), 7.02 (dd, *J* = 8.6, 2.7 Hz, 1H), 5.66 (d, *J* = 1.3 Hz, 1H), 4.98 (dd, *J* = 6.0, 1.4 Hz, 1H), 4.79

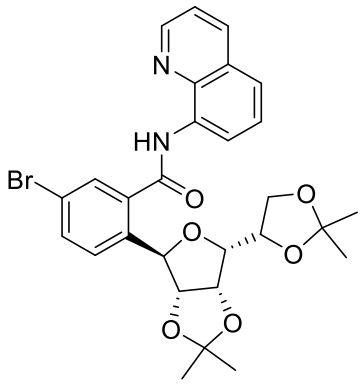
(dd, *J* = 6.0, 3.9 Hz, 1H), 4.43 (ddd, *J* = 7.9, 6.3, 4.5 Hz, 1H), 4.14 (dd, *J* = 8.7, 4.5 Hz, 1H), 4.06 (dd, *J* = 8.7, 6.3 Hz, 1H), 3.91 (dd, *J* = 7.8, 4.0 Hz, 1H), 3.87 (s, 3H), 1.47 (s, 3H), 1.39 (s, 3H), 1.35 (s, 3H), 1.25 (s, 3H).
^{13}C NMR (101 MHz, Chloroform-*d*) δ 167.3, 159.1, 148.2, 138.6, 137.3, 136.3, 134.4, 128.7, 128.0, 127.9, 127.3, 122.0, 121.6, 117.0, 115.4, 114.0, 112.6, 109.1, 86.7, 83.5, 81.2, 81.0, 73.5, 67.0, 55.5, 26.9, 26.2, 25.2, 24.6.
HRMS (ESI-TOF) m/z: $[M + Na]^+$ Calcd for $C_{29}H_{32}N_2O_7Na$ 543.2102; Found 543.2097.



2-((3a*R*,4*R*,6*R*,6a*S*)-6-((*R*)-2,2-dimethyl-1,3-dioxolan-4-yl)-2,2-dimethyltetrahydrofuro[3,4-*d*][1,3]dioxol-4-yl)-5-fluoro-*N*-(quinolin-8-yl)benzamide **(3f)** (α:β= 5:1)
White solid, 60% (30.3mg)
^{1}H NMR (400 MHz, Chloroform-*d*) δ 10.27 (s, 1H), 8.90 (dd, *J* = 6.3, 2.2 Hz, 2H), 8.80 (dd, *J* = 4.3, 1.7 Hz, 1H), 8.19 (dd, *J* = 8.3, 1.7 Hz, 1H), 7.63 – 7.55 (m, 2H), 7.52 – 7.39 (m, 3H), 7.20 (td, *J* = 8.3, 2.6 Hz, 1H), 5.69 (s, 1H), 4.95 (dd, *J* = 6.0, 1.7 Hz, 1H), 4.77 (dd, *J* = 6.0, 4.0 Hz, 1H), 4.44 (ddd, *J* = 7.6, 6.3, 4.6 Hz, 1H), 4.20 – 4.03 (m, 2H), 4.00 – 3.86 (m, 1H), 1.47 (s, 3H), 1.39 (s, 3H), 1.35 (s, 3H), 1.23 (s, 3H).
^{13}C NMR (101 MHz, Chloroform-*d*) δ 166.0 (d, *J* = 2.1 Hz), 161.9 (d, *J* = 249.1 Hz), 148.3, 138.6, 137.5 (d, *J* = 6.4 Hz), 136.3, 134.2, 133.1 (d, *J* = 3.4 Hz), 128.6 (d, *J* = 7.9 Hz), 127.9, 127.3, 122.2, 121.7, 117.2 (d, *J* = 20.9 Hz), 117.0, 115.4 (d, *J* = 23.0 Hz), 112.9, 109.1, 87.0, 83.7, 81.5, 80.9, 73.5, 66.8, 26.8, 26.3, 25.2, 24.7.
^{19}F NMR (376 MHz, Chloroform-*d*) δ -113.3.

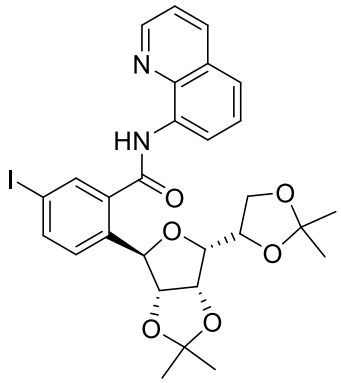


5-chloro-2-((3a*R*,4*R*,6*R*,6a*S*)-6-((*R*)-2,2-dimethyl-1,3-dioxolan-4-yl)-2,2-dimethyltetrahydrofuro[3,4-*d*][1,3]dioxol-4-yl)-*N*-(quinolin-8-yl)benzamide **(3g)**
White solid, 59% (30.7mg)
^{1}H NMR (400 MHz, Chloroform-*d*) δ 10.26 (s, 1H), 8.90 (dd, *J* = 5.9, 3.1 Hz, 1H), 8.81 (dd, *J* = 4.3, 1.7 Hz, 1H), 8.20 (dd, *J* = 8.3, 1.7 Hz, 1H), 7.73 (d, *J* = 2.1 Hz, 1H), 7.60 (d, *J* = 2.9 Hz, 1H), 7.59 (s, 1H), 7.51 – 7.46 (m, 2H), 7.42 (d, *J* = 8.4 Hz, 1H), 5.69 (d, *J* = 1.5 Hz, 1H), 4.93 (dd, *J* = 6.0, 1.6 Hz, 1H), 4.76 (dd, *J* = 6.0, 3.9 Hz, 1H), 4.44 (ddd, *J* = 7.6, 6.3, 4.5 Hz, 1H), 4.13 – 4.05 (m, 2H), 3.92 (dd, *J* = 7.6, 3.9 Hz, 1H), 1.47 (s, 3H), 1.39 (s, 3H), 1.35 (s, 3H), 1.22 (s, 3H).
^{13}C NMR (101 MHz, Chloroform-*d*) δ 166.0, 148.4, 138.5, 137.1, 136.4, 135.8, 134.1, 133.9, 130.4, 128.1, 127.9, 127.3, 122.3, 121.7, 117.0, 112.9, 109.1, 86.9, 83.7, 81.5, 80.8, 73.4, 66.8, 26.8, 26.3, 25.2, 24.7.
HRMS (ESI-TOF) m/z: $[M + Na]^+$ Calcd for $C_{28}H_{29}ClN_2O_6Na$ 547.1606; Found 547.1602.

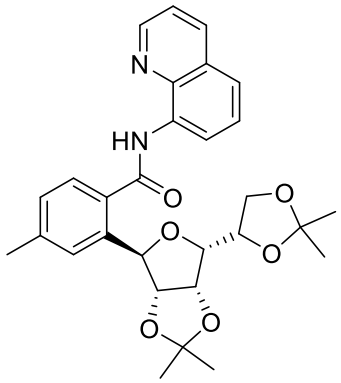


5-bromo-2-((3a*R*,4*R*,6*R*,6a*S*)-6-((*R*)-2,2-dimethyl-1,3-dioxolan-4-yl)-2,2-dimethyltetrahydrofuro[3,4-*d*][1,3]dioxol-4-yl)-*N*-(quinolin-8-yl)benzamide **(3h)**
White solid, 60% (33.4mg)
^{1}H NMR (400 MHz, Chloroform-*d*) δ 10.24 (s, 1H), 8.89 (dd, *J* = 6.0, 3.0 Hz, 1H), 8.81 (dd, *J* = 4.3, 1.8 Hz, 1H), 8.20 (dd, *J* = 8.3, 1.8 Hz, 1H), 7.87 (d, *J* = 2.1 Hz, 1H), 7.66 – 7.57 (m, 3H), 7.48 (dd, *J* = 8.3, 4.2 Hz, 1H), 7.35 (d, *J* = 8.4 Hz, 1H), 5.65 (s, 1H), 4.93 (dd, *J* = 6.0, 1.8 Hz, 1H), 4.75 (dd, *J* = 6.0, 3.9 Hz, 1H), 4.47 – 4.39 (m, 1H), 4.13 – 4.04 (m, 2H), 3.92 (dd, *J* = 7.6, 3.9 Hz, 1H), 1.46 (s, 3H), 1.38 (s, 3H), 1.35 (s, 3H), 1.22 (s, 3H).

^{13}C NMR (101 MHz, Chloroform-*d*) δ 165.9, 148.4, 138.6, 137.5, 136.4, 136.4, 134.2, 133.4, 130.9, 128.3, 127.9, 127.3, 122.3, 121.8, 121.7, 117.0, 112.9, 109.1, 86.9, 83.8, 81.6, 80.9, 73.5, 66.8, 26.8, 26.3, 25.2, 24.7.
HRMS (ESI-TOF) m/z: $[M + Na]^+$ Calcd for $C_{28}H_{29}BrN_2O_6Na$ 591.1101; Found 591.1098.



2-((3a*R*,4*R*,6*R*,6a*S*)-6-((*R*)-2,2-dimethyl-1,3-dioxolan-4-yl)-2,2-dimethyltetrahydrofuro[3,4-*d*][1,3]dioxol-4-yl)-5-iodo-*N*-(quinolin-8-yl)benzamide **(3i)**
Yellow solid, 50% (30.9mg)
^{1}H NMR (400 MHz, Chloroform-*d*) δ 10.23 (s, 1H), 8.89 (dd, *J* = 5.8, 3.2 Hz, 1H), 8.82 (dd, *J* = 4.2, 1.6 Hz, 1H), 8.20 (dd, *J* = 8.3, 1.7 Hz, 1H), 8.05 (d, *J* = 1.8 Hz, 1H), 7.84 (dd, *J* = 8.2, 1.8 Hz, 1H), 7.62 – 7.57 (m, 2H), 7.48 (dd, *J* = 8.3, 4.2 Hz, 1H), 7.21 (d, *J* = 8.3 Hz, 1H), 5.64 (s, 1H), 4.92 (dd, *J* = 6.0, 1.6 Hz, 1H), 4.75 (dd, *J* = 6.0, 3.9 Hz, 1H), 4.43 (ddd, *J* = 7.6, 6.2, 4.5 Hz, 1H), 4.13 – 4.04 (m, 2H), 3.90 (dd, *J* = 7.6, 3.9 Hz, 1H), 1.46 (s, 3H), 1.38 (s, 3H), 1.35 (s, 3H), 1.21 (s, 3H).
^{13}C NMR (101 MHz, Chloroform-*d*) δ 165.8, 148.4, 139.4, 138.5, 137.6, 136.9, 136.6, 136.4, 134.1, 128.4, 127.9, 127.3, 122.2, 121.7, 117.0, 112.9, 109.1, 93.1, 86.8, 83.8, 81.5, 80.8, 73.4, 66.8, 26.8, 26.3, 25.2, 24.7.
HRMS (ESI-TOF) m/z: $[M + Na]^+$ Calcd for $C_{28}H_{29}IN_2O_6Na$ 639.0963; Found 639.0961.



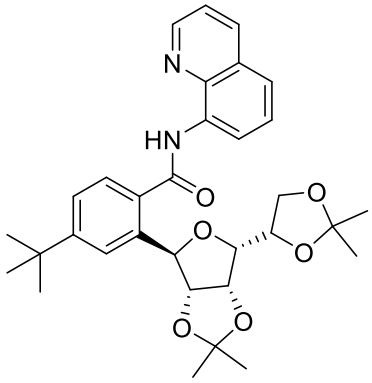
2-((3a*R*,4*R*,6*R*,6a*S*)-6-((*R*)-2,2-dimethyl-1,3-dioxolan-4-yl)-2,2-dimethyltetrahydrofuro[3,4-*d*][1,3]dioxol-4-yl)-4-methyl-*N*-(quinolin-8-yl)benzamide **(3j)**

Colorless oil, 47% (23.7mg)

^{1}H NMR (400 MHz, Chloroform-*d*) δ 10.27 (s, 1H), 8.93 (d, *J* = 6.1 Hz, 1H), 8.78 (dd, *J* = 4.2, 1.7 Hz, 1H), 8.18 (dd, *J* = 8.3, 1.7 Hz, 1H), 7.67 (d, *J* = 8.3 Hz, 1H), 7.61 – 7.53 (m, 2H), 7.45 (dd, *J* = 8.3, 4.3 Hz, 1H), 7.24 (d, *J* = 6.6 Hz, 2H), 5.74 (d, *J* = 1.5 Hz, 1H), 4.98 (dd, *J* = 6.0, 1.6 Hz, 1H), 4.78 (dd, *J* = 6.0, 4.0 Hz, 1H), 4.45 (ddd, *J* = 7.7, 6.3, 4.7 Hz, 1H), 4.15 – 4.08 (m, 2H), 3.97 (dd, *J* = 7.6, 4.0 Hz, 1H), 2.44 (s, 3H), 1.50 (s, 3H), 1.40 (s, 3H), 1.36 (s, 3H), 1.25 (s, 3H).

^{13}C NMR (101 MHz, Chloroform-*d*) δ 167.6, 148.2, 140.7, 138.6, 137.4, 136.3, 134.6, 133.0, 128.5, 128.2, 127.9, 127.4, 127.3, 121.8, 121.6, 116.8, 112.7, 109.1, 87.1, 84.0, 81.5, 80.9, 73.6, 67.0, 26.8, 26.3, 25.2, 24.7, 21.7.

HRMS (ESI-TOF) m/z: $[M + Na]^+$ Calcd for $C_{29}H_{32}N_2O_6Na$ 527.2153; Found 527.2148.



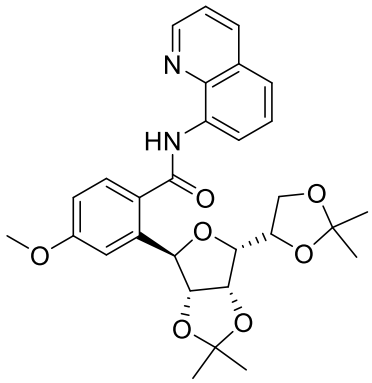
4-(tert-butyl)-2-((3a*R*,4*R*,6*R*,6a*S*)-6-((*R*)-2,2-dimethyl-1,3-dioxolan-4-yl)-2,2-dimethyl tetrahydrofuro[3,4-*d*][1,3]dioxol-4-yl)-*N*-(quinolin-8-yl)benzamide. **(3k)**

Light yellow oil, 37% (20.1mg)

^{1}H NMR (400 MHz, Chloroform-*d*) δ 10.34 (s, 1H), 8.95 (dd, *J* = 7.3, 1.7 Hz, 1H), 8.79 (dd, *J* = 4.2, 1.7 Hz, 1H), 8.19 (dd, *J* = 8.3, 1.7 Hz, 1H), 7.75 (d, *J* = 8.0 Hz, 1H), 7.62 – 7.54 (m, 3H), 7.49 – 7.44 (m, 2H), 5.84 (s, 1H), 4.93 (dd, *J* = 6.0, 1.3 Hz, 1H), 4.71 (dd, *J* = 6.0, 3.8 Hz, 1H), 4.50 (ddd, *J* = 7.6, 6.2, 4.3 Hz, 1H), 4.23 (dd, *J* = 8.7, 4.3 Hz, 1H), 4.14 (dd, *J* = 8.7, 6.2 Hz, 1H), 3.93 (dd, *J* = 7.6, 3.8 Hz, 1H), 1.51 (s, 3H), 1.40 – 1.37 (m, 15H), 1.23 (s, 3H).

^{13}C NMR (101 MHz, Chloroform-*d*) δ 167.4, 154.0, 148.2, 138.7, 137.1, 136.3, 134.6, 132.5, 128.0, 128.0, 127.4, 124.6, 123.8, 121.8, 121.6, 116.8, 112.7, 109.1, 87.6, 84.4, 81.4, 80.7, 73.5, 67.0, 35.0, 31.1, 26.9, 26.3, 25.3, 24.8.

HRMS (ESI-TOF) m/z: $[M + Na]^+$ Calcd for $C_{32}H_{38}N_2O_6Na$ 569.2622; Found 569.2618.



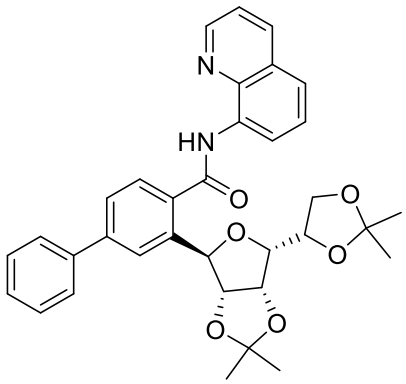
2-((3a*R*,4*R*,6*R*,6a*S*)-6-((*R*)-2,2-dimethyl-1,3-dioxolan-4-yl)-2,2-dimethyltetrahydrofuro[3,4-*d*][1,3]dioxol-4-yl)-4-methoxy-*N*-(quinolin-8-yl)benzamide **(3l)**

Yellow oil, 52% (27.0mg)

^{1}H NMR (400 MHz, Chloroform-*d*) δ 10.31 (s, 1H), 8.93 (dd, *J* = 7.4, 1.6 Hz, 1H), 8.80 (dd, *J* = 4.3, 1.7 Hz, 1H), 8.19 (dd, *J* = 8.3, 1.7 Hz, 1H), 7.77 (d, *J* = 8.4 Hz, 1H), 7.61 – 7.53 (m, 2H), 7.47 (dd, *J* = 8.2, 4.2 Hz, 1H), 7.07 (d, *J* = 2.3 Hz, 1H), 6.93 (dd, *J* = 8.5, 2.6 Hz, 1H), 5.85 (s, 1H), 4.91 (dd, *J* = 6.0, 1.3 Hz, 1H), 4.72 (dd, *J* = 6.0, 3.9 Hz, 1H), 4.48 (ddd, *J* = 7.5, 6.3, 4.5 Hz, 1H), 4.20 (dd, *J* = 8.7, 4.5 Hz, 1H), 4.13 (dd, *J* = 8.8, 6.2 Hz, 1H), 3.97 (dd, *J* = 7.5, 3.9 Hz, 1H), 3.89 (s, 3H), 1.50 (s, 3H), 1.42 (s, 3H), 1.37 (s, 3H), 1.23 (s, 3H).

^{13}C NMR (101 MHz, Chloroform-*d*) δ 167.0, 161.4, 148.2, 140.0, 138.7, 136.3, 134.7, 130.1, 128.0, 127.7, 127.4, 121.7, 121.6, 116.7, 112.7, 112.3, 109.1, 87.4, 84.0, 81.5, 80.7, 73.6, 67.0, 55.4, 26.9, 26.3, 25.2, 24.7.

HRMS (ESI-TOF) m/z: $[M + Na]^+$ Calcd for $C_{29}H_{32}N_2O_7Na$ 543.2102; Found 543.2097.

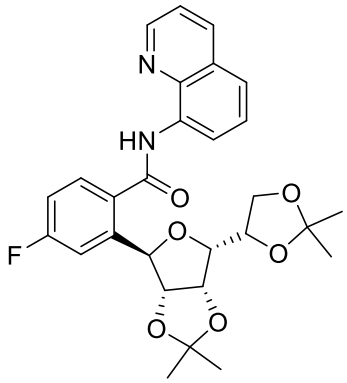


3-((3a*R*,4*R*,6*R*,6a*S*)-6-((*R*)-2,2-dimethyl-1,3-dioxolan-4-yl)-2,2-dimethyltetrahydrofuro[3,4-*d*][1,3]dioxol-4-yl)-*N*-(quinolin-8-yl)-[1,1'-biphenyl]-4-carboxamide **(3m)**

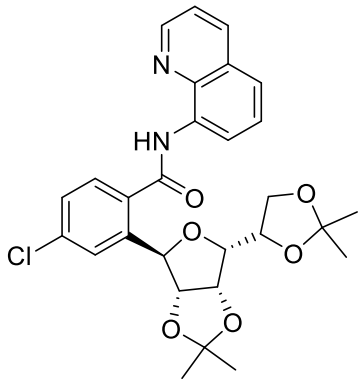
White solid, 51% (29.1mg)

^{1}H NMR (400 MHz, Chloroform-*d*) δ 10.4 (s, 1H), 9.0 (d, *J* = 7.1 Hz, 1H), 8.8 (dd, *J* = 4.2, 1.7 Hz, 1H), 8.2 (dd, *J* = 8.3, 1.7 Hz, 1H), 7.9 (d, *J* = 7.9 Hz, 1H), 7.7 (s, 1H), 7.7 – 7.6 (m, 5H), 7.5 – 7.4 (m, 4H), 5.8 (s, 1H), 5.0 (dd, *J* = 6.0, 1.6 Hz, 1H), 4.8 (dd,

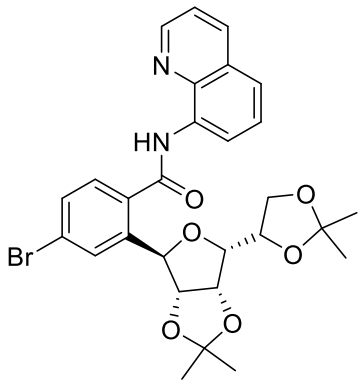
J = 6.0, 3.9 Hz, 1H), 4.5 (ddd, *J* = 7.5, 6.3, 4.6 Hz, 1H), 4.2 (dd, *J* = 8.7, 4.6 Hz, 1H), 4.1 (dd, *J* = 8.7, 6.3 Hz, 1H), 4.0 (dd, *J* = 7.5, 3.9 Hz, 1H), 1.5 (s, 3H), 1.4 (s, 3H), 1.4 (s, 3H), 1.3 (s, 3H).
^{13}C NMR (101 MHz, Chloroform-*d*) δ 167.3, 148.3, 143.3, 140.0, 138.6, 137.9, 136.4, 134.5, 134.3, 129.0, 128.7, 128.1, 127.9, 127.4, 127.1, 126.5, 125.5, 121.9, 121.7, 116.9, 112.8, 109.1, 87.1, 84.1, 81.6, 80.9, 73.5, 66.9, 26.8, 26.3, 25.2, 24.8.
HRMS (ESI-TOF) m/z: $[M + Na]^+$ Calcd for $C_{34}H_{34}N_2O_6Na$ 589.2309; Found 589.2305.



2-((3a*R*,4*R*,6*R*,6a*S*)-6-((*R*)-2,2-dimethyl-1,3-dioxolan-4-yl)-2,2-dimethyltetrahydrofuro[3,4-*d*][1,3]dioxol-4-yl)-4-fluoro-*N*-(quinolin-8-yl)benzamide **(3n)**
Yellow oil, 60% (30.5mg)
^{1}H NMR (400 MHz, Chloroform-*d*) δ 10.29 (s, 1H), 8.91 (dd, *J* = 6.8, 2.2 Hz, 1H), 8.80 (dd, *J* = 4.2, 1.7 Hz, 1H), 8.20 (dd, *J* = 8.3, 1.7 Hz, 1H), 7.79 (dd, *J* = 8.5, 5.5 Hz, 1H), 7.63 – 7.56 (m, 2H), 7.48 (dd, *J* = 8.3, 4.2 Hz, 1H), 7.22 (ddd, *J* = 10.0, 2.7, 0.9 Hz, 1H), 7.13 (td, *J* = 8.1, 2.6 Hz, 1H), 5.79 (s, 1H), 4.91 (dd, *J* = 6.0, 1.6 Hz, 1H), 4.74 (dd, *J* = 6.0, 3.9 Hz, 1H), 4.46 (ddd, *J* = 7.4, 6.3, 4.7 Hz, 1H), 4.18 – 4.09 (m, 2H), 3.96 (dd, *J* = 7.4, 3.9 Hz, 1H), 1.48 (s, 3H), 1.42 (s, 3H), 1.37 (s, 3H), 1.22 (s, 3H).
^{13}C NMR (101 MHz, Chloroform-*d*) δ 166.4, 163.8 (d, *J* = 251.3 Hz), 148.3, 141.1 (d, *J* = 7.1 Hz), 138.6, 136.4, 134.3, 131.5 (d, *J* = 3.3 Hz), 130.3 (d, *J* = 8.7 Hz), 127.9, 127.4, 122.0, 121.7, 116.9, 114.7 (d, *J* = 21.7 Hz), 114.0 (d, *J* = 23.4 Hz), 112.9, 109.1, 87.2, 83.7, 81.7, 80.7, 73.5, 66.8, 26.8, 26.2, 25.2, 24.7.
^{19}F NMR (376 MHz, Chloroform-*d*) δ -108.3.
HRMS (ESI-TOF) m/z: $[M + Na]^+$ Calcd for $C_{28}H_{29}FN_2O_6Na$ 531.1902; Found 531.1897.

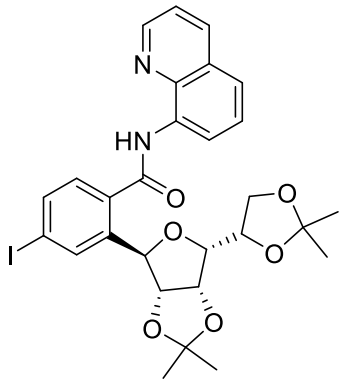


4-chloro-2-((3a*R*,4*R*,6*R*,6a*S*)-6-((*R*)-2,2-dimethyl-1,3-dioxolan-4-yl)-2,2-dimethyltetrahydrofuro[3,4-*d*][1,3]dioxol-4-yl)-*N*-(quinolin-8-yl)benzamide **(3o)**
White solid, 53% (27.8mg)
^{1}H NMR (400 MHz, Chloroform-*d*) δ 10.26 (s, 1H), 8.90 (d, *J* = 5.0 Hz, 1H), 8.85 – 8.77 (m, 1H), 8.19 (d, *J* = 7.5 Hz, 1H), 7.70 (d, *J* = 8.1 Hz, 1H), 7.64 – 7.55 (m, 2H), 7.50 – 7.41 (m, 3H), 5.70 (s, 1H), 4.94 (dd, *J* = 5.9, 1.9 Hz, 1H), 4.78 (dd, *J* = 6.0, 4.0 Hz, 1H), 4.44 (q, *J* = 6.2 Hz, 1H), 4.15 – 4.06 (m, 2H), 3.97 (dd, *J* = 7.5, 4.0 Hz, 1H), 1.47 (s, 3H), 1.40 (s, 3H), 1.36 (s, 3H), 1.23 (s, 3H).
^{13}C NMR (101 MHz, Chloroform-*d*) δ 166.5, 148.3, 139.8, 138.6, 136.7, 136.4, 134.3, 134.0, 129.5, 128.1, 127.9, 127.3, 126.9, 122.1, 121.7, 116.9, 113.0, 109.1, 87.0, 83.7, 81.8, 80.9, 73.5, 66.9, 26.8, 26.3, 25.2, 24.8.
HRMS (ESI-TOF) m/z: $[M + Na]^+$ Calcd for $C_{28}H_{29}ClN_2O_6Na$ 547.1606; Found 547.1602.

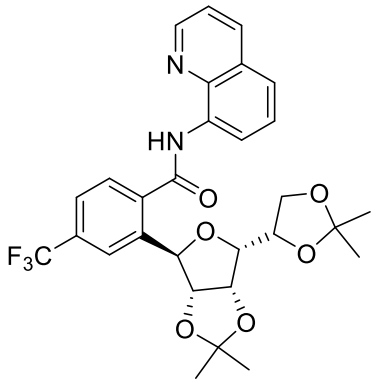


4-bromo-2-((3a*R*,4*R*,6*R*,6a*S*)-6-((*R*)-2,2-dimethyl-1,3-dioxolan-4-yl)-2,2-dimethyltetrahydrofuro[3,4-*d*][1,3]dioxol-4-yl)-*N*-(quinolin-8-yl)benzamide **(3p)**
White solid, 60% (34.2mg)
^{1}H NMR (400 MHz, Chloroform-*d*) δ 10.24 (s, 1H), 8.89 (dd, *J* = 6.5, 2.5 Hz, 1H), 8.79 (dd, *J* = 4.2, 1.7 Hz, 1H), 8.19 (dd, *J* = 8.3, 1.7 Hz, 1H), 7.64 – 7.56 (m, 5H), 7.47 (dd, *J* = 8.3, 4.2 Hz, 1H), 5.68 (s, 1H), 4.94 (dd, *J* = 6.0, 1.9 Hz, 1H), 4.78 (dd, *J* = 6.0, 4.0 Hz, 1H), 4.43 (dt, *J* = 7.3, 5.6 Hz, 1H), 4.07 (dd, *J* = 5.7, 1.6 Hz, 2H), 3.97 (dd, *J* = 7.4, 4.0 Hz, 1H), 1.47 (s, 3H), 1.39 (s, 3H), 1.35 (s, 3H), 1.24 (s, 3H).

^{13}C NMR (101 MHz, Chloroform-*d*) δ 166.6, 148.3, 139.8, 138.6, 136.4, 134.5, 134.3, 131.1, 129.8, 129.6, 127.9, 127.3, 125.0, 122.1, 121.7, 116.9, 113.0, 109.1, 87.0, 83.7, 81.8, 80.9, 73.5, 66.9, 26.8, 26.4, 25.2, 24.8.
HRMS (ESI-TOF) m/z: $[M + Na]^+$ Calcd for $C_{28}H_{29}BrN_2O_6Na$ 591.1101; Found 591.1099.



2-((3a*R*,4*R*,6*R*,6a*S*)-6-((*R*)-2,2-dimethyl-1,3-dioxolan-4-yl)-2,2-dimethyltetrahydrofuro[3,4-*d*][1,3]dioxol-4-yl)-4-iodo-*N*-(quinolin-8-yl)benzamide **(3q)**
Light yellow solid, 60% (36.5mg)
^{1}H NMR (400 MHz, Chloroform-*d*) δ 10.25 (s, 1H), 8.89 (dd, *J* = 6.4, 2.6 Hz, 1H), 8.78 (dd, *J* = 4.3, 1.7 Hz, 1H), 8.19 (dd, *J* = 8.3, 1.7 Hz, 1H), 7.82 – 7.78 (m, 2H), 7.61 – 7.56 (m, 2H), 7.47 (dd, *J* = 8.2, 3.1 Hz, 2H), 5.65 (s, 1H), 4.94 (dd, *J* = 6.0, 2.0 Hz, 1H), 4.78 (dd, *J* = 6.0, 3.9 Hz, 1H), 4.43 (dt, *J* = 7.5, 5.6 Hz, 1H), 4.07 (d, *J* = 5.6 Hz, 2H), 3.95 (dd, *J* = 7.6, 4.0 Hz, 1H), 1.47 (s, 3H), 1.39 (s, 3H), 1.35 (s, 3H), 1.24 (s, 3H).
^{13}C NMR (101 MHz, Chloroform-*d*) δ 166.7, 148.3, 139.5, 138.5, 137.1, 136.4, 135.8, 135.1, 134.2, 129.5, 127.9, 127.3, 122.1, 121.7, 116.9, 113.0, 109.1, 97.0, 86.9, 83.6, 81.8, 80.9, 73.4, 66.9, 26.7, 26.4, 25.2, 24.8.
HRMS (ESI-TOF) m/z: $[M + Na]^+$ Calcd for $C_{28}H_{29}IN_2O_6Na$ 639.0963; Found 639.0959.



2-((3a*R*,4*R*,6*R*,6a*S*)-6-((*R*)-2,2-dimethyl-1,3-dioxolan-4-yl)-2,2-dimethyltetrahydrofuro[3,4-*d*][1,3]dioxol-4-yl)-*N*-(quinolin-8-yl)-4-(trifluoromethyl)benzamide **(3r)**

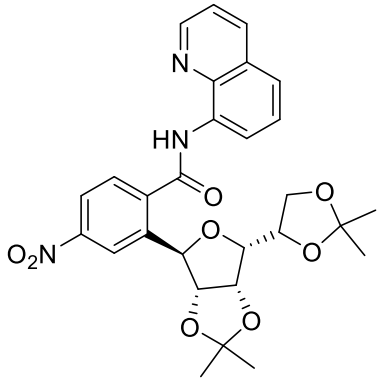
Yellow oil, 44% (24.6mg)

^{1}H NMR (400 MHz, Chloroform-*d*) δ 10.29 (s, 1H), 8.91 (dd, *J* = 5.7, 3.2 Hz, 1H), 8.79 (dd, *J* = 4.2, 1.7 Hz, 1H), 8.21 (dd, *J* = 8.3, 1.7 Hz, 1H), 7.86 (d, *J* = 7.7 Hz, 1H), 7.75 – 7.70 (m, 2H), 7.63 – 7.58 (m, 2H), 7.48 (dd, *J* = 8.3, 4.2 Hz, 1H), 5.70 (s, 1H), 4.97 (dd, *J* = 5.9, 2.1 Hz, 1H), 4.79 (dd, *J* = 6.0, 3.9 Hz, 1H), 4.44 (dt, *J* = 7.5, 5.5 Hz, 1H), 4.06 (d, *J* = 5.5 Hz, 2H), 3.96 (dd, *J* = 7.5, 3.9 Hz, 1H), 1.49 – 1.46 (m, 3H), 1.36 (s, 3H), 1.35 (s, 3H), 1.24 (s, 3H).

^{13}C NMR (101 MHz, Chloroform-*d*) δ 166.3, 148.4, 138.9, 138.7, 138.5, 136.4, 134.1, 132.3 (d, *J* = 32.7 Hz), 128.5, 127.9, 127.3, 125.0 (d, *J* = 4.0 Hz), 123.7 (d, *J* = 3.7 Hz), 123.5 (d, *J* = 272.8 Hz), 122.4, 121.8, 117.0, 113.2, 109.2, 86.9, 84.0, 81.9, 80.9, 73.4, 66.8, 26.7, 26.4, 25.3, 24.8.

^{19}F NMR (376 MHz, Chloroform-*d*) δ -63.0.

HRMS (ESI-TOF) m/z: $[M + Na]^+$ Calcd for $C_{29}H_{29}F_3N_2O_6Na$ 581.1870; Found 581.1867.



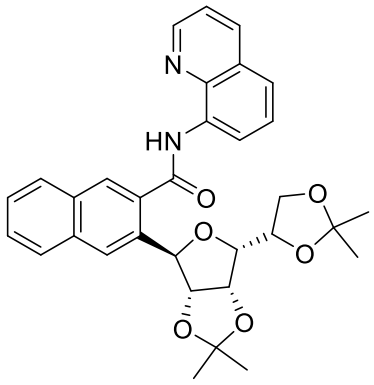
2-((3a*R*,4*R*,6*R*,6a*S*)-6-((*R*)-2,2-dimethyl-1,3-dioxolan-4-yl)-2,2-dimethyltetrahydrofuro[3,4-*d*][1,3]dioxol-4-yl)-4-nitro-*N*-(quinolin-8-yl)benzamide **(3s)**

Yellow oil, 51% (27.4mg)

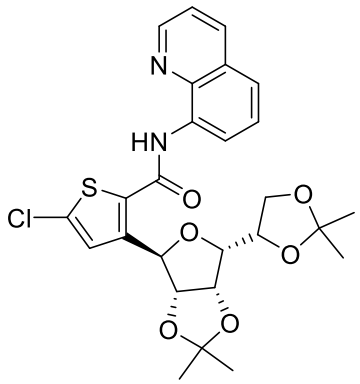
^{1}H NMR (400 MHz, Chloroform-*d*) δ 10.31 (s, 1H), 8.92 – 8.88 (m, 1H), 8.80 (dd, *J* = 4.2, 1.8 Hz, 1H), 8.35 – 8.26 (m, 2H), 8.24 – 8.20 (m, 1H), 7.90 (d, *J* = 8.3 Hz, 1H), 7.62 (d, *J* = 3.8 Hz, 2H), 7.50 (dd, *J* = 8.2, 4.2 Hz, 1H), 5.68 (s, 1H), 4.98 (dd, *J* = 6.0, 2.2 Hz, 1H), 4.82 (dd, *J* = 6.0, 3.9 Hz, 1H), 4.44 (dt, *J* = 7.6, 5.6 Hz, 1H), 4.06 (d, *J* = 5.5 Hz, 2H), 3.98 (dd, *J* = 7.5, 3.9 Hz, 1H), 1.47 (s, 3H), 1.37 (s, 3H), 1.35 (s, 3H), 1.25 (s, 3H).

^{13}C NMR (101 MHz, Chloroform-*d*) δ 165.5, 148.7, 148.4, 141.1, 140.0, 138.4, 136.5, 133.9, 129.2, 127.9, 127.3, 124.0, 123.1, 122.6, 121.9, 117.1, 113.4, 109.2, 86.7, 83.8, 82.0, 80.9, 73.3, 66.8, 26.7, 26.4, 25.2, 24.8.

HRMS (ESI-TOF) m/z: $[M + Na]^+$ Calcd for $C_{28}H_{29}N_3O_8Na$ 558.1847; Found 558.1842.

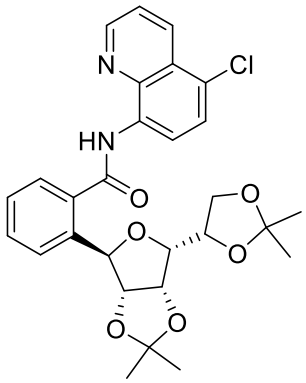


3-((3a*R*,4*R*,6*R*,6a*S*)-6-((*R*)-2,2-dimethyl-1,3-dioxolan-4-yl)-2,2-dimethyltetrahydrofuro[3,4-*d*][1,3]dioxol-4-yl)-*N*-(quinolin-8-yl)-2-naphthamide **(3t)**
White solid, 65% (34.9mg)
^{1}H NMR (400 MHz, Chloroform-*d*) δ 10.41 (s, 1H), 8.97 (dd, *J* = 7.3, 1.7 Hz, 1H), 8.79 (dd, *J* = 4.2, 1.7 Hz, 1H), 8.26 (s, 1H), 8.19 (dd, *J* = 8.3, 1.7 Hz, 1H), 7.96 – 7.87 (m, 3H), 7.64 – 7.55 (m, 4H), 7.47 (dd, *J* = 8.3, 4.2 Hz, 1H), 5.92 (s, 1H), 5.14 (dd, *J* = 6.0, 1.6 Hz, 1H), 4.80 (dd, *J* = 6.0, 4.0 Hz, 1H), 4.47 (ddd, *J* = 7.6, 6.3, 4.7 Hz, 1H), 4.15 – 4.06 (m, 2H), 4.01 (dd, *J* = 7.7, 4.0 Hz, 1H), 1.53 (s, 3H), 1.37 (s, 3H), 1.35 (s, 3H), 1.26 (s, 3H).
^{13}C NMR (101 MHz, Chloroform-*d*) δ 167.6, 148.3, 138.6, 136.3, 134.6, 133.8, 133.8, 133.5, 132.0, 128.3, 128.2, 128.1, 128.0, 127.8, 127.4, 127.0, 126.0, 121.9, 121.6, 116.9, 112.8, 109.1, 86.5, 84.1, 81.5, 81.0, 73.5, 67.0, 26.8, 26.3, 25.2, 24.7.
HRMS (ESI-TOF) m/z: $[M + Na]^+$ Calcd for $C_{32}H_{32}N_2O_6Na$ 563.2153; Found 563.2148.

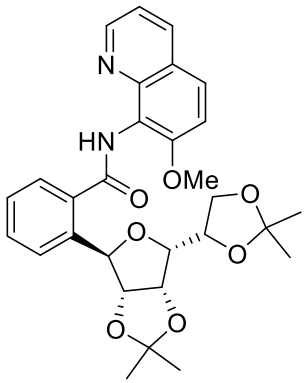


5-chloro-3-((3a*R*,4*R*,6*R*,6a*S*)-6-((*R*)-2,2-dimethyl-1,3-dioxolan-4-yl)-2,2-dimethyltetrahydrofuro[3,4-*d*][1,3]dioxol-4-yl)-*N*-(quinolin-8-yl)thiophene-2-carboxamide **(3u)**
Colorless oil, 26% (13.5mg)
^{1}H NMR (400 MHz, Chloroform-*d*) δ 10.42 (s, 1H), 8.87 – 8.78 (m, 2H), 8.18 (dd, *J* = 8.2, 1.7 Hz, 1H), 7.56 (d, *J* = 4.7 Hz, 2H), 7.48 (dd, *J* = 8.3, 4.2 Hz, 1H), 6.93 (s, 1H), 5.69 (s, 1H), 4.97 (dd, *J* = 6.0, 1.1 Hz, 1H), 4.80 (dd, *J* = 6.1, 3.9 Hz, 1H), 4.51 (td, *J* = 6.7, 4.6 Hz, 1H), 4.24 – 4.15 (m, 2H), 3.99 (dd, *J* = 7.2, 3.9 Hz, 1H), 1.57 (s, 3H), 1.48 (s, 3H), 1.41 (s, 3H), 1.35 (s, 3H).

^{13}C NMR (101 MHz, Chloroform-*d*) δ 159.1, 148.3, 144.7, 138.6, 136.3, 134.1, 133.2, 131.0, 127.9, 127.5, 127.3, 122.1, 121.7, 117.3, 112.9, 109.2, 87.3, 82.6, 82.0, 80.5, 73.5, 66.8, 26.9, 26.2, 25.2, 24.9.
HRMS (ESI-TOF) m/z: $[M + Na]^+$ Calcd for $C_{26}H_{27}ClN_2O_6Na$ 553.1171; Found 553.1165.

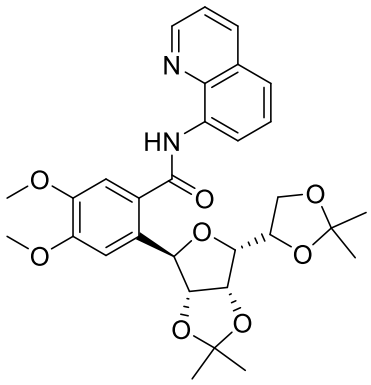


N-(5-chloroquinolin-8-yl)-2-((3a*R*,4*R*,6*R*,6a*S*)-6-((*R*)-2,2-dimethyl-1,3-dioxolan-4-yl)-2,2-dimethyltetrahydrofuro[3,4-*d*][1,3]dioxol-4-yl)benzamide **(3v)**
Light yellow solid, 51% (26.7mg)
^{1}H NMR (400 MHz, Chloroform-*d*) δ 10.26 (s, 1H), 8.89 (d, *J* = 8.4 Hz, 1H), 8.84 (dd, *J* = 4.2, 1.6 Hz, 1H), 8.59 (dd, *J* = 8.5, 1.6 Hz, 1H), 7.76 (dd, *J* = 7.5, 1.4 Hz, 1H), 7.66 (d, *J* = 8.4 Hz, 1H), 7.58 (dd, *J* = 8.5, 4.2 Hz, 1H), 7.56 – 7.44 (m, 3H), 5.76 (s, 1H), 4.96 (dd, *J* = 6.0, 1.5 Hz, 1H), 4.76 (dd, *J* = 6.0, 3.9 Hz, 1H), 4.46 (ddd, *J* = 7.7, 6.3, 4.4 Hz, 1H), 4.16 (dd, *J* = 8.7, 4.4 Hz, 1H), 4.09 (dd, *J* = 8.7, 6.3 Hz, 1H), 3.95 (dd, *J* = 7.7, 4.0 Hz, 1H), 1.49 (s, 3H), 1.40 (s, 3H), 1.36 (s, 3H), 1.24 (s, 3H).
^{13}C NMR (101 MHz, Chloroform-*d*) δ 167.4, 148.7, 139.2, 137.4, 135.4, 133.7, 133.4, 130.7, 128.0, 128.0, 127.2, 126.6, 125.9, 124.7, 122.4, 116.8, 112.8, 109.1, 87.1, 84.0, 81.4, 80.8, 73.5, 66.9, 26.9, 26.3, 25.2, 24.7.
HRMS (ESI-TOF) m/z: $[M + Na]^+$ Calcd for $C_{28}H_{29}ClN_2O_6Na$ 547.1606; Found 547.1603.

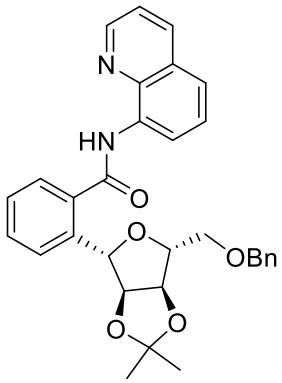


2-((3a*R*,4*R*,6*R*,6a*S*)-6-((*R*)-2,2-dimethyl-1,3-dioxolan-4-yl)-2,2-dimethyltetrahydrofuro[3,4-*d*][1,3]dioxol-4-yl)-*N*-(7-methoxyquinolin-8-yl)benzamide **(3w)**

Yellow oil, 33% (16.9mg)
^{1}H NMR (400 MHz, Chloroform-*d*) δ 10.25 (s, 1H), 8.67 (d, *J* = 2.6 Hz, 1H), 8.61 (dd, *J* = 4.2, 1.7 Hz, 1H), 8.06 (d, *J* = 9.2 Hz, 1H), 7.75 (d, *J* = 7.3 Hz, 1H), 7.54 – 7.38 (m, 4H), 6.84 (d, *J* = 2.3 Hz, 1H), 5.74 (s, 1H), 4.98 (dd, *J* = 5.9, 1.6 Hz, 1H), 4.78 (dd, *J* = 6.0, 3.9 Hz, 1H), 4.49 – 4.40 (m, 1H), 4.16 – 4.07 (m, 2H), 3.96 (s, 4H), 1.50 (s, 3H), 1.40 (s, 3H), 1.36 (s, 3H), 1.26 (s, 3H).
^{13}C NMR (101 MHz, Chloroform-*d*) δ 167.5, 158.5, 145.6, 137.3, 135.6, 135.4, 135.2, 135.0, 130.6, 128.9, 128.1, 128.0, 126.6, 122.1, 112.8, 109.4, 109.1, 100.0, 87.1, 84.0, 81.5, 80.9, 73.6, 67.0, 55.6, 26.9, 26.3, 25.2, 24.7.
HRMS (ESI-TOF) m/z: $[M + Na]^+$ Calcd for $C_{29}H_{32}N_2O_7Na$ 543.2102; Found 543.2097.



2-((3a*R*,4*R*,6*R*,6a*S*)-6-((*R*)-2,2-dimethyl-1,3-dioxolan-4-yl)-2,2-dimethyltetrahydrofuro[3,4-*d*][1,3]dioxol-4-yl)-4,5-dimethoxy-*N*-(quinolin-8-yl)benzamide **(3x)**
Colorless oil, 60% (32.6mg)
^{1}H NMR (400 MHz, Chloroform-*d*) δ 10.30 (s, 1H), 8.91 (d, *J* = 6.0 Hz, 1H), 8.80 (dd, *J* = 4.2, 1.7 Hz, 1H), 8.19 (dd, *J* = 8.3, 1.6 Hz, 1H), 7.63 – 7.54 (m, 2H), 7.47 (dd, *J* = 8.3, 4.2 Hz, 1H), 7.30 (s, 1H), 7.05 (s, 1H), 5.75 (s, 1H), 4.90 (dd, *J* = 6.0, 1.4 Hz, 1H), 4.72 (dd, *J* = 6.0, 3.8 Hz, 1H), 4.47 (td, *J* = 6.7, 4.4 Hz, 1H), 4.21 (dd, *J* = 8.7, 4.4 Hz, 1H), 4.12 (dd, *J* = 8.7, 6.3 Hz, 1H), 3.99 – 3.95 (m, 7H), 1.44 (s, 3H), 1.41 (s, 3H), 1.37 (s, 3H), 1.22 (s, 3H).
^{13}C NMR (101 MHz, Chloroform-*d*) δ 167.0, 150.6, 148.2, 148.0, 138.7, 136.3, 134.6, 130.6, 127.9, 127.8, 127.4, 121.8, 121.6, 116.8, 112.8, 111.7, 109.6, 109.1, 87.5, 83.9, 81.3, 80.7, 73.5, 66.8, 56.2, 56.0, 26.9, 26.2, 25.2, 24.8.
HRMS (ESI-TOF) m/z: $[M + Na]^+$ Calcd for $C_{30}H_{34}N_2O_8Na$ 573.2207; Found 573.2204.



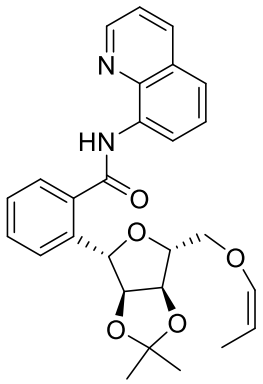
2-((3a*S*,4*S*,6*R*,6a*R*)-6-((benzyloxy)methyl)-2,2-dimethyltetrahydrofuro[3,4-d][1,3]dioxol-4-yl)-N-(quinolin-8-yl)benzamide **(4a)**

Yellow oil, 37% (18.7mg)

^{1}H NMR (400 MHz, Chloroform-*d*) δ 10.16 (s, 1H), 8.92 (dd, *J* = 7.4, 1.6 Hz, 1H), 8.73 (dd, *J* = 4.2, 1.7 Hz, 1H), 8.15 (dd, *J* = 8.3, 1.7 Hz, 1H), 7.66 – 7.52 (m, 4H), 7.49 – 7.39 (m, 3H), 7.24 – 7.14 (m, 3H), 7.04 (dd, *J* = 7.2, 2.4 Hz, 2H), 5.24 (d, *J* = 4.7 Hz, 1H), 4.93 (dd, *J* = 6.9, 4.7 Hz, 1H), 4.68 (dd, *J* = 6.9, 5.2 Hz, 1H), 4.19 – 4.04 (m, 3H), 3.60 (dd, *J* = 10.3, 3.8 Hz, 1H), 3.45 (dd, *J* = 10.3, 6.4 Hz, 1H), 1.47 (s, 3H), 1.27 (s, 3H).

^{13}C NMR (101 MHz, Chloroform-*d*) δ 168.4, 148.3, 138.5, 137.9, 137.7, 136.2, 136.2, 134.9, 130.1, 128.2, 128.1, 127.9, 127.6, 127.5, 127.4, 127.3, 127.3, 121.7, 121.6, 116.6, 115.0, 86.8, 85.1, 83.5, 81.9, 73.1, 70.3, 27.4, 25.5.

HRMS (ESI-TOF) m/z: $[M + Na]^+$ Calcd for $C_{31}H_{30}N_2O_5Na$ 533.2047; Found 533.2045.

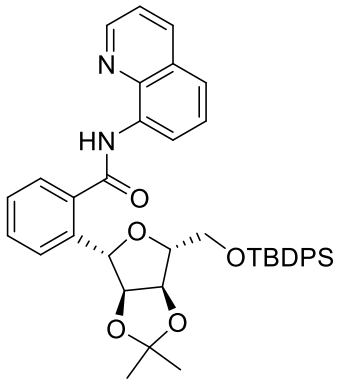


2-((3a*S*,4*S*,6*R*,6a*R*)-2,2-dimethyl-6-((((Z)-prop-1-en-1-yl)oxy)methyl)tetrahydrofuro[3,4-d][1,3]dioxol-4-yl)-N-(quinolin-8-yl)benzamide **(4b)**

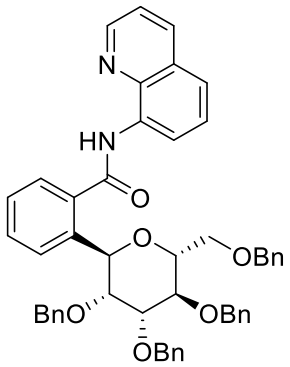
Colorless oil, 27% (12.4mg)

^{1}H NMR (400 MHz, Chloroform-*d*) δ 10.17 (s, 1H), 8.92 (dd, *J* = 7.2, 1.6 Hz, 1H), 8.75 (dd, *J* = 4.3, 1.6 Hz, 1H), 8.17 (dd, *J* = 8.3, 1.8 Hz, 1H), 7.70 – 7.53 (m, 4H), 7.51 – 7.39 (m, 3H), 5.64 (dt, *J* = 5.6, 1.7 Hz, 1H), 5.32 (d, *J* = 4.8 Hz, 1H), 4.87 (dd, *J* = 6.7, 4.8 Hz, 1H), 4.73 (dd, *J* = 6.8, 5.1 Hz, 1H), 4.18 – 4.07 (m, 2H), 3.90 (dd, *J* = 11.3, 3.2 Hz, 1H), 3.75 (dd, *J* = 11.3, 5.5 Hz, 1H), 1.46 – 1.43 (m, 6H), 1.26 (s, 3H).

^{13}C NMR (101 MHz, Chloroform-*d*) δ 168.2, 148.2, 145.7, 138.6, 137.7, 136.2, 136.2, 134.8, 130.2, 128.1, 128.0, 127.2, 127.2, 121.8, 121.6, 116.6, 115.1, 114.8, 100.8, 86.9, 84.5, 83.3, 81.3, 71.6, 27.4, 25.5, 9.1.
HRMS (ESI-TOF) m/z: $[M + Na]^+$ Calcd for $C_{24}H_{23}N_2O_4Na$ 483.1890; Found 483.1886.

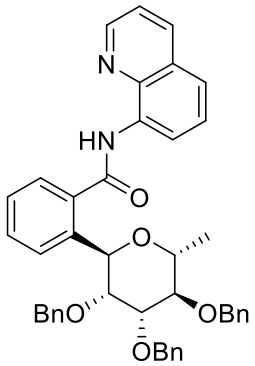


2-((3a*S*,4*S*,6*R*,6a*R*)-6-(((tert-butyldiphenylsilyl)oxy)methyl)-2,2-dimethyltetrahydrofuro[3,4-d][1,3]dioxol-4-yl)-N-(quinolin-8-yl)benzamide **(4c)**
Yellow oil, 49% (32.2mg)
^{1}H NMR (400 MHz, Chloroform-*d*) δ 10.20 (s, 1H), 8.91 (dd, *J* = 5.7, 3.3 Hz, 1H), 8.72 (dd, *J* = 4.2, 1.7 Hz, 1H), 8.14 (dd, *J* = 8.3, 1.7 Hz, 1H), 7.77 – 7.71 (m, 1H), 7.69 – 7.62 (m, 5H), 7.55 – 7.50 (m, 2H), 7.45 – 7.37 (m, 5H), 7.37 – 7.31 (m, 4H), 5.43 (d, *J* = 4.9 Hz, 1H), 4.82 (dd, *J* = 6.6, 4.4 Hz, 1H), 4.75 (dd, *J* = 6.6, 5.0 Hz, 1H), 4.10 (q, *J* = 4.0 Hz, 1H), 3.93 (dd, *J* = 11.1, 3.8 Hz, 1H), 3.80 (dd, *J* = 11.1, 4.0 Hz, 1H), 1.37 (s, 3H), 1.22 (s, 3H), 1.03 (s, 9H).
^{13}C NMR (101 MHz, Chloroform-*d*) δ 167.7, 148.1, 138.6, 138.1, 136.2, 135.6, 135.6, 134.8, 133.4, 133.2, 130.3, 129.6, 129.6, 128.0, 127.9, 127.6, 127.5, 127.3, 127.2, 121.7, 121.5, 116.7, 114.4, 87.0, 84.3, 82.8, 81.5, 63.8, 27.4, 26.8, 25.6, 19.2.
HRMS (ESI-TOF) m/z: $[M + Na]^+$ Calcd for $C_{40}H_{42}N_2O_5SiNa$ 681.2755; Found 681.2756.

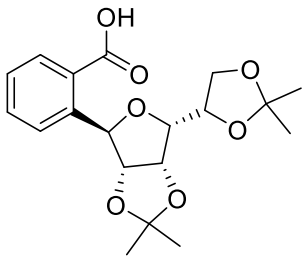


N-(quinolin-8-yl)-2-((2*R*,3*R*,4*R*,5*R*,6*R*)-3,4,5-tris(benzyloxy)-6-((benzyloxy)methyl)tetrahydro-2*H*-pyran-2-yl)benzamide **(4d)**
Yellow oil, 19% (14.8mg)

^{1}H NMR (400 MHz, Chloroform-*d*) δ 10.48 (s, 1H), 8.92 (dd, *J* = 7.6, 1.5 Hz, 1H), 8.63 (dd, *J* = 4.2, 1.7 Hz, 1H), 8.10 (dd, *J* = 8.3, 1.7 Hz, 1H), 7.69 – 7.61 (m, 1H), 7.56 (t, *J* = 7.9 Hz, 1H), 7.52 – 7.48 (m, 1H), 7.45 – 7.42 (m, 1H), 7.38 (ddd, *J* = 12.7, 7.1, 3.4 Hz, 3H), 7.30 – 7.20 (m, 7H), 7.16 – 7.10 (m, 7H), 7.09 – 7.03 (m, 4H), 6.90 – 6.84 (m, 2H), 5.63 (d, *J* = 7.5 Hz, 1H), 4.48 – 4.25 (m, 8H), 4.08 (dd, *J* = 7.5, 2.6 Hz, 1H), 4.02 (dt, *J* = 6.1, 3.0 Hz, 1H), 3.84 – 3.73 (m, 3H), 3.67 (dd, *J* = 10.2, 5.9 Hz, 1H).
^{13}C NMR (101 MHz, Chloroform-*d*) δ 168.3, 148.0, 139.0, 138.4, 138.2, 138.1, 138.0, 137.6, 136.8, 136.1, 135.0, 130.0, 128.3, 128.1, 128.1, 128.0, 127.9, 127.7, 127.7, 127.7, 127.5, 127.5, 127.3, 127.3, 127.3, 127.2, 127.2, 121.8, 121.4, 117.5, 75.2, 74.9, 73.2, 72.4, 72.2, 71.4, 69.7, 68.5.
HRMS (ESI-TOF) m/z: $[M + Na]^+$ Calcd for $C_{50}H_{46}N_2O_6Na$ 793.3248; Found 793.3244.



N-(quinolin-8-yl)-2-((2*R*,3*R*,4*S*,5*R*,6*R*)-3,4,5-tris(benzyloxy)-6-methyltetrahydro-2*H*-pyran-2-yl)benzamide **(4e)**
Yellow oil, 21% (13.9mg)
^{1}H NMR (400 MHz, Chloroform-*d*) δ 10.39 (s, 1H), 8.91 (d, *J* = 6.8 Hz, 1H), 8.65 (dd, *J* = 4.2, 1.7 Hz, 1H), 8.11 (dd, *J* = 8.3, 1.7 Hz, 1H), 7.63 (dd, *J* = 7.5, 1.5 Hz, 1H), 7.57 – 7.48 (m, 2H), 7.40 – 7.25 (m, 6H), 7.22 – 7.11 (m, 11H), 7.03 – 6.97 (m, 2H), 5.68 (d, *J* = 6.0 Hz, 1H), 4.63 – 4.41 (m, 6H), 4.14 (dd, *J* = 6.0, 2.8 Hz, 1H), 3.82 – 3.72 (m, 2H), 3.53 (dd, *J* = 6.3, 5.0 Hz, 1H), 1.22 (d, *J* = 6.7 Hz, 3H).
^{13}C NMR (101 MHz, Chloroform-*d*) δ 168.4, 148.0, 138.9, 138.3, 138.3, 138.1, 137.6, 136.7, 136.1, 134.8, 129.9, 128.3, 128.2, 128.1, 128.0, 128.0, 127.9, 127.9, 127.7, 127.6, 127.4, 127.4, 127.4, 127.3, 127.3, 121.8, 121.4, 117.4, 79.6, 76.5, 76.4, 73.1, 72.4, 71.6, 71.5, 69.7, 17.2.
HRMS (ESI-TOF) m/z: $[M + Na]^+$ Calcd for $C_{43}H_{40}N_2O_5Na$ 687.2829; Found 687.2828.



2-((3aR,4R,6R,6aS)-6-((R)-2,2-dimethyl-1,3-dioxolan-4-yl)-2,2-dimethyltetrahydrofuro[3,4-d][1,3] dioxol-4-yl)benzoic acid **(5a)**

White solid, 70% (25.7mg)

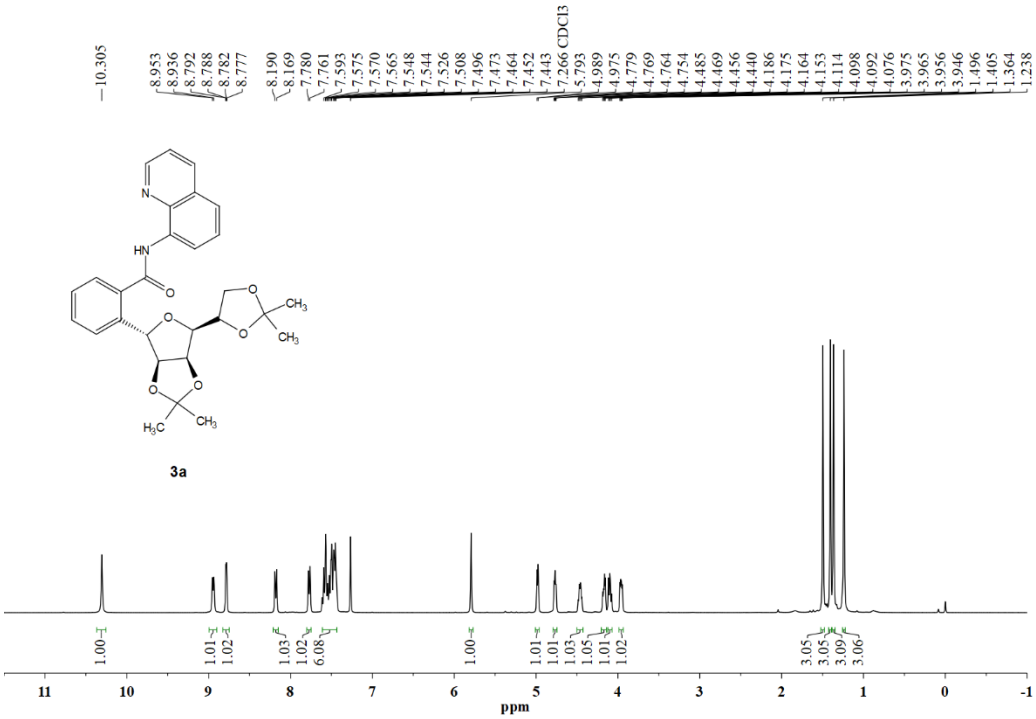
1H NMR (400 MHz, Chloroform-d) δ 8.01 (d, J = 7.7 Hz, 1H), 7.49 (d, J = 4.0 Hz, 2H), 7.35 – 7.31 (m, 1H), 5.85 (s, 1H), 4.76 (d, J = 6.0 Hz, 1H), 4.64 (dd, J = 6.1, 3.6 Hz, 1H), 4.50 (td, J = 6.7, 4.5 Hz, 1H), 4.27 (dd, J = 8.8, 4.4 Hz, 1H), 4.20 (dd, J = 8.8, 6.4 Hz, 1H), 3.95 (dd, J = 7.2, 3.6 Hz, 1H), 1.60 (s, 3H), 1.45 (s, 3H), 1.40 (s, 3H), 1.33 (s, 3H).

13C NMR (101 MHz, Chloroform-d) δ 172.8, 139.3, 131.8, 131.5, 130.9, 127.4, 125.4, 112.6, 109.2, 88.9, 84.8, 81.4, 80.6, 73.5, 66.8, 26.9, 26.2, 25.1, 24.7.

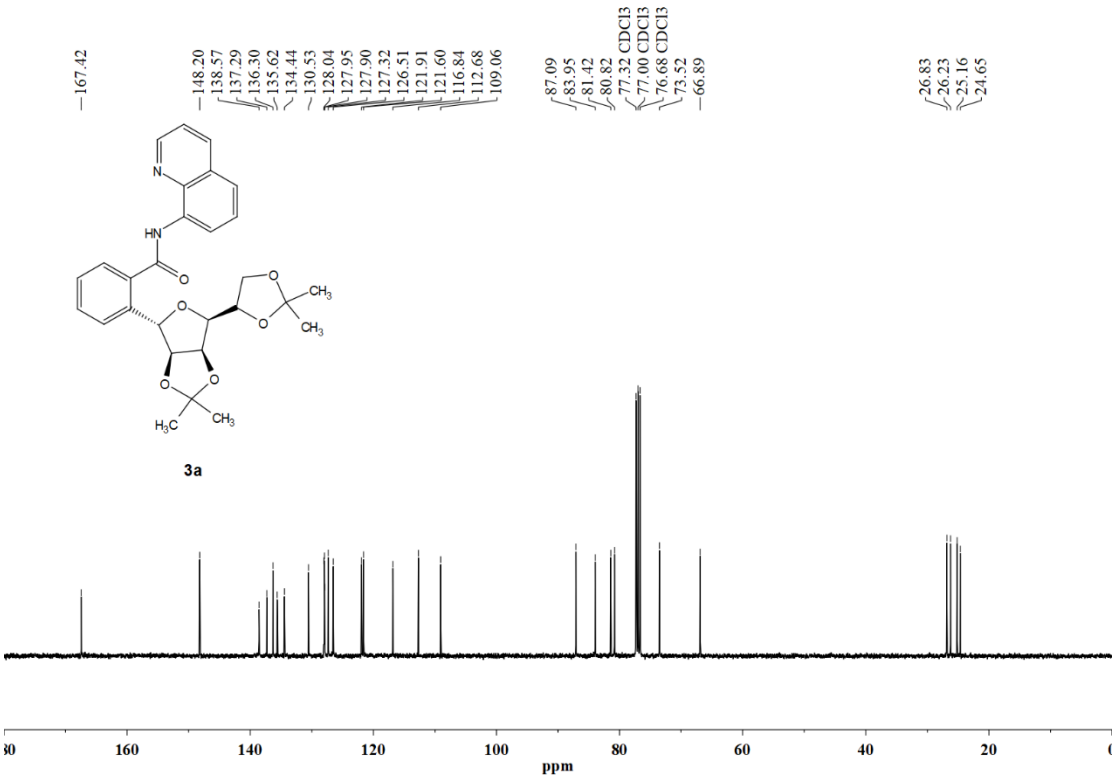
HRMS (ESI-TOF) m/z: $[M + Na]^+$ Calcd for $C_{19}H_{24}O_7Na$ 387.1414; Found 387.1411.

10. NMR Spectroscopic Data

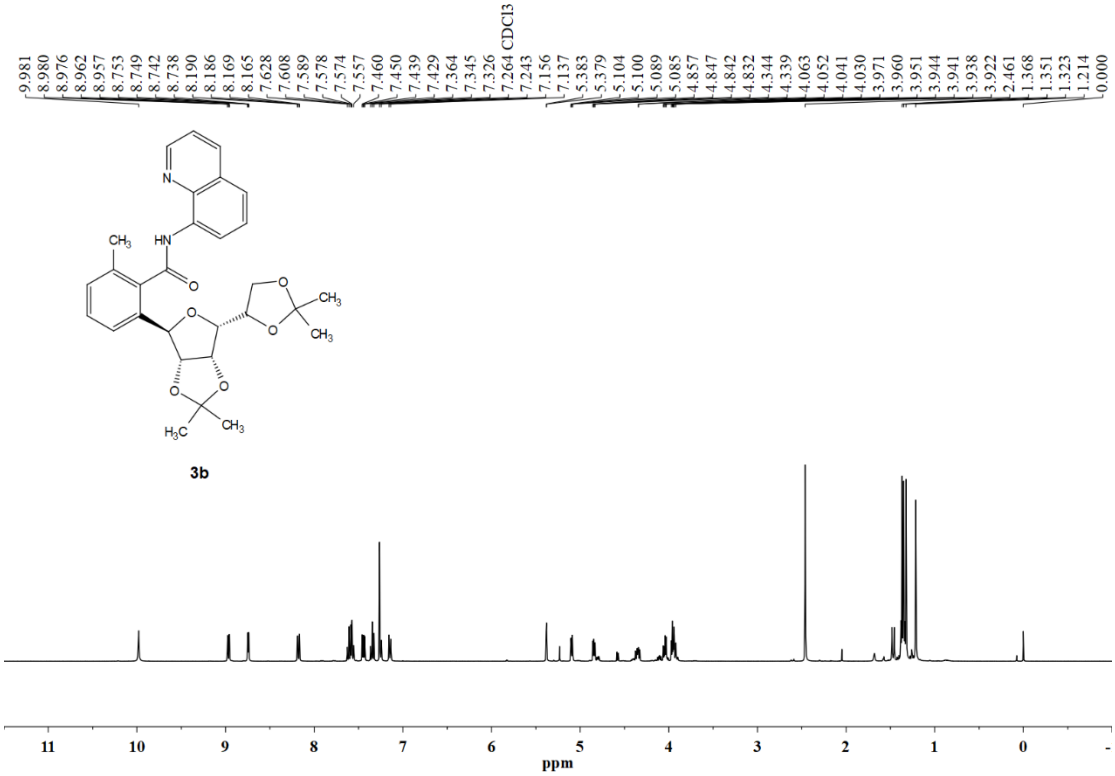
^{1}H NMR (400 MHz, Chloroform-*d*)



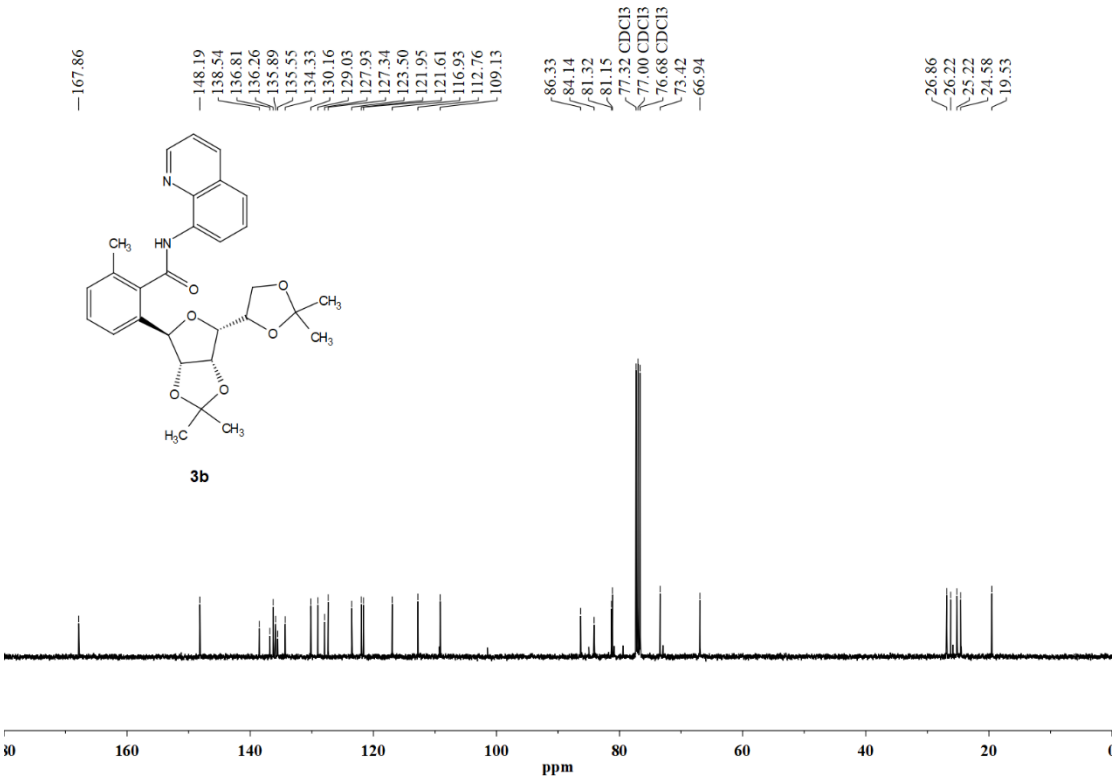
^{13}C NMR (101 MHz, Chloroform-*d*)



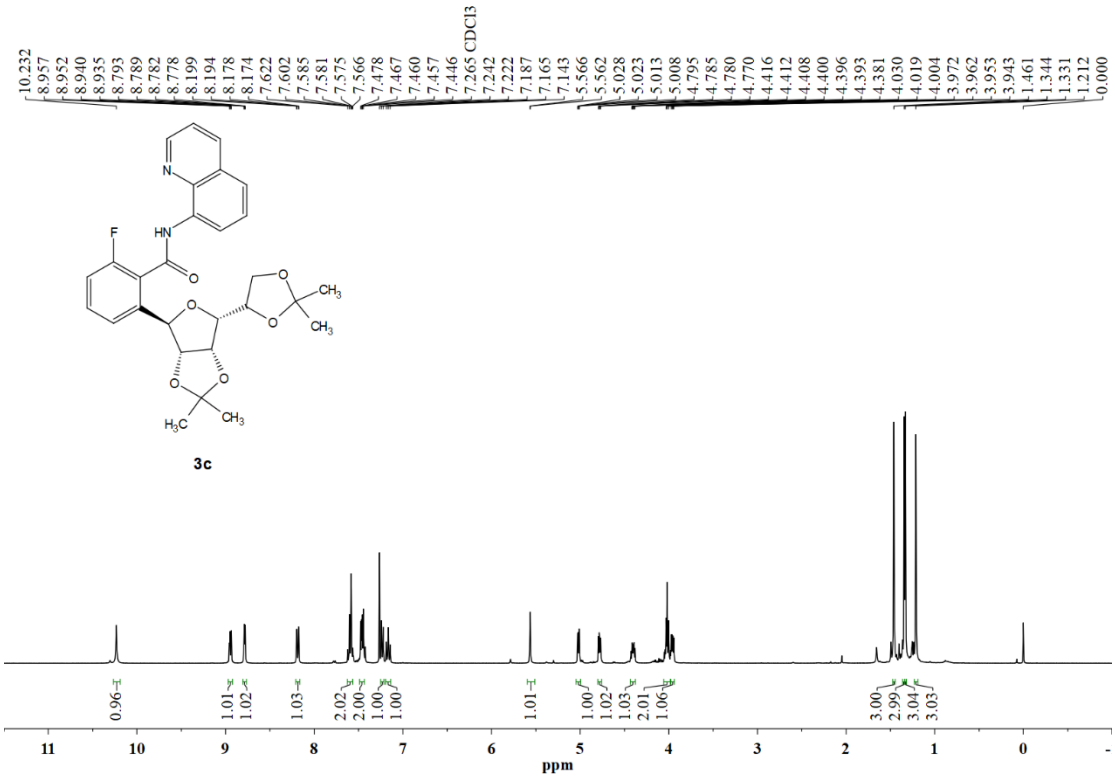
^{1}H NMR (400 MHz, Chloroform-*d*)



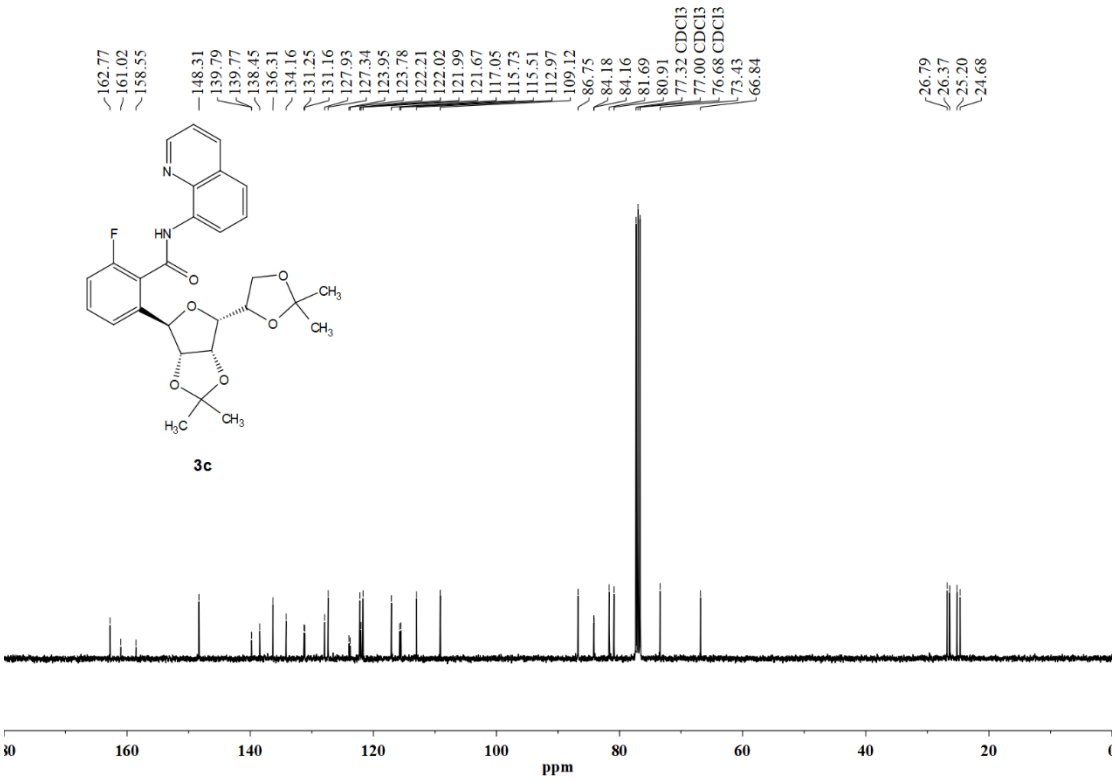
^{13}C NMR (101 MHz, Chloroform-*d*)



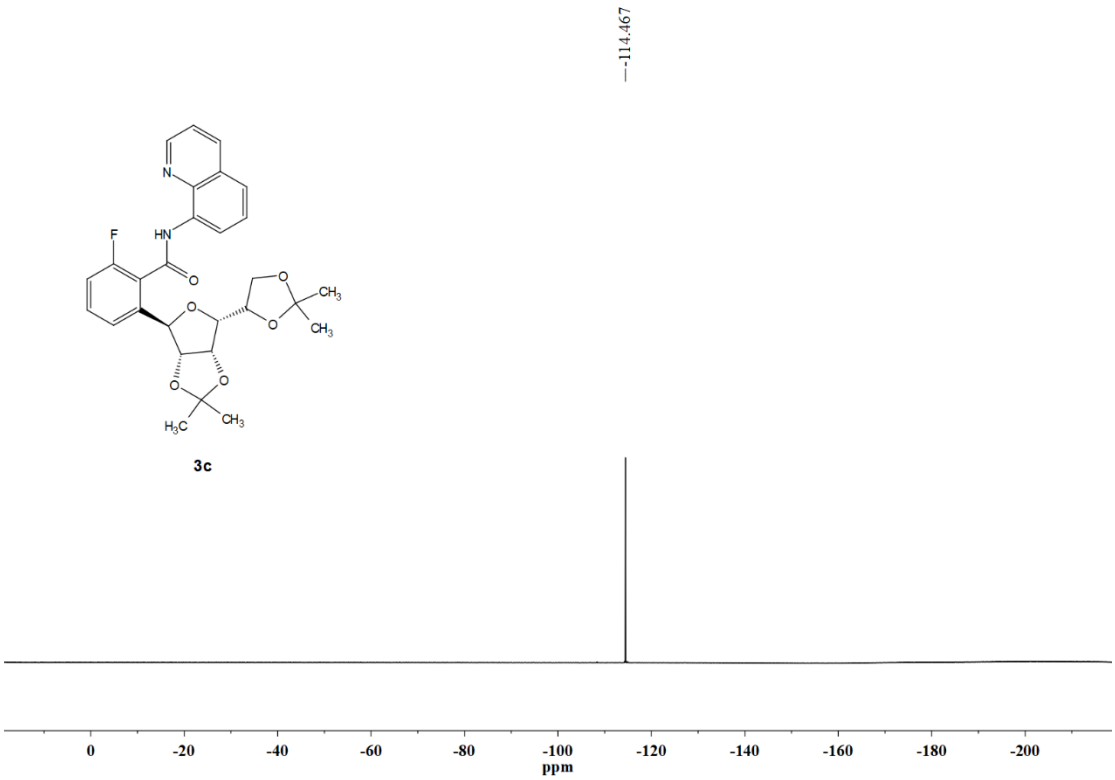
^{1}H NMR (400 MHz, Chloroform-*d*)



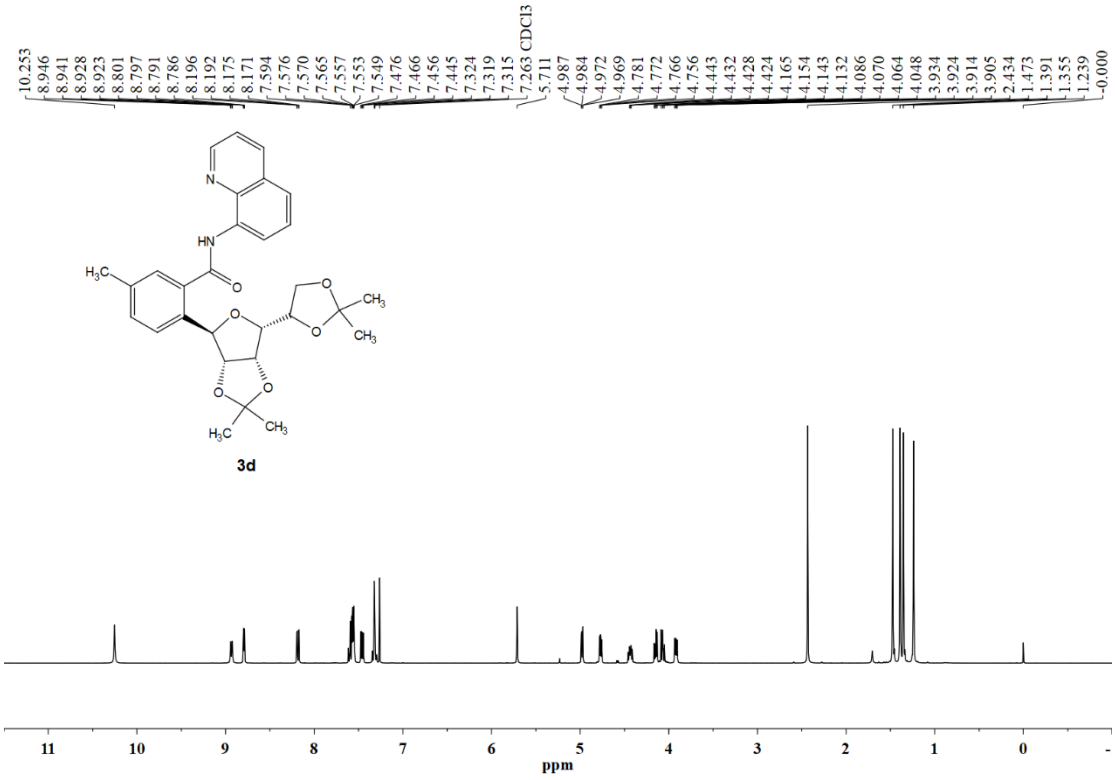
^{13}C NMR (101 MHz, Chloroform-*d*)



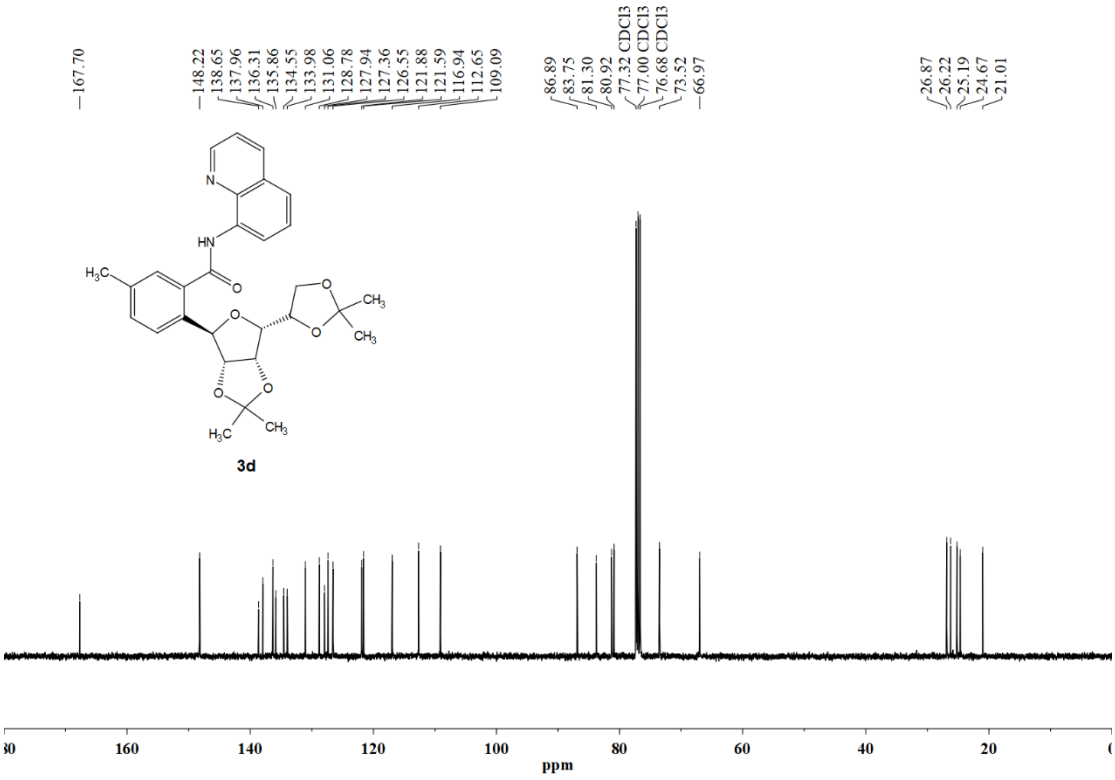
^{19}F NMR (376 MHz, Chloroform-*d*)



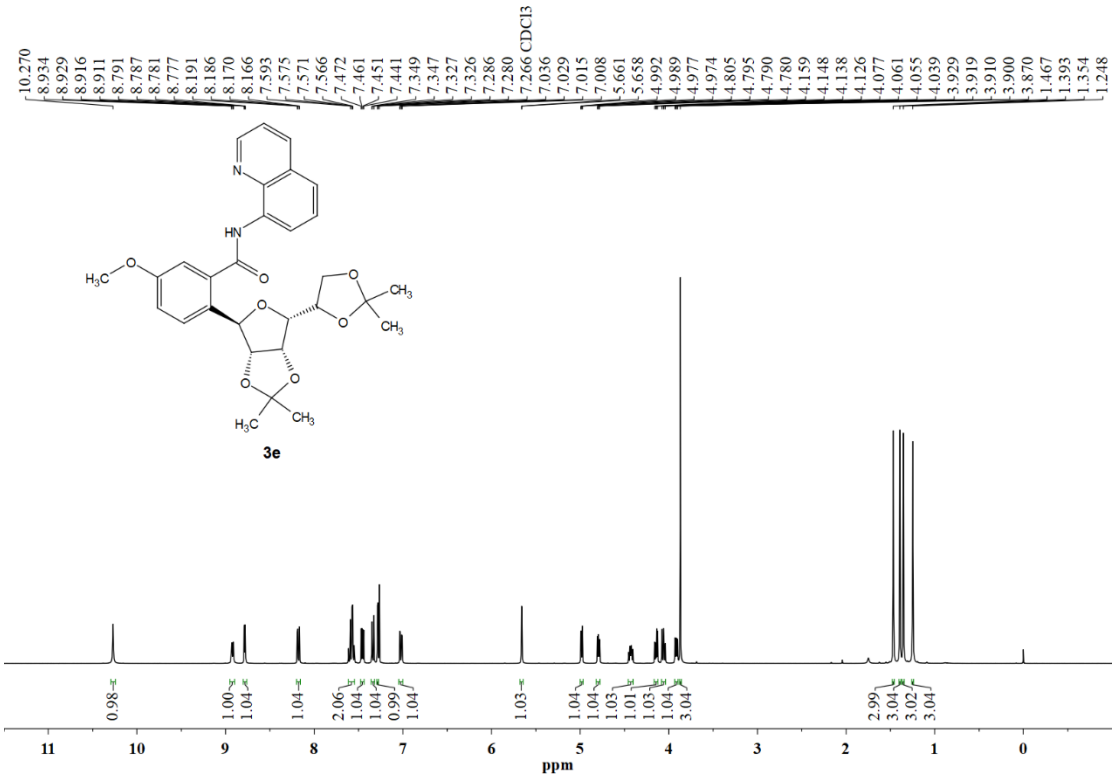
^{1}H NMR (400 MHz, Chloroform-*d*)



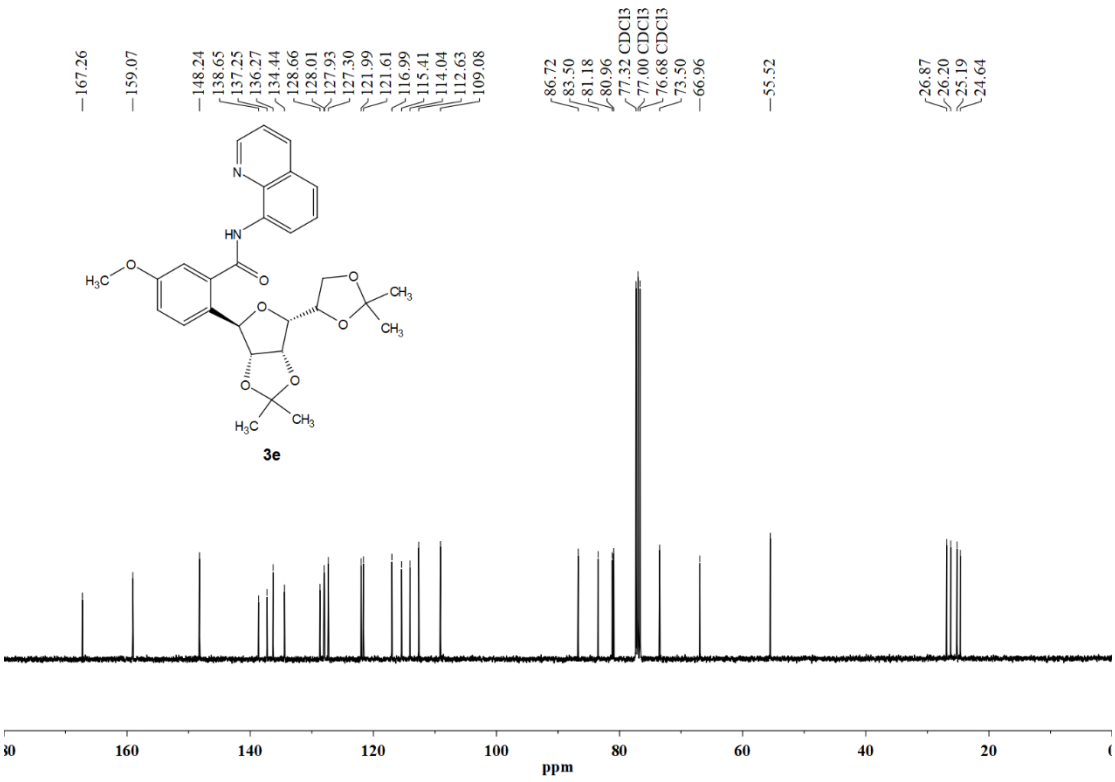
^{13}C NMR (101 MHz, Chloroform-*d*)

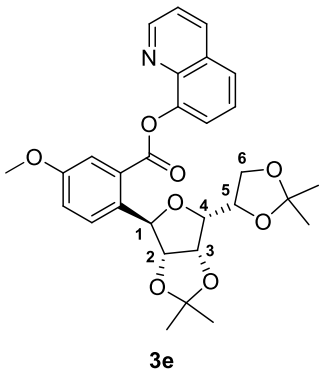


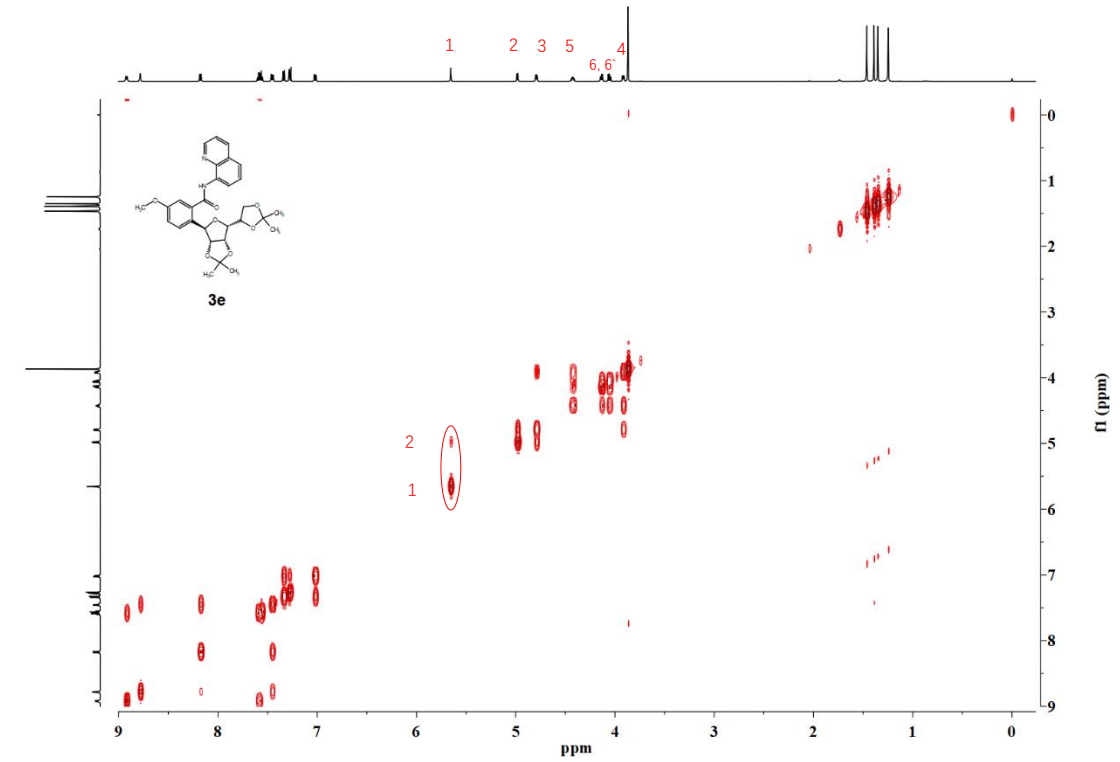
^{1}H NMR (400 MHz, Chloroform-*d*)

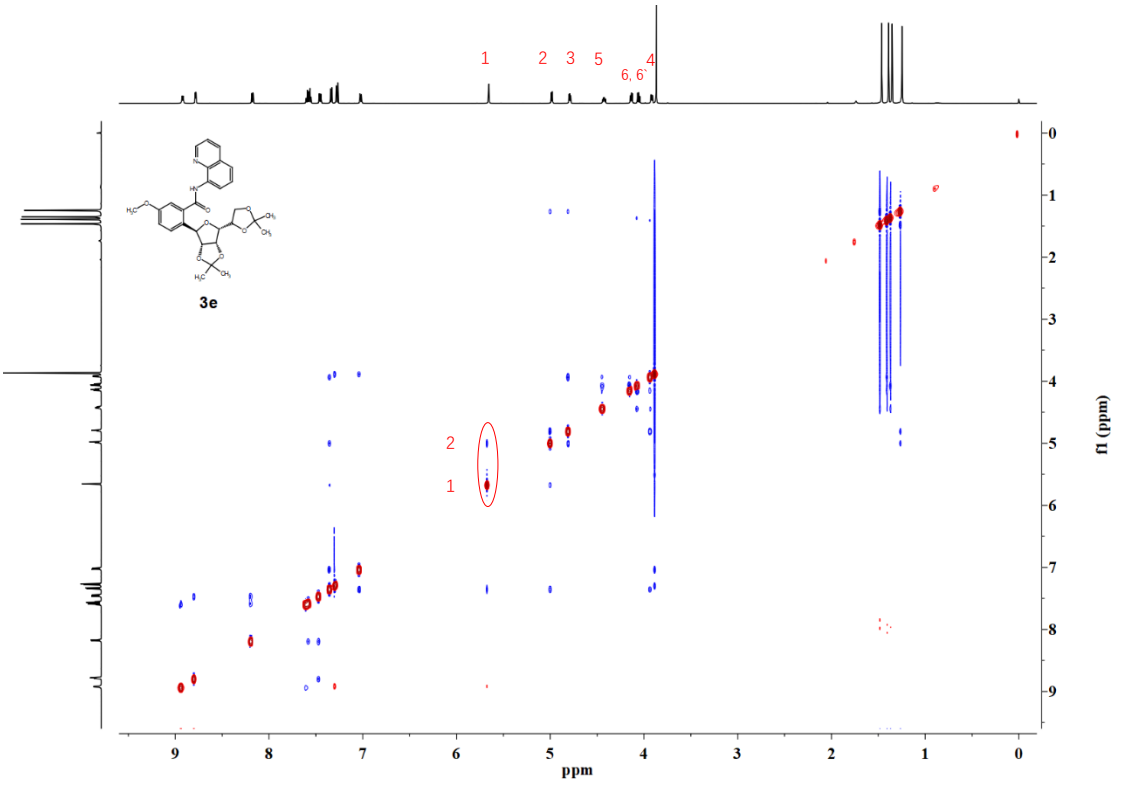


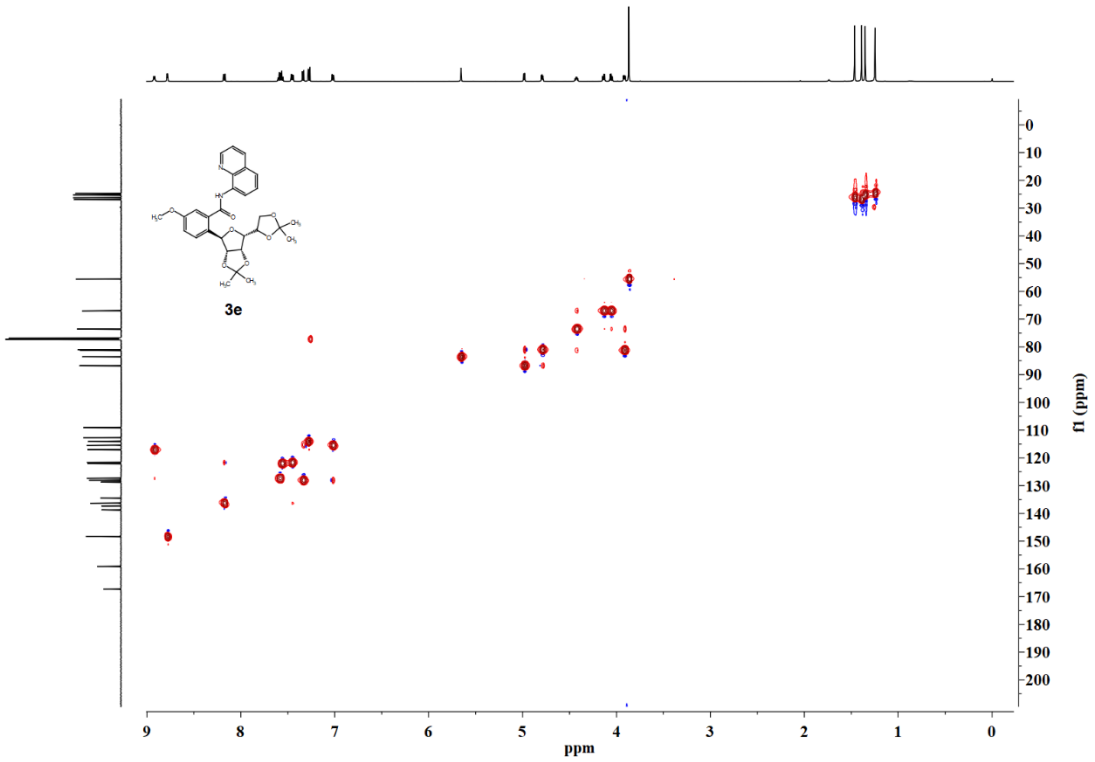
^{13}C NMR (101 MHz, Chloroform-*d*)



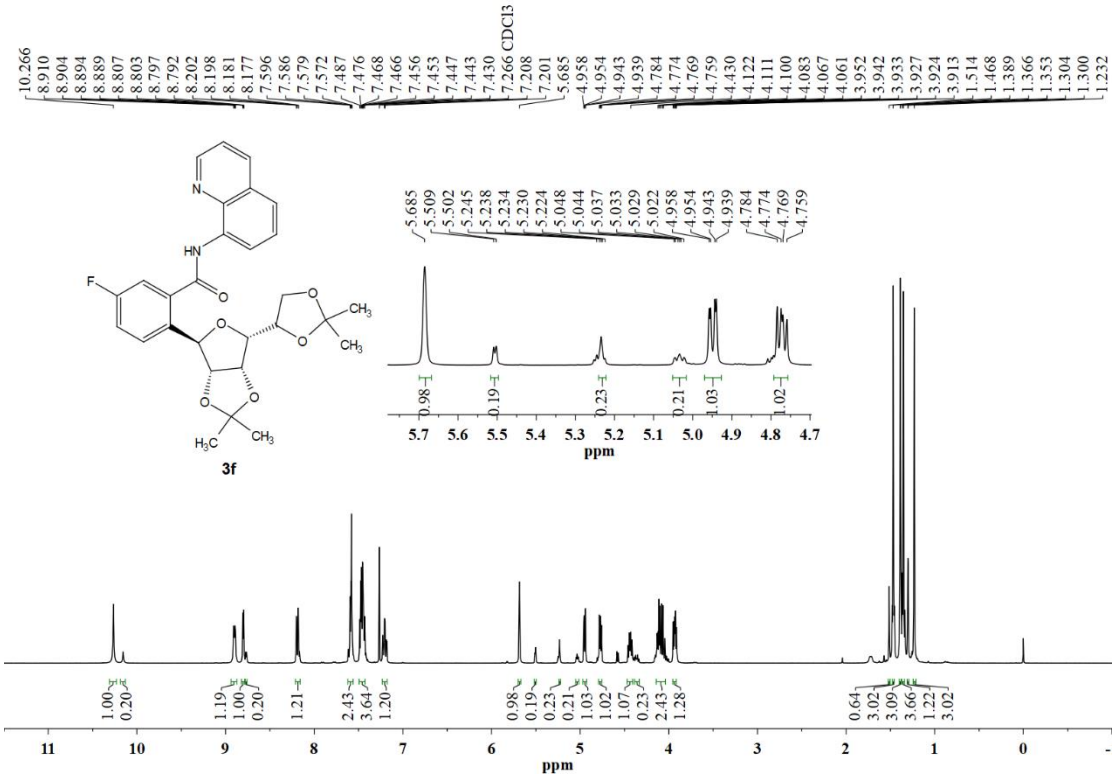



1
2
3
5
6, 6`
4
3e
2
1
ppm
f1 (ppm)

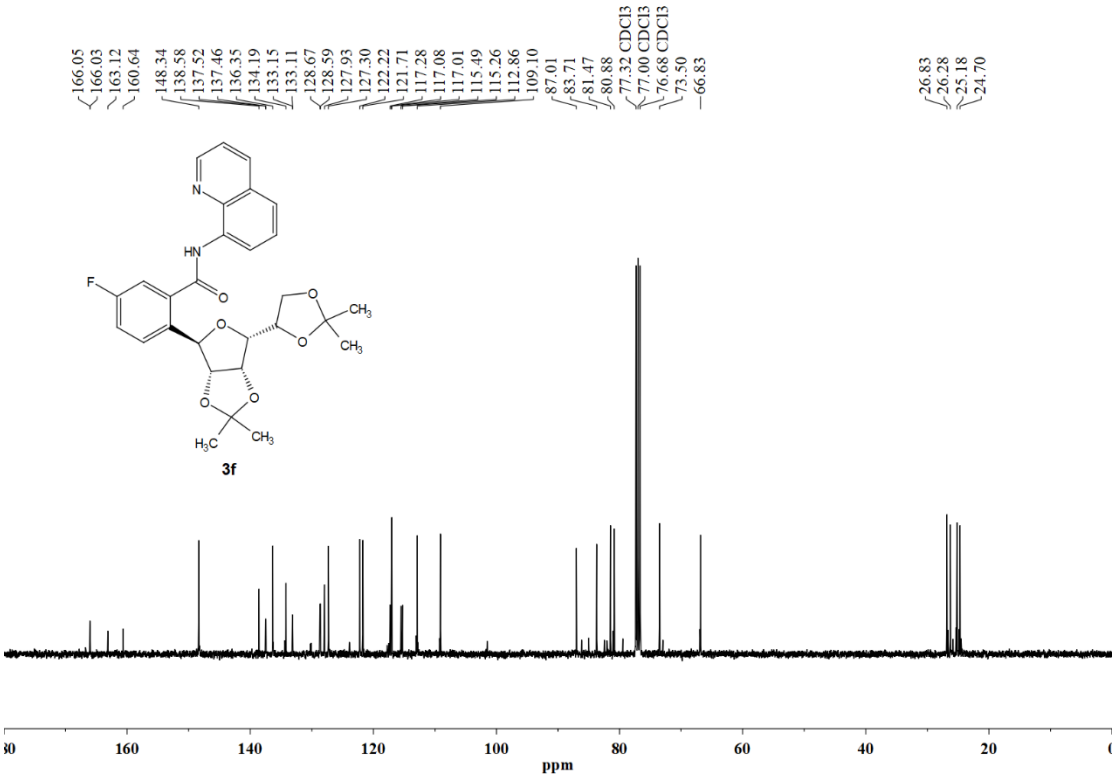

1
2
3
5
6, 6`
4
3e
2
1
ppm
f1 (ppm)



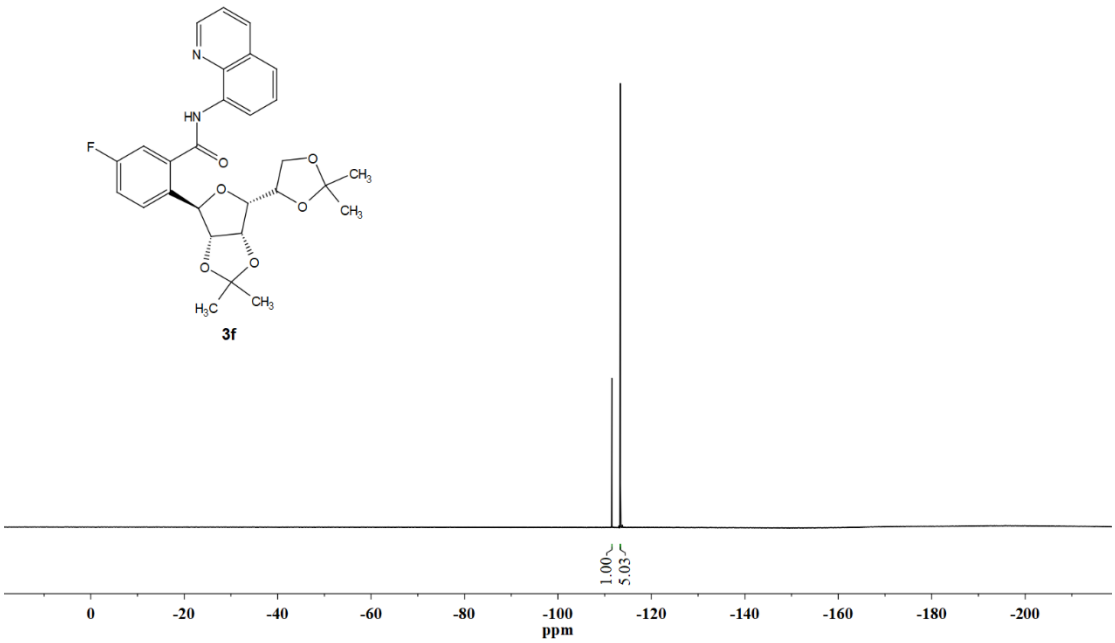
^{1}H NMR (400 MHz, Chloroform-*d*)



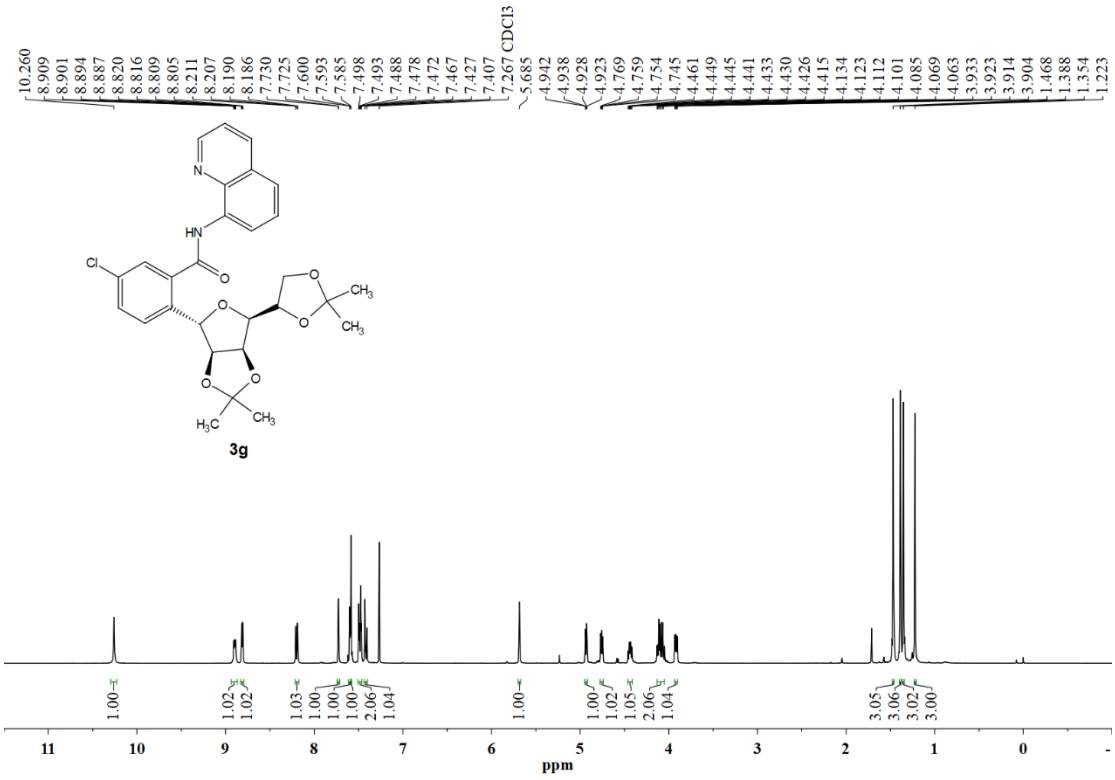
^{13}C NMR (101 MHz, Chloroform-*d*)



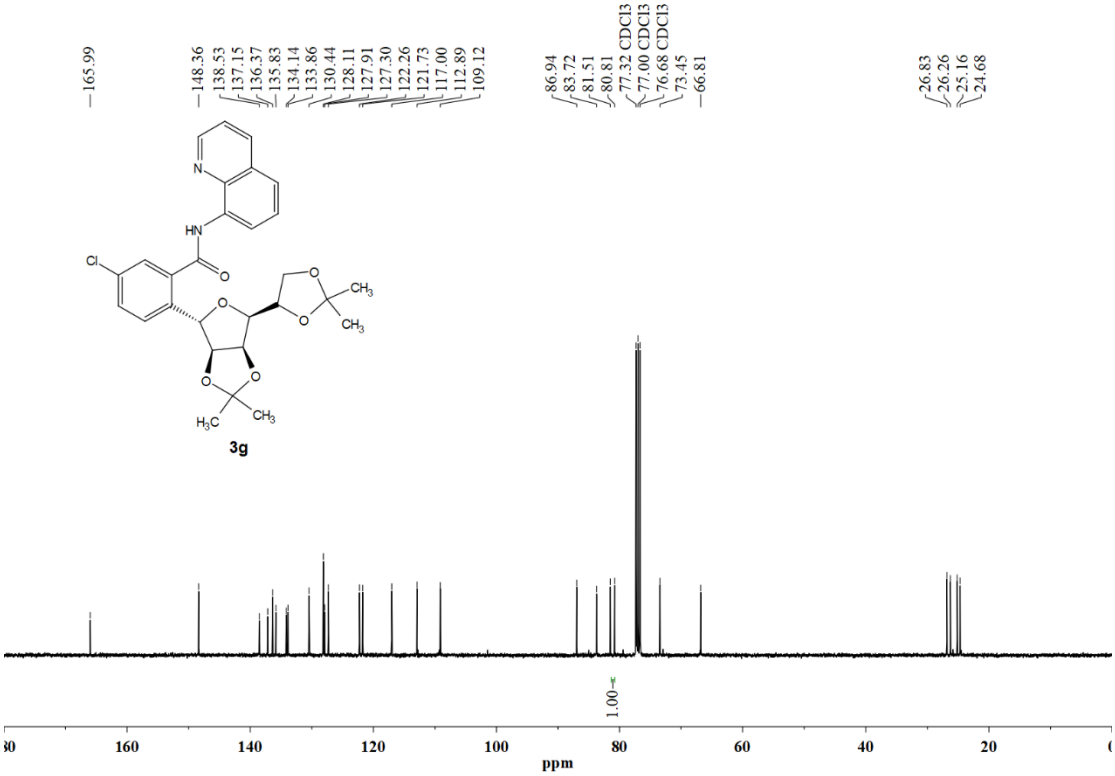
^{19}F NMR (376 MHz, Chloroform-*d*)



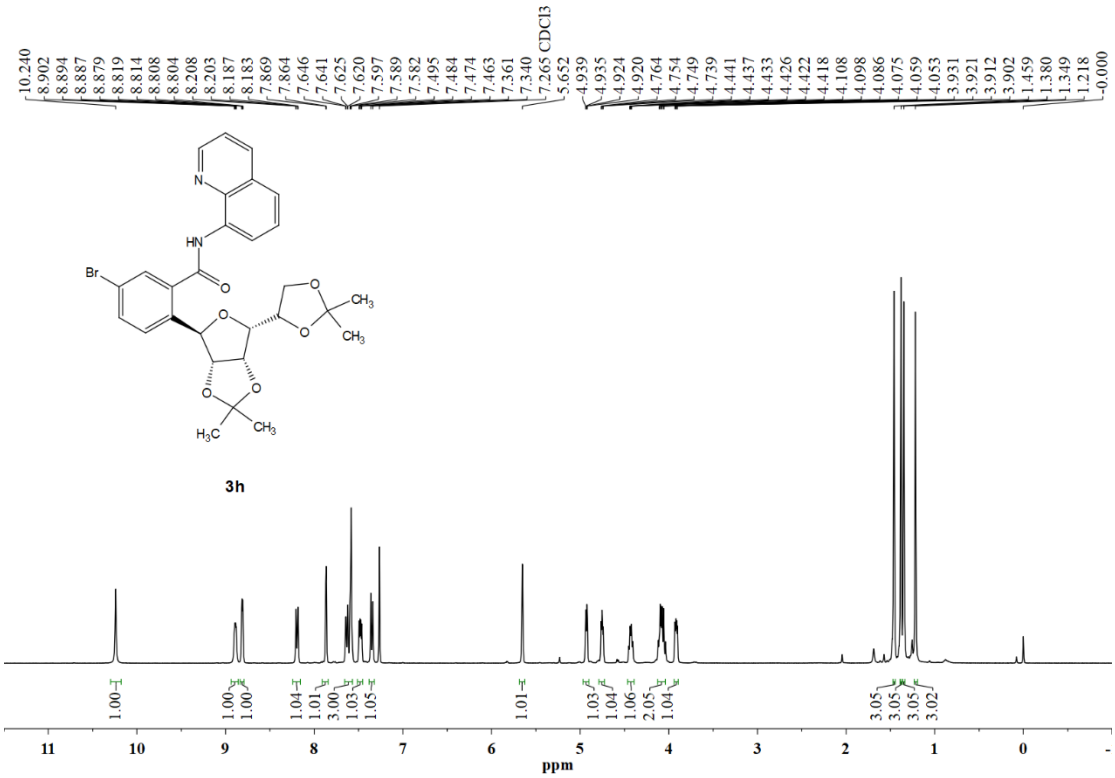
^{1}H NMR (400 MHz, Chloroform-*d*)



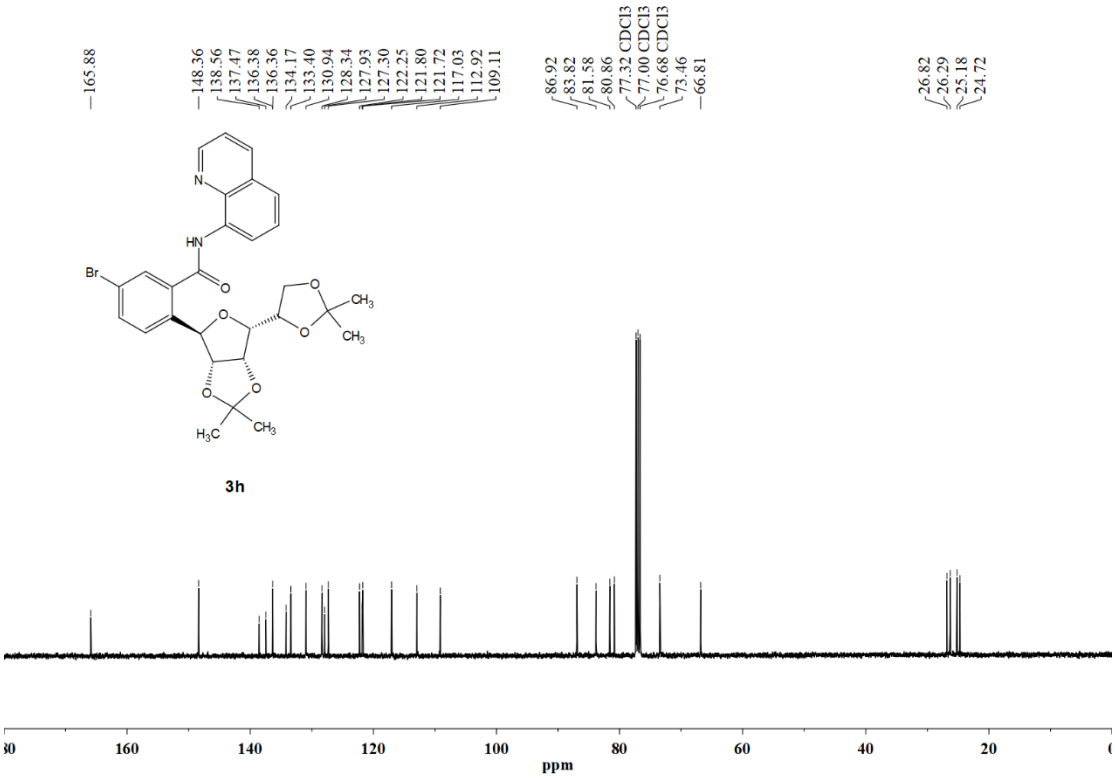
^{13}C NMR (101 MHz, Chloroform-*d*)



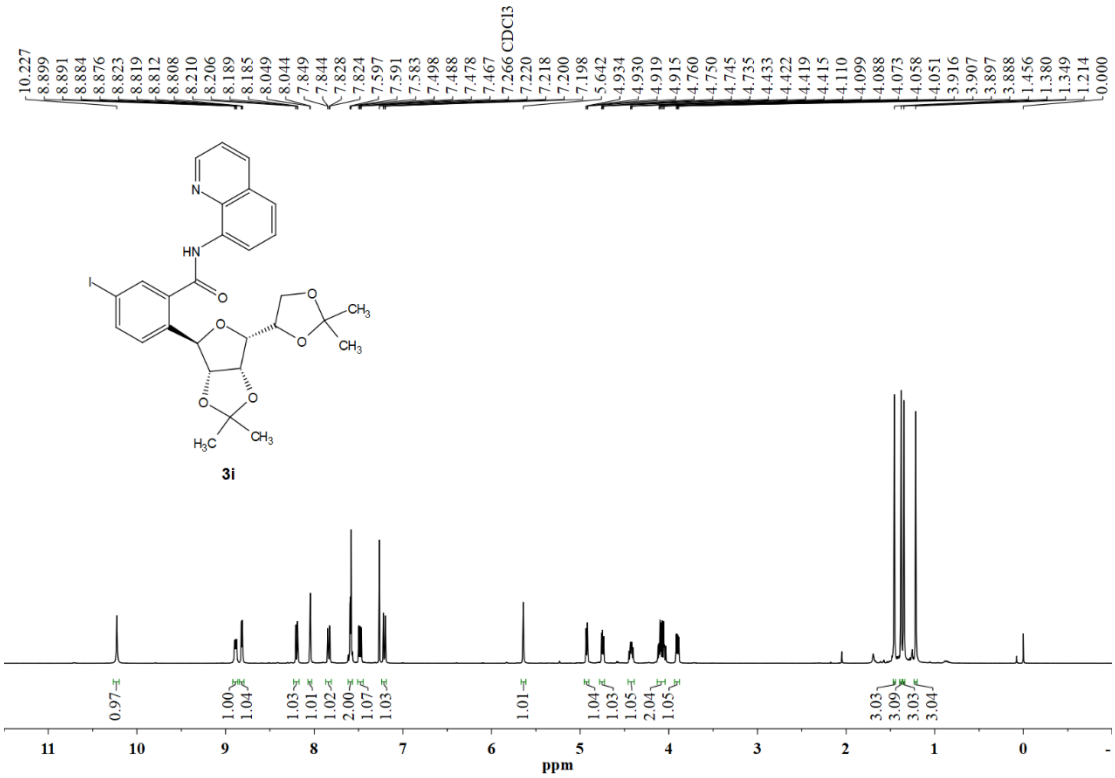
^{1}H NMR (400 MHz, Chloroform-*d*)



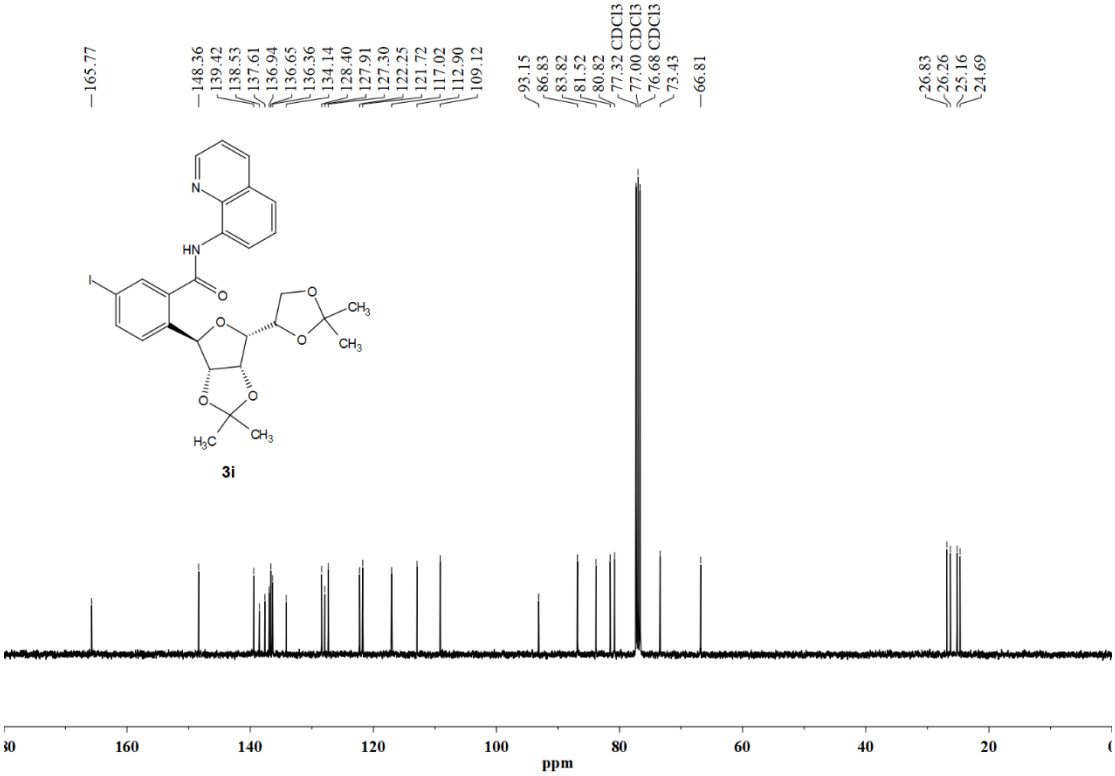
^{13}C NMR (101 MHz, Chloroform-*d*)



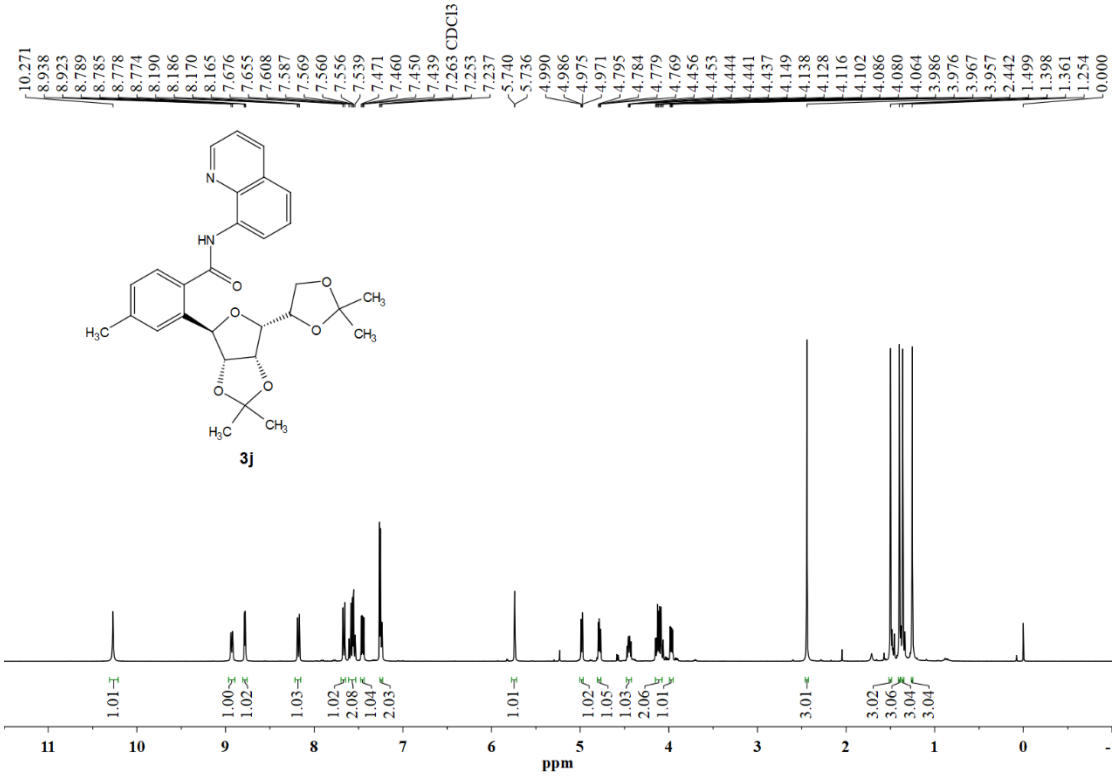
^{1}H NMR (400 MHz, Chloroform-*d*)



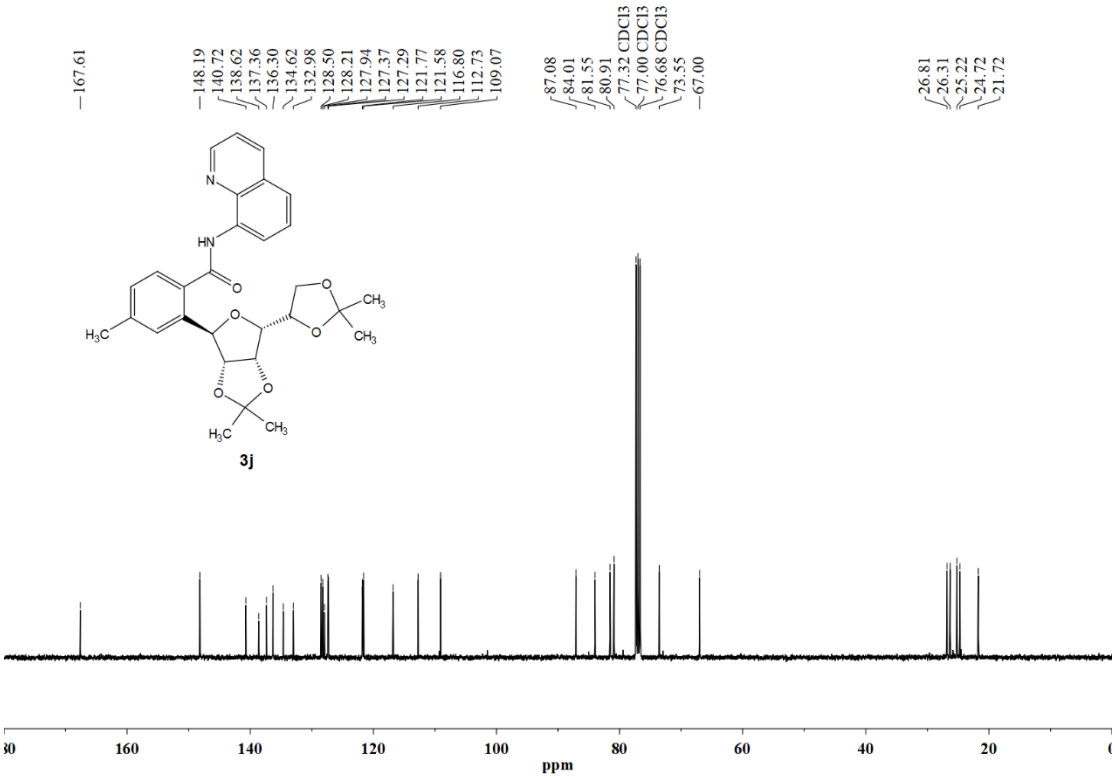
^{13}C NMR (101 MHz, Chloroform-*d*)



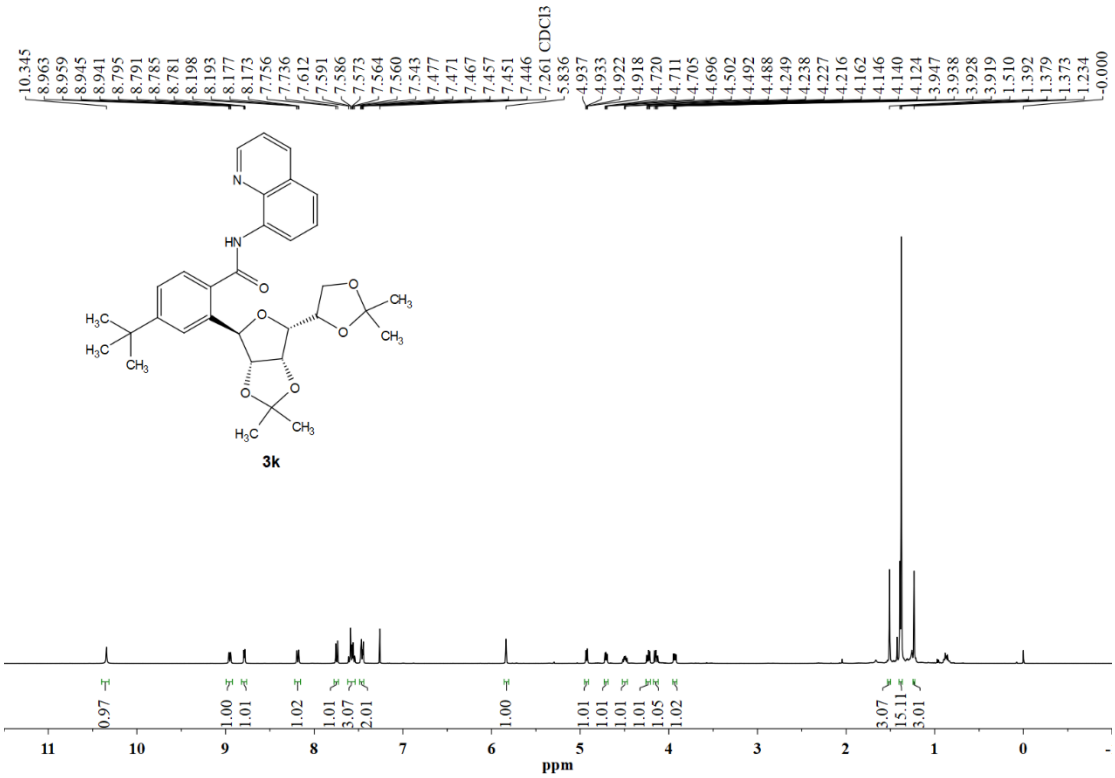
^{1}H NMR (400 MHz, Chloroform-*d*)



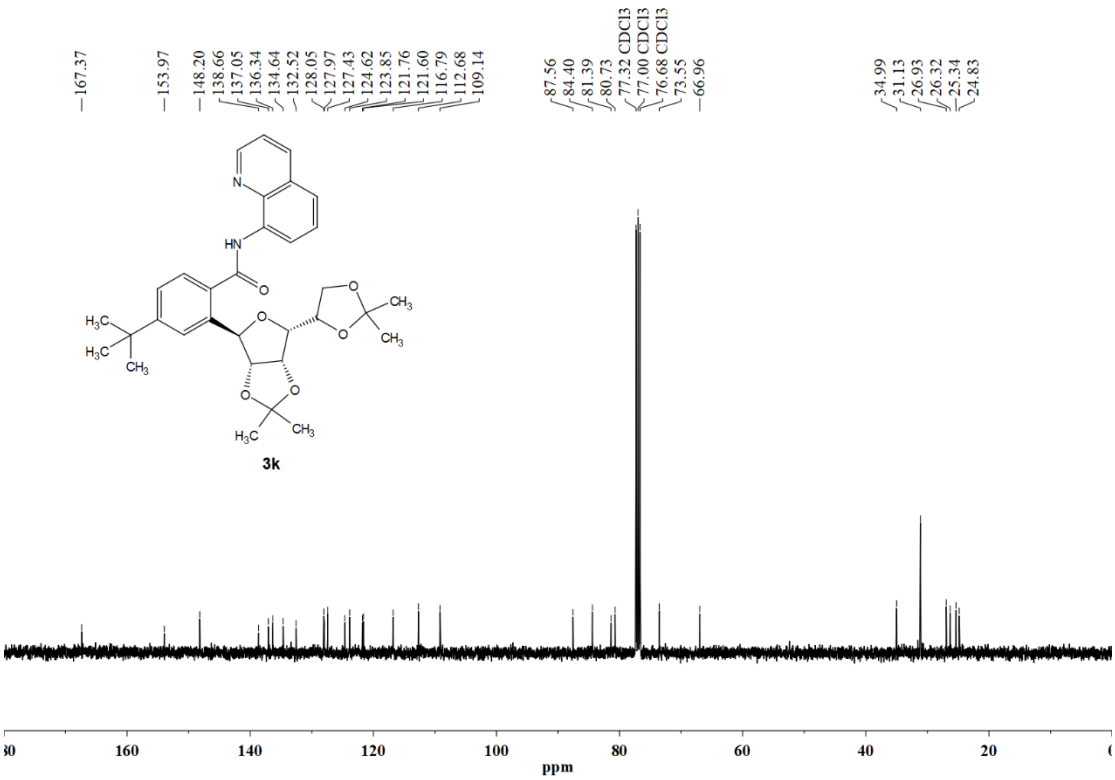
^{13}C NMR (101 MHz, Chloroform-*d*)



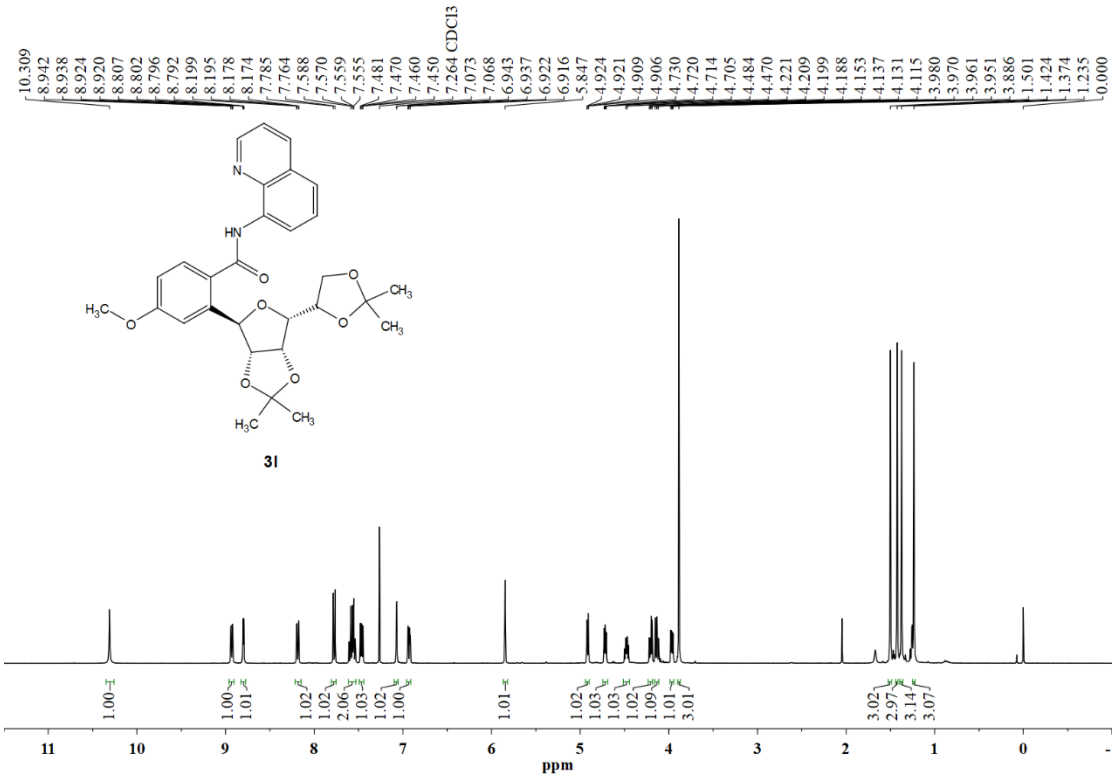
^{1}H NMR (400 MHz, Chloroform-*d*)



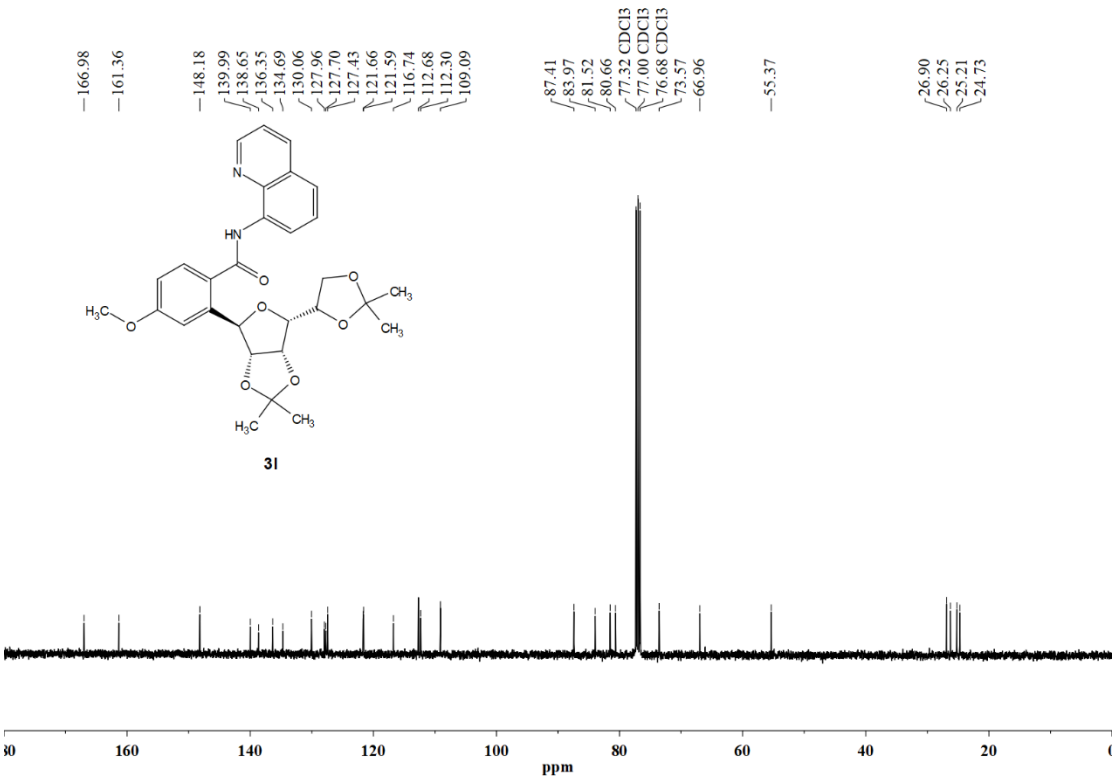
^{13}C NMR (101 MHz, Chloroform-*d*)



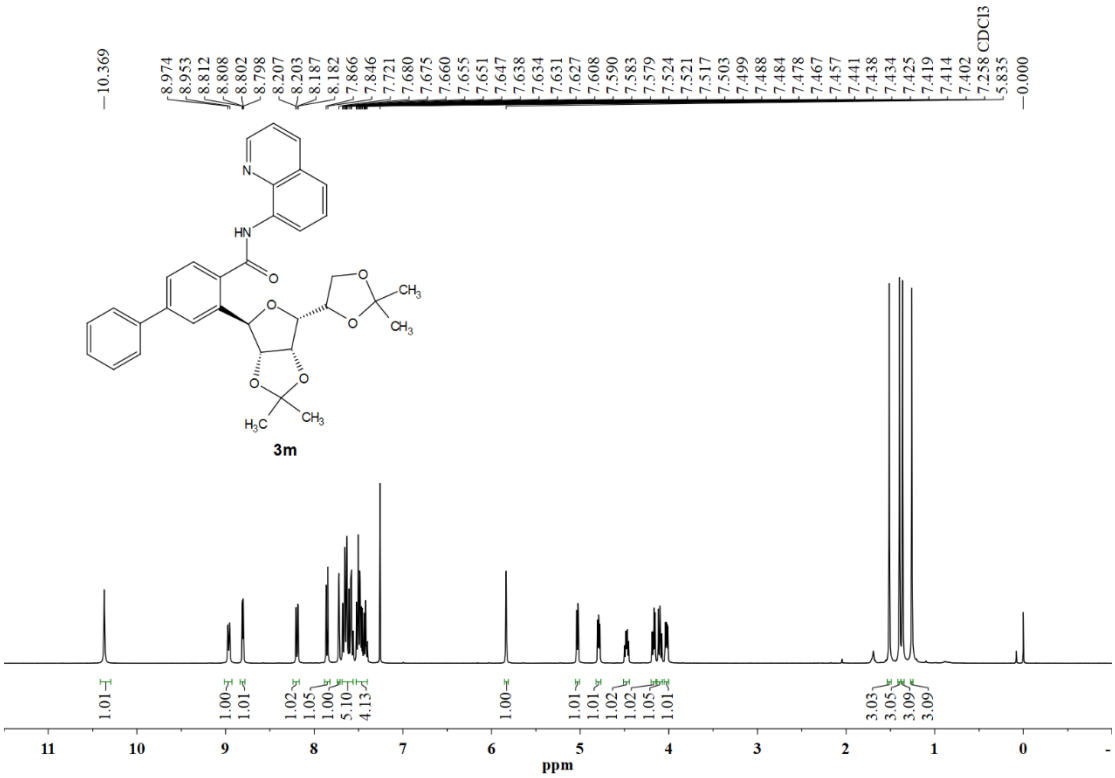
^{1}H NMR (400 MHz, Chloroform-*d*)



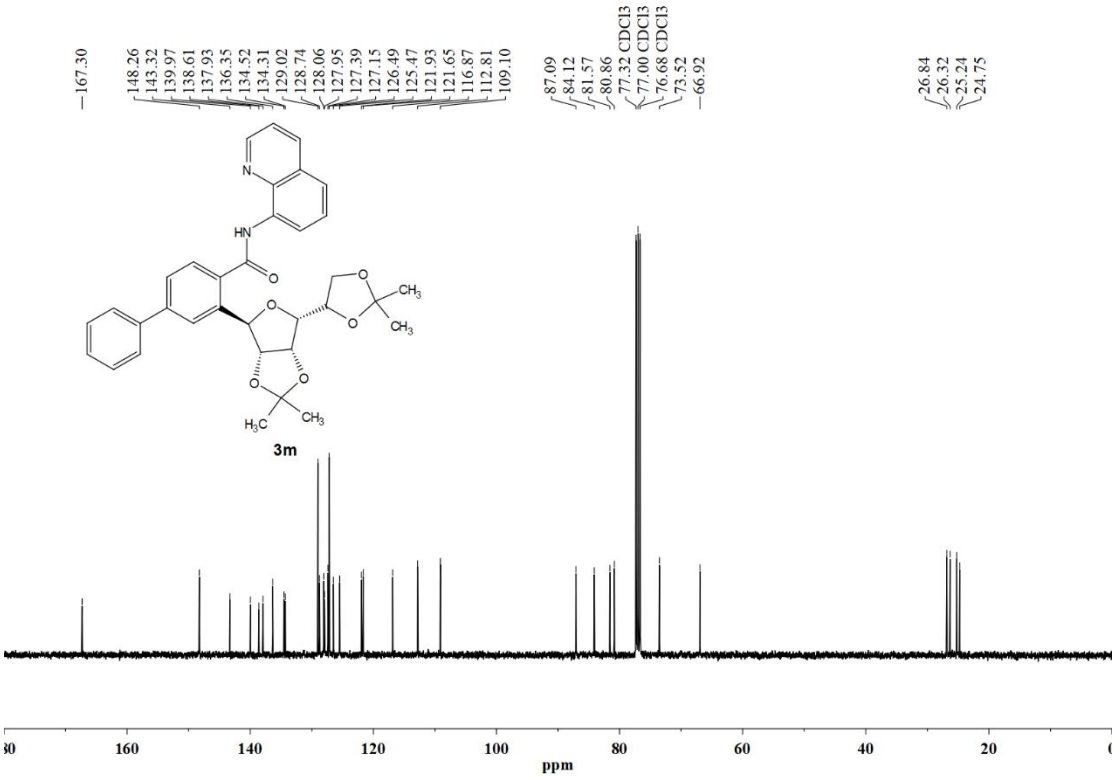
^{13}C NMR (101 MHz, Chloroform-*d*)



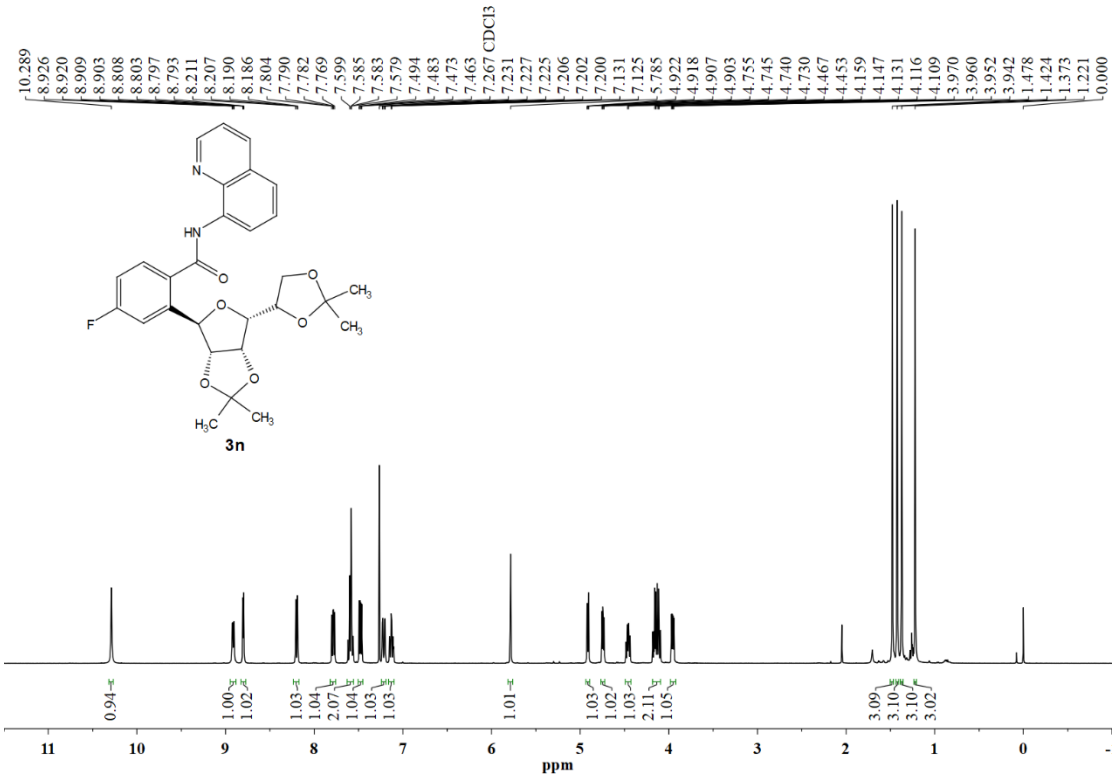
^{1}H NMR (400 MHz, Chloroform-*d*)



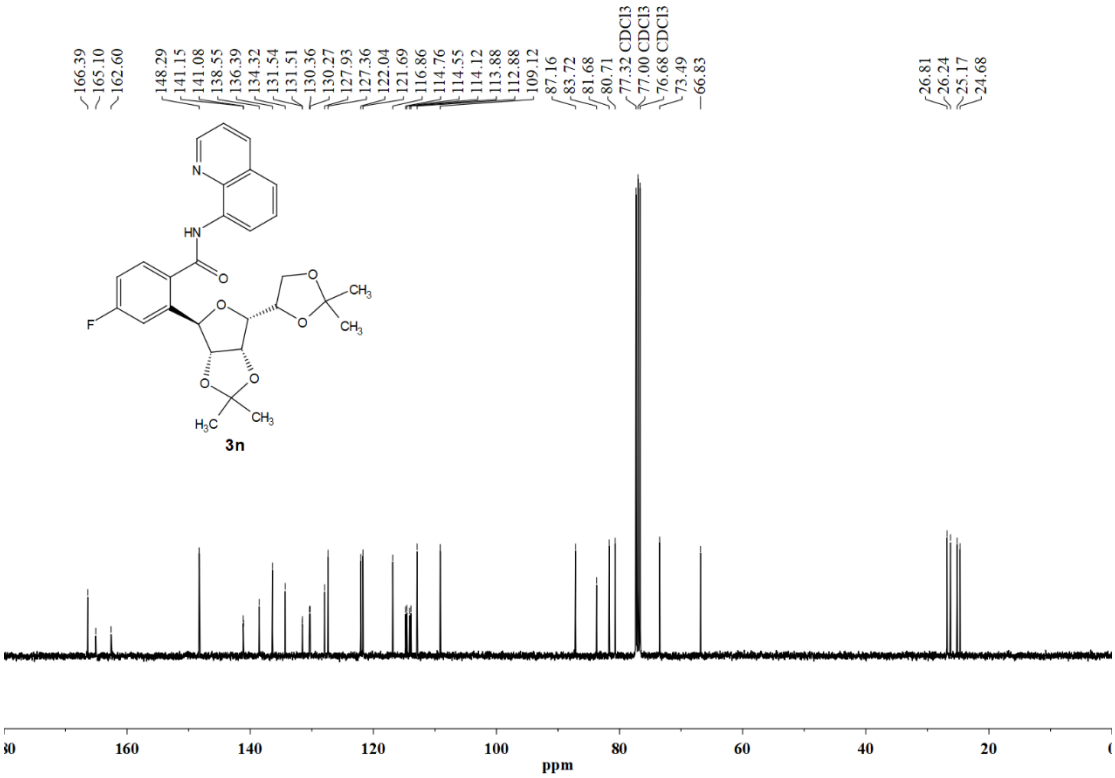
^{13}C NMR (101 MHz, Chloroform-*d*)



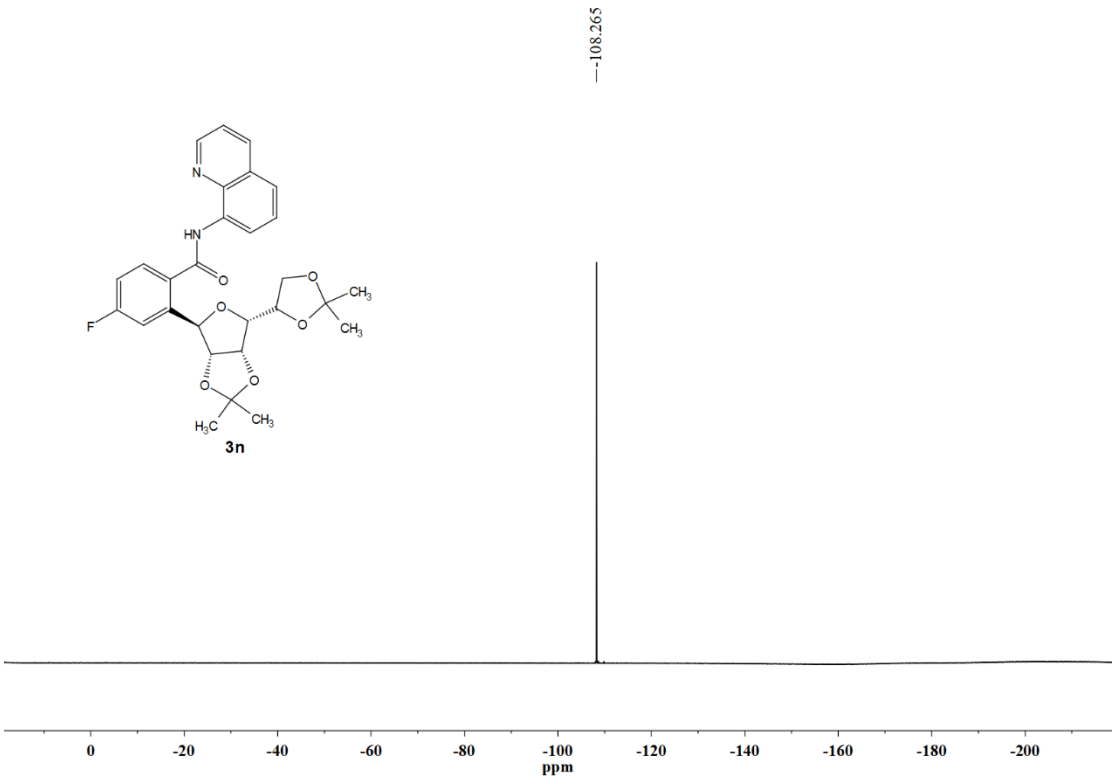
^{1}H NMR (400 MHz, Chloroform-*d*)



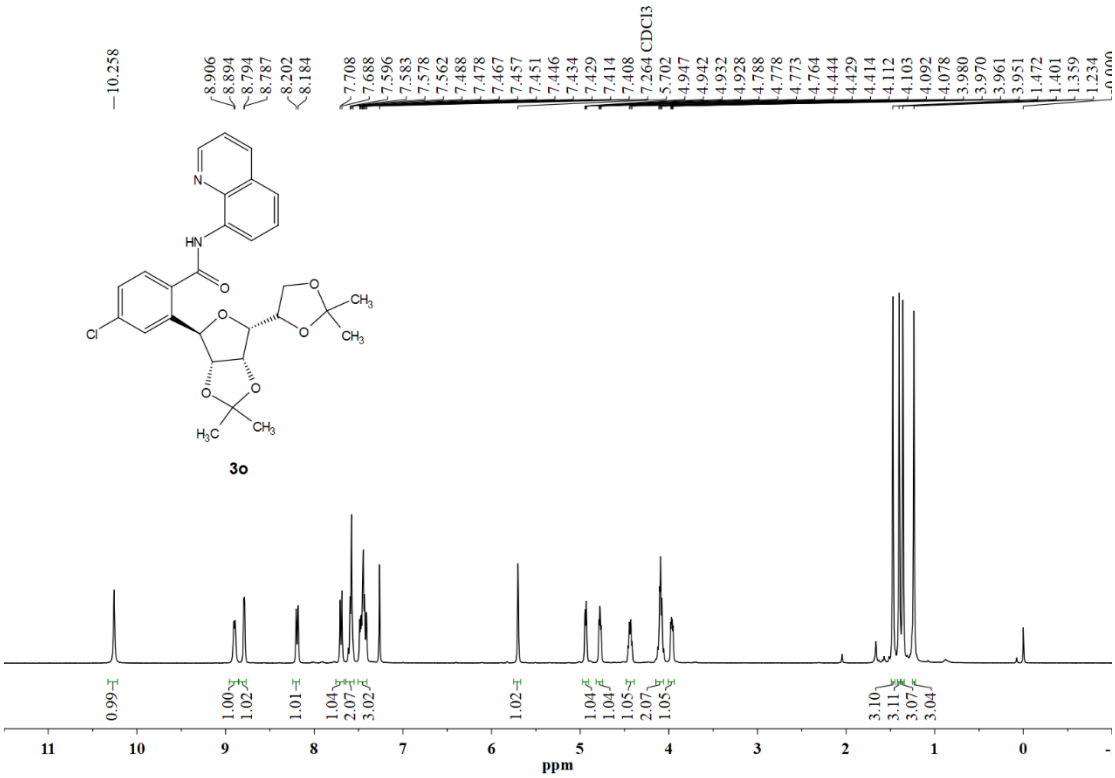
^{13}C NMR (101 MHz, Chloroform-*d*)



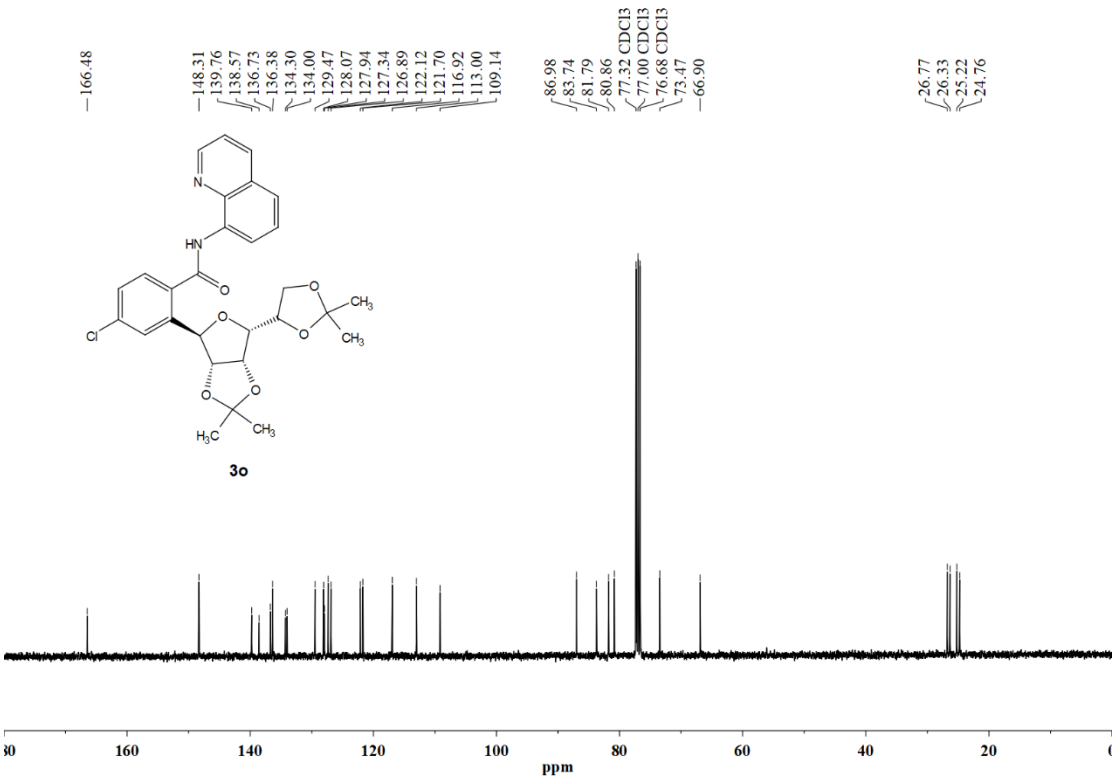
^{19}F NMR (376 MHz, Chloroform-*d*)



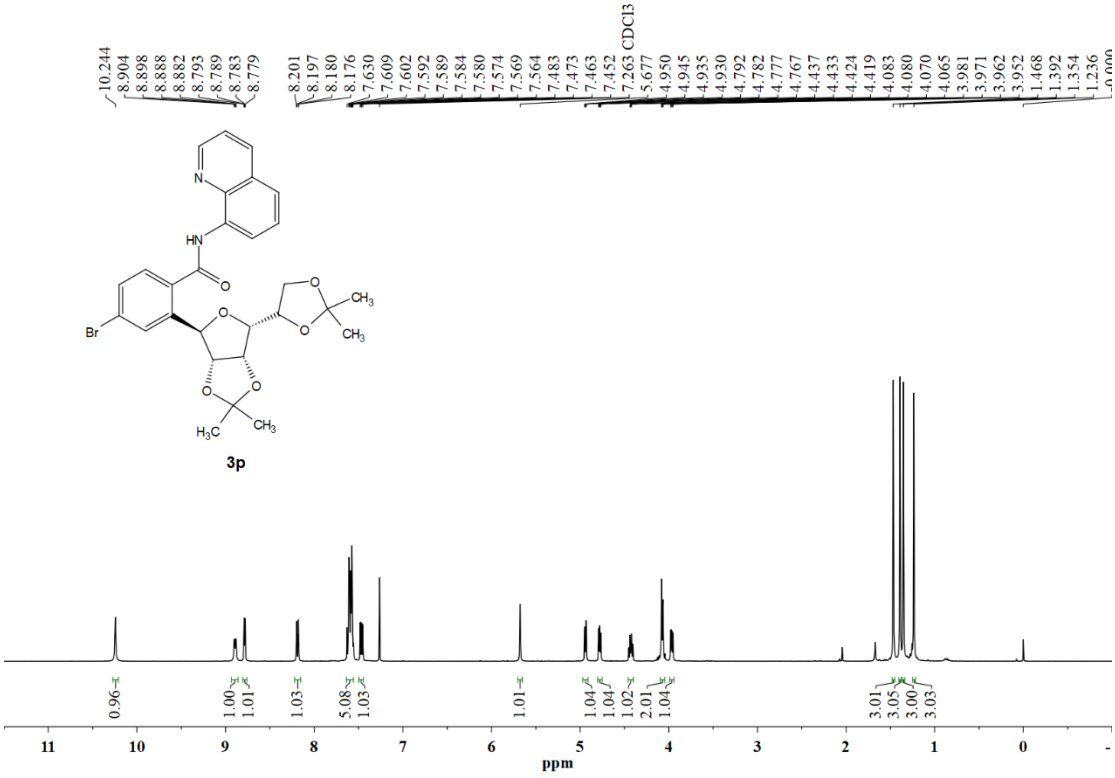
^{1}H NMR (400 MHz, Chloroform-*d*)



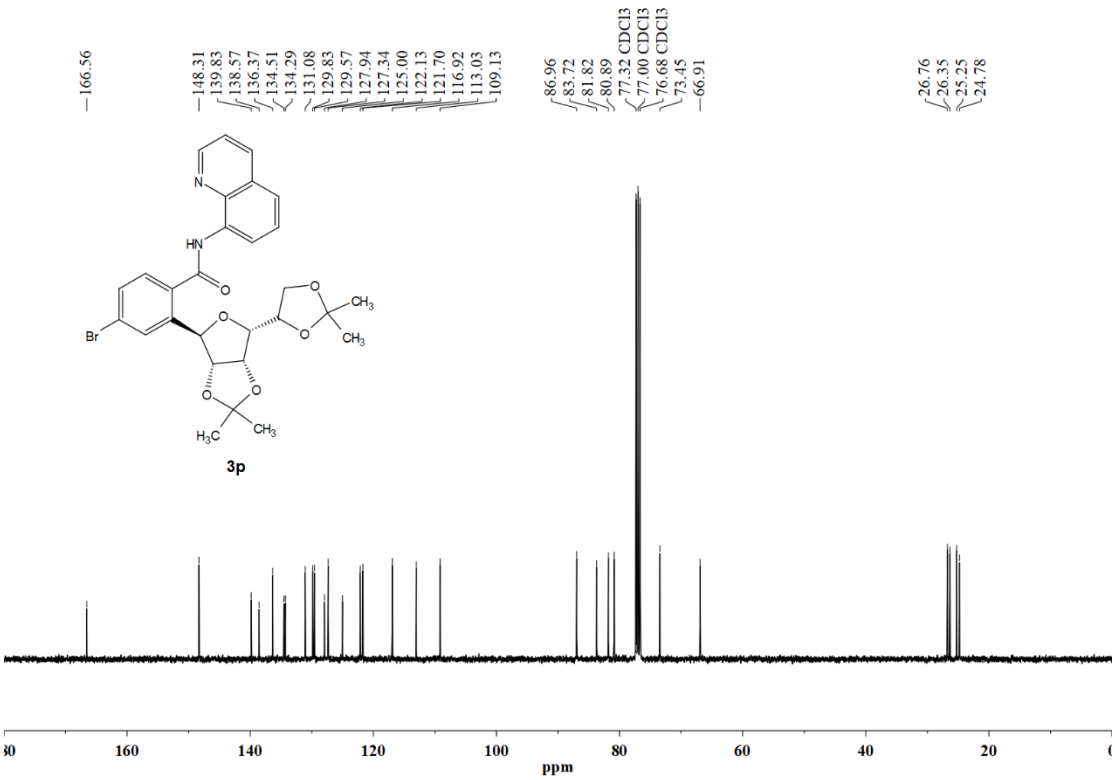
^{13}C NMR (101 MHz, Chloroform-*d*)



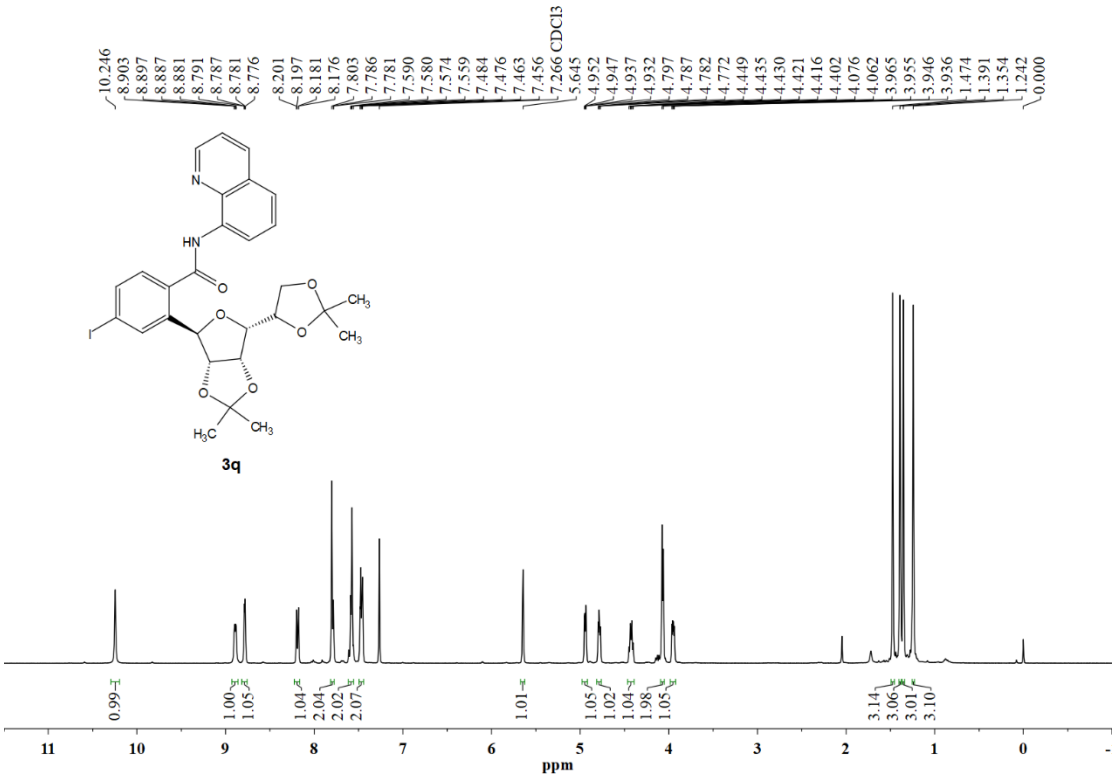
^{1}H NMR (400 MHz, Chloroform-*d*)



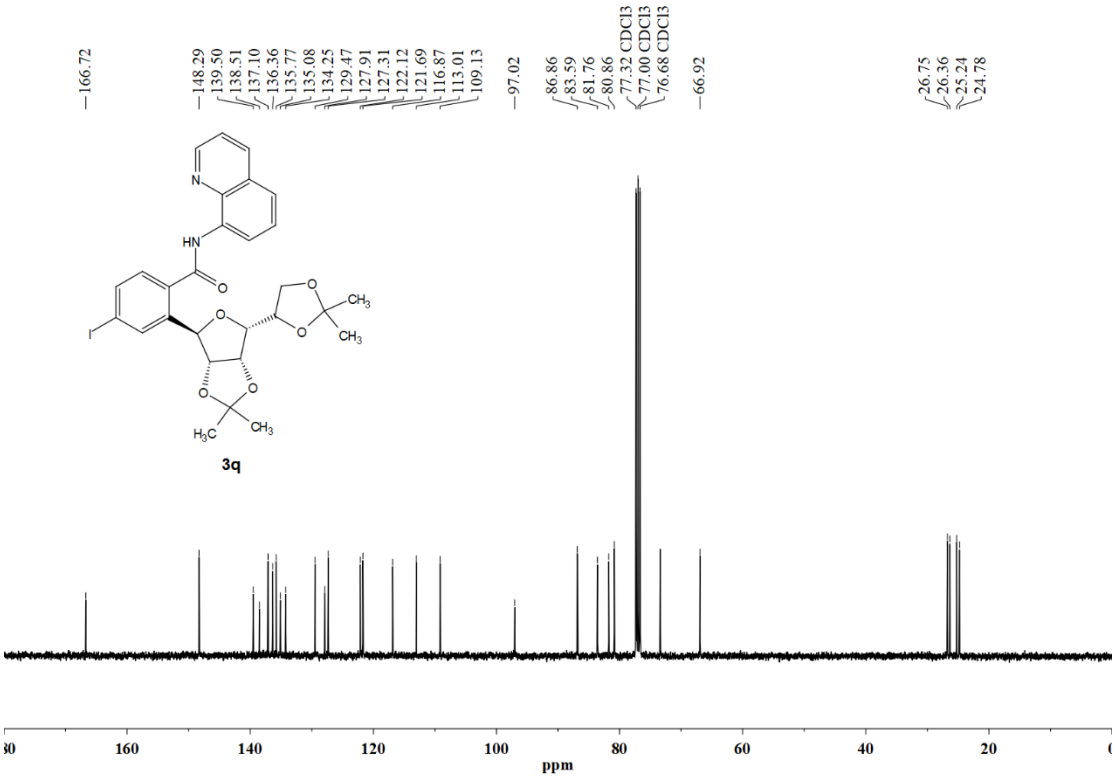
^{13}C NMR (101 MHz, Chloroform-*d*)



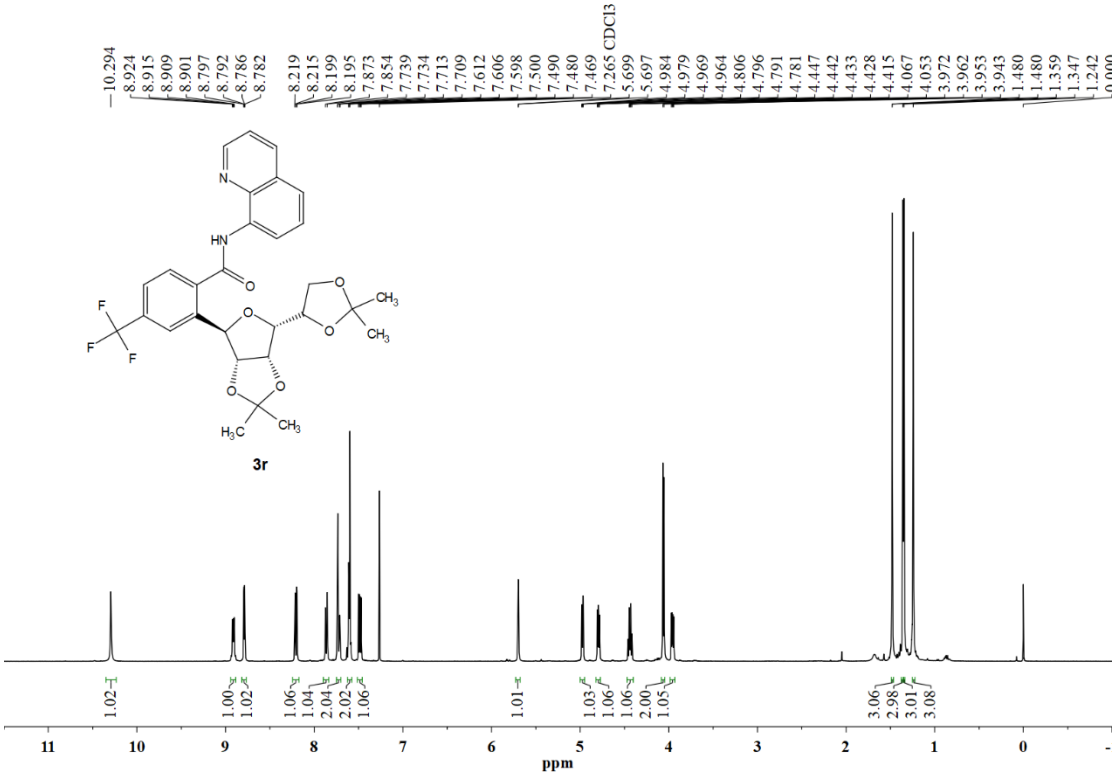
^{1}H NMR (400 MHz, Chloroform-*d*)



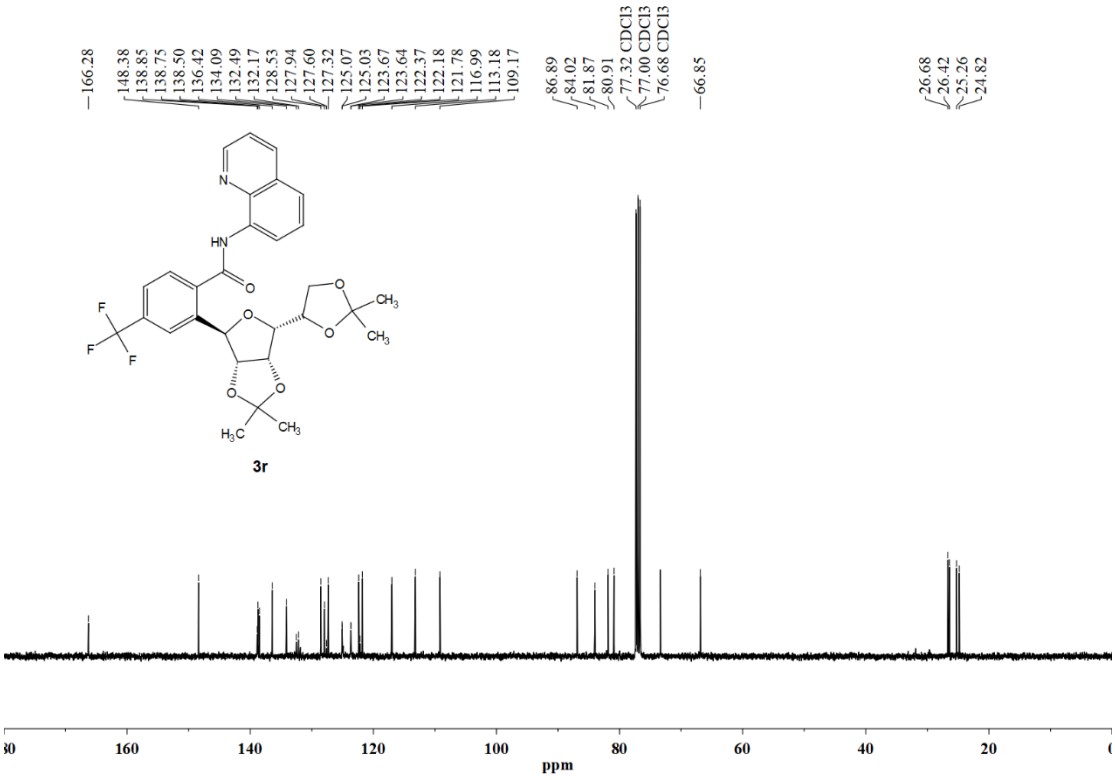
^{13}C NMR (101 MHz, Chloroform-*d*)



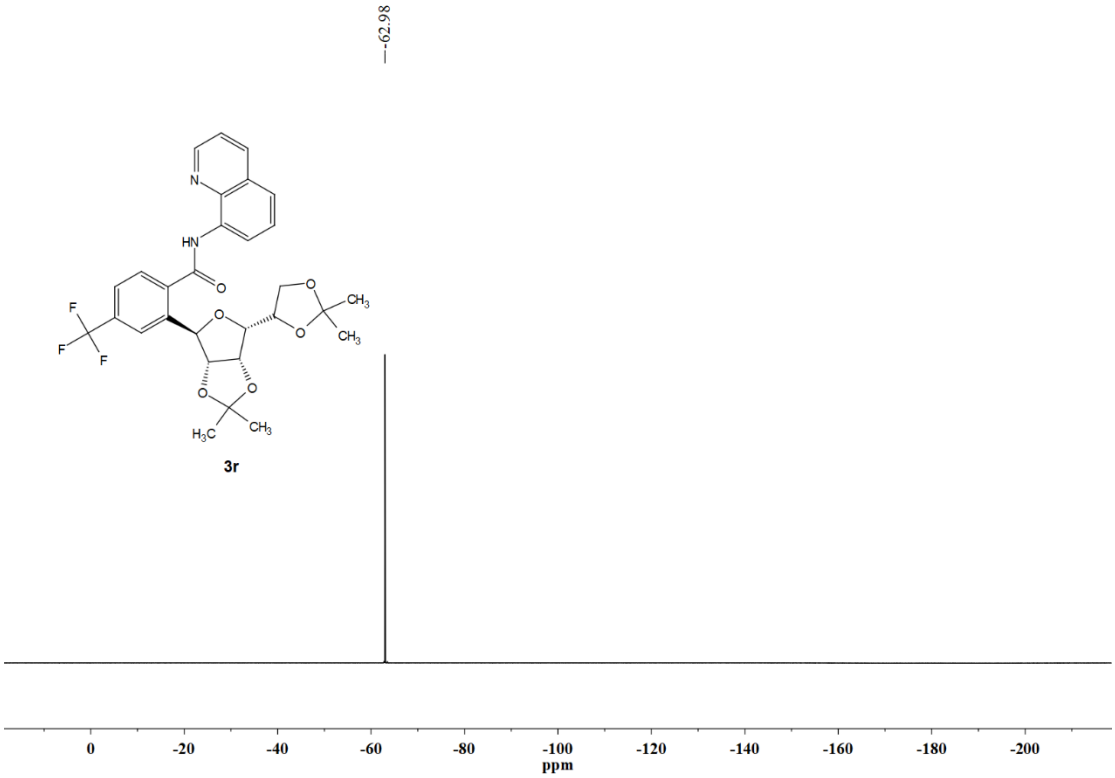
^{1}H NMR (400 MHz, Chloroform-*d*)



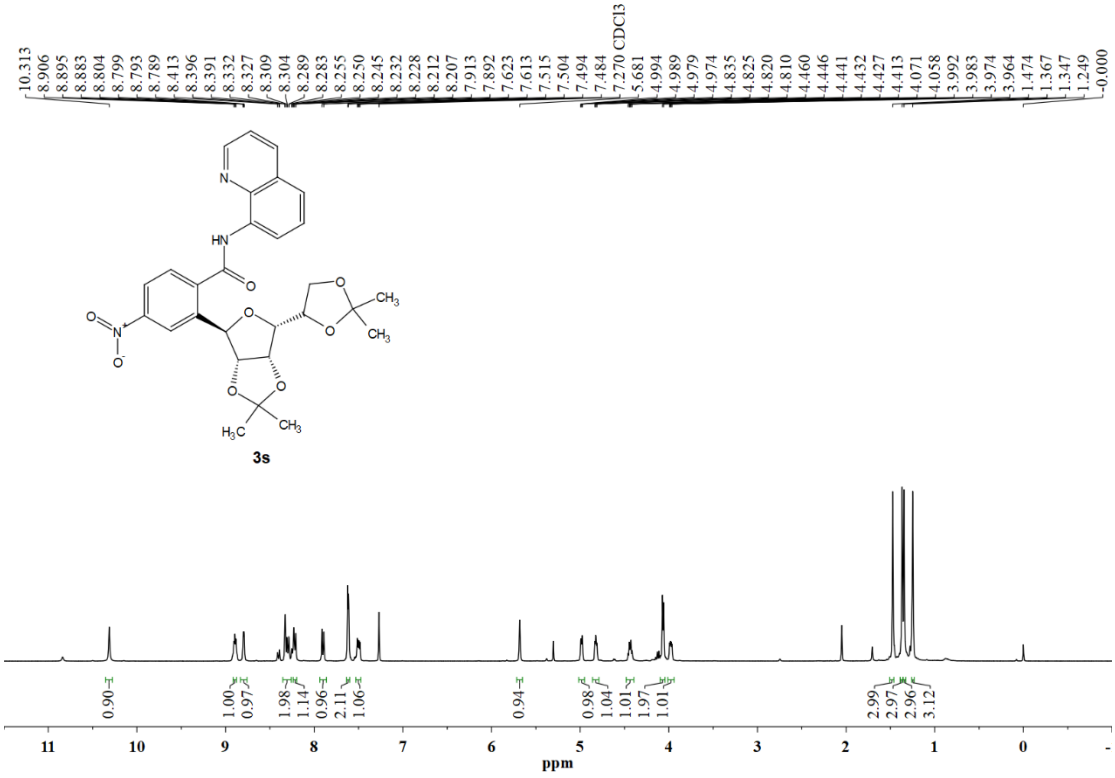
^{13}C NMR (101 MHz, Chloroform-*d*)



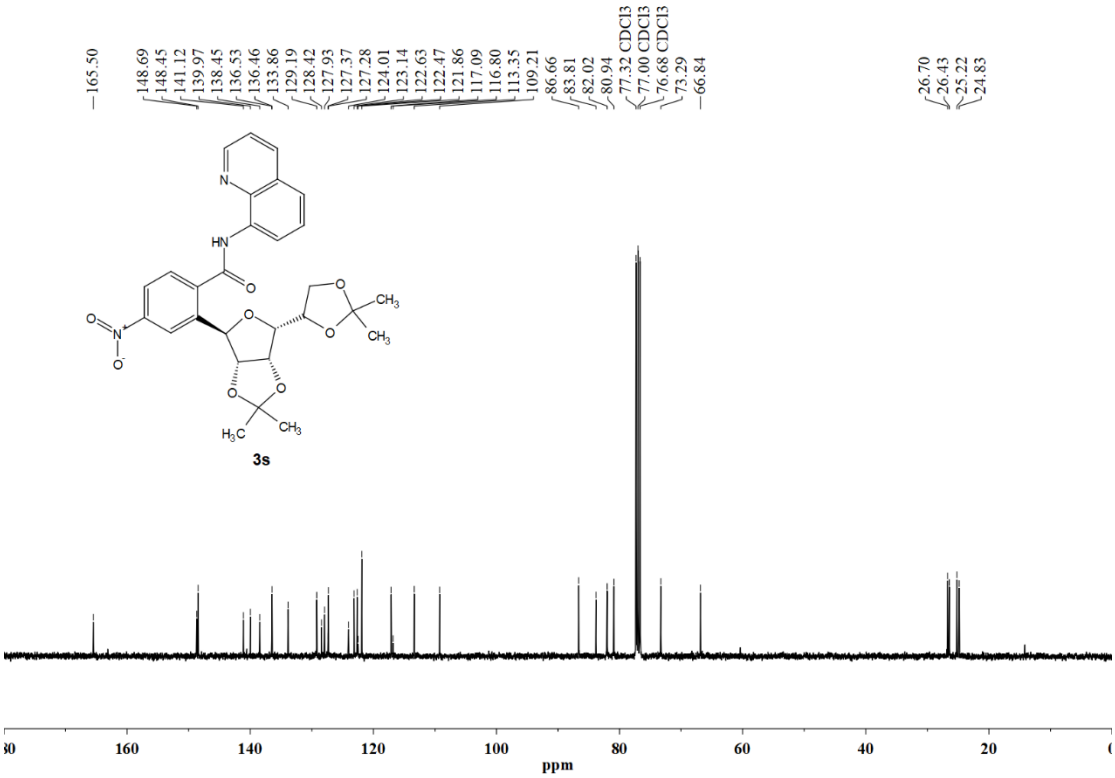
^{19}F NMR (376 MHz, Chloroform-*d*)



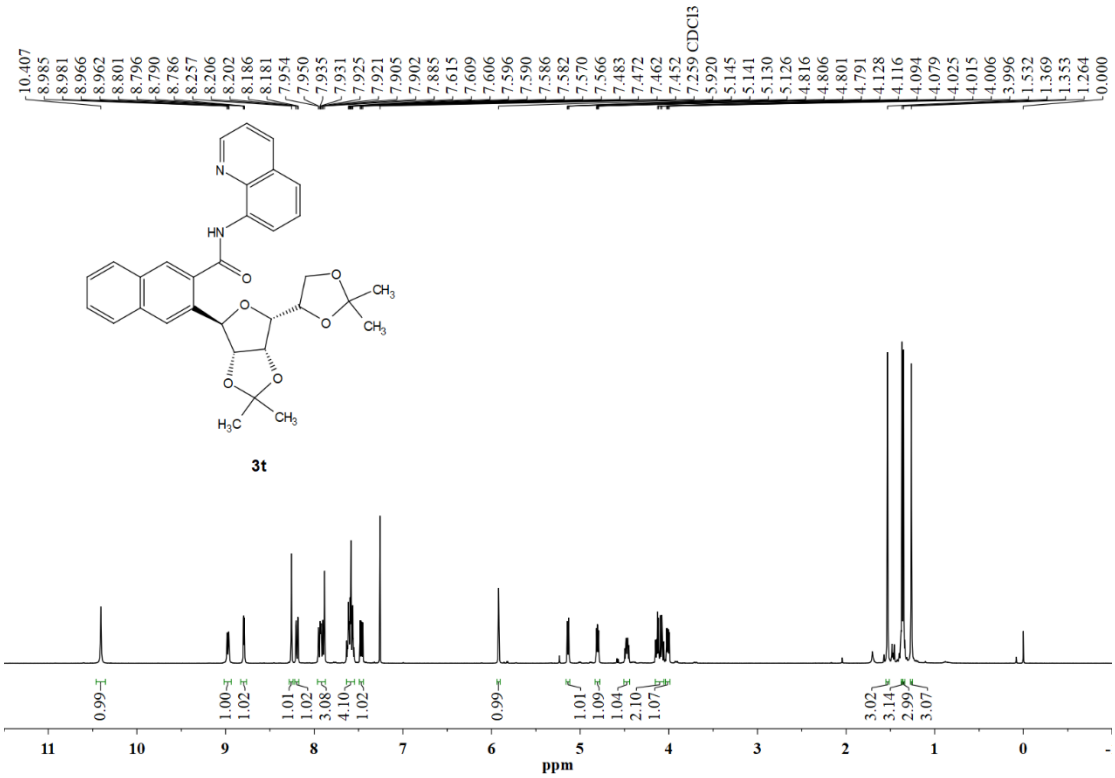
^{1}H NMR (400 MHz, Chloroform-*d*)



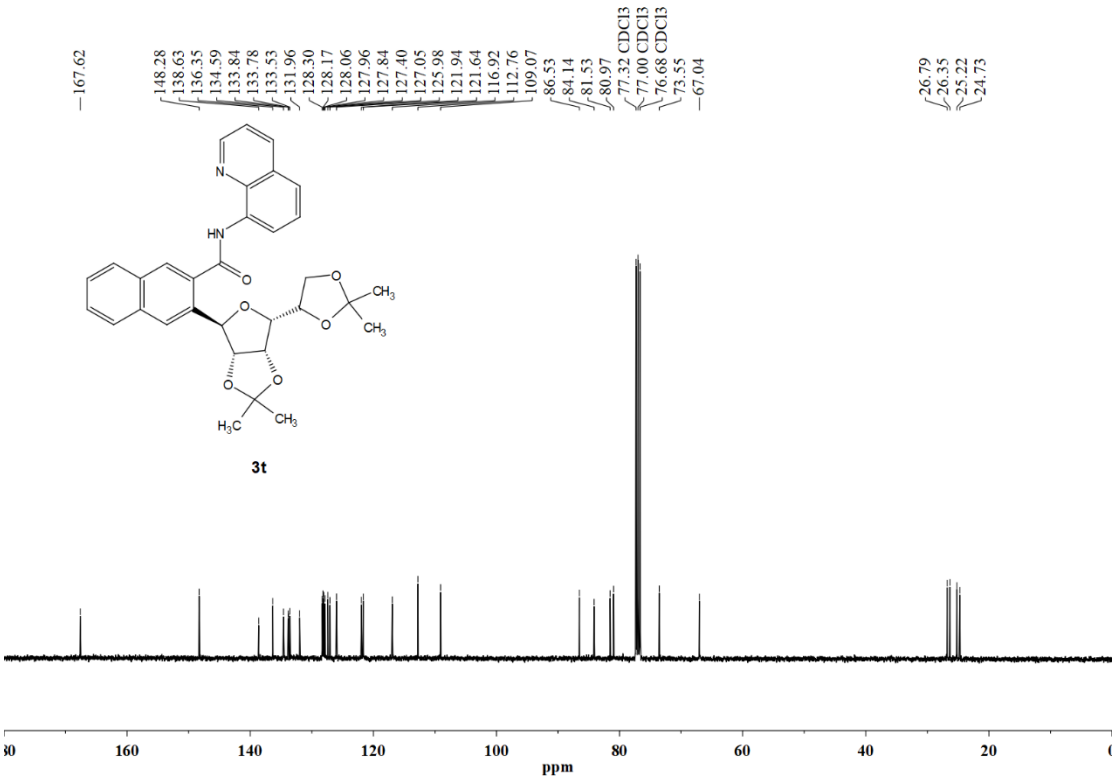
^{13}C NMR (101 MHz, Chloroform-*d*)



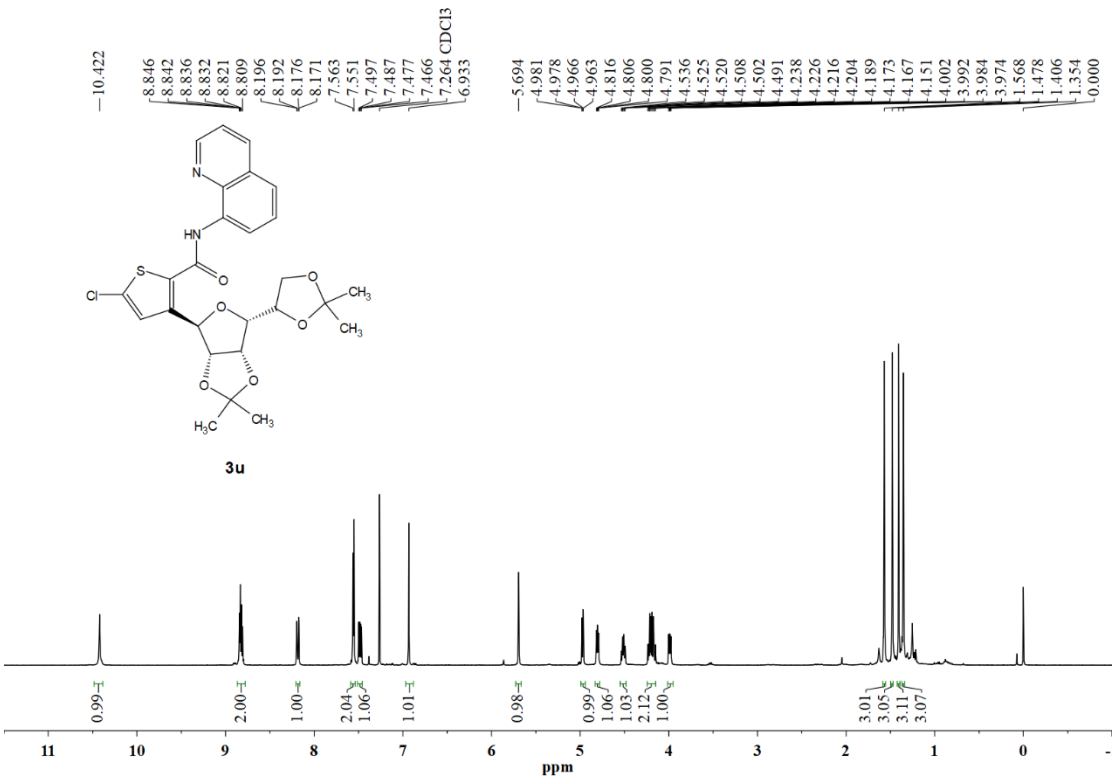
^{1}H NMR (400 MHz, Chloroform-*d*)



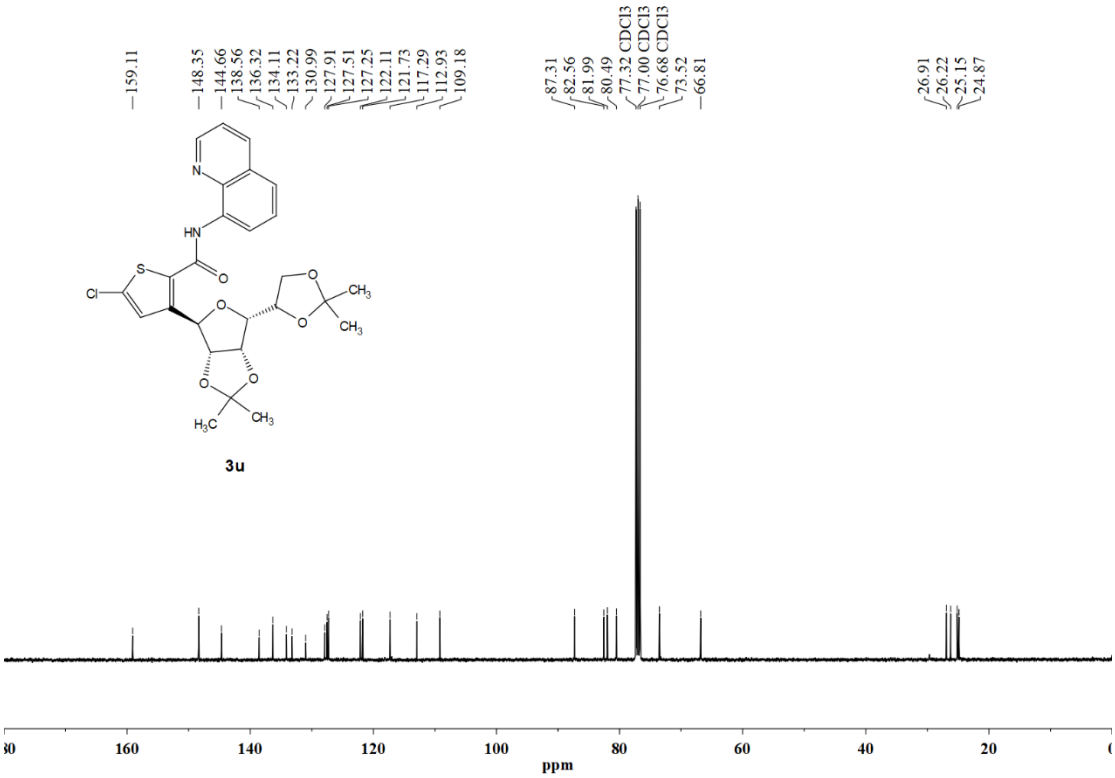
^{13}C NMR (101 MHz, Chloroform-*d*)



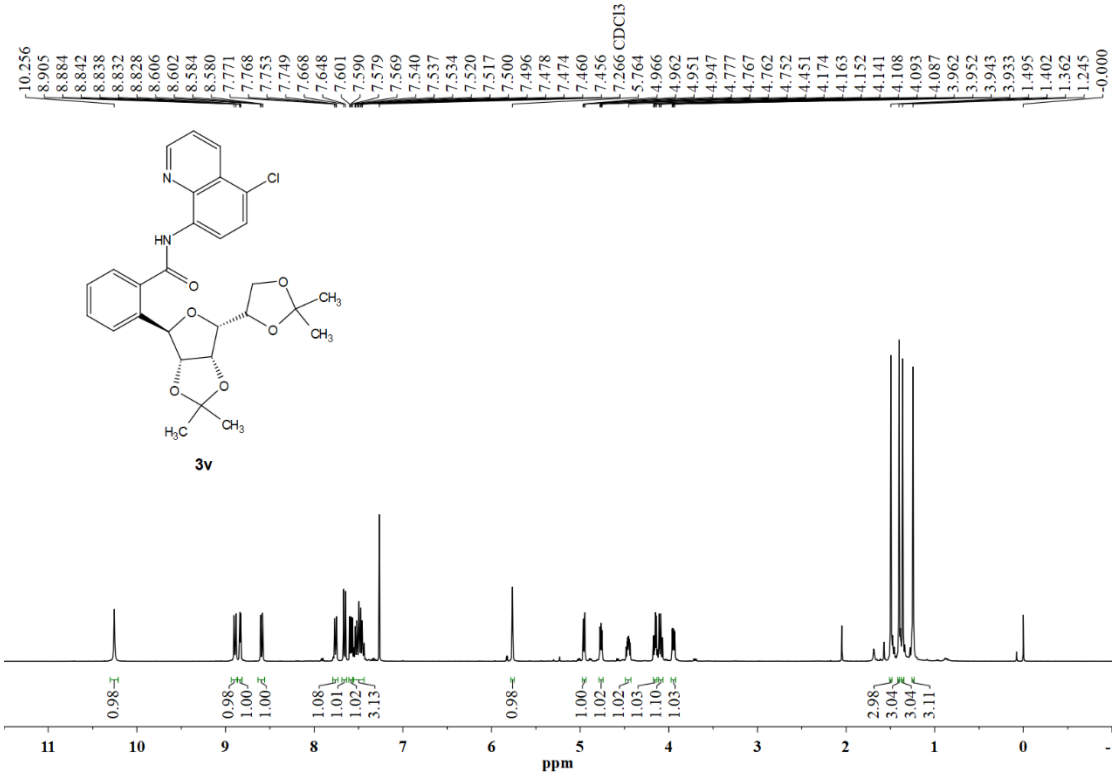
^{1}H NMR (400 MHz, Chloroform-*d*)



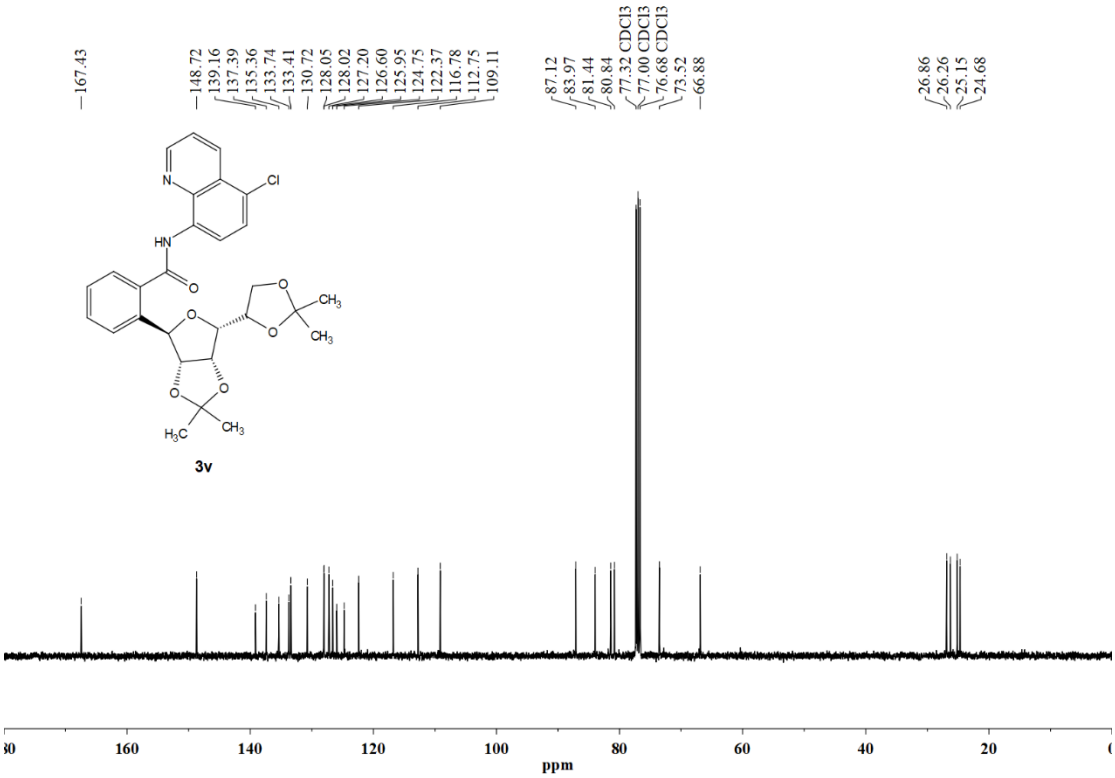
^{13}C NMR (101 MHz, Chloroform-*d*)



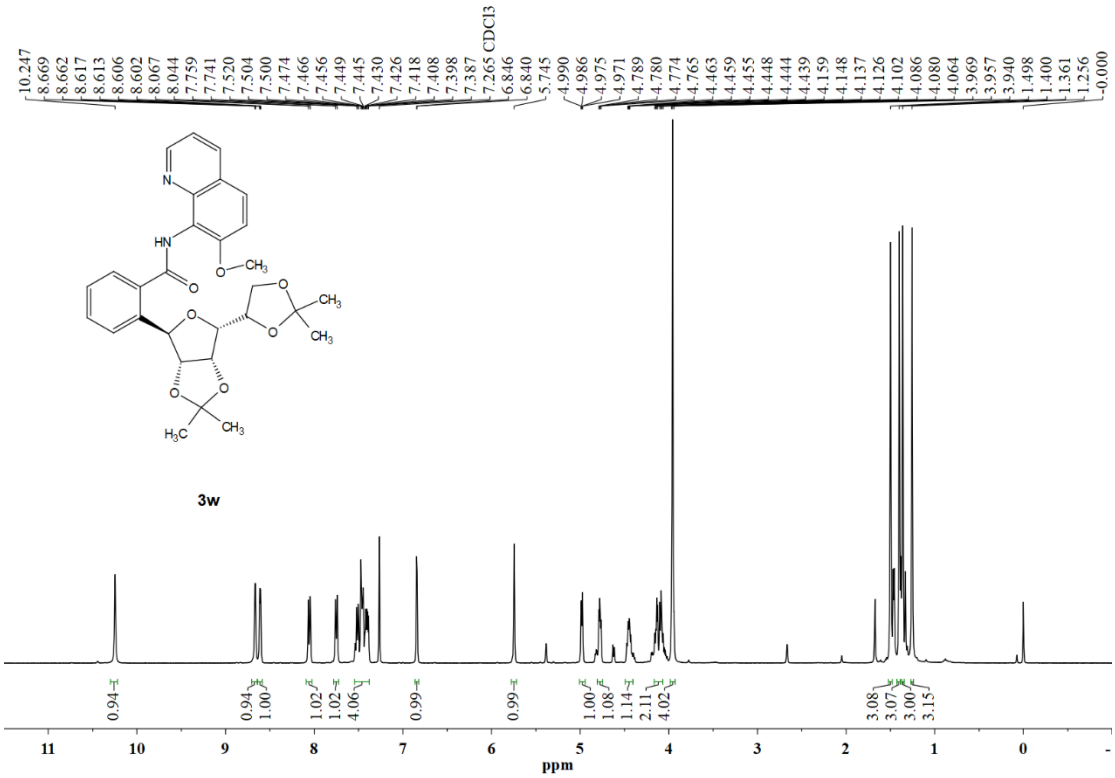
^{1}H NMR (400 MHz, Chloroform-*d*)



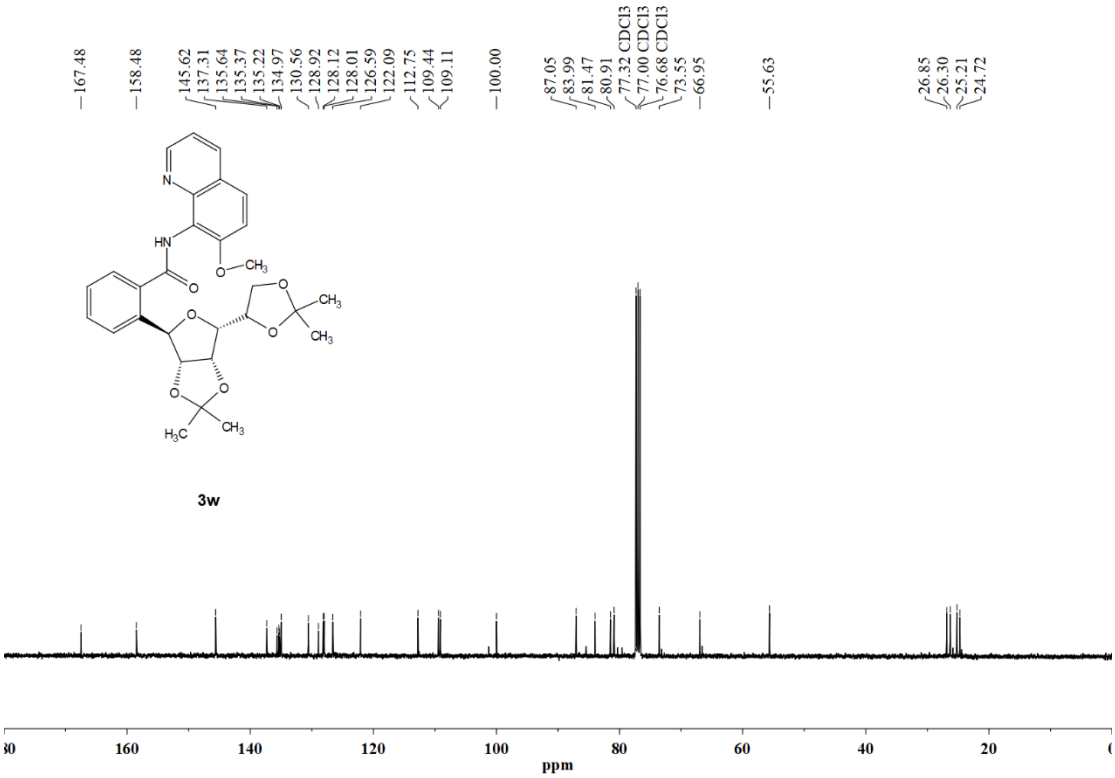
^{13}C NMR (101 MHz, Chloroform-*d*)



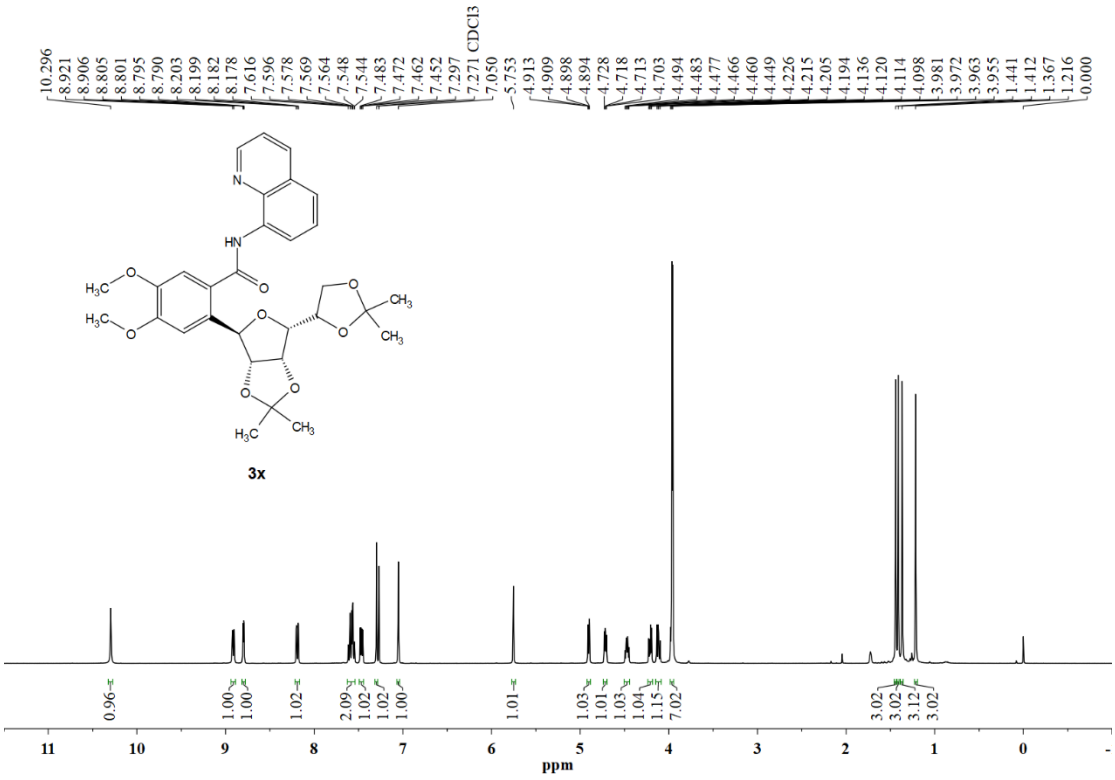
^{1}H NMR (400 MHz, Chloroform-*d*)



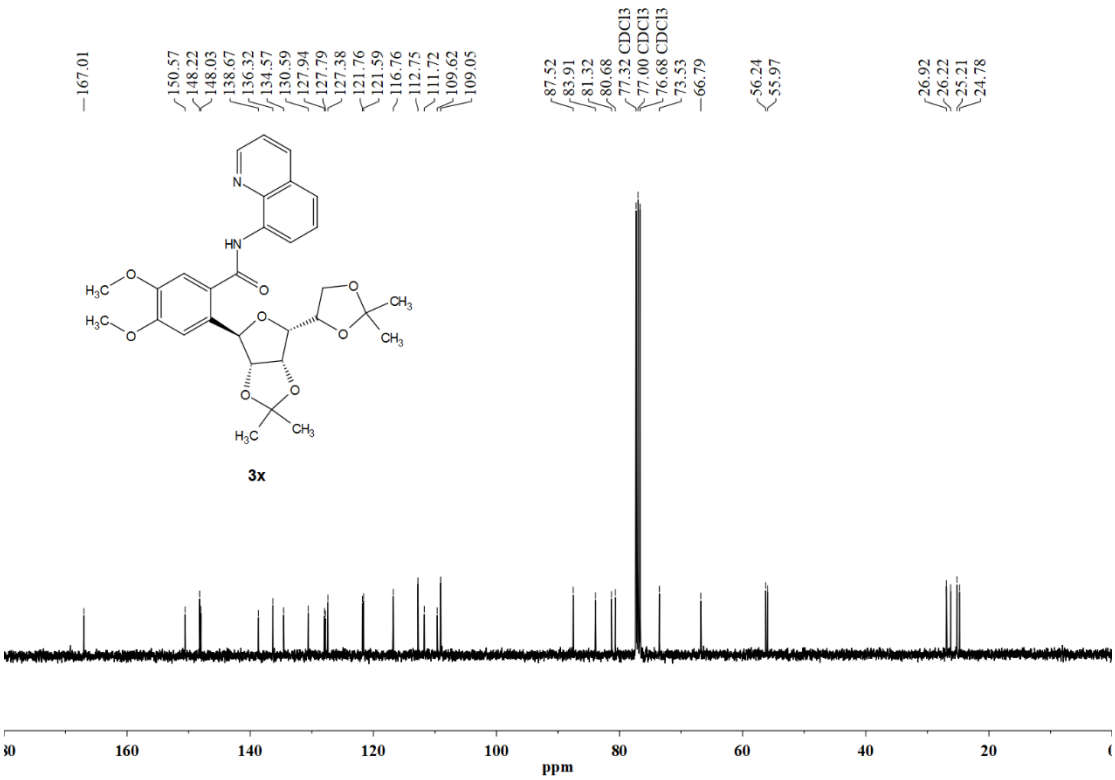
^{13}C NMR (101 MHz, Chloroform-*d*)



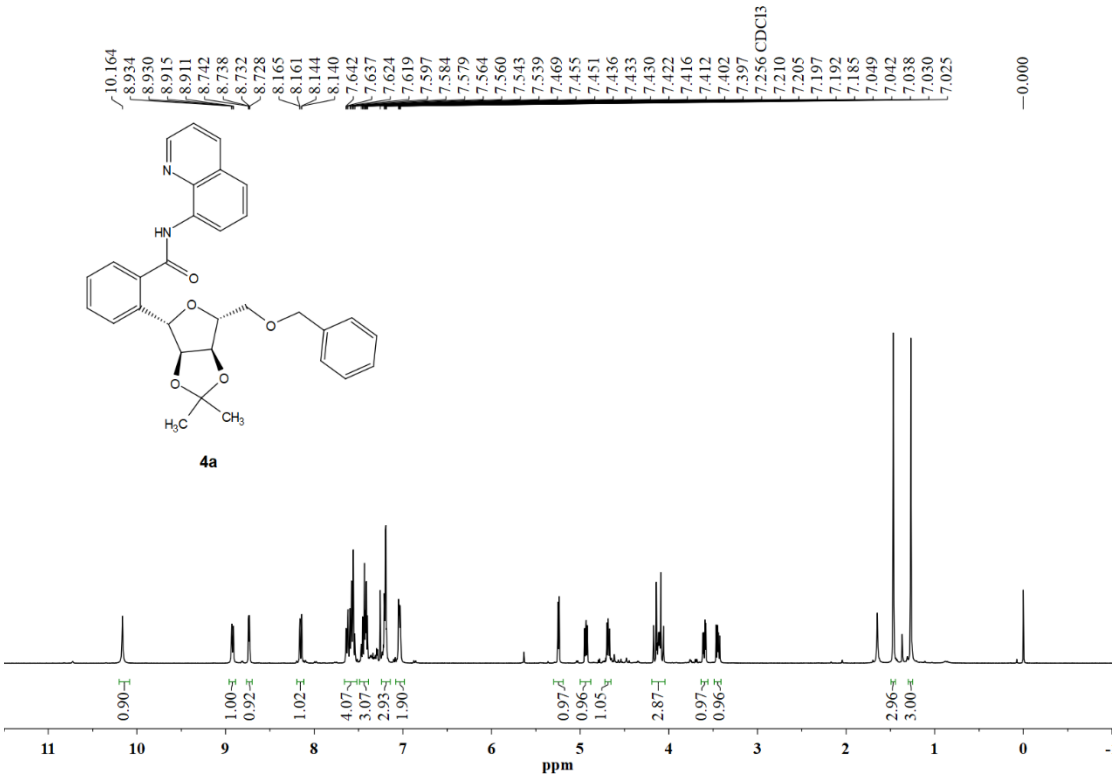
^{1}H NMR (400 MHz, Chloroform-*d*)



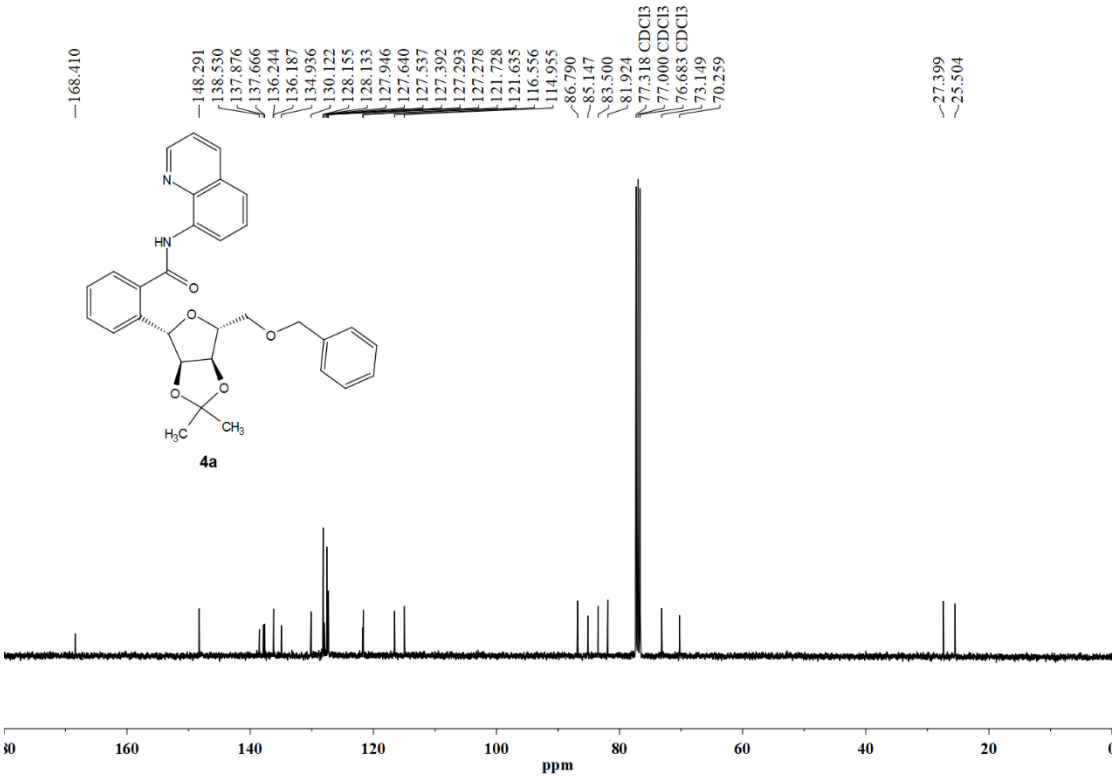
^{13}C NMR (101 MHz, Chloroform-*d*)



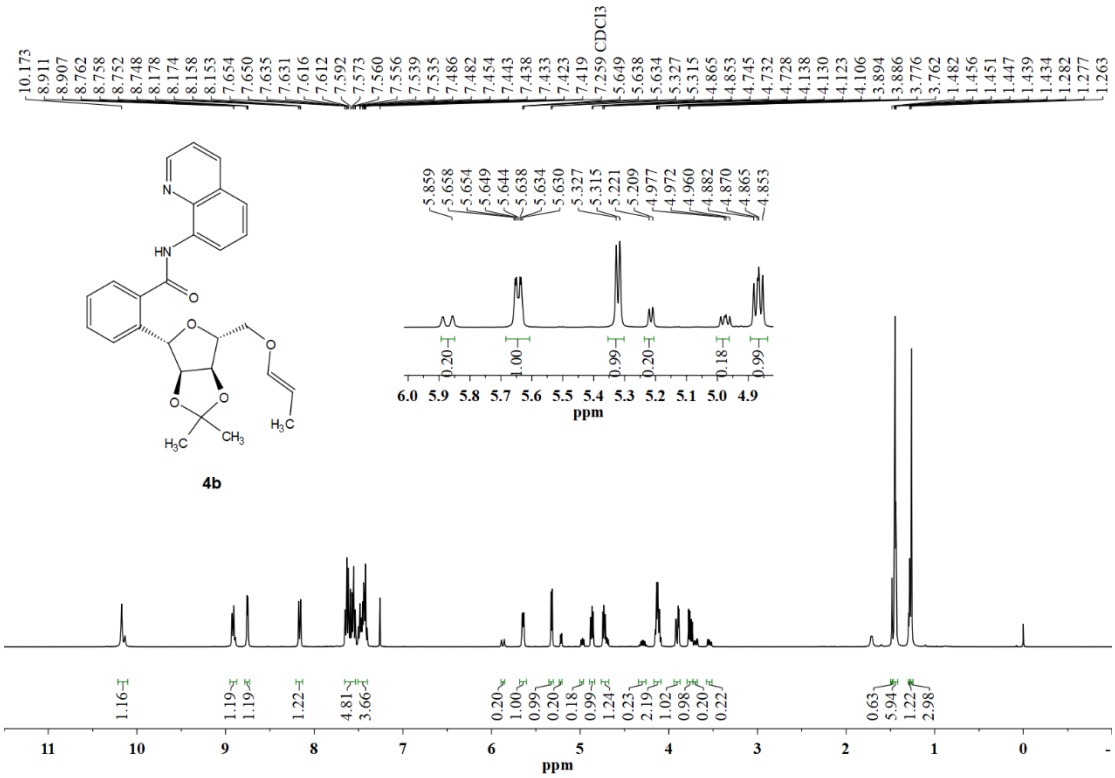
^{1}H NMR (400 MHz, Chloroform-*d*)



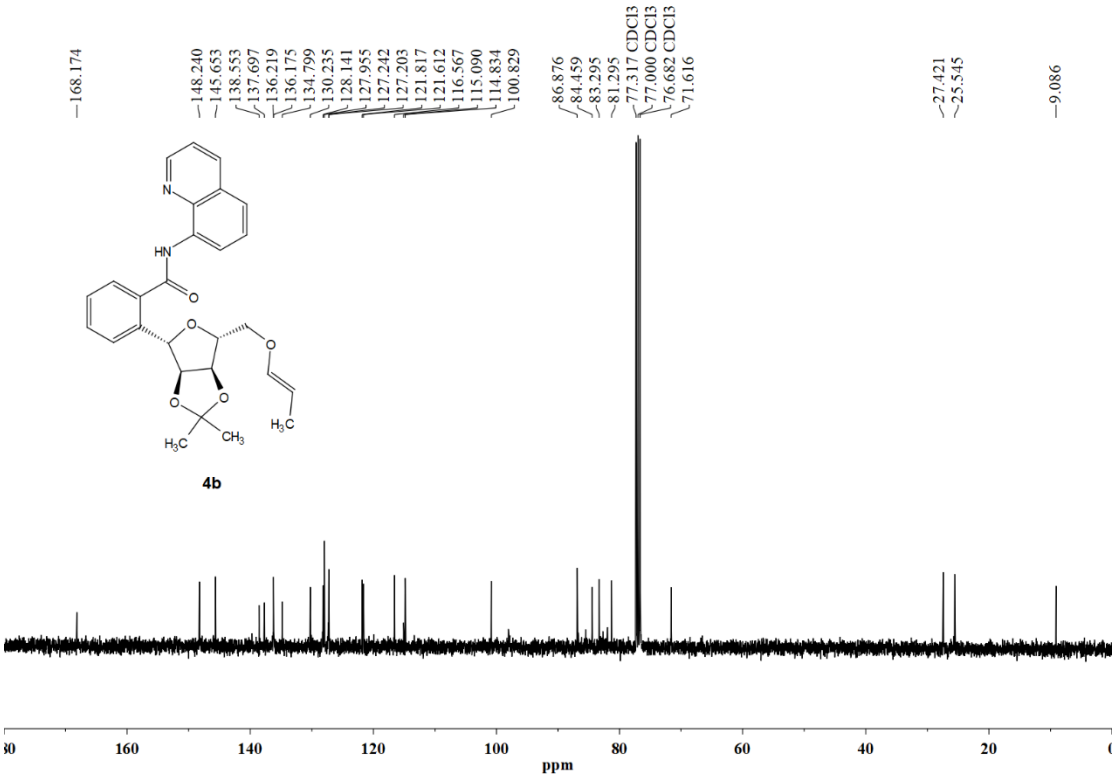
^{13}C NMR (101 MHz, Chloroform-*d*)



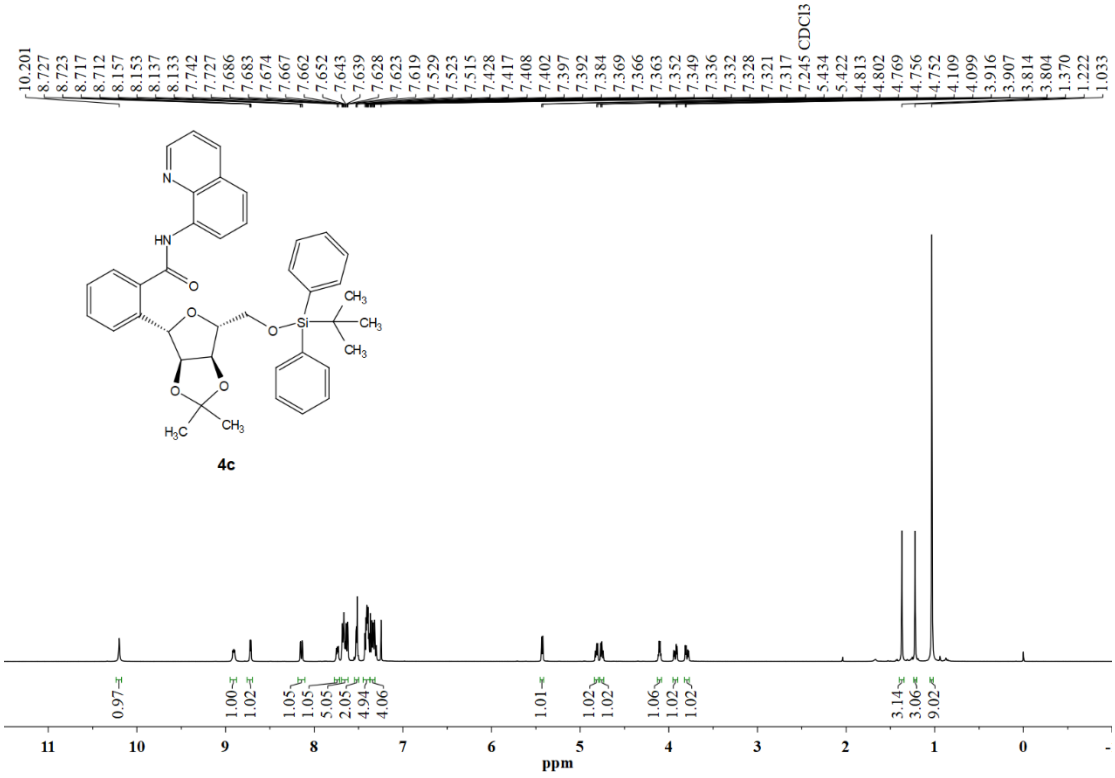
^{1}H NMR (400 MHz, Chloroform-*d*)



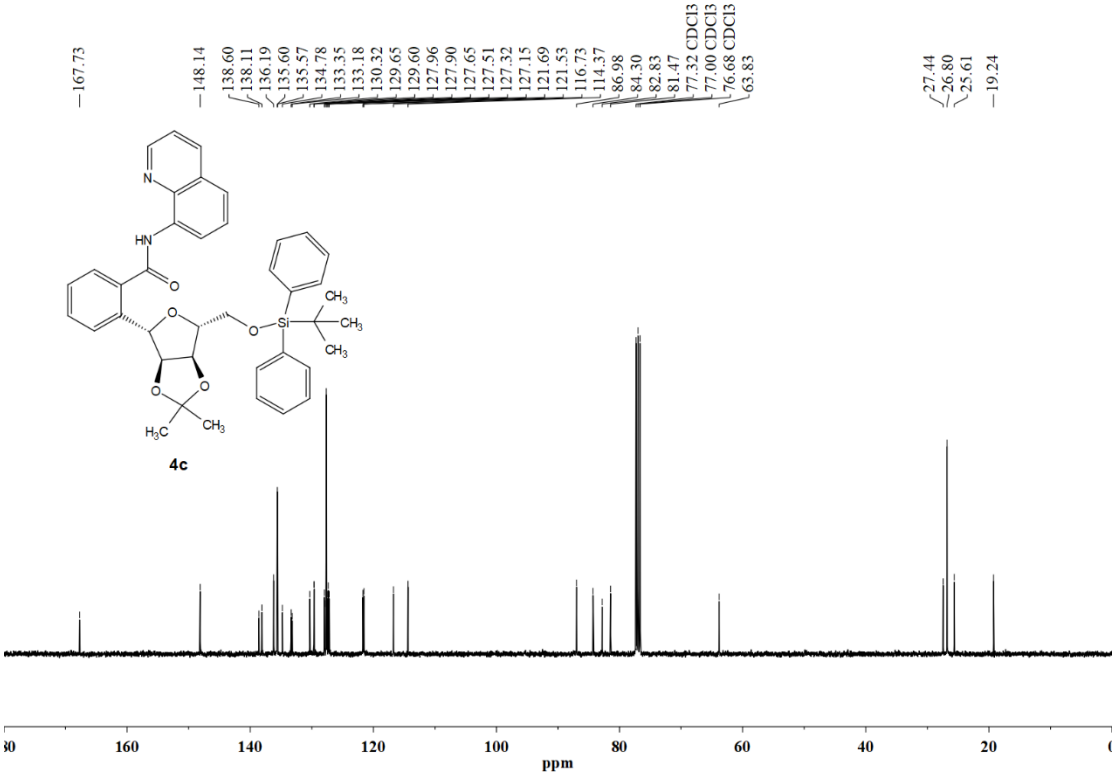
^{13}C NMR (101 MHz, Chloroform-*d*)

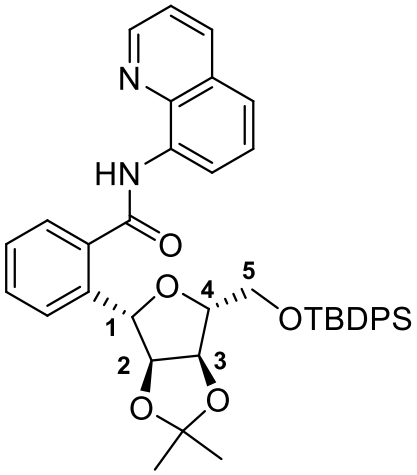


^{1}H NMR (400 MHz, Chloroform-*d*)

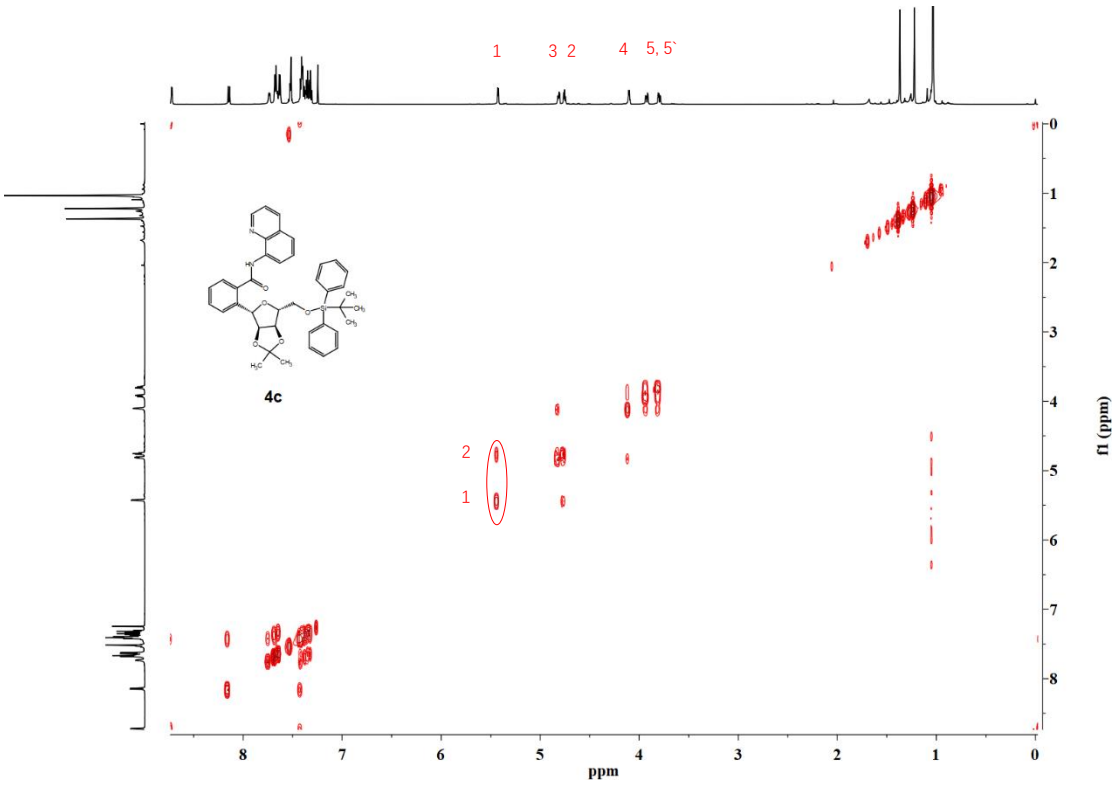


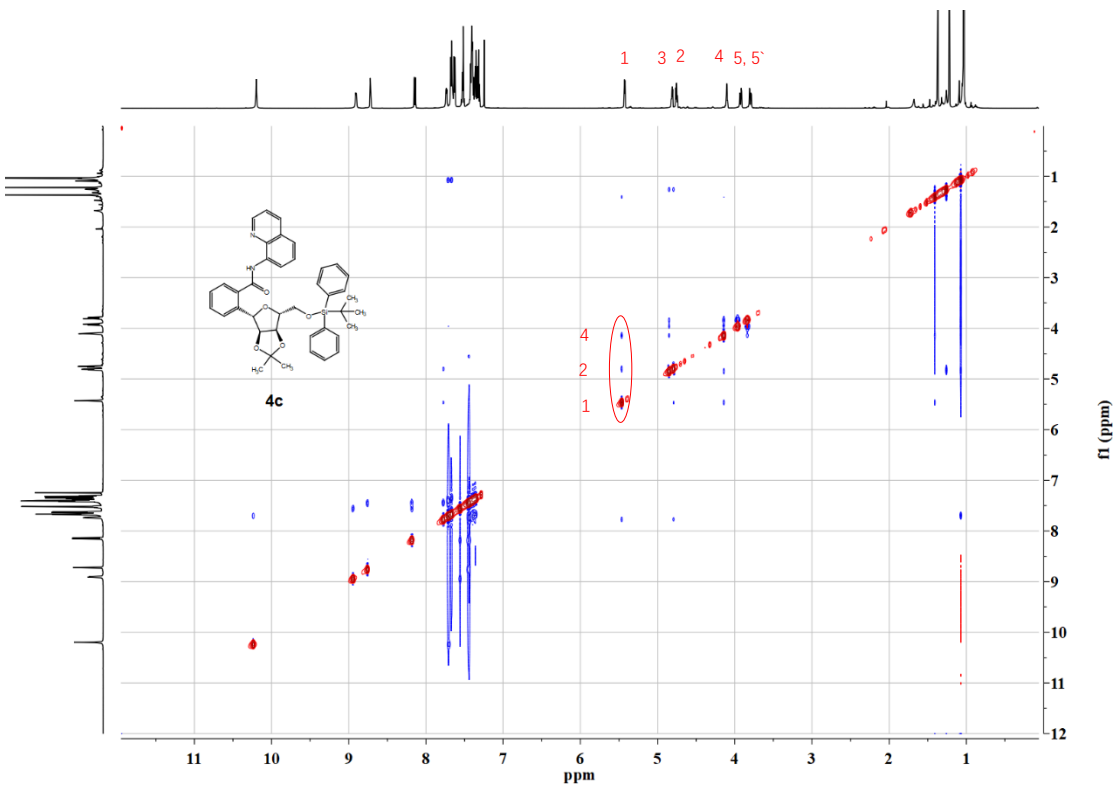
^{13}C NMR (101 MHz, Chloroform-*d*)

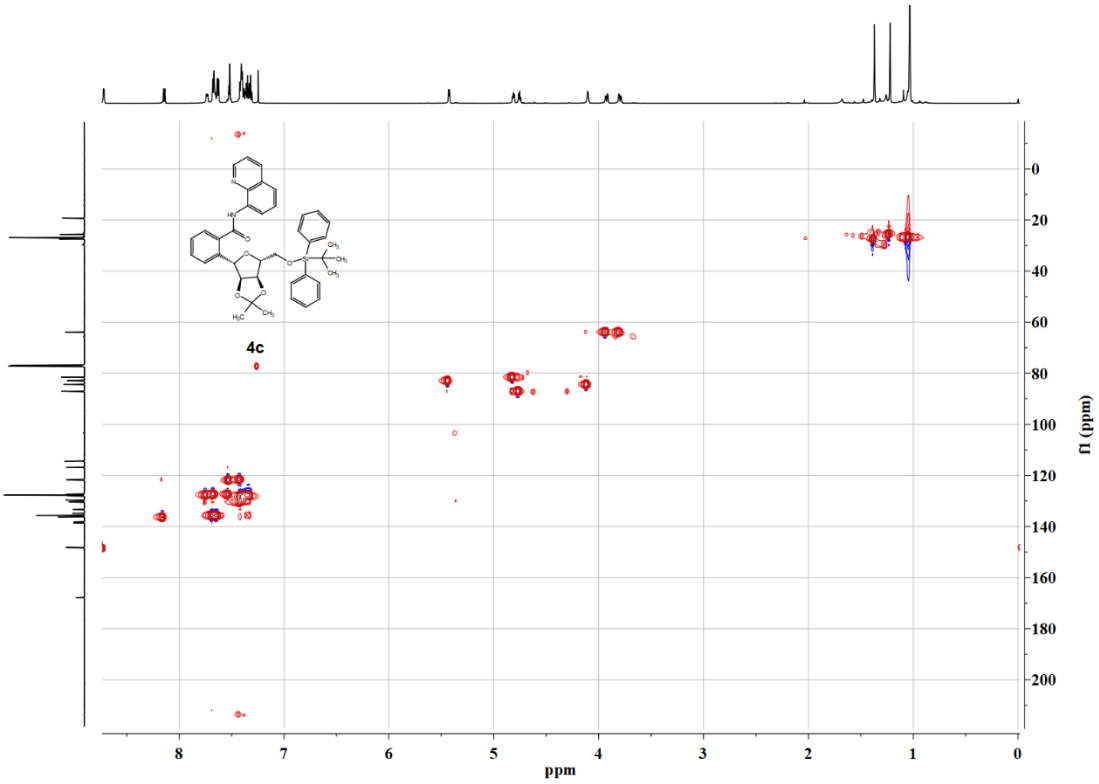


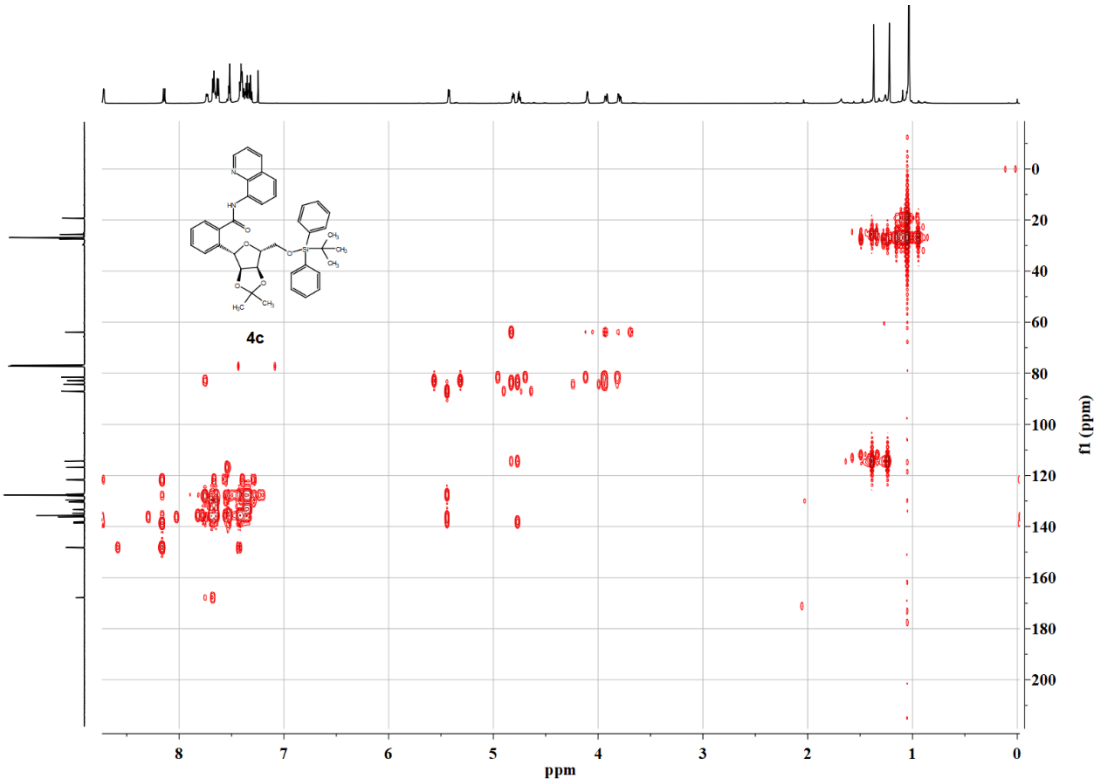


4c

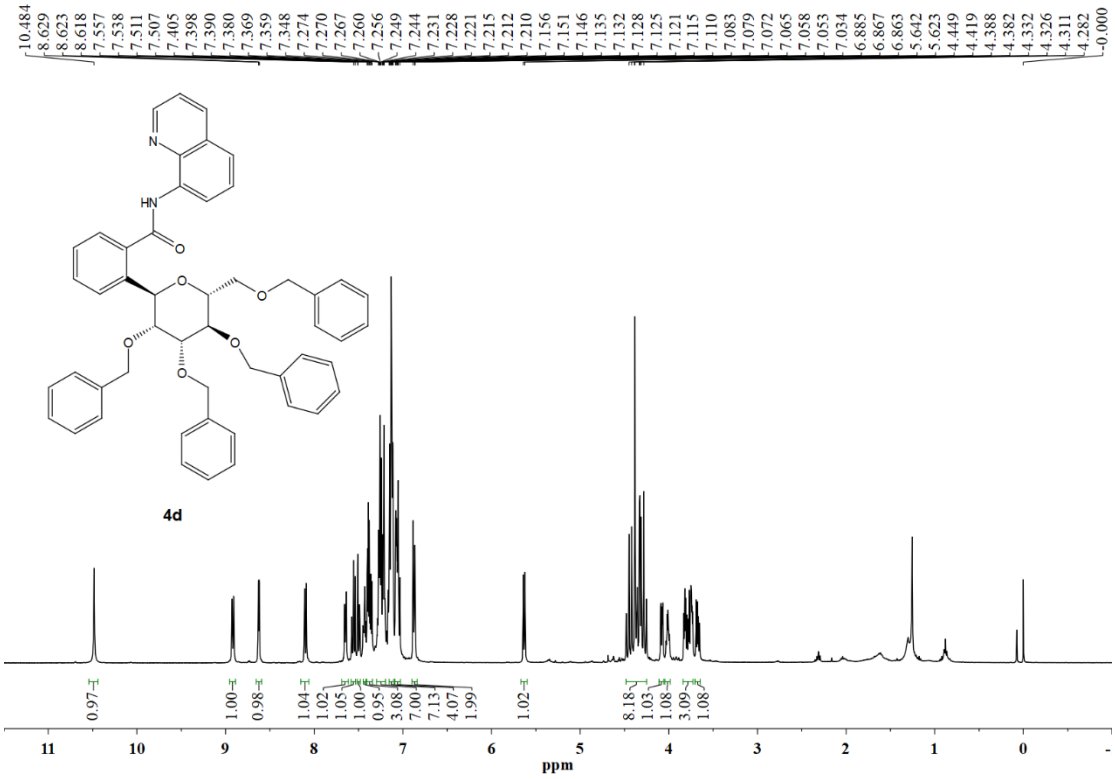



1
3
2
4
5, 5`
4c
4
2
1
f1 (ppm)
ppm

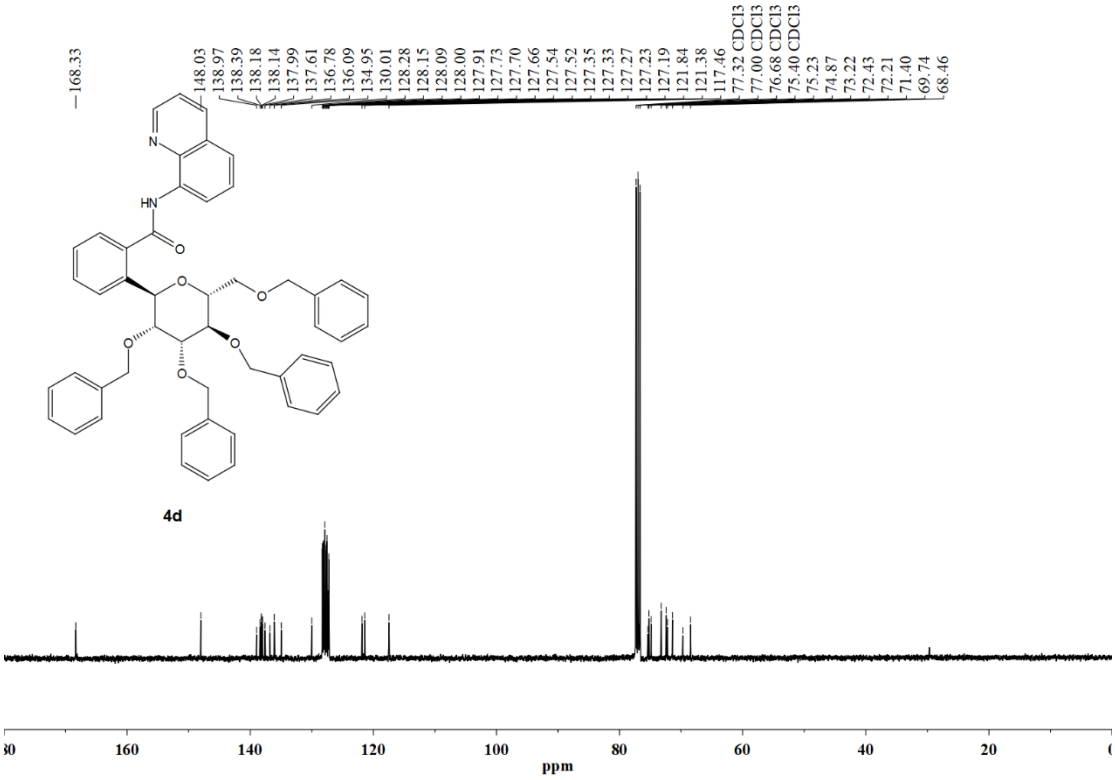

4c
f1 (ppm)
ppm


4c
ppm
f1 (ppm)

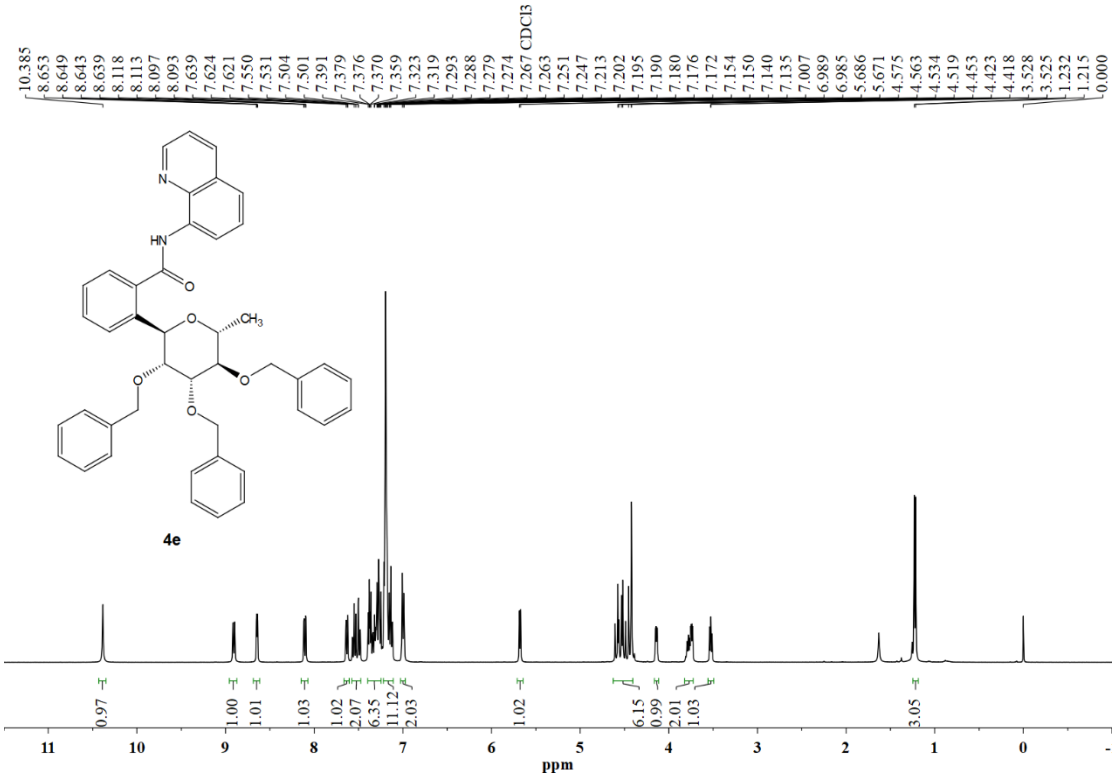
^{1}H NMR (400 MHz, Chloroform-*d*)



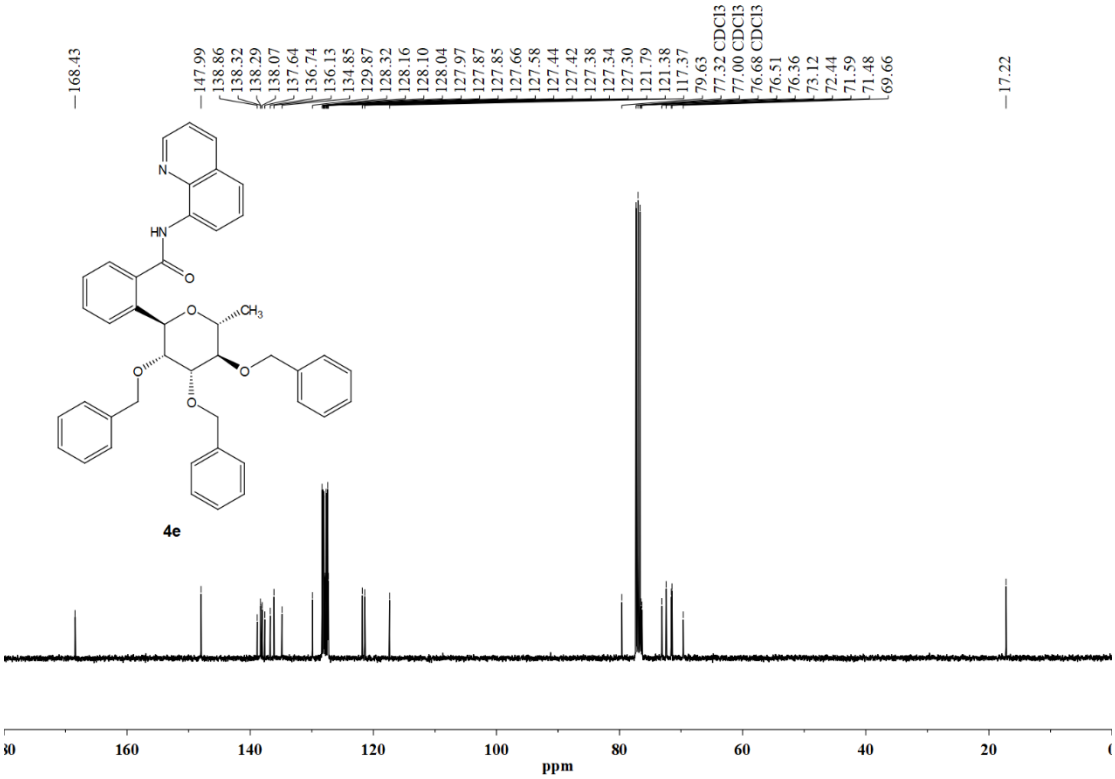
^{13}C NMR (101 MHz, Chloroform-*d*)



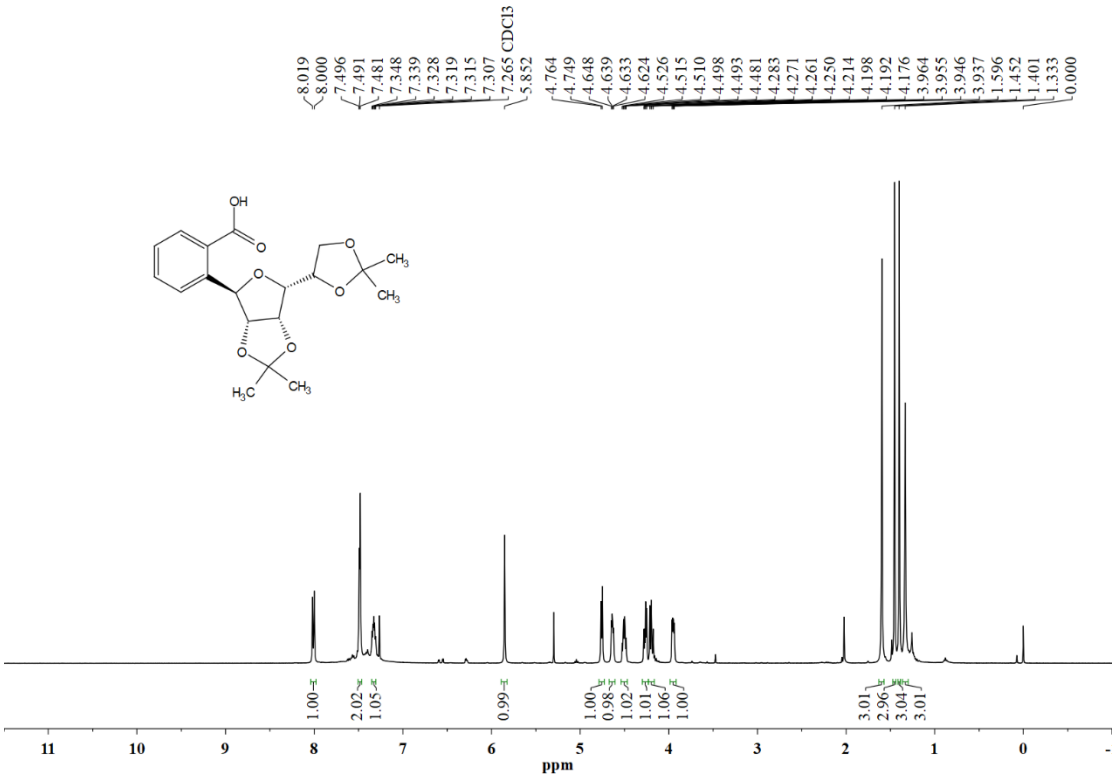
^{1}H NMR (400 MHz, Chloroform-*d*)



^{13}C NMR (101 MHz, Chloroform-*d*)



^{1}H NMR (400 MHz, Chloroform-*d*)



^{13}C NMR (101 MHz, Chloroform-*d*)