Supporting Information

Switchable synthesis of benzimidazoles/quinoxalines C-glycoside with o-phenylenediamines and sulfoxonium ylide glyco-reagents

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General Information

Unless otherwise noted, all reactions were carried out under an atmosphere of nitrogen in flame-dried glassware. If reaction was not carried out at room temperature, reaction temperatures are reported as the temperature of the bath surrounding the vessel unless otherwise stated. The dry solvents used were purified by distillation over the drying agents indicated in parentheses and were transferred under nitrogen. Commercially available chemicals were obtained from commercial suppliers and used without further purification unless otherwise stated.

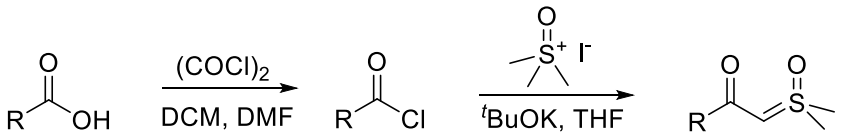
Proton NMR (^{1}H) were recorded at 300/400/500/600 MHz, and Carbon NMR (^{13}C) at 75/101/126/151 MHz NMR spectrometer unless otherwise stated. The following abbreviations are used for the multiplicities: s: singlet, d = doublet, t = triplet, q = quartet, m = multiplet, br s: broad singlet for proton spectra. Coupling constants (*J*) are reported in Hertz (Hz).

High–resolution mass spectra (HRMS, LCMS-IT-TOF) were recorded on a Bruker VPEXII spectrometer with EI and ESI mode unless otherwise stated.

Analytical thin layer chromatography was performed on Polygram SIL G/UV254 plates. Visualization was accomplished with short wave UV light, $KMnO_4$ or Phosphomolybdic acid hydrate staining solutions followed by heating. Flash column chromatography was performed using silica gel (300-400 mesh) with solvents distilled prior to use.

1. Synthesis of Starting Materials

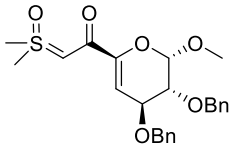
1.1 Synthesis of Carbonyl sulfoxonium ylides glycogen anomeric[1][2] (General procedure 1)



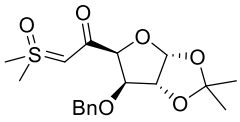
Step-I: To a stirred solution of a carboxylic acid (5 mmol) and DMF (2 drops) in CH_2Cl_2 (25 mL), $(COCl)_2$ (10 mmol, 0.9 mL) was added dropwise. The reaction was allowed to stir at room temperature 2 h. Evaporation of the reaction mixture gave a residue which was dissolved in THF (20 mL). The resulting solution was used as acid chloride solution in subsequent reactions.

Step-II: To a stirred solution of potassium tert-butoxide (16.75 mmol, 2.1 g) in dry THF (20 mL), trimethylsulfoxonium iodide (10.25 mmol, 5.5 g) was added and the reaction was allowed to reflux (oil bath) for 2 h under N_2. The reaction mixture was cooled to 0 °C and the solution of the acid chloride (obtained by step-I) was added dropwise to it. Then, the reaction was allowed to stir at room temperature for additional 1-2 h. Next, the solvent was evaporated, water and ethyl acetate were then added to the resulting slurry. The layers were separated and the aqueous layer was extracted with ethyl acetate and the organic layers were combined. The organic solution was dried over anhydrous Na_2SO_4, filtered, and evaporated to dryness. The crude product was purified by flash chromatography over silica gel using CH_2Cl_2 and MeOH to afford the corresponding carbonyl sulfoxonium ylides glycogen anomeric.

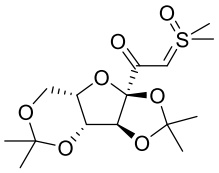
Scheme 1 carbonyl sulfoxonium ylide glyco-reagents[1][2]



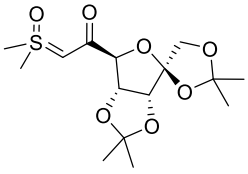
SI-1-1



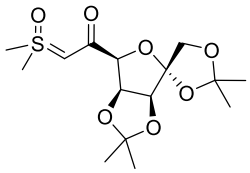
SI-1-2



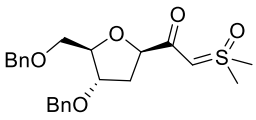
SI-1-3



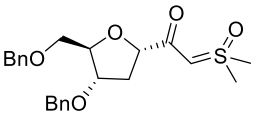
SI-1-4



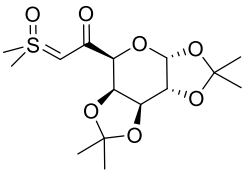
SI-1-5



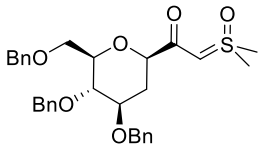
SI-1-6



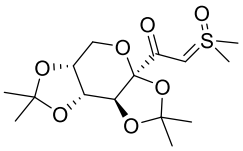
SI-1-7



SI-1-8



SI-1-9

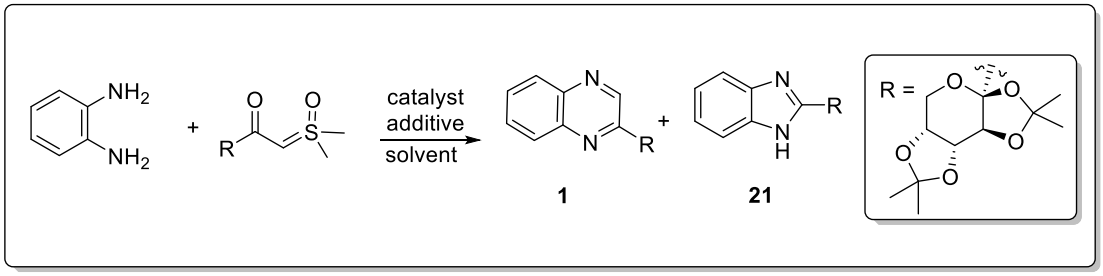


SI-1-10

2. Optimization reaction and general procedure

2.1 Optimization reaction

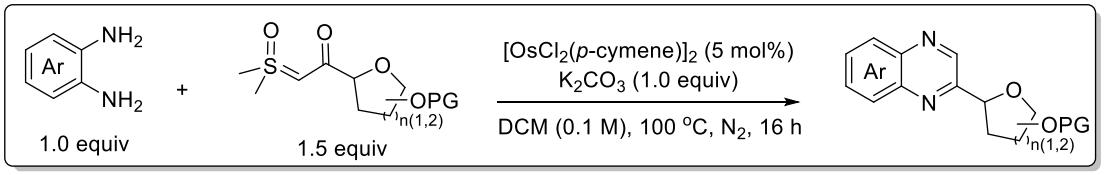
Reaction *o*-phenylenediamines with carbonyl sulfoxonium ylides glycogen anomeric **SI-1-10**.



Entry	Catalyst (mol %)	Ag salt (mol %)	Solvent (M)	Additive (equiv.)	Yield (%)[b] **1**/**21**
1	Os(2.5)	$AgSbF_6$(10)	DCM(0.1)	$NaHCO_3$(1)	53/14
2	Os(2.5)	$AgSbF_6$(10)	DCE(0.1)	$NaHCO_3$(1)	30/10
3	Os(2.5)	$AgSbF_6$(10)	$PhCF_3$(0.1)	$NaHCO_3$(1)	28/7
4	Os(2.5)	AgOAc(10)	DCM(0.1)	$NaHCO_3$(1)	38/5
5	Os(2.5)	$AgNTf_2$(10)	DCM(0.1)	$NaHCO_3$(1)	33/<5
6	Os(2.5)	$AgSbF_6$(10)	DCM(0.1)	K_2CO_3(1)	63(72[c,d])/0
7[d]	Os(5)	$AgSbF_6$(10)	DCM(0.1)	K_2CO_3(1)	72[e]/0
8[d]	Os(2.5)	$AgSbF_6$(10)	DCM(0.1)	$ZnCl_2$(1)	<5/71
9[d]	Os(2.5)	$AgSbF_6$(10)	DCM(0.1)	$Zn(OPiv)_2$(1.4)	<5/74
10[d]		$AgSbF_6$(10)	DCM(0.1)	$Zn(OPiv)_2$(1.4)	0/76(49[e],39[f])
11[d]		$AgSbF_6$(10)	DCM(0.1)	$Zn(OPiv)_2$(0.2)	0/72

[a] Reaction conditions: 1a (0.2 mmol), 2a (0.3 mmol), $[OsCl_2(p\text{-cymene})]_2$ (2.5 mol %), Ag salts (10 mol %), additive (1.0 equiv.), solvent (0.1 M) under N_2 atmosphere at 80 °C for 16 h. [b] Isolated yields. [c] $[OsCl_2(p\text{-cymene})]_2$ (5.0 mol %), $AgSbF_6$ (20 mol %). [d] 100 °C. [e] without $AgSbF_6$. [f] without $Zn(OPiv)_2$.

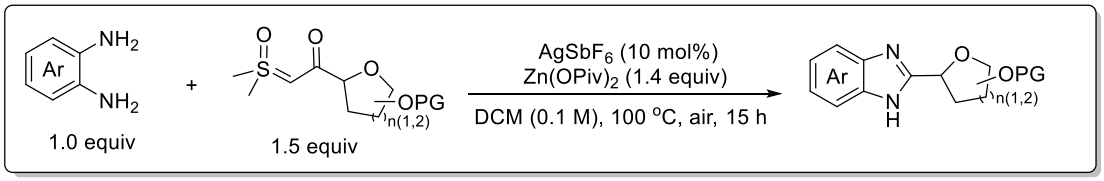
2.2 Procedure for the synthesis of 2-glycosides quinoxaline with *o*-phenylenediamines and carbonyl sulfoxonium ylides glycogen anomeric (General procedure 2)



A Schlenk tube (15 mL) equipped with a magnetic stir bar and a Teflon-lined screwed cap was charged with substituted *o*-phenylenediamines (0.2 mmol), carbonyl

sulfoxonium ylides glycogen anomeric SI-1 (0.3 mmol), $[OsCl_2(p\text{-cymene})]_2$ (5 mol %, 7.9 mg), K_2CO_3 (1.0 equiv, 27.6 mg) and DCM (0.1 M, 2 mL). The vial was then sealed and heated at 100 °C (oil bath) for 16 h under N_2. After that, the solvent was removed under reduced pressure and the residue was purified by silica gel chromatography using PE/EA to afford the product.

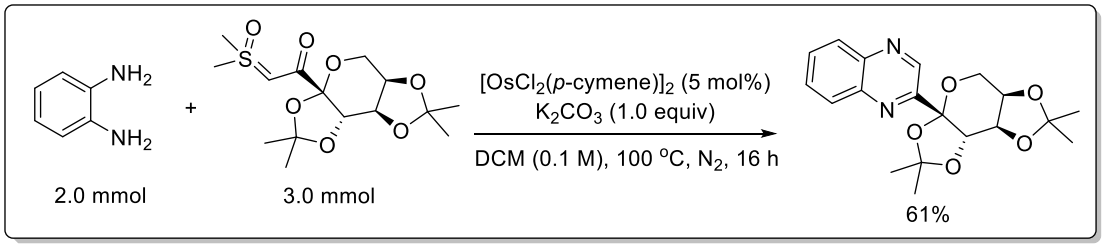
2.3 Procedure for the synthesis of 2-glycosyls benzimidazole with *o*-phenylenediamines and carbonyl sulfoxonium ylides glycogen anomeric (General procedure 3)



A Schlenk tube (15 mL) equipped with a magnetic stir bar and a Teflon-lined screwed cap was charged with substituted o-phenylenediamine (0.2 mmol), carbonyl sulfoxonium ylides glycogen anomeric SI-1 (0.3 mmol), $AgSbF_6$(10 mol %), $Zn(OPiv)_2$ (1.4 equiv) and DCM (0.1 M, 2 mL). The vial was then sealed and heated at 100 °C (oil bath) for 15 h under atmosphere. After that, the solvent was removed under reduced pressure and the residue was purified by silica gel chromatography using PE/EA to afford the product.

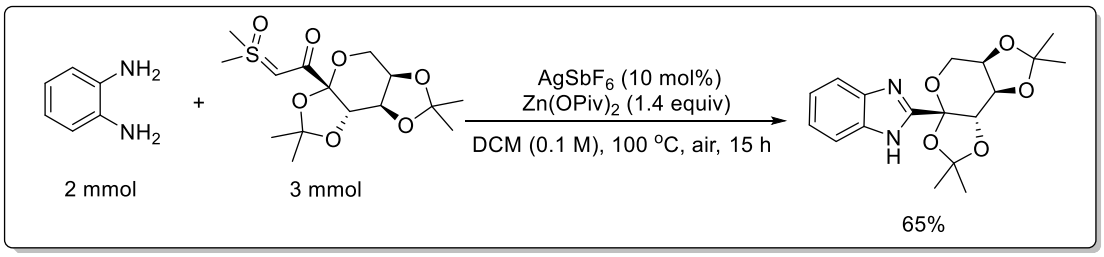
3. Experimental procedure for scale-up reaction

3.1 Gram-Scale Preparation of 1



A Schlenk tube (100 mL) equipped with a magnetic stir bar and a Teflon-lined screwed cap was charged with o-phenylenediamine (2.0 mmol, 1.0 equiv), carbonyl sulfoxonium ylides glycogen anomeric **SI-1-10** (3.0 mmol, 1.5 equiv), $[OsCl_2(p\text{-cymene})]_2$ (5 mol %), K_2CO_3 (1.0 equiv) and DCM (0.1 M). The vial was then sealed and heated at 100 °C (oil bath) for 16 h under N_2. After that, the solvent was removed under reduced pressure and the residue was purified by silica gel chromatography using PE/EA to afford the product **1** (437.2 mg, 61% yield) as yellow oil.

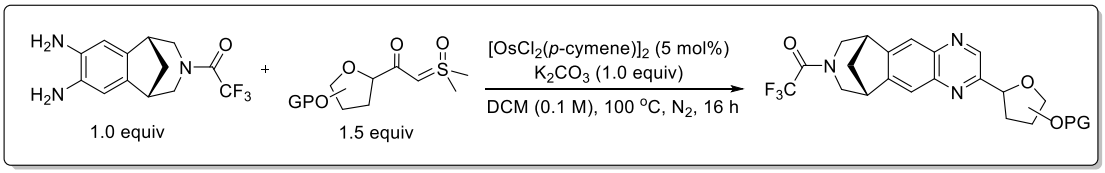
3.2 Gram-Scale Preparation of 21



A Schlenk tube (100 mL) equipped with a magnetic stir bar and a Teflon-lined screwed cap was charged with o-phenylenediamine (2.0 mmol, 1.0 equiv), carbonyl sulfoxonium ylides glycogen anomeric **SI-1-10** (3.0 mmol, 1.5 equiv), $AgSbF_6$(10 mol %), $Zn(OPiv)_2$ (1.4 equiv) and DCM (0.1 M). The vial was then sealed and heated at 100 °C (oil bath) for 15 h under air. After that, the solvent was removed under reduced pressure and the residue was purified by silica gel chromatography using PE/EA to afford the product **21** (450.2 mg, 65% yield) as yellow oil.

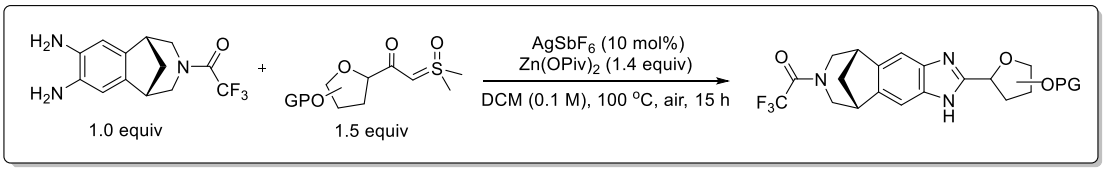
4. Late-stage modification of varenicline

4.1 The synthesis of 2-glycosides quinoxaline with the derivatives of varenicline and carbonyl sulfoxonium ylides glycogen anomeric (General procedure 4)



A Schlenk tube (15 mL) equipped with a magnetic stir bar and a Teflon-lined screwed cap was charged with the o-phenylenediamine derivative of varenicline (0.1 mmol), carbonyl sulfoxonium ylides glycogen anomeric SI-1 (0.15 mmol), $[OsCl_2(p\text{-cymene})]_2$ (5 mol %), K_2CO_3 (1.0 equiv) and DCM (0.1 M). The vial was then sealed and heated at 100 °C (oil bath) for 16 h under N_2. After that, the solvent was removed under reduced pressure and the residue was purified by silica gel chromatography using PE/EA to afford the product.

4.2 The synthesis of 2-glycosyls benzimidazole with the derivatives of varenicline and carbonyl sulfoxonium ylides glycogen anomeric (General procedure 5)

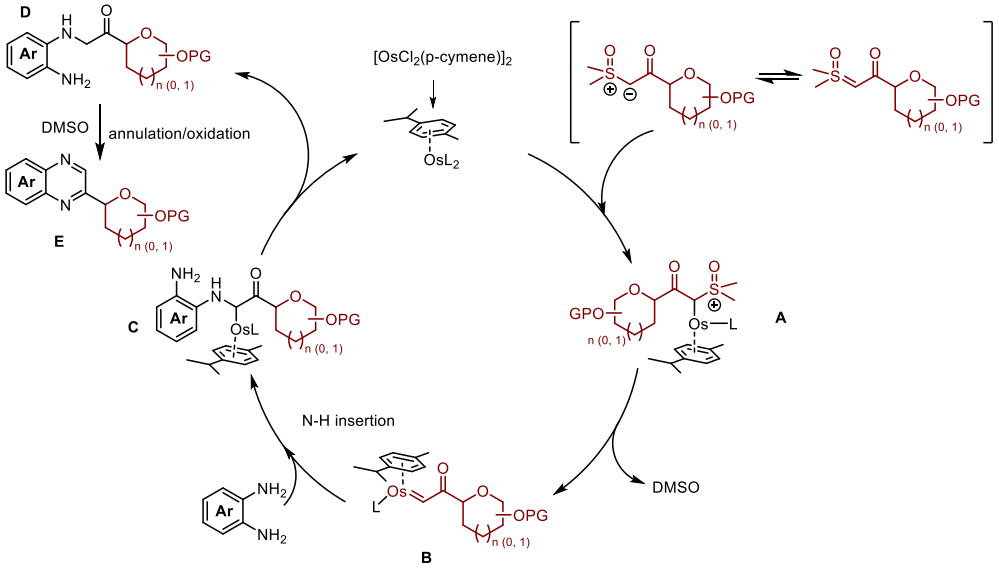


A Schlenk tube (15 mL) equipped with a magnetic stir bar and a Teflon-lined screwed cap was charged with the o-phenylenediamine derivative of varenicline (0.1 mmol), carbonyl sulfoxonium ylides glycogen anomeric SI-1 (0.15 mmol), $AgSbF_6$(10 mol %), $Zn(OPiv)_2$ (1.4 equiv) and DCM (0.1 M). The vial was then sealed and heated at 100 °C (oil bath) for 15 h under air. After that, the solvent was removed under reduced pressure and the residue was purified by silica gel chromatography using PE/EA to afford the product.

5. Proposed reaction mechanism

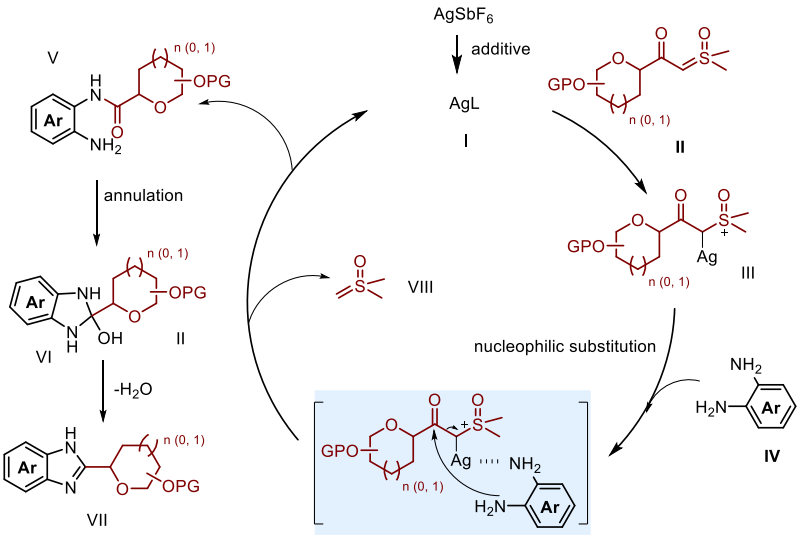
5.1 synthesis mechanism of 2-glycosides quinoxaline

Based on the experimental observations and relevant literatures[3], a plausible reaction mechanism has been proposed. Initially, the carbonyl sulfoxonium ylides glycogen anomeric is activated by an Os species, forming an Os-complex A. Subsequently, Os-complex A undergoes an elimination reaction involving DMSO to yield an osmium carbene complex B. This carbene intermediate then inserts into the N–H bond of *o*-phenylenediamines, resulting in the formation of complex C. Following this, the catalyst is regenerated, leading to the formation of intermediate D. Rapid cyclocondensation, ultimately yielding product E.



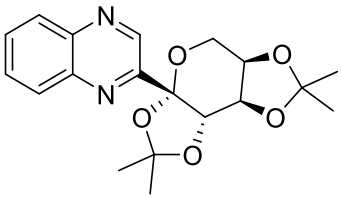
5.2 synthesis mechanism of 2-glycosyls benzimidazole

Based on our experiment results and literatures[3], we propose a plausible mechanism for these reactions. Initially, the carbonyl sulfoxonium ylides glycogen anomeric is activated by Ag catalyst, forming an Ag-complex III. Subsequently, Ag-complex III undergoes nucleophile substitution with *o*-phenylenediamines (IV) generate compound V. Subsequently, Ag-complex III undergoes nucleophilic substitution with o-phenylenediamines (IV) to generate compound V. Finaly, compound V undergoes annulation and dehydration reactions to afford product (VII).



6. Spectra Data of substrates and products

2-((3a*S*,5a*R*,8a*R*,8b*S*)-2,2,7,7-tetramethyltetrahydro-3a*H*-bis([1,3]dioxolo)[4,5-*b*:4',5'-*d*]pyran-3a-yl)quinoxaline(1)



Prepared from o-phenylenediamine (0.2 mmol, 1.0 equiv.) and **SI-1-10** (0.3 mmol, 1.5 equiv.) according to the general procedure **2**. Purification by flash column (Petroleum Ether: Ethyl acetate, 10:1) afforded **1** (51.6 mg, 72% yield) as yellow oil.

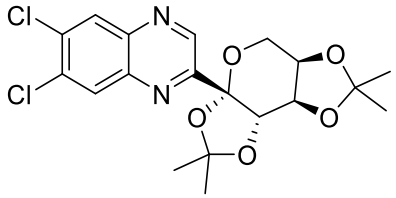
TLC: R*f* = 0.60 (Petroleum Ether: Ethyl acetate, 4:1)

^{1}H NMR (500 MHz, $CDCl_3$): δ 9.37 (s, 1H), 8.15 – 8.07 (m, 2H), 7.80 – 7.74 (m, 2H), 5.19 (d, *J* = 2.6 Hz, 1H), 4.72 (dd, *J* = 8.0, 2.6 Hz, 1H), 4.36 (dd, *J* = 8.0, 1.9 Hz, 1H), 4.19 (dd, *J* = 13.0, 2.0 Hz, 1H), 4.05 (d, *J* = 12.9 Hz, 1H), 1.66 (s, 3H), 1.65 (s, 3H), 1.29 (s, 3H), 1.27 (s, 3H).

^{13}C NMR (126 MHz, $CDCl_3$): δ 153.63, 144.21, 142.24, 141.41, 130.26, 130.01, 129.90, 129.28, 110.06, 109.28, 102.75, 73.93, 70.63, 70.59, 61.81, 26.54, 26.01, 25.61, 24.21.

HRMS (ESI): m/z calculated for $C_{19}H_{22}N_2NaO_5^+$ [M+Na] $^+$, 381.1421; found, 381.1430.

6,7-dichloro-2-((3a*S*,5a*R*,8a*R*,8b*S*)-2,2,7,7-tetramethyltetrahydro-3a*H*-bis([1,3]dioxolo)[4,5-*b*:4',5'-*d*]pyran-3a-yl)quinoxaline(2)



Prepared from substituted o-phenylenediamine (0.2 mmol, 1.0 equiv.) and **SI-1-10** (0.3 mmol, 1.5 equiv.) according to the general procedure **2**. Purification by flash column (Petroleum Ether: Ethyl acetate, 8:1) afforded **2** (52.9 mg, 62% yield) as yellow solid.

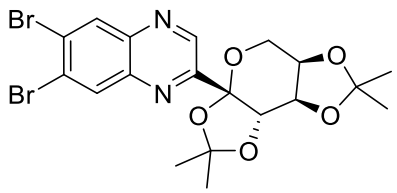
TLC: R*f* = 0.50 (Petroleum Ether: Ethyl acetate, 4:1)

^{1}H NMR (300 MHz, $CDCl_3$): δ 9.35 (s, 1H), 8.23 (d, *J* = 5.0 Hz, 2H), 5.13 (d, *J* = 2.6 Hz, 1H), 4.71 (dd, *J* = 8.0, 2.6 Hz, 1H), 4.34 (d, *J* = 8.0 Hz, 1H), 4.17 (dd, *J* = 13.0, 1.9 Hz, 1H), 4.03 (d, *J* = 13.0 Hz, 1H), 1.64 (s, 3H), 1.62 (s, 3H), 1.29 (s, 3H), 1.24 (s, 3H).

^{13}C NMR (101 MHz, $CDCl_3$): δ 154.76, 145.34, 140.96, 140.08, 134.95, 134.81, 130.39, 129.98, 110.27, 109.26, 102.40, 73.85, 70.49, 70.42, 61.83, 26.50, 25.97, 25.54, 24.14.

HRMS (ESI): m/z calculated for $C_{19}H_{21}Cl_2N_2O_5^+$ [M+H] $^+$, 427.0822; found, 427.0829.

6,7-dibromo-2-((3a*S*,5a*R*,8a*R*,8b*S*)-2,2,7,7-tetramethyltetrahydro-3a*H*-bis([1,3]dioxolo)[4,5-*b*:4',5'-*d*]pyran-3a-yl)quinoxaline(3)



Prepared from substituted o-phenylenediamine (0.2 mmol, 1.0 equiv.) and **SI-1-10** (0.3 mmol, 1.5 equiv.) according to the general procedure **2**. Purification by flash column (Petroleum Ether: Ethyl acetate, 8:1) afforded **3** (56.7 mg, 55% yield) as white solid.

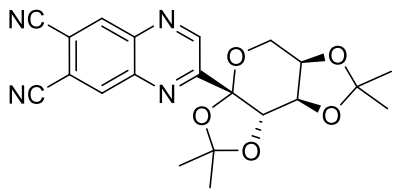
TLC: R*f* = 0.70 (Petroleum Ether: Ethyl acetate, 4:1)

^{1}H NMR (300 MHz, $CDCl_3$): δ 9.35 (s, 1H), 8.42 (d, *J* = 5.2 Hz, 2H), 5.14 (d, *J* = 2.6 Hz, 1H), 4.71 (dd, *J* = 7.9, 2.6 Hz, 1H), 4.34 (dd, *J* = 7.9, 1.8 Hz, 1H), 4.17 (dd, *J* = 13.0, 1.8 Hz, 1H), 4.03 (d, *J* = 12.9 Hz, 1H), 1.63 (s, 3H), 1.61 (s, 3H), 1.29 (s, 3H), 1.23 (s, 3H).

^{13}C NMR (75 MHz, $CDCl_3$): δ 154.74, 145.36, 141.33, 140.44, 133.70, 133.30, 126.88, 126.74, 110.18, 109.15, 102.30, 73.71, 70.39, 70.31, 61.73, 26.39, 25.87, 25.45, 24.04.

HRMS (ESI): m/z calculated for $C_{19}H_{21}Br_2N_2O_5^+$[M+H] $^+$, 514.9812; found, 516.9809.

2-((3a*S*,5a*R*,8a*R*,8b*S*)-2,2,7,7-tetramethyltetrahydro-3a*H*-bis([1,3]dioxolo)[4,5-*b*:4',5'-*d*]pyran-3a-yl)quinoxaline-6,7-dicarbonitrile(4)



Prepared from substituted o-phenylenediamine (0.2 mmol, 1.0 equiv.) and **SI-1-10** (0.3 mmol, 1.5 equiv.) according to the general procedure **2**. Purification by flash column (Petroleum Ether: Ethyl acetate, 8:1) afforded **4** (30.2 mg, 37% yield) as

white solid.

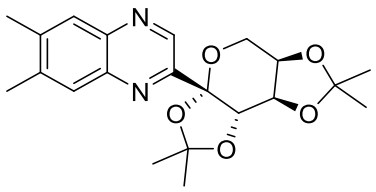
TLC: R*f* = 0.45 (Petroleum Ether: Ethyl acetate, 4:1)

^{1}H NMR (300 MHz, $CDCl_3$): δ 9.57 (s, 1H), 8.61 (d, *J* = 6.3 Hz, 2H), 5.11 (d, *J* = 2.6 Hz, 1H), 4.72 (dd, *J* = 7.9, 2.6 Hz, 1H), 4.36 (dd, *J* = 7.9, 1.7 Hz, 1H), 4.19 (dd, *J* = 13.0, 1.9 Hz, 1H), 4.06 (d, *J* = 13.0 Hz, 1H), 1.65 (s, 3H), 1.61 (s, 3H), 1.29 (s, 3H), 1.22 (s, 3H).

^{13}C NMR (75 MHz, $CDCl_3$): δ 158.08, 148.60, 142.59, 141.79, 137.43, 137.15, 114.78, 114.72, 114.68, 110.74, 109.20, 101.90, 70.20, 70.11, 61.88, 26.36, 25.86, 25.38, 23.95.

HRMS (ESI): m/z calculated for $C_{21}H_{21}N_4O_5^+$[M+H] $^+$, 409.1506; found, 409.1513.

6,7-dimethyl-2-((3a*S*,5a*R*,8a*R*,8b*S*)-2,2,7,7-tetramethyltetrahydro-3a*H*-bis([1,3]dioxolo)[4,5-*b*:4',5'-*d*]pyran-3a-yl)quinoxaline(5)



Prepared from substituted o-phenylenediamine (0.2 mmol, 1.0 equiv.) and **SI-1-10** (0.3 mmol, 1.5 equiv.) according to the general procedure **2**. Purification by flash column (Petroleum Ether: Ethyl acetate, 8:1) afforded **5** (40.9 mg, 53% yield) as yellow oil.

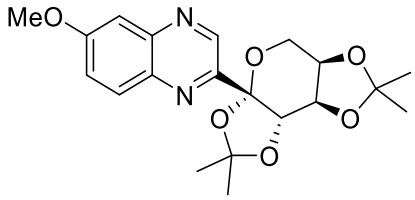
TLC: R*f* = 0.53 (Petroleum Ether: Ethyl acetate, 4:1)

^{1}H NMR (300 MHz, $CDCl_3$): δ 9.25 (s, 1H), 7.83 (d, *J* = 3.0 Hz, 2H), 5.18 (d, *J* = 2.5 Hz, 1H), 4.70 (dd, *J* = 7.9, 2.5 Hz, 1H), 4.34 (d, *J* = 8.0 Hz, 1H), 4.18 (d, *J* = 13.2 Hz, 1H), 4.02 (d, *J* = 12.9 Hz, 1H), 2.47 (s, 6H), 1.65 (s, 3H), 1.63 (s, 3H), 1.28 (s, 3H), 1.25 (s, 3H).

^{13}C NMR (101 MHz, $CDCl_3$): δ 152.58, 143.17, 141.17, 140.79, 140.46, 140.32, 128.84, 128.21, 109.82, 109.19, 102.80, 73.81, 70.62, 70.58, 61.70, 26.51, 25.96, 25.60, 24.18, 20.49, 20.36.

HRMS (ESI): m/z calculated for $C_{21}H_{26}N_2NaO_5^+$ $[M+Na]^+$, 409.1734; found, 409.1743.

6-methoxy-2-((3a*S*,5a*R*,8a*R*,8b*S*)-2,2,7,7-tetramethyltetrahydro-3a*H*-bis([1,3]dioxolo)[4,5-*b*:4',5'-*d*]pyran-3a-yl)quinoxaline(6a)



Prepared from substituted o-phenylenediamine (0.2 mmol, 1.0 equiv.) and **SI-1-10** (0.3 mmol, 1.5 equiv.) according to the general procedure **2**. Purification by flash column (Petroleum Ether: Ethyl acetate, 8:1) afforded **6a** (27.1 mg, 35% yield) as white solid.

TLC: R*f* = 0.30 (Petroleum Ether: Ethyl acetate, 4:1)

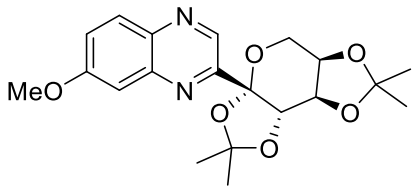
^{1}H NMR (300 MHz, $CDCl_3$): δ 9.21 (s, 1H), 7.98 (d, *J* = 9.1 Hz, 1H), 7.41 (dd, *J* = 9.3, 2.9 Hz, 1H), 7.34 (d, *J* = 2.8 Hz, 1H), 5.18 (t, *J* = 1.9 Hz, 1H), 4.75 – 4.67 (m, 1H), 4.35 (d, *J* = 8.0 Hz, 1H), 4.18 (d, *J* = 13.0 Hz, 1H), 4.03 (d, *J* = 13.0 Hz, 1H), 3.97 (s, 3H), 1.65 (s, 6H), 1.30 (s, 3H), 1.28 (s, 3H).

^{13}C NMR (101 MHz, $CDCl_3$): δ 160.88, 153.57, 143.10, 141.62, 138.45, 130.16, 123.62, 109.91, 109.29, 107.16, 102.81, 73.84, 70.67, 70.62, 61.77, 55.96, 26.54, 25.99, 25.71, 24.22.

HRMS (ESI): m/z calculated for $C_{20}H_{25}N_2O_6^+$ $[M+H]^+$, 389.1707; found, 389.1716.

8-methoxy-2-((3a*S*,5a*R*,8a*R*,8b*S*)-2,2,7,7-tetramethyltetrahydro-3a*H*-

bis([1,3]dioxolo)[4,5-*b*:4',5'-*d*]pyran-3a-yl)quinoxaline(6b)



Prepared from substituted o-phenylenediamine (0.2 mmol, 1.0 equiv.) and **SI-1-10** (0.3 mmol, 1.5 equiv.) according to the general procedure **2**. Purification by flash column (Petroleum Ether: Ethyl acetate, 8:1) afforded **6b** (20.9 mg, 27% yield) as white solid.

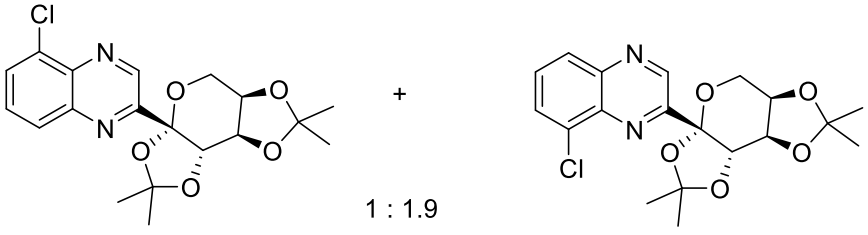
TLC: R*f* = 0.25 (Petroleum Ether: Ethyl acetate, 4:1)

^{1}H NMR (300 MHz, $CDCl_3$): δ 9.28 (s, 1H), 7.96 (d, *J* = 10.0 Hz, 1H), 7.40 (dd, *J* = 6.8, 2.5 Hz, 2H), 5.13 (d, *J* = 2.6 Hz, 1H), 4.71 (dd, *J* = 8.0, 2.6 Hz, 1H), 4.35 (d, *J* = 8.0 Hz, 1H), 4.19 (dd, *J* = 13.0, 2.0 Hz, 1H), 4.04 (d, *J* = 12.9 Hz, 1H), 3.97 (s, 3H), 1.66 (s, 3H), 1.64 (s, 3H), 1.29 (s, 6H).

^{13}C NMR (101 MHz, $CDCl_3$): δ 161.12, 151.18, 144.08, 143.88, 137.59, 130.81, 123.40, 109.89, 109.26, 106.58, 102.82, 74.01, 70.68, 70.63, 61.76, 55.94, 26.57, 26.00, 25.65, 24.20.

HRMS (ESI): m/z calculated for $C_{20}H_{25}N_2O_6^+$ $[M+H]^+$, 389.1707; found, 389.1715.

5-chloro-2-((3a*S*,5a*R*,8a*R*,8b*S*)-2,2,7,7-tetramethyltetrahydro-3a*H*-bis([1,3]dioxolo)[4,5-*b*:4',5'-*d*]pyran-3a-yl)quinoxaline and 8-chloro-2-((3a*S*,5a*R*,8a*R*,8b*S*)-2,2,7,7-tetramethyltetrahydro-3a*H*-bis([1,3]dioxolo)[4,5-*b*:4',5'-*d*]pyran-3a-yl)quinoxaline(7)



Prepared from substituted o-phenylenediamine (0.2 mmol, 1.0 equiv.) and **SI-1-10** (0.3 mmol, 1.5 equiv.) according to the general procedure **2**. Purification by flash column (Petroleum Ether: Ethyl acetate, 8:1) afforded **7** (25.1 mg, 32% yield) as yellow oil.

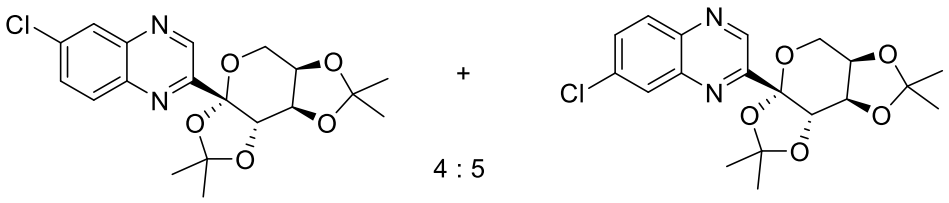
TLC: R*f* = 0.50 (Petroleum Ether: Ethyl acetate, 4:1)

^{1}H NMR (300 MHz, $CDCl_3$): δ 9.44 (dt, *J* = 10.1, 2.7 Hz, 1H), 8.05 (dd, *J* = 8.7, 3.5 Hz, 1H), 7.86 (q, *J* = 3.5 Hz, 1H), 7.68 (t, *J* = 8.1 Hz, 1H), 5.21 – 5.14 (m, 1H), 4.72 (d, *J* = 7.7 Hz, 1H), 4.35 (d, *J* = 7.9 Hz, 1H), 4.21 (d, *J* = 13.2 Hz, 1H), 4.11 – 4.00 (m, 1H), 1.82 (s, 2H), 1.65 (s, 4H), 1.28 (s, 6H).

^{13}C NMR (101 MHz, $CDCl_3$): δ 154.51, 154.33, 144.61, 144.57, 143.17, 142.39, 139.06, 138.48, 133.91, 133.16, 130.22, 130.06, 129.98, 129.76, 128.98, 128.34, 110.94, 110.21, 109.34, 109.24, 102.54, 75.07, 73.95, 70.58, 70.53, 70.50, 61.92, 61.88, 26.65, 26.50, 26.12, 26.05, 25.57, 24.25, 24.15.

HRMS (ESI): m/z calculated for $C_{19}H_{21}ClN_2NaO_5^+$ $[M+Na]^+$, 415.1031; found, 415.1039.

6-chloro-2-((3a*S*,5a*R*,8a*R*,8b*S*)-2,2,7,7-tetramethyltetrahydro-3a*H*-bis([1,3]dioxolo)[4,5-*b*:4',5'-*d*]pyran-3a-yl)quinoxaline and 7-chloro-2-((3a*S*,5a*R*,8a*R*,8b*S*)-2,2,7,7-tetramethyltetrahydro-3a*H*-bis([1,3]dioxolo)[4,5-*b*:4',5'-*d*]pyran-3a-yl)quinoxaline(8)



Prepared from substituted o-phenylenediamine (0.2 mmol, 1.0 equiv.) and **SI-1-10** (0.3 mmol, 1.5 equiv.) according to the general procedure **2**. Purification by flash column (Petroleum Ether: Ethyl acetate, 8:1) afforded **8** (42.4 mg, 54% yield) as yellow oil.

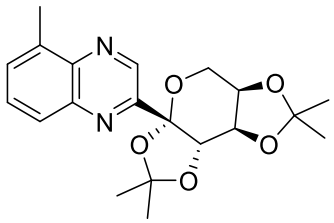
TLC: R*f* = 0.60 (Petroleum Ether: Ethyl acetate, 4:1)

^{1}H NMR (300 MHz, $CDCl_3$): δ 9.35 (s, 1H), 8.13 – 7.97 (m, 2H), 7.69 (dd, *J* = 9.1, 2.4 Hz, 1H), 5.14 (dd, *J* = 5.0, 2.5 Hz, 1H), 4.71 (d, *J* = 8.1 Hz, 1H), 4.34 (d, *J* = 8.0 Hz, 1H), 4.18 (d, *J* = 13.0 Hz, 1H), 4.03 (d, *J* = 12.9 Hz, 1H), 1.63 (s, 6H), 1.28 (s, 3H), 1.25 (s, 3H).

^{13}C NMR (101 MHz, $CDCl_3$): δ 154.58, 153.88, 145.13, 144.41, 142.51, 141.66, 140.77, 139.89, 136.08, 135.90, 131.27, 131.09, 131.03, 130.53, 128.68, 128.24, 110.17, 110.12, 109.25, 102.57, 102.54, 77.48, 77.16, 76.84, 73.91, 73.90, 70.56, 70.51, 61.83, 61.81, 26.51, 25.98, 25.56, 24.17.

HRMS (ESI): m/z calculated for $C_{19}H_{21}ClN_2NaO_5^+$ $[M+Na]^+$, 415.1031; found, 415.1039.

5-methyl-2-((3a*S*,5a*R*,8a*R*,8b*S*)-2,2,7,7-tetramethyltetrahydro-3a*H*-bis([1,3]dioxolo)[4,5-*b*:4',5'-*d*]pyran-3a-yl)quinoxaline(9a)



Prepared from substituted o-phenylenediamine (0.2 mmol, 1.0 equiv.) and **SI-1-10** (0.3 mmol, 1.5 equiv.) according to the general procedure **2**. Purification by flash column (Petroleum Ether: Ethyl acetate, 10:1) afforded **9a** (4.4 mg, 6% yield) as yellow oil.

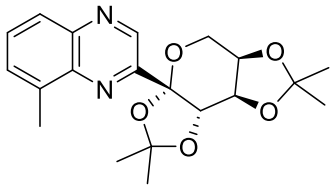
TLC: R*f* = 0.50 (Petroleum Ether: Ethyl acetate, 4:1)

^{1}H NMR (500 MHz, $CDCl_3$): δ 9.35 (s, 1H), 7.93 (dd, *J* = 8.3, 1.5 Hz, 1H), 7.64 (dd, *J* = 8.3, 7.1 Hz, 1H), 7.60 (dt, *J* = 7.0, 1.3 Hz, 1H), 5.21 (d, *J* = 2.6 Hz, 1H), 4.72 (dd, *J* = 7.9, 2.6 Hz, 1H), 4.36 (dd, *J* = 8.0, 1.8 Hz, 1H), 4.19 (dd, *J* = 13.0, 2.0 Hz, 1H), 4.04 (d, *J* = 12.9 Hz, 1H), 2.81 (s, 3H), 1.65 (s, 3H), 1.64 (s, 3H), 1.29 (s, 3H), 1.28 (s, 3H).

^{13}C NMR (126 MHz, $CDCl_3$): δ 153.09, 142.82, 141.55, 141.44, 137.54, 130.21, 129.72, 127.76, 109.96, 109.28, 102.83, 73.83, 70.68, 70.64, 61.84, 26.53, 26.09, 25.63, 24.28, 17.55.

HRMS (ESI): m/z calculated for $C_{20}H_{24}N_2NaO_5^+$ $[M+Na]^+$, 395.1577; found, 395.1583.

8-methyl-2-((3a*S*,5a*R*,8a*R*,8b*S*)-2,2,7,7-tetramethyltetrahydro-3a*H*-bis([1,3]dioxolo)[4,5-*b*:4',5'-*d*]pyran-3a-yl)quinoxaline(9b)



Prepared from substituted o-phenylenediamine (0.2 mmol, 1.0 equiv.) and **SI-1-10** (0.3 mmol, 1.5 equiv.) according to the general procedure **2**. Purification by flash column (Petroleum Ether: Ethyl acetate, 10:1) afforded **9b** (14.8 mg, 20% yield) as yellow oil.

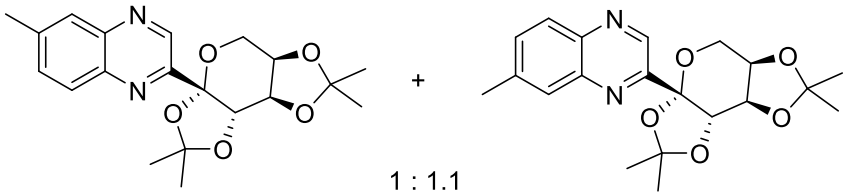
TLC: R*f* = 0.40 (Petroleum Ether: Ethyl acetate, 4:1)

^{1}H NMR (500 MHz, $CDCl_3$): δ 9.37 (s, 1H), 7.96 (dd, *J* = 8.3, 1.5 Hz, 1H), 7.66 (dd, *J* = 8.4, 6.9 Hz, 1H), 7.60 (dt, *J* = 7.1, 1.3 Hz, 1H), 5.16 (d, *J* = 2.6 Hz, 1H), 4.72 (dd, *J* = 7.9, 2.6 Hz, 1H), 4.36 (dd, *J* = 8.0, 1.8 Hz, 1H), 4.20 (dd, *J* = 13.0, 1.9 Hz, 1H), 4.07 (d, *J* = 12.9 Hz, 1H), 2.80 (s, 3H), 1.75 (s, 3H), 1.66 (s, 3H), 1.28 (s, 3H), 1.27 (s, 3H).

^{13}C NMR (126 MHz, $CDCl_3$): δ 152.46, 143.62, 142.34, 140.68, 137.98, 130.10, 127.13, 110.37, 109.26, 102.77, 74.79, 70.63, 70.56, 61.79, 26.63, 26.03, 25.67, 24.17, 17.54.

HRMS (ESI): m/z calculated for $C_{20}H_{25}N_2O_5^+$ $[M+H]^+$, 373.1758; found, 373.1768.

6-methyl-2-((3a*S*,5a*R*,8a*R*,8b*S*)-2,2,7,7-tetramethyltetrahydro-3a*H*-bis([1,3]dioxolo)[4,5-*b*:4',5'-*d*]pyran-3a-yl)quinoxaline and 7-methyl-2-((3a*S*,5a*R*,8a*R*,8b*S*)-2,2,7,7-tetramethyltetrahydro-3a*H*-bis([1,3]dioxolo)[4,5-*b*:4',5'-*d*]pyran-3a-yl)quinoxaline(10)



Prepared from substituted o-phenylenediamine (0.2 mmol, 1.0 equiv.) and **SI-1-10** (0.3 mmol, 1.5 equiv.) according to the general procedure **2**. Purification by flash column (Petroleum Ether: Ethyl acetate, 8:1) afforded **10** (51.3 mg, 69% yield) as yellow oil.

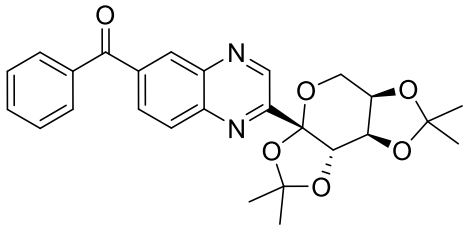
TLC: R*f* = 0.40 (Petroleum Ether: Ethyl acetate, 4:1)

^{1}H NMR (300 MHz, $CDCl_3$): δ 9.30 (d, *J* = 7.1 Hz, 1H), 7.98 (t, *J* = 7.6 Hz, 1H), 7.87 (s, 1H), 7.58 (d, *J* = 8.6 Hz, 1H), 5.18 (dd, *J* = 8.0, 2.4 Hz, 1H), 4.71 (d, *J* = 8.0 Hz, 1H), 4.35 (d, *J* = 8.0 Hz, 1H), 4.18 (d, *J* = 13.0 Hz, 1H), 4.03 (d, *J* = 12.9 Hz, 1H), 2.58 (s, 3H), 1.65 (s, 3H), 1.64 (s, 3H), 1.28 (s, 3H), 1.26 (s, 3H).

^{13}C NMR (101 MHz, $CDCl_3$): δ 153.49, 152.72, 144.08, 143.28, 142.31, 141.47, 140.81, 140.73, 140.49, 139.88, 132.54, 132.28, 129.38, 128.75, 128.70, 128.09, 109.94, 109.92, 109.25, 102.79, 73.91, 73.87, 70.65, 70.62, 61.78, 26.53, 26.00, 25.62, 24.21, 21.98, 21.86.

HRMS (ESI): m/z calculated for $C_{20}H_{25}N_2O_5^+$ $[M+H]^+$, 373.1758; found, 373.1762.

phenyl(2-((3a*S*,5a*R*,8a*R*,8b*S*)-2,2,7,7-tetramethyltetrahydro-3a*H*-bis([1,3]dioxolo)[4,5-*b*:4',5'-*d*]pyran-3a-yl)quinoxalin-6-yl)methanone(11a)



Prepared from substituted o-phenylenediamine (0.2 mmol, 1.0 equiv.) and **SI-1-10** (0.3 mmol, 1.5 equiv.) according to the general procedure **2**. Purification by flash column (Petroleum Ether: Ethyl acetate, 8:1) afforded **11a** (18.5 mg, 20% yield) as yellow oil.

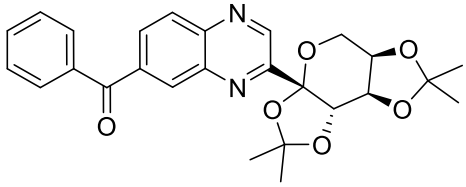
TLC: R*f* = 0.6 (Petroleum Ether: Ethyl acetate, 4:1)

^{1}H NMR (300 MHz, $CDCl_3$): δ 9.44 (s, 1H), 8.48 (d, *J* = 1.8 Hz, 1H), 8.29 – 8.17 (m, 2H), 7.93 – 7.83 (m, 2H), 7.64 (t, *J* = 7.4 Hz, 1H), 7.52 (t, *J* = 7.5 Hz, 2H), 5.20 (d, *J* = 2.6 Hz, 1H), 4.74 (dd, *J* = 7.9, 2.6 Hz, 1H), 4.37 (d, *J* = 7.9 Hz, 1H), 4.20 (dd, *J* = 12.9, 1.9 Hz, 1H), 4.06 (d, *J* = 13.0 Hz, 1H), 1.67 (d, *J* = 2.8 Hz, 6H), 1.30 (s, 3H), 1.27 (s, 3H).

^{13}C NMR (75 MHz, $CDCl_3$): δ 195.63, 154.79, 145.95, 143.78, 140.44, 138.72, 137.11, 132.98, 132.38, 130.22, 130.08, 129.65, 128.58, 110.11, 109.19, 102.45, 73.81, 70.47, 70.44, 61.76, 26.39, 25.90, 25.53, 24.07.

HRMS (ESI): m/z calculated for $C_{26}H_{26}N_2NaO_6^+$[M+Na] $^+$, 485.1683; found, 485.1690.

phenyl(3-((3a*S*,5a*R*,8a*R*,8b*S*)-2,2,7,7-tetramethyltetrahydro-3a*H*-bis([1,3]dioxolo)[4,5-*b*:4',5'-*d*]pyran-3a-yl)quinoxalin-6-yl)methanone(11b)



Prepared from substituted o-phenylenediamine (0.2 mmol, 1.0 equiv.) and **SI-1-10**

(0.3 mmol, 1.5 equiv.) according to the general procedure **2**. Purification by flash column (Petroleum Ether: Ethyl acetate, 8:1) afforded **11b** (16.6 mg, 18% yield) as yellow oil.

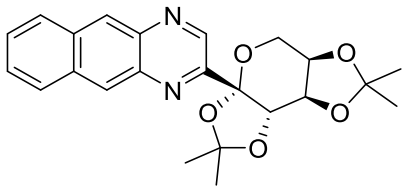
TLC: R*f* = 0.7 (Petroleum Ether: Ethyl acetate, 4:1)

^{1}H NMR (300 MHz, $CDCl_3$): δ 9.46 (s, 1H), 8.46 (d, *J* = 1.7 Hz, 1H), 8.28 – 8.16 (m, 2H), 7.93 – 7.85 (m, 2H), 7.70 – 7.61 (m, 1H), 7.54 (t, *J* = 7.6 Hz, 2H), 5.16 (d, *J* = 2.6 Hz, 1H), 4.72 (dd, *J* = 7.9, 2.6 Hz, 1H), 4.36 (dd, *J* = 8.0, 1.7 Hz, 1H), 4.20 (dd, *J* = 13.0, 1.9 Hz, 1H), 4.06 (d, *J* = 13.0 Hz, 1H), 1.64 (s, 3H), 1.61 (s, 3H), 1.30 (s, 3H), 1.28 (s, 3H).

^{13}C NMR (75 MHz, $CDCl_3$): δ 195.49, 155.36, 145.26, 141.19, 138.60, 137.06, 132.94, 132.28, 130.23, 130.16, 129.84, 128.57, 110.19, 109.19, 102.48, 73.86, 70.46, 61.76, 26.42, 25.90, 25.48, 24.07.

HRMS (ESI): m/z calculated for $C_{26}H_{27}N_2O_6^+$ $[M+H]^+$, 463.1864; found, 463.1871.

2-((3a*S*,5a*R*,8a*R*,8b*S*)-2,2,7,7-tetramethyltetrahydro-3a*H*-bis([1,3]dioxolo)[4,5-*b*:4',5'-*d*]pyran-3a-yl)benzo[g]quinoxaline(12)



Prepared from substituted o-phenylenediamine (0.2 mmol, 1.0 equiv.) and **SI-1-10** (0.3 mmol, 1.5 equiv.) according to the general procedure **2**. Purification by flash column (Petroleum Ether: Ethyl acetate, 8:1) afforded **12** (53.0 mg, 65% yield) as yellow solid.

TLC: R*f* = 0.50 (Petroleum Ether: Ethyl acetate, 4:1)

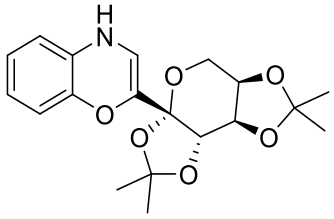
^{1}H NMR (300 MHz, $CDCl_3$): δ 9.39 (s, 1H), 8.69 (d, *J* = 2.0 Hz, 2H), 8.10 (td, *J* = 6.0, 2.9 Hz, 2H), 7.58 (dt, *J* = 6.5, 2.9 Hz, 2H), 5.34 (s, 1H), 4.76 (d, *J* = 7.6 Hz, 1H), 4.37 (d, *J* = 8.0 Hz, 1H), 4.21 (d, *J* = 12.9 Hz, 1H), 4.06 (d, *J* = 13.0 Hz, 1H), 1.66 (s,

6H), 1.31 (s, 3H), 1.27 (s, 3H).

^{13}C NMR (101 MHz, $CDCl_3$): δ 153.88, 145.21, 138.71, 137.81, 134.14, 134.00, 128.69, 128.52, 128.39, 127.67, 127.03, 126.99, 109.99, 109.29, 102.84, 73.45, 70.66, 61.84, 26.50, 26.04, 25.58, 24.26.

HRMS (ESI): m/z calculated for $C_{23}H_{24}N_2NaO_5^+$ $[M+Na]^+$, 431.1577; found, 431.1584.

2-((3a*R*,5a*R*,8a*R*,8b*S*)-2,2,7,7-tetramethyltetrahydro-3a*H*-bis([1,3]dioxolo)[4,5-*b*:4',5'-*d*]pyran-3a-yl)-4*H*-benzo[*b*][1,4]oxazine(13)



Prepared from o-aminophenol (0.2 mmol, 1.0 equiv.) and **SI-1-10** (0.3 mmol, 1.5 equiv.) according to the general procedure **2**. Purification by flash column (Petroleum Ether: Ethyl acetate, 8:1) afforded **13** (41.1 mg, 57% yield) as yellow oil.

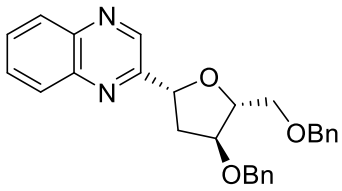
TLC: R*f* = 0.45 (Petroleum Ether: Ethyl acetate, 4:1)

^{1}H NMR (300 MHz, $CDCl_3$): δ 7.90 (s, 1H), 7.48 (d, *J* = 7.7 Hz, 1H), 7.20 (t, *J* = 7.7 Hz, 1H), 7.03 (t, *J* = 7.6 Hz, 1H), 6.93 (d, *J* = 8.0 Hz, 1H), 5.43 (s, 1H), 4.97 (d, *J* = 2.9 Hz, 1H), 4.74 (dd, *J* = 7.8, 2.9 Hz, 1H), 4.33 (d, *J* = 7.7 Hz, 1H), 3.97 (dd, *J* = 12.8, 2.1 Hz, 1H), 3.89 (d, *J* = 13.0 Hz, 1H), 1.55 (s, 3H), 1.53 (s, 3H), 1.42 (s, 3H), 1.37 (s, 3H).

^{13}C NMR (101 MHz, $CDCl_3$): δ 151.81, 144.44, 130.91, 129.34, 128.35, 122.38, 116.42, 111.22, 110.19, 104.40, 89.10, 71.06, 69.62, 69.32, 61.74, 26.65, 25.41, 25.27, 24.24.

HRMS (ESI): m/z calculated for $C_{19}H_{23}KNO_6^+$ $[M+K]^+$, 400.1157; found, 400.1405.

2-((2*R*,4*S*,5*R*)-4-(benzyloxy)-5-((benzyloxy)methyl)tetrahydrofuran-2-yl)quinoxaline(14)



Prepared from o-phenylenediamine (0.2 mmol, 1.0 equiv.) and **SI-1-6** (0.3 mmol, 1.5 equiv.) according to the general procedure **2**. Purification by flash column (Petroleum Ether: Ethyl acetate, 8:1) afforded **14** (24.7 mg, 29% yield) as yellow oil.

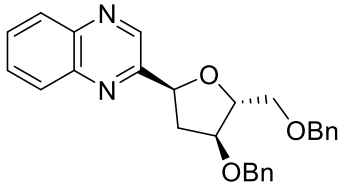
TLC: R*f* = 0.45 (Petroleum Ether: Ethyl acetate, 4:1)

^{1}H NMR (500 MHz, $CDCl_3$): δ 9.15 (s, 1H), 8.13 – 8.10 (m, 1H), 8.06 – 8.04 (m, 1H), 7.78 – 7.73 (m, 2H), 7.38 – 7.35 (m, 4H), 7.33 – 7.27 (m, 6H), 5.49 (dd, *J* = 10.2, 5.9 Hz, 1H), 4.62 (dd, *J* = 12.0, 9.2 Hz, 2H), 4.57 (dd, *J* = 12.0, 2.3 Hz, 2H), 4.44 (td, *J* = 4.5, 2.3 Hz, 1H), 4.25 (dt, *J* = 5.8, 2.0 Hz, 1H), 3.70 – 3.64 (m, 2H), 2.68-2.63 (m, 1H), 2.29-2.23 (m, 1H).

^{13}C NMR (126 MHz, $CDCl_3$): δ 156.46, 144.10, 142.20, 141.57, 138.06, 130.17, 129.68, 129.38, 129.23, 128.59, 128.53, 127.86, 127.81, 127.79, 127.75, 84.85, 81.23, 80.65, 73.65, 71.27, 71.03, 39.24.

HRMS (ESI): m/z calculated for $C_{27}H_{27}N_2O_3^+$ $[M+H]^+$, 427.2016; found, 427.2024.

2-((2*S*,4*S*,5*R*)-4-(benzyloxy)-5-((benzyloxy)methyl)tetrahydrofuran-2-yl)quinoxaline(15)



Prepared from o-phenylenediamine (0.2 mmol, 1.0 equiv.) and **SI-1-7** (0.3 mmol, 1.5 equiv.) according to the general procedure **2**. Purification by flash column (Petroleum

Ether: Ethyl acetate, 8:1) afforded **15** (29.8 mg, 35% yield) as yellow oil.

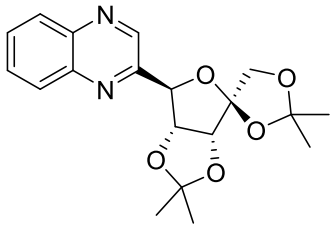
TLC: R*f* = 0.25 (Petroleum Ether: Ethyl acetate, 4:1)

^{1}H NMR (400 MHz, $CDCl_3$): δ 9.19 (s, 1H), 8.13 – 8.08 (m, 1H), 8.05 – 8.00 (m, 1H), 7.77 – 7.71 (m, 2H), 7.38 – 7.34 (m, 4H), 7.33 – 7.30 (m, 1H), 7.19 – 7.13 (m, 3H), 7.01 (dd, *J* = 7.3, 2.3 Hz, 2H), 5.50 (dd, *J* = 8.2, 4.9 Hz, 1H), 4.61 (d, *J* = 2.8 Hz, 2H), 4.55 (td, *J* = 4.6, 2.7 Hz, 1H), 4.39 (s, 2H), 4.26 (dt, *J* = 6.0, 3.1 Hz, 1H), 3.69 – 3.60 (m, 2H), 2.80-2.72 (m, 1H), 2.58-2.51 (m, 1H).

^{13}C NMR (101 MHz, $CDCl_3$): δ 157.99, 143.97, 141.95, 141.51, 138.18, 137.77, 130.03, 129.45, 129.43, 129.08, 128.59, 128.39, 127.87, 127.80, 127.70, 127.61, 84.37, 80.80, 80.76, 73.74, 71.27, 70.99, 38.74.

HRMS (ESI): m/z calculated for $C_{27}H_{26}N_2NaO_3^+[M+Na]^+$, 449.1836; found, 449.1842.

2-((3a*R*,4*S*,6*R*,6a*R*)-2,2,2',2'-tetramethyldihydro-6*H*-spiro[furo[3,4-*d*][1,3]dioxole-4,4'-[1,3]dioxolan]-6-yl)quinoxaline(16)



Prepared from o-phenylenediamine (0.2 mmol, 1.0 equiv.) and **SI-1-4** (0.3 mmol, 1.5 equiv.) according to the general procedure **2**. Purification by flash column (Petroleum Ether: Ethyl acetate, 8:1) afforded **16** (40.3 mg, 56% yield) as yellow white.

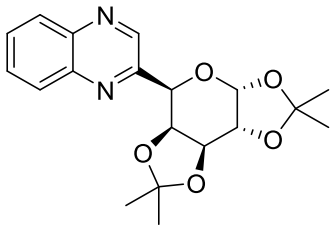
TLC: R*f* = 0.52 (Petroleum Ether: Ethyl acetate, 4:1)

^{1}H NMR (300 MHz, $CDCl_3$): δ 8.99 (s, 1H), 8.11 (dd, *J* = 6.4, 3.6 Hz, 1H), 8.06 (dd, *J* = 7.3, 3.1 Hz, 1H), 7.78 – 7.70 (m, 2H), 5.35 (d, *J* = 3.9 Hz, 1H), 5.16 – 5.09 (m, 1H), 4.79 (d, *J* = 5.6 Hz, 1H), 4.42 (d, *J* = 9.8 Hz, 1H), 4.30 (d, *J* = 9.8 Hz, 1H), 1.49 (s, 3H), 1.46 (s, 3H), 1.39 (s, 3H), 1.23 (s, 3H).

^{13}C NMR (101 MHz, $CDCl_3$): δ 151.68, 145.31, 142.23, 141.60, 130.00, 129.80, 129.47, 129.23, 113.19, 112.52, 112.36, 85.34, 81.85, 81.63, 69.67, 26.62, 26.60, 25.93, 24.47.

HRMS (ESI): m/z calculated for $C_{19}H_{22}N_2NaO_5^+[M+Na]^+$, 381.1421; found, 381.1428.

2-((3a*R*,5*R*,5a*S*,8a*S*,8b*R*)-2,2,7,7-tetramethyltetrahydro-5*H*-bis([1,3]dioxolo)[4,5-*b*:4',5'-*d*]pyran-5-yl)quinoxaline(17)



Prepared from o-phenylenediamine (0.2 mmol, 1.0 equiv.) and **SI-1-8** (0.3 mmol, 1.5 equiv.) according to the general procedure **2**. Purification by flash column (Petroleum Ether: Ethyl acetate, 8:1) afforded **17** (34.1 mg, 48% yield) as yellow oil.

TLC: R*f* = 0.45 (Petroleum Ether: Ethyl acetate, 4:1)

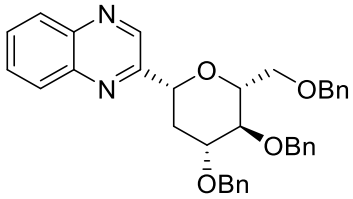
^{1}H NMR (300 MHz, $CDCl_3$): δ 9.05 (s, 1H), 8.13 – 8.07 (m, 1H), 8.06 – 7.99 (m, 1H), 7.73 (p, *J* = 5.1 Hz, 2H), 5.81 (d, *J* = 5.0 Hz, 1H), 5.20 (d, *J* = 2.0 Hz, 1H), 4.78 (dd, *J* = 7.8, 2.4 Hz, 1H), 4.69 (dd, *J* = 7.8, 2.0 Hz, 1H), 4.47 (dd, *J* = 5.0, 2.4 Hz, 1H), 1.61 (s, 3H), 1.45 (s, 3H), 1.39 (s, 3H), 1.25 (s, 3H).

^{13}C NMR (101 MHz, $CDCl_3$): δ 153.34, 144.99, 142.06, 141.51, 129.92, 129.59, 129.47, 129.05, 109.66, 109.24, 96.74, 73.46, 70.99, 70.65, 26.30, 26.01, 25.05, 24.30.

HRMS (ESI): m/z calculated for $C_{19}H_{22}N_2NaO_5^+[M+Na]^+$, 381.1421; found, 381.1426.

2-((2*R*,4*R*,5*S*,6*R*)-4,5-bis(benzyloxy)-6-((benzyloxy)methyl)tetrahydro-2*H*-pyran-

2-yl)quinoxaline(18)



Prepared from o-phenylenediamine (0.2 mmol, 1.0 equiv.) and **SI-1-9** (0.3 mmol, 1.5 equiv.) according to the general procedure **2**. Purification by flash column (Petroleum Ether: Ethyl acetate, 8:1) afforded **18** (60.2 mg, 55% yield) as yellow oil.

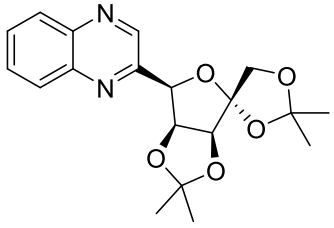
TLC: R*f* = 0.30 (Petroleum Ether: Ethyl acetate, 4:1)

^{1}H NMR (400 MHz, $CDCl_3$): δ 9.17 (s, 1H), 8.16 – 8.11 (m, 1H), 8.08 – 8.03 (m, 1H), 7.77 (td, *J* = 6.0, 3.1 Hz, 2H), 7.40-7.36 (m, 5H), 7.35 (d, *J* = 2.0 Hz, 2H), 7.33 (d, *J* = 1.9 Hz, 2H), 7.32 – 7.30 (m, 4H), 7.28 (t, *J* = 2.7 Hz, 2H), 4.99 (d, *J* = 10.8 Hz, 1H), 4.83 – 4.80 (m, 1H), 4.80 – 4.77 (m, 1H), 4.70 (d, *J* = 2.2 Hz, 1H), 4.67 (t, *J* = 1.8 Hz, 2H), 4.64 (d, *J* = 4.1 Hz, 1H), 3.98-3.92 (m, 1H), 3.86 (d, *J* = 2.6 Hz, 2H), 3.71 (dd, *J* = 6.9, 3.8 Hz, 2H), 2.83-2.77 (m, 1H), 1.83 (dt, *J* = 13.0, 11.6 Hz, 1H).

^{13}C NMR (75 MHz, $CDCl_3$): δ 155.15, 143.73, 142.29, 141.41, 138.50, 138.38, 130.28, 129.82, 129.48, 129.14, 128.57, 128.53, 128.21, 128.09, 128.02, 127.88, 127.81, 127.76, 81.11, 79.83, 78.18, 77.69, 75.36, 73.67, 71.56, 69.63, 37.25.

HRMS (ESI): m/z calculated for $C_{35}H_{35}N_2O_4^+$ $[M+H]^+$, 547.2591; found, 547.2598.

2-((3a*S*,4*R*,6*R*,6a*S*)-2,2,2',2'-tetramethyldihydro-6*H*-spiro[furo[3,4-*d*][1,3]dioxole-4,4'-[1,3]dioxolan]-6-yl)quinoxaline(19)



Prepared from o-phenylenediamine (0.2 mmol, 1.0 equiv.) and **SI-1-5** (0.3 mmol, 1.5

equiv.) according to the general procedure **2**. Purification by flash column (Petroleum Ether: Ethyl acetate, 8:1) afforded **19** (33.1 mg, 46% yield) as yellow oil.

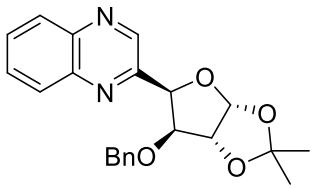
TLC: R*f* = 0.50 (Petroleum Ether: Ethyl acetate, 4:1)

^{1}H NMR (300 MHz, $CDCl_3$): δ 9.17 (s, 1H), 8.09 (q, *J* = 4.4 Hz, 2H), 7.75 (p, *J* = 5.0 Hz, 2H), 5.78 (d, *J* = 5.8 Hz, 1H), 5.44 (s, 1H), 4.63 (d, *J* = 5.9 Hz, 1H), 4.45 (d, *J* = 9.9 Hz, 1H), 4.24 (d, *J* = 10.0 Hz, 1H), 1.56 (s, 3H), 1.47 (s, 3H), 1.42 (s, 3H), 1.24 (s, 3H).

^{13}C NMR (101 MHz, $CDCl_3$): δ 154.64, 144.88, 141.73, 141.34, 130.10, 129.81, 129.44, 129.33, 114.66, 113.10, 112.28, 86.36, 85.44, 84.26, 69.80, 26.76, 26.26, 26.20, 25.49.

HRMS (ESI): m/z calculated for $C_{19}H_{22}N_2NaO_5^+[M+Na]^+$, 381.1421; found, 381.1428.

2-((3a*R*,5*R*,6*S*,6a*R*)-6-(benzyloxy)-2,2-dimethyltetrahydrofuro[2,3-*d*][1,3]dioxol-5-yl)quinoxaline(20)



Prepared from o-phenylenediamine (0.2 mmol, 1.0 equiv.) and **SI-1-2** (0.3 mmol, 1.5 equiv.) according to the general procedure **1**. Purification by flash column (Petroleum Ether: Ethyl acetate, 8:1) afforded **20** (45.9 mg, 61% yield) as yellow oil.

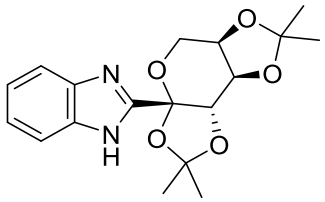
TLC: R*f* = 0.45 (Petroleum Ether: Ethyl acetate, 4:1)

^{1}H NMR (400 MHz, $CDCl_3$): δ 9.10 (s, 1H), 8.17 – 8.13 (m, 1H), 8.02 – 7.97 (m, 1H), 7.78 (dt, *J* = 6.4, 3.5 Hz, 2H), 7.12 – 7.06 (m, 1H), 7.01 (dd, *J* = 8.2, 6.7 Hz, 2H), 6.76 – 6.71 (m, 2H), 6.25 (d, *J* = 3.6 Hz, 1H), 5.57 (d, *J* = 3.3 Hz, 1H), 4.78 (d, *J* = 3.6 Hz, 1H), 4.39 (d, *J* = 12.1 Hz, 1H), 4.34 (d, *J* = 3.3 Hz, 1H), 4.14 (d, *J* = 12.1 Hz, 1H), 1.58 (s, 3H), 1.40 (s, 3H).

^{13}C NMR (101 MHz, $CDCl_3$): δ 152.15, 145.35, 142.15, 141.42, 136.76, 130.05, 129.78, 129.52, 129.05, 128.30, 127.89, 127.50, 112.47, 105.95, 83.65, 83.10, 82.94, 72.36, 27.05, 26.50.

HRMS (ESI): m/z calculated for $C_{22}H_{23}N_2O_4^+$ $[M+H]^+$, 379.1652; found, 379.1661.

2-((3a*S*,5a*R*,8a*R*,8b*S*)-2,2,7,7-tetramethyltetrahydro-3a*H*-bis([1,3]dioxolo)[4,5-*b*:4',5'-*d*]pyran-3a-yl)-1*H*-benzo[*d*]imidazole(21)



Prepared from o-phenylenediamine (0.2 mmol, 1.0 equiv.) and **SI-1-10** (0.3 mmol, 1.5 equiv.) according to the general procedure **3**. Purification by flash column (Petroleum Ether: Ethyl acetate, 10:1) afforded **21** (52.6 mg, 76% yield) as yellow solid.

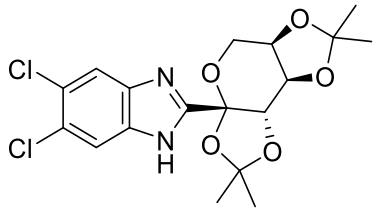
TLC: R*f* = 0.30 (Petroleum Ether: Ethyl acetate, 4:1)

^{1}H NMR (300 MHz, $CDCl_3$): δ 9.67 (s, 1H), 7.80 (s, 1H), 7.41 (s, 1H), 7.26 – 7.21 (m, 2H), 5.04 (d, *J* = 2.5 Hz, 1H), 4.70 (dd, *J* = 7.9, 2.5 Hz, 1H), 4.33 (d, *J* = 8.0 Hz, 1H), 4.12 (dd, *J* = 11.4, 2.7 Hz, 1H), 3.95 (d, *J* = 13.0 Hz, 1H), 1.66 (s, 3H), 1.63 (s, 3H), 1.32 (s, 6H).

^{13}C NMR (75 MHz, $CDCl_3$): δ 152.38, 143.38, 133.12, 123.42, 122.25, 120.58, 111.02, 110.35, 109.23, 99.52, 74.09, 70.52, 70.19, 61.56, 26.32, 25.98, 25.24, 24.04.

HRMS (ESI): m/z calculated for $C_{18}H_{23}N_2O_5^+$ $[M+H]^+$, 347.1601; found, 347.1610.

5,6-dichloro-2-((3a*S*,5a*R*,8a*R*,8b*S*)-2,2,7,7-tetramethyltetrahydro-3a*H*-bis([1,3]dioxolo)[4,5-*b*:4',5'-*d*]pyran-3a-yl)-1*H*-benzo[d]imidazole(22)



Prepared from substituted o-phenylenediamine (0.2 mmol, 1.0 equiv.) and **SI-1-10** (0.3 mmol, 1.5 equiv.) according to the general procedure **3**. Purification by flash column (Petroleum Ether: Ethyl acetate, 10:1) afforded **22** (69.7 mg, 84% yield) as yellow oil.

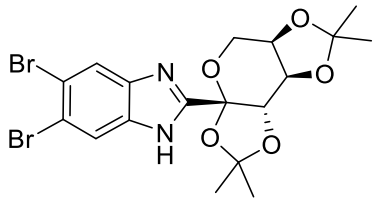
TLC: R*f* = 0.50 (Petroleum Ether: Ethyl acetate, 3:1)

^{1}H NMR (500 MHz, $CDCl_3$): δ 9.85 (s, 1H), 7.87 (s, 1H), 7.54 (s, 1H), 4.99 (d, *J* = 2.5 Hz, 1H), 4.70 (dd, *J* = 7.9, 2.5 Hz, 1H), 4.33 (dd, *J* = 7.9, 1.7 Hz, 1H), 4.10 (dd, *J* = 13.0, 1.9 Hz, 1H), 3.95 (d, *J* = 13.0 Hz, 1H), 1.63 (s, 3H), 1.62 (s, 3H), 1.32 (s, 3H), 1.30 (s, 3H).

^{13}C NMR (126 MHz, $CDCl_3$): δ 154.48, 146.02, 121.71, 112.57, 110.67, 109.25, 99.14, 74.13, 70.39, 70.01, 61.58, 26.30, 26.00, 25.12, 23.96.

HRMS (ESI): m/z calculated for $C_{18}H_{21}Cl_2N_2O_5^+$ $[M+H]^+$, 415.0822; found, 415.0827.

5,6-dibromo-2-((3a*S*,5a*R*,8a*R*,8b*S*)-2,2,7,7-tetramethyltetrahydro-3a*H*-bis([1,3]dioxolo)[4,5-*b*:4',5'-*d*]pyran-3a-yl)-1*H*-benzo[*d*]imidazole(23)



Prepared from substituted o-phenylenediamine (0.2 mmol, 1.0 equiv.) and **SI-1-10** (0.3 mmol, 1.5 equiv.) according to the general procedure **3**. Purification by flash column (Petroleum Ether: Ethyl acetate, 10:1) afforded **23** (51.4 mg, 51% yield) as

red solid.

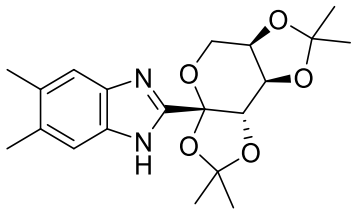
TLC: R*f* = 0.50 (Petroleum Ether: Ethyl acetate, 4:1)

^{1}H NMR (400 MHz, $CDCl_3$): δ 9.79 (s, 1H), 8.08 (s, 1H), 7.73 (s, 1H), 4.97 (d, *J* = 2.5 Hz, 1H), 4.69 (dd, *J* = 7.9, 2.5 Hz, 1H), 4.35 – 4.30 (m, 1H), 4.10 (dd, *J* = 13.0, 1.9 Hz, 1H), 3.95 (dd, *J* = 13.0, 0.9 Hz, 1H), 1.63 (s, 3H), 1.62 (s, 3H), 1.32 (s, 3H), 1.29 (s, 3H).

^{13}C NMR (75 MHz, $CDCl_3$): δ 154.28, 143.80, 133.09, 124.97, 118.63, 117.54, 115.50, 110.60, 109.16, 99.01, 74.08, 70.28, 69.91, 61.47, 26.22, 25.90, 25.02, 23.85.

HRMS (ESI): m/z calculated for $C_{18}H_{21}Br_2N_2O_5^+$[M+H] $^+$, 502.9812; found, 504.9804.

5,6-dimethyl-2-((3a*S*,5a*R*,8a*R*,8b*S*)-2,2,7,7-tetramethyltetrahydro-3a*H*-bis([1,3]dioxolo)[4,5-*b*:4',5'-*d*]pyran-3a-yl)-1*H*-benzo[*d*]imidazole(24)



Prepared from substituted o-phenylenediamine (0.2 mmol, 1.0 equiv.) and **SI-1-10** (0.3 mmol, 1.5 equiv.) according to the general procedure **3**. Purification by flash column (Petroleum Ether: Ethyl acetate, 10:1) afforded **24** (56.1 mg, 75% yield) as yellow oil.

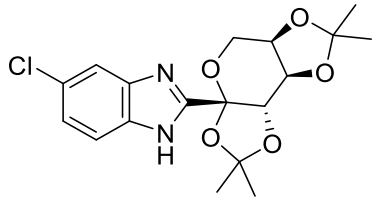
TLC: R*f* = 0.40 (Petroleum Ether: Ethyl acetate, 3:1)

^{1}H NMR (500 MHz, $CDCl_3$): δ 9.45 (s, 1H), 7.57 (s, 1H), 7.18 (s, 1H), 5.00 (d, *J* = 2.5 Hz, 1H), 4.69 (dd, *J* = 7.9, 2.5 Hz, 1H), 4.33 (dd, *J* = 7.8, 0.8 Hz, 1H), 4.11 (dd, *J* = 13.0, 1.9 Hz, 1H), 3.94 (dd, *J* = 13.0, 0.8 Hz, 1H), 2.35 (s, 6H), 1.65 (s, 3H), 1.62 (s, 3H), 1.32 (s, 6H).

^{13}C NMR (126 MHz, $CDCl_3$): δ 151.52, 142.07, 132.57, 131.68, 131.05, 120.56, 111.12, 110.22, 109.20, 99.62, 74.07, 70.55, 70.22, 61.53, 26.32, 26.03, 25.24, 24.06, 20.59, 20.44.

HRMS (ESI): m/z calculated for $C_{20}H_{27}N_2O_5^+$ [M+H] $^+$, 375.1914; found, 375.1922.

5-chloro-2-((3a*S*,5a*R*,8a*R*,8b*S*)-2,2,7,7-tetramethyltetrahydro-3a*H*-bis([1,3]dioxolo)[4,5-*b*:4',5'-*d*]pyran-3a-yl)-1*H*-benzo[d]imidazole(25)



Prepared from substituted o-phenylenediamine (0.2 mmol, 1.0 equiv.) and **SI-1-10** (0.3 mmol, 1.5 equiv.) according to the general procedure **3**. Purification by flash column (Petroleum Ether: Ethyl acetate, 10:1) afforded **25** (36.5 mg, 48% yield) as yellow oil.

TLC: R*f* = 0.48 (Petroleum Ether: Ethyl acetate, 3:1)

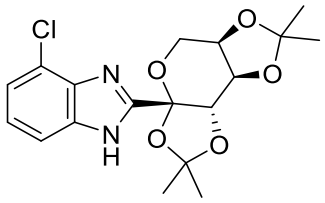
^{1}H NMR (400 MHz, $CDCl_3$): δ 9.73 (s, 1H), 7.74 (d, *J* = 34.2 Hz, 1H), 7.37 (d, *J* = 34.3 Hz, 1H), 7.22 (dd, *J* = 8.6, 2.0 Hz, 1H), 5.00 (d, *J* = 2.5 Hz, 1H), 4.70 (dd, *J* = 7.9, 2.5 Hz, 1H), 4.33 (dd, *J* = 8.0, 1.8 Hz, 1H), 4.11 (dd, *J* = 13.0, 1.9 Hz, 1H), 3.94 (d, *J* = 13.0 Hz, 1H), 1.65 (s, 3H), 1.62 (s, 3H), 1.32 (s, 3H), 1.31 (s, 3H).

^{13}C NMR (101 MHz, $CDCl_3$): δ 153.65, 146.14, 130.34, 123.98, 123.10, 121.46, 110.53, 109.23, 99.29, 74.14, 70.45, 70.09, 61.57, 26.31, 25.99, 25.18, 23.99.

HRMS (ESI): m/z calculated for $C_{18}H_{22}ClN_2O_5^+$ [M+H] $^+$, 381.1212; found, 381.1221.

4-chloro-2-((3a*S*,5a*R*,8a*R*,8b*S*)-2,2,7,7-tetramethyltetrahydro-3a*H*-

bis([1,3]dioxolo)[4,5-*b*:4',5'-d]pyran-3a-yl)-1*H*-benzo[*d*]imidazole(26)



Prepared from substituted o-phenylenediamine (0.2 mmol, 1.0 equiv.) and **SI-1-10** (0.3 mmol, 1.5 equiv.) according to the general procedure **3**. Purification by flash column (Petroleum Ether: Ethyl acetate, 10:1) afforded **26** (37.3 mg, 49% yield) as yellow oil.

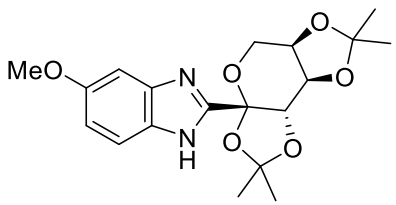
TLC: R*f* = 0.50 (Petroleum Ether: Ethyl acetate, 4:1)

^{1}H NMR (300 MHz, $CDCl_3$): δ 9.81 (s, 1H), 7.70 (d, *J* = 7.9 Hz, 1H), 7.25 (d, *J* = 5.4 Hz, 1H), 7.19 (t, *J* = 7.7 Hz, 1H), 4.90 (d, *J* = 2.6 Hz, 1H), 4.72 (dd, *J* = 7.9, 2.6 Hz, 1H), 4.35 (dd, *J* = 7.8, 1.8 Hz, 1H), 4.11 (dd, *J* = 13.0, 1.9 Hz, 1H), 3.96 (d, *J* = 13.0 Hz, 1H), 1.65 (s, 3H), 1.64 (s, 3H), 1.45 (s, 3H), 1.36 (s, 3H).

^{13}C NMR (75 MHz, $CDCl_3$): δ 152.74, 144.15, 131.55, 122.94, 122.88, 119.12, 116.02, 110.59, 109.31, 99.45, 74.00, 70.42, 70.03, 61.57, 26.13, 25.96, 24.99, 23.94.

HRMS (ESI): m/z calculated for $C_{18}H_{22}ClN_2O_5^+$ $[M+H]^+$, 381.1212; found, 381.1222.

5-methoxy-2-((3a*S*,5a*R*,8a*R*,8b*S*)-2,2,7,7-tetramethyltetrahydro-3a*H*-bis([1,3]dioxolo)[4,5-*b*:4',5'-*d*]pyran-3a-yl)-1*H*-benzo[d]imidazole(27)



Prepared from substituted o-phenylenediamine (0.2 mmol, 1.0 equiv.) and **SI-1-10** (0.3 mmol, 1.5 equiv.) according to the general procedure **3**. Purification by flash

column (Petroleum Ether: Ethyl acetate, 10:1) afforded **27** (32.3 mg, 43% yield) as yellow oil.

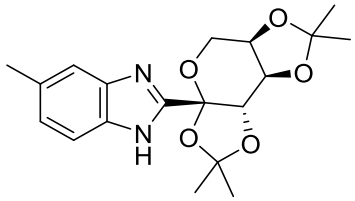
TLC: R*f* = 0.30 (Petroleum Ether: Ethyl acetate, 4:1)

^{1}H NMR (500 MHz, $CDCl_3$): δ 9.62 (s, 1H), 7.63 (s, 1H), 6.89 (dd, *J* = 8.8, 2.4 Hz, 2H), 5.02 (d, *J* = 2.5 Hz, 1H), 4.69 (dd, *J* = 7.9, 2.5 Hz, 1H), 4.33 (dd, *J* = 7.9, 1.7 Hz, 1H), 4.11 (dd, *J* = 13.0, 1.9 Hz, 1H), 3.97 – 3.92 (m, 1H), 3.83 (s, 3H), 1.65 (s, 3H), 1.62 (s, 3H), 1.32 (s, 6H).

^{13}C NMR (126 MHz, $CDCl_3$): δ 151.78, 145.04, 142.53, 130.54, 123.67, 111.78, 110.27, 109.20, 106.75, 99.47, 74.08, 70.51, 70.17, 61.54, 55.88, 26.32, 26.01, 25.25, 24.03.

HRMS (ESI): m/z calculated for $C_{19}H_{25}N_2O_6^+$ $[M+H]^+$, 377.1707; found, 377.1716.

5-methyl-2-((3a*S*,5a*R*,8a*R*,8b*S*)-2,2,7,7-tetramethyltetrahydro-3a*H*-bis([1,3]dioxolo)[4,5-*b*:4',5'-*d*]pyran-3a-yl)-1*H*-benzo[d]imidazole(28)



Prepared from substituted o-phenylenediamine (0.2 mmol, 1.0 equiv.) and **SI-1-10** (0.3 mmol, 1.5 equiv.) according to the general procedure **3**. Purification by flash column (Petroleum Ether: Ethyl acetate, 10:1) afforded **28** (38.2 mg, 53% yield) as yellow oil.

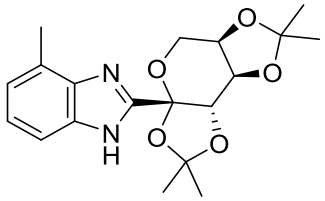
TLC: R*f* = 0.48 (Petroleum Ether: Ethyl acetate, 3:1)

^{1}H NMR (300 MHz, $CDCl_3$): δ 9.55 (s, 1H), 7.21 (s, 1H), 7.07 (d, *J* = 8.3 Hz, 1H), 5.01 (d, *J* = 2.2 Hz, 1H), 4.70 (dd, *J* = 8.0, 2.4 Hz, 1H), 4.33 (d, *J* = 8.1 Hz, 1H), 4.15 – 4.06 (m, 1H), 3.94 (d, *J* = 13.1 Hz, 1H), 2.46 (s, 3H), 1.65 (s, 3H), 1.62 (s, 3H), 1.32 (s, 6H).

^{13}C NMR (101 MHz, $CDCl_3$): δ 151.34, 144.24, 133.18, 131.09, 127.75, 122.53, 118.50, 110.26, 109.19, 99.55, 74.05, 70.52, 70.18, 61.53, 26.30, 26.00, 25.23, 24.04, 21.77.

HRMS (ESI): m/z calculated for $C_{19}H_{25}N_2O_5^+$ $[M+H]^+$, 361.1758; found, 361.1764.

4-methyl-2-((3a*S*,5a*R*,8a*R*,8b*S*)-2,2,7,7-tetramethyltetrahydro-3a*H*-bis([1,3]dioxolo)[4,5-*b*:4',5'-d]pyran-3a-yl)-1H-benzo[*d*]imidazole(29)



Prepared from substituted o-phenylenediamine (0.2 mmol, 1.0 equiv.) and **SI-1-10** (0.3 mmol, 1.5 equiv.) according to the general procedure **3**. Purification by flash column (Petroleum Ether: Ethyl acetate, 10:1) afforded **29** (45.4 mg, 63% yield) as yellow oil.

TLC: R*f* = 0.50 (Petroleum Ether: Ethyl acetate, 4:1)

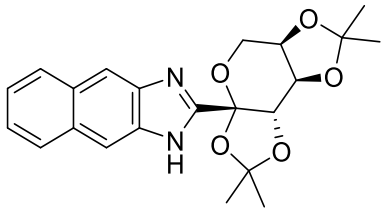
^{1}H NMR (300 MHz, $CDCl_3$): δ 9.61 (s, 1H), 7.59 (s, 1H), 7.16 (t, *J* = 7.6 Hz, 1H), 7.05 (d, *J* = 7.3 Hz, 1H), 4.99 (d, *J* = 2.5 Hz, 1H), 4.71 (dd, *J* = 7.9, 2.5 Hz, 1H), 4.34 (dd, *J* = 7.9, 1.7 Hz, 1H), 4.12 (dd, *J* = 13.0, 1.9 Hz, 1H), 3.95 (d, *J* = 13.0 Hz, 1H), 2.55 (s, 3H), 1.68 (s, 3H), 1.64 (s, 3H), 1.38 (s, 3H), 1.34 (s, 3H).

^{13}C NMR (75 MHz, $CDCl_3$): δ 151.72, 149.67, 143.83, 134.68, 122.51, 116.79, 114.20, 110.31, 109.10, 99.63, 74.06, 70.46, 70.14, 61.44, 26.21, 25.97, 25.06, 23.92, 16.86.

HRMS (ESI): m/z calculated for $C_{19}H_{25}N_2O_5^+$ $[M+H]^+$, 361.1758; found, 361.1768.

2-((3a*S*,5a*R*,8a*R*,8b*S*)-2,2,7,7-tetramethyltetrahydro-3a*H*-bis([1,3]dioxolo)[4,5-

***b*:4',5'-*d*]pyran-3a-yl)-1*H*-naphtho[2,3-*d*]imidazole(30)**



Prepared from substituted o-phenylenediamine (0.2 mmol, 1.0 equiv.) and **SI-1-10** (0.3 mmol, 1.5 equiv.) according to the general procedure **3**. Purification by flash column (Petroleum Ether: Ethyl acetate, 10:1) afforded **30** (40.4 mg, 51% yield) as yellow oil.

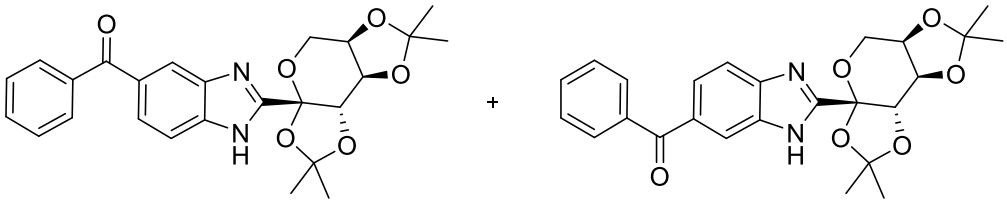
TLC: R*f* = 0.30 (Petroleum Ether: Ethyl acetate, 3:1)

^{1}H NMR (500 MHz, $CDCl_3$): δ 9.71 (s, 1H), 8.30 (s, 1H), 7.88 (d, *J* = 43.4 Hz, 3H), 7.40 (dd, *J* = 6.8, 3.5 Hz, 2H), 5.11 (d, *J* = 2.4 Hz, 1H), 4.73 (dd, *J* = 7.9, 2.5 Hz, 1H), 4.38 – 4.34 (m, 1H), 4.15 (dd, *J* = 13.0, 1.9 Hz, 1H), 3.99 (dd, *J* = 13.0, 0.8 Hz, 1H), 1.70 (s, 3H), 1.65 (s, 3H), 1.33 (s, 3H), 1.33 (s, 3H).

^{13}C NMR (126 MHz, $CDCl_3$): δ 156.37, 128.66, 127.45, 124.51, 123.56, 117.65, 110.60, 109.27, 99.44, 74.14, 70.48, 70.12, 61.60, 26.33, 25.98, 25.22, 24.03.

HRMS (ESI): m/z calculated for $C_{22}H_{25}N_2O_5^+$ $[M+H]^+$, 397.1758; found, 397.1761.

phenyl(2-((3a*S*,5a*R*,8a*R*,8b*S*)-2,2,7,7-tetramethyltetrahydro-3a*H*-bis([1,3]dioxolo)[4,5-*b*:4',5'-*d*]pyran-3a-yl)-1*H*-benzo[*d*]imidazol-5-yl)methanone and phenyl(2-((3a*S*,5a*R*,8a*R*,8b*S*)-2,2,7,7-tetramethyltetrahydro-3a*H*-bis([1,3]dioxolo)[4,5-*b*:4',5'-*d*]pyran-3a-yl)-1*H*-benzo[*d*]imidazol-6-yl)methanone(31)



1.1:1

Prepared from substituted o-phenylenediamine (0.2 mmol, 1.0 equiv.) and **SI-1-10** (0.3 mmol, 1.5 equiv.) according to the general procedure **3**. Purification by flash column (Petroleum Ether: Ethyl acetate, 10:1) afforded **31** (29.7 mg, 33% yield) as yellow oil.

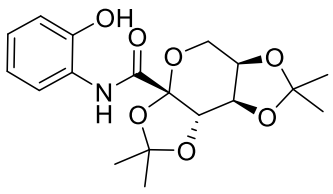
TLC: R*f* = 0.40 (Petroleum Ether: Ethyl acetate, 4:1)

^{1}H NMR (300 MHz, $CDCl_3$): δ 10.07 (d, *J* = 30.5 Hz, 1H), 8.12 (dd, *J* = 87.3, 1.5 Hz, 1H), 7.92 – 7.83 (m, 1H), 7.80 (ddd, *J* = 7.6, 5.9, 1.4 Hz, 2H), 7.75 – 7.51 (m, 2H), 7.47 (td, *J* = 7.6, 3.6 Hz, 2H), 5.05 (dd, *J* = 2.5, 1.3 Hz, 1H), 4.71 (dt, *J* = 7.9, 2.5 Hz, 1H), 4.34 (dd, *J* = 7.9, 1.6 Hz, 1H), 4.16 – 4.09 (m, 1H), 3.96 (d, *J* = 13.0 Hz, 1H), 1.69 – 1.60 (m, 6H), 1.32 (s, 3H), 1.31 (s, 3H).

^{13}C NMR (75 MHz, $CDCl_3$): δ 196.83, 155.44, 154.28, 146.64, 142.62, 138.35, 136.17, 132.81, 132.14, 132.08, 131.99, 130.05, 128.25, 128.22, 125.48, 124.96, 124.38, 119.91, 113.99, 111.18, 110.58, 110.51, 109.18, 99.18, 74.11, 70.34, 69.98, 61.50, 26.23, 25.92, 25.11, 23.88.

HRMS (ESI): m/z calculated for $C_{25}H_{27}N_2O_6^+$ $[M+H]^+$, 451.1864; found, 451.1872.

(3a*R*,5a*R*,8a*R*,8b*S*)-*N*-(2-hydroxyphenyl)-2,2,7,7-tetramethyltetrahydro-3a*H*-bis([1,3]dioxolo)[4,5-*b*:4',5'-*d*]pyran-3a-carboxamide(32)



Prepared from *o*-aminophenol (0.2 mmol, 1.0 equiv.) and **SI-1-10** (0.3 mmol, 1.5

equiv.) according to the general procedure **3**. Purification by flash column (Petroleum Ether: Ethyl acetate, 10:1) afforded **32** (53.3 mg, 73% yield) as yellow oil.

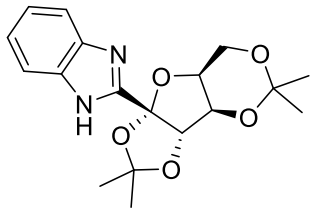
TLC: R*f* = 0.40 (Petroleum Ether: Ethyl acetate, 3:1)

^{1}H NMR (500 MHz, $CDCl_3$): δ 8.88 (s, 1H), 8.48 (s, 1H), 7.15 – 7.08 (m, 2H), 7.01 (dd, *J* = 8.1, 1.4 Hz, 1H), 6.90 – 6.82 (m, 1H), 4.78 (d, *J* = 2.5 Hz, 1H), 4.66 (dd, *J* = 7.9, 2.6 Hz, 1H), 4.30 (d, *J* = 7.9 Hz, 1H), 4.03 (dd, *J* = 12.9, 1.7 Hz, 1H), 3.97 (d, *J* = 13.0 Hz, 1H), 1.59 (s, 3H), 1.58 (s, 3H), 1.41 (s, 3H), 1.34 (s, 3H).

^{13}C NMR (126 MHz, $CDCl_3$): δ 167.69, 148.89, 127.54, 124.64, 122.49, 120.57, 119.81, 111.25, 109.32, 99.65, 72.99, 70.25, 69.95, 62.07, 26.41, 26.13, 24.81, 23.95.

HRMS (ESI): m/z calculated for $C_{18}H_{23}NNaO_7^+$ $[M+Na]^+$, 388.1367; found, 388.1375.

2-((3a*S*,3b*R*,7a*S*,8a*S*)-2,2,5,5-tetramethyltetrahydro-8a*H*-[1,3]dioxolo[4',5':4,5]furo[3,2-*d*][1,3]dioxin-8a-yl)-1*H*-benzo[d]imidazole(33)



Prepared from o-phenylenediamine (0.2 mmol, 1.0 equiv.) and **SI-1-3** (0.3 mmol, 1.5 equiv.) according to the general procedure **3**. Purification by flash column (Petroleum Ether: Ethyl acetate, 10:1) afforded **33** (40.1 mg, 58% yield) as yellow solid.

TLC: R*f* = 0.23 (Petroleum Ether: Ethyl acetate, 3:1)

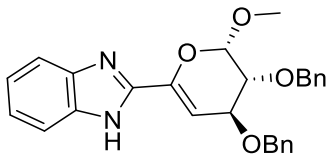
^{1}H NMR (400 MHz, $CDCl_3$): δ 9.92 (s, 1H), 7.83 (s, 1H), 7.45 (s, 1H), 7.28 – 7.25 (m, 2H), 4.67 (s, 1H), 4.48 (d, *J* = 2.4 Hz, 1H), 4.37 (t, *J* = 1.9 Hz, 1H), 4.25 – 4.22 (m, 2H), 1.73 (s, 3H), 1.64 (s, 3H), 1.47 (s, 3H), 1.30 (s, 3H).

^{13}C NMR (75 MHz, $CDCl_3$): δ 151.45, 128.69, 123.02, 122.27, 114.53, 110.38,

97.97, 89.18, 73.67, 73.22, 60.85, 29.28, 27.29, 26.39, 18.70.

HRMS (ESI): m/z calculated for $C_{18}H_{23}N_2O_5^+$ $[M+H]^+$, 347.1601; found, 347.1610.

2-((2*S*,3*R*,4*S*)-3,4-bis(benzyloxy)-2-methoxy-3,4-dihydro-2*H*-pyran-6-yl)-1*H*-benzo[d]imidazole(34)



Prepared from o-phenylenediamine (0.2 mmol, 1.0 equiv.) and **SI-1-1** (0.3 mmol, 1.5 equiv.) according to the general procedure **3**. Purification by flash column (Petroleum Ether: Ethyl acetate, 10:1) afforded **34** (40.7 mg, 46% yield) as yellow oil.

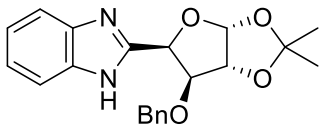
TLC: R*f* = 0.25 (Petroleum Ether: Ethyl acetate, 3:1)

^{1}H NMR (500 MHz, $CDCl_3$): δ 10.16 (s, 1H), 7.52 (s, 2H), 7.26 (dd, *J* = 7.3, 1.5 Hz, 4H), 7.23 – 7.20 (m, 6H), 7.17 (dd, *J* = 6.1, 3.1 Hz, 2H), 6.29 (d, *J* = 3.3 Hz, 1H), 4.91 (d, *J* = 2.3 Hz, 1H), 4.73 (d, *J* = 12.4 Hz, 1H), 4.66 (d, *J* = 12.2 Hz, 1H), 4.58 (d, *J* = 11.6 Hz, 1H), 4.49 (d, *J* = 11.6 Hz, 1H), 4.28 (dd, *J* = 6.6, 3.3 Hz, 1H), 3.79 (dd, *J* = 6.6, 2.3 Hz, 1H), 3.43 (s, 3H).

^{13}C NMR (126 MHz, $CDCl_3$): δ 146.70, 141.28, 138.09, 138.05, 128.56, 128.52, 128.24, 128.15, 128.08, 128.02, 127.90, 127.83, 123.31, 102.39, 100.43, 75.79, 73.41, 72.79, 71.21, 57.24.

HRMS (ESI): m/z calculated for $C_{27}H_{27}N_2O_4^+$ $[M+H]^+$, 443.1965; found, 443.1973.

2-((3a*R*,5*R*,6*S*,6a*R*)-6-(benzyloxy)-2,2-dimethyltetrahydrofuro[2,3-*d*][1,3]dioxol-5-yl)-1*H*-benzo[*d*]imidazole(35)



Prepared from o-phenylenediamine (0.2 mmol, 1.0 equiv.) and **SI-1-2** (0.3 mmol, 1.5 equiv.) according to the general procedure **3**. Purification by flash column (Petroleum Ether: Ethyl acetate, 10:1) afforded **35** (14.6 mg, 20% yield) as yellow solid.

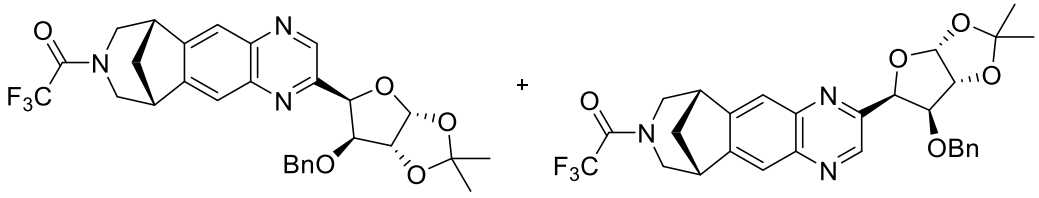
TLC: R*f* = 0.30 (Petroleum Ether: Ethyl acetate, 3:1)

^{1}H NMR (400 MHz, $CDCl_3$): δ 9.72 (s, 1H), 7.84 – 7.68 (m, 1H), 7.42 (d, *J* = 1.5 Hz, 1H), 7.27 (dd, *J* = 6.2, 3.3 Hz, 2H), 7.20 – 7.12 (m, 3H), 6.87 (d, *J* = 6.6 Hz, 2H), 6.09 (d, *J* = 3.6 Hz, 1H), 5.63 (d, *J* = 3.0 Hz, 1H), 4.71 (d, *J* = 3.6 Hz, 1H), 4.38 – 4.33 (m, 2H), 4.13 (d, *J* = 11.4 Hz, 1H), 1.55 (s, 3H), 1.36 (s, 3H).

^{13}C NMR (75 MHz, $CDCl_3$): δ 149.52, 136.78, 128.39, 128.04, 127.76, 112.68, 105.28, 83.74, 83.23, 77.86, 73.07, 26.93, 26.40.

HRMS (ESI): m/z calculated for $C_{21}H_{23}N_2O_4^+$ $[M+H]^+$, 367.1652; found, 367.1661.

1-((6*S*,10*R*)-2-((3a*R*,5*R*,6*S*,6a*R*)-6-(benzyloxy)-2,2-dimethyltetrahydrofuro[2,3-*d*][1,3]dioxol-5-yl)-6,7,9,10-tetrahydro-8*H*-6,10-methanoazepino[4,5-*g*]quinoxalin-8-yl)-2,2,2-trifluoroethan-1-one and 1-((6*R*,10*S*)-2-((3a*R*,5*R*,6*S*,6a*R*)-6-(benzyloxy)-2,2-dimethyltetrahydrofuro[2,3-*d*][1,3]dioxol-5-yl)-6,7,9,10-tetrahydro-8*H*-6,10-methanoazepino[4,5-*g*]quinoxalin-8-yl)-2,2,2-trifluoroethan-1-one(37)



1:1

Prepared from the o-phenylenediamine derivative of varenicline (0.1 mmol, 1.0 equiv.)

and **SI-1-2** (0.15 mmol, 1.5 equiv.) according to the general procedure **4**. Purification by flash column (Petroleum Ether: Ethyl acetate, 8:1) afforded **37** (19.4 mg, 35% yield) as yellow oil.

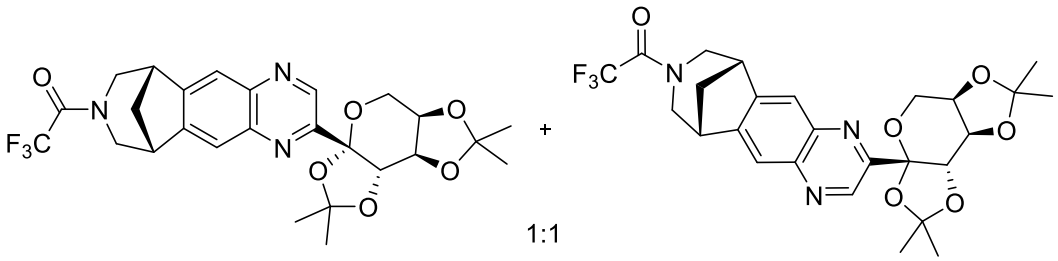
TLC: R*f* = 0.30 (Petroleum Ether: Ethyl acetate, 4:1)

^{1}H NMR (300 MHz, $CDCl_3$): δ 9.03 (d, *J* = 5.6 Hz, 1H), 7.94 (d, *J* = 4.2 Hz, 1H), 7.79 (dd, *J* = 14.6, 12.4 Hz, 1H), 7.13 – 6.86 (m, 3H), 6.80 – 6.63 (m, 2H), 6.23 (d, *J* = 3.6 Hz, 1H), 5.58 – 5.47 (m, 1H), 4.76 (dd, *J* = 7.2, 3.7 Hz, 1H), 4.49 (t, *J* = 13.1 Hz, 1H), 4.34 (tt, *J* = 14.8, 5.9 Hz, 2H), 4.20 – 4.06 (m, 2H), 3.69 (dd, *J* = 12.6, 8.0 Hz, 1H), 3.60 – 3.50 (m, 2H), 3.30 (t, *J* = 11.0 Hz, 1H), 2.50 (s, 1H), 2.15 (d, *J* = 11.3 Hz, 1H), 1.57 (s, 3H), 1.39 (s, 3H).

^{13}C NMR (101 MHz, $CDCl_3$): δ 151.70 – 151.11 (m), 146.81, 146.73, 146.48, 146.29, 146.26, 145.98, 145.91, 144.77, 144.52, 144.42, 142.40, 141.72, 141.57, 136.87, 136.61, 136.49, 128.25, 128.19, 128.17, 128.09, 127.89, 127.86, 127.69, 127.67, 127.43, 127.34, 122.89, 122.87, 122.64, 122.61, 122.42, 122.38, 122.15, 119.11 – 113.38 (m), 112.34, 112.31, 112.28, 105.85, 105.80, 105.77, 83.73, 83.38, 83.24, 83.10, 83.02, 82.89, 82.77, 82.71, 72.31, 50.86, 48.73, 41.75, 39.92, 39.87, 39.73, 26.94, 26.40, 26.37.

HRMS (ESI): m/z calculated for $C_{29}H_{29}F_3N_3O_5^+$ $[M+H]^+$, 556.2054; found, 556.2061.

2,2,2-trifluoro-1-((6*S*,10*R*)-2-((3a*S*,5a*R*,8a*R*,8b*S*)-2,2,7,7-tetramethyltetrahydro-3a*H*-bis([1,3]dioxolo)[4,5-*b*:4',5'-*d*]pyran-3a-yl)-6,7,9,10-tetrahydro-8*H*-6,10-methanoazepino[4,5-*g*]quinoxalin-8-yl)ethan-1-one and 2,2,2-trifluoro-1-((6*R*,10*S*)-2-((3a*S*,5a*R*,8a*R*,8b*S*)-2,2,7,7-tetramethyltetrahydro-3a*H*-bis([1,3]dioxolo)[4,5-*b*:4',5'-*d*]pyran-3a-yl)-6,7,9,10-tetrahydro-8*H*-6,10-methanoazepino[4,5-g]quinoxalin-8-yl)ethan-1-one(38)



Prepared from the o-phenylenediamine derivative of varenicline (0.1 mmol, 1.0 equiv.) and **SI-1-10** (0.15 mmol, 1.5 equiv.) according to the general procedure **4**.
Purification by flash column (Petroleum Ether: Ethyl acetate, 8:1) afforded **38** (27.2 mg, 51% yield) as yellow oil.

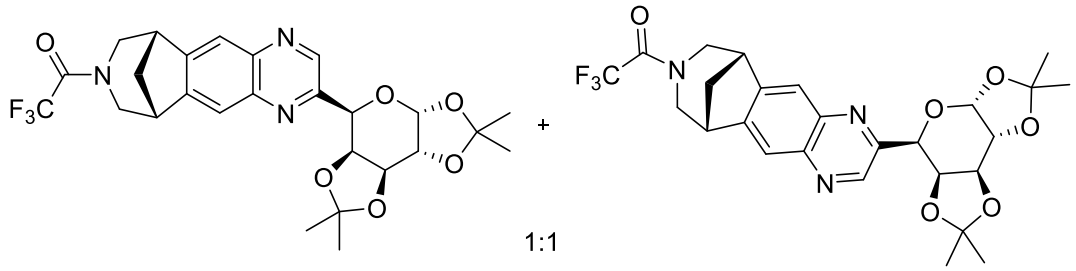
TLC: R*f* = 0.20 (Petroleum Ether: Ethyl acetate, 4:1)

^{1}H NMR (500 MHz, $CDCl_3$): δ 9.30 (d, *J* = 1.9 Hz, 1H), 7.93 – 7.89 (m, 2H), 5.24 – 5.07 (m, 1H), 4.73-4.69 (m, 1H), 4.47 (dd, *J* = 13.1, 2.9 Hz, 1H), 4.35 (dt, *J* = 8.1, 1.8 Hz, 1H), 4.18 (dt, *J* = 13.0, 2.5 Hz, 1H), 4.03 (dd, *J* = 13.0, 4.8 Hz, 2H), 3.72 – 3.64 (m, 1H), 3.58 – 3.49 (m, 2H), 3.29 (dd, *J* = 14.3, 9.0 Hz, 1H), 2.51-2.45 (m, 1H), 2.14 (dd, *J* = 11.2, 2.5 Hz, 1H), 1.68 (s, 1H), 1.67 (s, 1H), 1.64 (s, 3H), 1.63 (s, 1H), 1.33 (s, 1H), 1.31 (s, 1H), 1.30 (s, 1H), 1.28 (s, 1H), 1.26 (s, 1H), 1.22 (s, 1H).

^{13}C NMR (126 MHz, $CDCl_3$): δ 153.23 – 152.88 (m), 147.28, 147.23, 146.96, 146.91, 146.72, 146.70, 146.38, 143.54, 143.40, 143.34, 142.53, 142.41, 141.88, 141.77, 141.71, 141.68, 123.32, 123.29, 123.10, 123.06, 122.67, 122.42, 120.39 – 112.90 (m), 110.09, 110.06, 109.94, 109.90, 109.36, 109.34, 109.21, 109.20, 102.83, 102.79, 102.73, 102.60, 74.24, 73.88, 73.82, 73.74, 70.67, 70.62, 70.59, 70.56, 70.54, 70.52, 61.88, 61.77, 61.72, 50.92, 48.88, 48.83, 48.76, 41.89, 41.84, 41.81, 41.78, 39.98, 39.93, 39.90, 39.79, 39.76, 26.53, 26.51, 26.06, 26.00, 25.98, 25.74, 25.65, 25.58, 25.54, 24.23, 24.20, 24.15.

HRMS (ESI): m/z calculated for $C_{26}H_{29}F_3N_3O_6^+$ $[M+H]^+$, 536.2003; found, 536.2005.

2,2,2-trifluoro-1-((6*S*,10*R*)-2-((3a*R*,5*R*,5a*S*,8a*S*,8b*R*)-2,2,7,7-tetramethyltetrahydro-5*H*-bis([1,3]dioxolo)[4,5-*b*:4',5'-*d*]pyran-5-yl)-6,7,9,10-tetrahydro-8*H*-6,10-methanoazepino[4,5-*g*]quinoxalin-8-yl)ethan-1-one and 2,2,2-trifluoro-1-((6*R*,10*S*)-2-((3a*R*,5*R*,5a*S*,8a*S*,8b*R*)-2,2,7,7-tetramethyltetrahydro-5*H*-bis([1,3]dioxolo)[4,5-*b*:4',5'-*d*]pyran-5-yl)-6,7,9,10-tetrahydro-8*H*-6,10-methanoazepino[4,5-*g*]quinoxalin-8-yl)ethan-1-one(39)



Prepared from the o-phenylenediamine derivative of varenicline (0.1 mmol, 1.0 equiv.) and **SI-1-8** (0.15 mmol, 1.5 equiv.) according to the general procedure **4**. Purification by flash column (Petroleum Ether: Ethyl acetate, 8:1) afforded **39** (19.3 mg, 36% yield) as yellow oil.

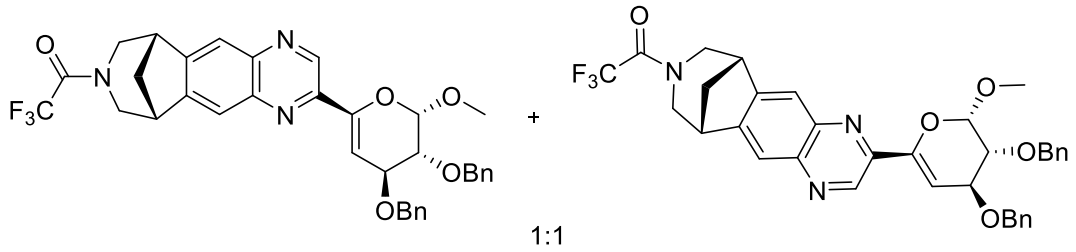
TLC: R*f* = 0.25 (Petroleum Ether: Ethyl acetate, 4:1)

^{1}H NMR (300 MHz, $CDCl_3$): δ 8.99 (t, *J* = 3.4 Hz, 1H), 7.89 (s, 1H), 7.83 (d, *J* = 5.0 Hz, 1H), 5.79 (d, *J* = 4.9 Hz, 1H), 5.17 (t, *J* = 2.5 Hz, 1H), 4.81 – 4.66 (m, 2H), 4.45 (t, *J* = 7.8 Hz, 2H), 4.13 – 3.99 (m, 1H), 3.67 (dd, *J* = 12.7, 5.1 Hz, 1H), 3.53 (d, *J* = 14.1 Hz, 2H), 3.28 (dd, *J* = 13.1, 6.3 Hz, 1H), 2.54 – 2.41 (m, 1H), 2.12 (d, *J* = 11.3 Hz, 1H), 1.61 (d, *J* = 3.1 Hz, 3H), 1.45 (dd, *J* = 14.9, 4.1 Hz, 3H), 1.39 (s, 3H), 1.29 – 1.24 (m, 3H).

^{13}C NMR (126 MHz, $CDCl_3$): δ 154.37 – 151.08 (m), 146.66, 146.28, 146.11, 144.35, 144.12, 143.93, 141.76, 141.66, 122.74, 122.53, 122.50, 122.46, 122.41, 122.22, 119.26 – 113.08 (m), 109.66, 109.59, 109.51, 109.17, 109.13, 109.09, 109.06, 96.66, 96.64, 70.96, 70.93, 70.87, 70.84, 70.69, 70.64, 70.60, 70.56, 50.83, 48.74, 48.67, 41.84, 41.71, 39.87, 39.82, 39.78, 39.73, 39.69, 39.62, 29.72, 26.21, 26.16, 25.92, 25.90, 24.98, 24.94, 24.24, 24.16, 24.13.

HRMS (ESI): m/z calculated for $C_{26}H_{28}F_3N_3NaO_6^+$ [M+Na] $^+$, 558.1822; found, 558.1826.

1-((6*S*,10*R*)-2-((2*S*,3*R*,4*S*)-3,4-bis(benzyloxy)-2-methoxy-3,4-dihydro-2*H*-pyran-6-yl)-6,7,9,10-tetrahydro-8*H*-6,10-methanoazepino[4,5-*g*]quinoxalin-8-yl)-2,2,2-trifluoroethan-1-one and 1-((6*R*,10*S*)-2-((2*S*,3*R*,4*S*)-3,4-bis(benzyloxy)-2-methoxy-3,4-dihydro-2*H*-pyran-6-yl)-6,7,9,10-tetrahydro-8*H*-6,10-methanoazepino[4,5-*g*]quinoxalin-8-yl)-2,2,2-trifluoroethan-1-one(40)



Prepared from the o-phenylenediamine derivative of varenicline (0.1 mmol, 1.0 equiv.) and **SI-1-1** (0.15 mmol, 1.5 equiv.) according to the general procedure **4**. Purification by flash column (Petroleum Ether: Ethyl acetate, 8:1) afforded **40** (25.3 mg, 40% yield) as yellow oil.

TLC: R*f* = 0.25 (Petroleum Ether: Ethyl acetate, 4:1)

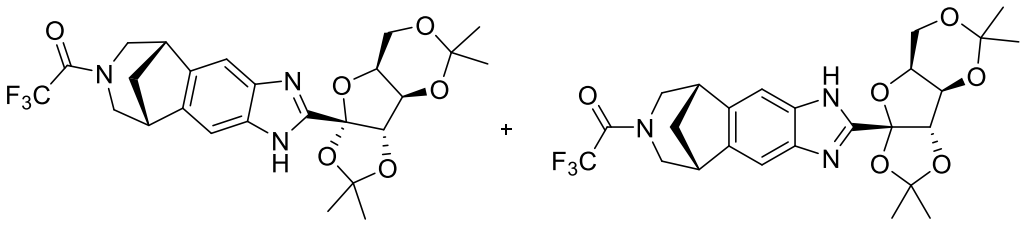
^{1}H NMR (300 MHz, $CDCl_3$): δ 9.12 (d, *J* = 4.9 Hz, 1H), 7.88 (s, 2H), 7.40 – 7.31 (m, 10H), 6.38 (q, *J* = 3.2 Hz, 1H), 5.12 (s, 1H), 4.83 (d, *J* = 7.3 Hz, 2H), 4.75 (t, *J* = 5.6 Hz, 2H), 4.46 (t, *J* = 9.4 Hz, 2H), 4.05 (d, *J* = 12.8 Hz, 1H), 3.94 (d, *J* = 6.8 Hz, 1H), 3.66 (d, *J* = 12.6 Hz, 1H), 3.59 (d, *J* = 6.1 Hz, 3H), 3.53 (d, *J* = 13.8 Hz, 2H), 3.27 (d, *J* = 13.0 Hz, 1H), 2.56 – 2.43 (m, 1H), 2.13 (d, *J* = 11.3 Hz, 1H).

^{13}C NMR (126 MHz, $CDCl_3$): δ 160.20 – 152.75 (m), 147.22, 146.95, 146.69, 146.67, 146.42, 146.07, 145.97, 145.95, 142.65, 142.50, 142.21, 142.16, 142.06, 141.39, 141.35, 141.32, 141.23, 138.33, 138.29, 138.06, 138.04, 128.50, 128.48, 128.16, 128.12, 127.97, 127.95, 127.86, 127.83, 127.82, 127.74, 122.99, 122.94, 122.77, 122.62, 122.38, 120.28 – 111.59 (m), 103.13, 103.02, 102.83, 100.17, 100.08,

100.06, 76.02, 75.82, 73.60, 73.55, 73.32, 73.29, 73.26, 71.68, 71.64, 71.51, 71.42, 57.10, 57.07, 56.99, 56.97, 50.87, 48.71, 41.67, 41.65, 39.91, 39.88, 39.74, 39.72, 29.72.

HRMS (ESI): m/z calculated for $C_{35}H_{33}F_3N_3O_5^+$ $[M+H]^+$, 632.2367; found, 632.2373.

2,2,2-trifluoro-1-((5*S*,9*R*)-2-((3a*S*,3b*R*,7a*S*,8a*S*)-2,2,5,5-tetramethyltetrahydro-8a*H*-[1,3]dioxolo[4',5':4,5]furo[3,2-*d*][1,3]dioxin-8a-yl)-5,6,8,9-tetrahydro-5,9-methanoimidazo[4',5':4,5]benzo[1,2-*d*]azepin-7(1*H*)-yl)ethan-1-one and 2,2,2-trifluoro-1-((5*R*,9*S*)-2-((3a*S*,3b*R*,7a*S*,8a*S*)-2,2,5,5-tetramethyltetrahydro-8a*H*-[1,3]dioxolo[4',5':4,5]furo[3,2-*d*][1,3]dioxin-8a-yl)-5,6,8,9-tetrahydro-5,9-methanoimidazo[4',5':4,5]benzo[1,2-*d*]azepin-7(1*H*)-yl)ethan-1-one(41)



Prepared from the o-phenylenediamine derivative of varenicline (0.2 mmol, 1.0 equiv.) and **SI-1-3** (0.3 mmol, 1.5 equiv.) according to the general procedure **5**. Purification by flash column (Petroleum Ether: Ethyl acetate, 10:1) afforded **41** (37.6 mg, 67% yield) as white solid.

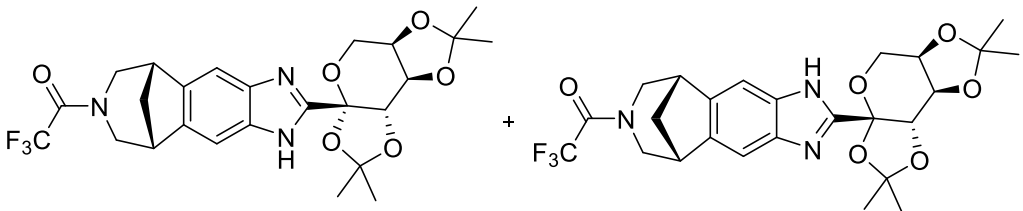
TLC: R*f* = 0.20 (Petroleum Ether: Ethyl acetate, 4:1)

^{1}H NMR (300 MHz, $CDCl_3$): δ 9.90 (s, 1H), 7.58 (s, 1H), 4.67 (d, *J* = 11.7 Hz, 1H), 4.46 (d, *J* = 2.5 Hz, 1H), 4.31 (t, *J* = 9.4 Hz, 2H), 4.24 – 4.16 (m, 2H), 4.10 (q, *J* = 7.1 Hz, 1H), 3.88 (s, 1H), 3.61 – 3.48 (m, 1H), 3.33 (d, *J* = 13.9 Hz, 2H), 3.16 (dd, *J* = 12.9, 5.2 Hz, 1H), 2.50 – 2.35 (m, 1H), 2.02 (s, 1H), 1.68 (d, *J* = 4.9 Hz, 3H), 1.61 (s, 3H), 1.45 (d, *J* = 5.0 Hz, 3H), 1.28 – 1.20 (m, 3H).

^{13}C NMR (75 MHz, $CDCl_3$): δ 157.30 – 149.77 (m), 150.88, 139.30, 129.39, 125.53, 118.91 – 108.52 (m), 105.81, 97.81, 88.98, 88.84, 85.97, 80.57, 73.57, 73.42, 73.22, 72.97, 60.78, 60.64, 50.78, 48.64, 42.60, 42.50, 39.84, 39.65, 29.28, 27.20, 26.26, 18.60, 18.58.

HRMS (ESI): m/z calculated for $C_{25}H_{29}F_3N_3O_6^+$[M+H] $^+$, 524.2003; found, 524.2012.

2,2,2-trifluoro-1-((5*S*,9*R*)-2-((3a*S*,5a*R*,8a*R*,8b*S*)-2,2,7,7-tetramethyltetrahydro-3a*H*-bis([1,3]dioxolo)[4,5-*b*:4',5'-*d*]pyran-3a-yl)-5,6,8,9-tetrahydro-5,9-methanoimidazo[4',5':4,5]benzo[1,2-*d*]azepin-7(1*H*)-yl)ethan-1-one and 2,2,2-trifluoro-1-((5*R*,9*S*)-2-((3a*S*,5a*R*,8a*R*,8b*S*)-2,2,7,7-tetramethyltetrahydro-3a*H*-bis([1,3]dioxolo)[4,5-*b*:4',5'-*d*]pyran-3a-yl)-5,6,8,9-tetrahydro-5,9-methanoimidazo[4',5':4,5]benzo[1,2-*d*]azepin-7(1*H*)-yl)ethan-1-one (42)



Prepared from the o-phenylenediamine derivative of varenicline (0.2 mmol, 1.0 equiv.) and **SI-1-10** (0.3 mmol, 1.5 equiv.) according to the general procedure **5**. Purification by flash column (Petroleum Ether: Ethyl acetate, 10:1) afforded **42** (22.4 mg, 41% yield) as white solid.

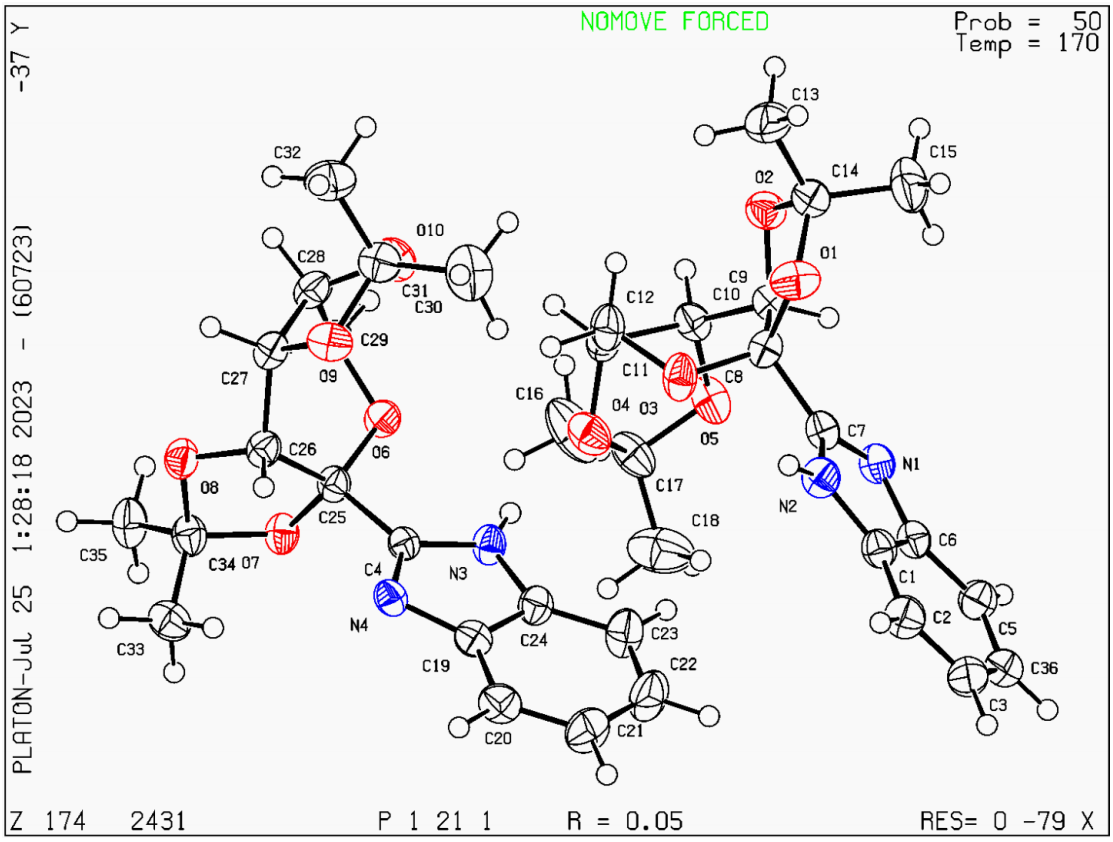
TLC: R*f* = 0.20 (Petroleum Ether: Ethyl acetate, 4:1)

^{1}H NMR (300 MHz, $CDCl_3$): δ 9.65 (s, 1H), 7.59 (s, 1H), 5.12 – 4.90 (m, 1H), 4.75 – 4.64 (m, 1H), 4.32 (d, *J* = 8.6 Hz, 2H), 4.17 – 4.05 (m, 2H), 3.95 (d, *J* = 4.0 Hz, 1H), 3.90 (d, *J* = 4.0 Hz, 1H), 3.56 (dd, *J* = 12.4, 2.0 Hz, 1H), 3.34 (d, *J* = 13.4 Hz, 2H), 3.17 (d, *J* = 12.9 Hz, 1H), 2.44 (dt, *J* = 10.9, 5.2 Hz, 1H), 2.04 (s, 1H), 1.65 (s, 3H), 1.62 (s, 3H), 1.31 (d, *J* = 6.0 Hz, 6H).

^{13}C NMR (75 MHz, $CDCl_3$): δ 158.60 – 153.06 (m), 151.86, 142.86, 139.57, 137.71, 137.71, 134.90, 133.04, 122.26 – 111.88 (m), 110.24, 109.12, 99.36, 83.84, 73.82, 72.43, 70.44, 70.38, 70.09, 61.40, 57.96, 49.78, 49.62, 42.56, 39.78, 39.62, 26.22, 25.91, 25.13, 23.92.

HRMS (ESI): m/z calculated for $C_{25}H_{29}F_3N_3O_6^+$[M+H] $^+$, 524.2003; found, 524.2011.

7. X-ray Crystallographic Data for Compounds 21



Experimental

Single crystal of $C_{18}H_{22}N2O_5$ was obtained by slow diffusion of Petroleum ether into a dichloromethane solution of **21** at room temperature under air. A suitable crystal was selected and on a **XtaLAB AFC12 (RINC): Kappa single** diffractometer. The crystal was kept at 100.0(2) K during data collection. Using Olex2, the structure was

solved with the SHELXT structure solution program using Intrinsic Phasing and refined with the SHELXL refinement package using Least Squares minimisation.

Crystal structure determination of 21

Crystal Data for $C_{18}H_{22}N_2O_5$ (*M* =346.37 g/mol): monoclinic, space group $P2_1$ (no. 4), *a* = 9.1504(4) Å, *b* = 19.6553(6) Å, *c* = 9.7569(4) Å, *β* = 102.207(4) °, *V* = 1715.15(11) $Å^3$, *Z* = 4, *T* = 170.00(10) K, μ(Cu Kα) = 0.816 mm^{-1}, *Dcalc* = 1.341 g/cm^3, 6872 reflections measured (8.998° ≤ 2Θ ≤ 146.4°), 4797 unique (R_{int} = 0.0472, R_{sigma} = 0.0587) which were used in all calculations. The final R_1 was 0.0511 (I > 2σ(I)) and wR_2 was 0.1319 (all data).

Table 1 Crystal data and structure refinement for 21.

Identification code	2431
Empirical formula	$C_{18}H_{22}N_2O_5$
Formula weight	346.37
Temperature/K	170.00(10)
Crystal system	monoclinic
Space group	$P2_1$
a/Å	9.1504(4)
b/Å	19.6553(6)
c/Å	9.7569(4)
α/°	90
β/°	102.207(4)
γ/°	90
Volume/$Å^3$	1715.15(11)
Z	4
$\rho_{calc}g/cm^3$	1.341
μ/mm^{-1}	0.816
F(000)	736.0
Crystal size/mm^3	0.11× 0.12 × 0.15

Radiation	Cu Kα (λ = 1.54184)
2Θ range for data collection/°	8.998 to 146.4
Index ranges	-7 ≤ h ≤ 11, -16 ≤ k ≤ 24, -12 ≤ l ≤ 7
Reflections collected	6872
Independent reflections	4797 [R_{int} = 0.0472, R_{sigma} = 0.0587]
Data/restraints/parameters	4797/1/459
Goodness-of-fit on F^2	1.022
Final R indexes [I>=2σ (I)]	R_1 = 0.0511, wR_2 = 0.1244
Final R indexes [all data]	R_1 = 0.0575, wR_2 = 0.1319
Largest diff. peak/hole / e $Å^{-3}$	0.24/-0.31
Flack parameter	0.3(3)

Table 2 Fractional Atomic Coordinates (×10^4) and Equivalent Isotropic Displacement Parameters ($Å^2$×10^3) for 2431. U_{eq} is defined as 1/3 of the trace of the orthogonalised U_{IJ} tensor.

Atom	*x*	*y*	*z*	U(eq)
O1	3555(4)	4049.7(18)	5045(3)	40.9(8)
O2	5316(3)	3267.9(16)	5899(3)	35.8(7)
O3	5247(3)	4531.5(14)	3892(3)	37.7(7)
O4	7790(4)	4115.9(15)	2982(3)	40.2(7)
O5	6940(3)	3044.5(15)	2902(3)	38.5(7)
N1	3057(4)	3391.3(17)	1753(4)	31.1(7)
N2	2519(4)	4484.4(17)	2048(4)	33.4(8)
C1	1668(5)	4303(2)	757(4)	31.0(9)
C2	642(5)	4663(2)	-231(5)	39.7(10)
C3	-46(5)	4308(3)	-1417(5)	42.4(11)
C5	1297(5)	3272(2)	-619(4)	36.3(9)
C6	2011(5)	3620(2)	579(4)	30.8(9)
C7	3314(5)	3924(2)	2574(4)	29.0(8)
C8	4375(5)	3953(2)	3973(4)	30.4(9)
C9	5266(5)	3292(2)	4429(4)	29.2(8)
C10	6881(5)	3281(2)	4263(4)	31.6(9)
C11	7627(5)	3989(2)	4371(4)	34.3(9)
C12	6684(5)	4532(2)	4799(5)	38.3(10)
C13	4229(6)	3889(3)	7529(5)	50.2(13)
C14	3957(5)	3544(2)	6127(4)	36.9(10)
C15	2762(6)	3010(3)	5964(6)	54.1(13)
C16	9505(6)	3231(3)	2723(8)	69.4(18)
C17	7907(6)	3475(2)	2330(5)	41.5(11)
C18	7308(9)	3548(3)	798(6)	70.0(19)

Table 2 Fractional Atomic Coordinates ($\times 10^4$) and Equivalent Isotropic Displacement Parameters ($Å^2 \times 10^3$) for 2431. U_{eq} is defined as 1/3 of the trace of the orthogonalised U_{IJ} tensor.

Atom	*x*	*y*	*z*	U(eq)
C36	272(5)	3625(3)	-1600(5)	38.7(10)
O6	10075(3)	5360.9(14)	4045(3)	31.4(6)
O7	11380(3)	5907.0(14)	2598(3)	30.6(6)
O8	12137(3)	6701.3(15)	4259(3)	33.9(6)
O9	8984(3)	6715.8(16)	5870(3)	36.0(7)
O10	9254(4)	5646.7(16)	6656(3)	39.5(7)
N3	7828(4)	5470.3(17)	1912(3)	29.7(7)
N4	8150(4)	6586.2(17)	1665(3)	28.4(7)
C4	8704(4)	6026(2)	2287(4)	24.1(7)
C19	6807(5)	6385(2)	807(4)	30.4(8)
C20	5724(5)	6767(3)	-117(4)	37.7(10)
C21	4489(5)	6426(3)	-820(5)	44.2(11)
C22	4279(6)	5734(3)	-642(6)	50.6(13)
C23	5325(5)	5348(3)	242(5)	43.9(11)
C24	6592(4)	5686(2)	957(4)	31.2(9)
C25	10184(4)	5964(2)	3321(4)	27.1(8)
C26	10592(5)	6608(2)	4241(4)	29.4(8)
C27	10463(5)	6543(2)	5765(4)	31.7(9)
C28	10684(5)	5817(2)	6376(4)	34.4(9)
C29	11091(5)	5308(2)	5359(4)	33.8(9)
C30	6894(6)	6190(3)	6528(6)	53.6(13)
C31	8576(5)	6279(2)	6878(4)	37.6(10)
C32	9137(6)	6531(3)	8355(5)	50.9(13)
C33	12008(5)	7026(2)	1837(5)	39.3(10)
C34	12388(5)	6479(2)	2944(4)	33.1(9)
C35	13976(5)	6234(3)	3148(5)	42.7(11)

Table 3 Anisotropic Displacement Parameters ($Å^2 \times 10^3$) for 2431. The Anisotropic displacement factor exponent takes the form: $-2\pi^2[h^2a^{*2}U_{11}+2hka^*b^*U_{12}+\ldots]$.

Atom	U_{11}	U_{22}	U_{33}	U_{23}	U_{13}	U_{12}
O1	43.4(19)	46.4(19)	34.2(14)	0.3(13)	11.0(13)	15.3(15)
O2	32.7(16)	39.6(17)	35.6(14)	5.7(13)	8.5(12)	2.7(13)
O3	32.5(16)	21.9(14)	54.9(18)	1.6(13)	0.4(14)	-2.5(12)
O4	53(2)	24.3(15)	46.6(16)	3.2(13)	16.9(15)	-1.4(14)
O5	39.4(18)	28.2(15)	53.8(18)	-5.0(13)	22.9(14)	-1.2(13)
N1	31.2(19)	25.8(17)	36.8(16)	-1.5(14)	8.6(14)	0.1(15)
N2	38(2)	22.1(17)	38.7(18)	0.6(13)	4.8(15)	1.4(15)
C1	30(2)	27(2)	37(2)	1.2(17)	7.8(17)	-0.2(17)
C2	42(3)	27(2)	47(2)	6.4(19)	3(2)	2.2(19)

Table 3 Anisotropic Displacement Parameters ($Å^2 \times 10^3$) for 2431. The Anisotropic displacement factor exponent takes the form: $-2\pi^2[h^2a^{*2}U_{11}+2hka^*b^*U_{12}+\ldots]$.

Atom	U_{11}	U_{22}	U_{33}	U_{23}	U_{13}	U_{12}
C3	39(2)	44(3)	41(2)	11(2)	-0.4(19)	-3(2)
C5	40(2)	34(2)	36(2)	-3.2(18)	8.1(18)	-3.2(19)
C6	27(2)	33(2)	33.4(19)	0.8(16)	8.4(17)	-2.9(17)
C7	27(2)	24.7(19)	36.6(19)	0.3(16)	9.8(16)	0.3(16)
C8	27(2)	31(2)	31.9(19)	-3.4(16)	3.5(16)	-0.3(17)
C9	30(2)	27(2)	32.2(18)	1.5(16)	10.2(16)	0.4(17)
C10	27(2)	29(2)	39(2)	7.7(17)	8.8(17)	3.0(17)
C11	28(2)	34(2)	38(2)	2.7(17)	0.0(17)	-3.5(18)
C12	38(2)	26(2)	49(2)	-4.4(18)	6(2)	-7.7(19)
C13	52(3)	67(4)	34(2)	-7(2)	12(2)	-6(3)
C14	37(2)	42(3)	34(2)	-0.2(18)	10.1(19)	-4(2)
C15	42(3)	56(3)	69(3)	-13(3)	25(3)	-16(2)
C16	52(3)	55(4)	115(5)	21(4)	49(3)	13(3)
C17	50(3)	27(2)	55(2)	4.2(19)	27(2)	1(2)
C18	119(6)	47(3)	50(3)	-1(3)	31(3)	10(3)
C36	41(3)	43(3)	33.4(19)	-0.2(18)	9.6(19)	-8(2)
O6	37.2(16)	20.5(13)	33.5(13)	3.2(11)	0.6(12)	-1.0(12)
O7	28.1(15)	27.2(14)	37.2(14)	-6.4(11)	8.2(12)	-1.0(12)
O8	32.2(15)	32.5(15)	36.2(14)	-5.0(12)	5.5(12)	-6.3(13)
O9	43.2(18)	30.7(15)	35.7(14)	2.6(12)	12.0(13)	9.4(13)
O10	41.2(17)	31.4(16)	47.8(16)	5.0(13)	13.5(14)	3.6(14)
N3	28.6(18)	20.5(16)	38.4(16)	-0.1(13)	3.2(14)	-0.7(14)
N4	28.2(18)	24.0(16)	33.6(15)	3.2(13)	8.2(13)	-0.7(14)
C4	23.5(19)	23.6(19)	26.2(16)	-0.7(14)	7.4(14)	0.2(15)
C19	30(2)	31(2)	32.0(18)	-0.1(16)	10.6(16)	3.1(17)
C20	36(2)	35(2)	41(2)	8.4(18)	7.2(18)	7.8(19)
C21	30(2)	51(3)	47(2)	4(2)	-0.9(19)	10(2)
C22	30(2)	58(3)	58(3)	0(3)	-6(2)	-2(2)
C23	37(3)	36(3)	55(3)	-2(2)	1(2)	-4(2)
C24	24(2)	34(2)	35.3(19)	-1.5(17)	6.1(16)	1.7(17)
C25	29(2)	20.9(18)	30.9(18)	-0.9(15)	4.4(15)	-0.8(16)
C26	32(2)	23.2(19)	31.1(18)	-2.3(16)	3.2(15)	-0.4(17)
C27	30(2)	31(2)	31.8(18)	-3.0(16)	1.4(16)	-1.6(18)
C28	32(2)	37(2)	31.0(19)	0.1(17)	-1.3(16)	1.2(18)
C29	32(2)	30(2)	36(2)	4.3(17)	1.3(17)	3.5(18)
C30	45(3)	47(3)	72(3)	-7(3)	19(3)	6(2)
C31	43(3)	33(2)	37(2)	-1.7(18)	11.0(19)	3(2)
C32	58(3)	60(3)	36(2)	-2(2)	15(2)	5(3)
C33	46(3)	33(2)	41(2)	3.3(18)	14(2)	0(2)
C34	34(2)	28(2)	39(2)	-5.2(17)	9.5(17)	-4.1(17)
C35	29(2)	39(3)	59(3)	-1(2)	6(2)	-4(2)

Table 4 Bond Lengths for 21.

Atom	Atom	Length/Å	Atom	Atom	Length/Å
O1	C8	1.424(5)	O6	C25	1.394(5)
O1	C14	1.440(5)	O6	C29	1.419(5)
O2	C9	1.426(5)	O7	C25	1.426(5)
O2	C14	1.417(5)	O7	C34	1.449(5)
O3	C8	1.401(5)	O8	C26	1.422(5)
O3	C12	1.422(5)	O8	C34	1.419(5)
O4	C11	1.416(5)	O9	C27	1.421(5)
O4	C17	1.426(6)	O9	C31	1.415(5)
O5	C10	1.418(5)	O10	C28	1.432(5)
O5	C17	1.421(5)	O10	C31	1.426(5)
N1	C6	1.402(5)	N3	C4	1.359(5)
N1	C7	1.309(5)	N3	C24	1.372(5)
N2	C1	1.380(5)	N4	C4	1.306(5)
N2	C7	1.360(5)	N4	C19	1.390(5)
C1	C2	1.389(6)	C4	C25	1.513(5)
C1	C6	1.398(6)	C19	C20	1.406(6)
C2	C3	1.384(7)	C19	C24	1.401(6)
C3	C36	1.394(7)	C20	C21	1.367(7)
C5	C6	1.392(6)	C21	C22	1.390(8)
C5	C36	1.378(6)	C22	C23	1.373(7)
C7	C8	1.500(6)	C23	C24	1.389(6)
C8	C9	1.547(6)	C25	C26	1.551(5)
C9	C10	1.520(6)	C26	C27	1.522(5)
C10	C11	1.545(6)	C27	C28	1.542(6)
C11	C12	1.487(6)	C28	C29	1.510(6)
C13	C14	1.500(6)	C30	C31	1.514(7)
C14	C15	1.500(7)	C31	C32	1.507(6)
C16	C17	1.509(7)	C33	C34	1.512(6)
C17	C18	1.486(7)	C34	C35	1.504(6)

Table 5 Bond Angles for 21.

Atom	Atom	Atom	Angle/°	Atom	Atom	Atom	Angle/°
C8	O1	C14	110.7(3)	C25	O6	C29	114.6(3)
C14	O2	C9	107.6(3)	C25	O7	C34	110.0(3)
C8	O3	C12	115.4(3)	C34	O8	C26	107.4(3)
C11	O4	C17	107.7(3)	C31	O9	C27	107.5(3)
C10	O5	C17	108.9(3)	C31	O10	C28	105.7(3)
C7	N1	C6	104.3(3)	C4	N3	C24	106.8(3)
C7	N2	C1	106.8(3)	C4	N4	C19	104.3(3)

Table 5 Bond Angles for 21.

Atom	Atom	Atom	Angle/°	Atom	Atom	Atom	Angle/°
N2	C1	C2	132.0(4)	N3	C4	C25	120.5(3)
N2	C1	C6	105.3(3)	N4	C4	N3	113.8(3)
C2	C1	C6	122.7(4)	N4	C4	C25	125.7(4)
C3	C2	C1	116.3(4)	N4	C19	C20	130.4(4)
C2	C3	C36	121.6(4)	N4	C19	C24	110.0(3)
C36	C5	C6	117.8(4)	C24	C19	C20	119.7(4)
C1	C6	N1	109.8(3)	C21	C20	C19	117.2(4)
C5	C6	N1	130.3(4)	C20	C21	C22	122.5(4)
C5	C6	C1	119.9(4)	C23	C22	C21	121.5(5)
N1	C7	N2	113.9(4)	C22	C23	C24	116.6(5)
N1	C7	C8	125.8(4)	N3	C24	C19	105.1(3)
N2	C7	C8	120.3(4)	N3	C24	C23	132.4(4)
O1	C8	C7	109.5(3)	C23	C24	C19	122.5(4)
O1	C8	C9	103.2(3)	O6	C25	O7	109.2(3)
O3	C8	O1	109.1(3)	O6	C25	C4	104.9(3)
O3	C8	C7	104.3(3)	O6	C25	C26	115.8(3)
O3	C8	C9	115.2(3)	O7	C25	C4	110.4(3)
C7	C8	C9	115.5(3)	O7	C25	C26	103.5(3)
O2	C9	C8	102.7(3)	C4	C25	C26	113.0(3)
O2	C9	C10	106.3(3)	O8	C26	C25	103.2(3)
C10	C9	C8	116.6(3)	O8	C26	C27	106.3(3)
O5	C10	C9	109.5(3)	C27	C26	C25	116.0(3)
O5	C10	C11	104.8(3)	O9	C27	C26	108.8(3)
C9	C10	C11	113.9(4)	O9	C27	C28	104.0(3)
O4	C11	C10	103.2(3)	C26	C27	C28	115.1(3)
O4	C11	C12	109.1(4)	O10	C28	C27	103.9(3)
C12	C11	C10	113.1(4)	O10	C28	C29	109.4(4)
O3	C12	C11	109.9(4)	C29	C28	C27	112.9(3)
O1	C14	C13	108.9(4)	O6	C29	C28	109.9(3)
O1	C14	C15	109.8(4)	O9	C31	O10	103.6(3)
O2	C14	O1	104.3(3)	O9	C31	C30	108.5(4)
O2	C14	C13	109.5(4)	O9	C31	C32	112.2(4)
O2	C14	C15	111.1(4)	O10	C31	C30	108.7(4)
C13	C14	C15	112.9(4)	O10	C31	C32	111.1(4)
O4	C17	C16	109.1(4)	C32	C31	C30	112.3(4)
O4	C17	C18	108.5(4)	O7	C34	C33	110.3(3)
O5	C17	O4	103.8(3)	O7	C34	C35	109.4(4)
O5	C17	C16	111.2(4)	O8	C34	O7	103.5(3)
O5	C17	C18	109.0(5)	O8	C34	C33	111.8(4)
C18	C17	C16	114.7(5)	O8	C34	C35	108.4(3)
C5	C36	C3	121.7(4)	C35	C34	C33	113.1(4)

Table 6 Torsion Angles for 21.

A	B	C	D	Angle/°	A	B	C	D	Angle/°
O1	C8	C9	O2	-22.8(4)	O6	C25	C26	O8	101.9(4)
O1	C8	C9	C10	-138.6(3)	O6	C25	C26	C27	-13.9(5)
O2	C9	C10	O5	157.7(3)	O7	C25	C26	O8	-17.6(4)
O2	C9	C10	C11	-85.3(4)	O7	C25	C26	C27	-133.4(4)
O3	C8	C9	O2	96.0(4)	O8	C26	C27	O9	157.3(3)
O3	C8	C9	C10	-19.8(5)	O8	C26	C27	C28	-86.5(4)
O4	C11	C12	O3	60.6(5)	O9	C27	C28	O10	4.3(4)
O5	C10	C11	O4	9.5(4)	O9	C27	C28	C29	122.7(4)
O5	C10	C11	C12	127.1(4)	O10	C28	C29	O6	65.1(4)
N1	C7	C8	O1	-113.7(5)	N3	C4	C25	O6	-20.6(5)
N1	C7	C8	O3	129.6(4)	N3	C4	C25	O7	96.9(4)
N1	C7	C8	C9	2.2(6)	N3	C4	C25	C26	-147.7(4)
N2	C1	C2	C3	-178.3(5)	N4	C4	C25	O6	160.4(4)
N2	C1	C6	N1	0.1(5)	N4	C4	C25	O7	-82.1(5)
N2	C1	C6	C5	178.2(4)	N4	C4	C25	C26	33.4(5)
N2	C7	C8	O1	66.7(5)	N4	C19	C20	C21	-179.3(4)
N2	C7	C8	O3	-49.9(5)	N4	C19	C24	N3	-0.3(4)
N2	C7	C8	C9	-177.4(4)	N4	C19	C24	C23	178.8(4)
C1	N2	C7	N1	-0.4(5)	C4	N3	C24	C19	0.1(4)
C1	N2	C7	C8	179.3(4)	C4	N3	C24	C23	-178.8(5)
C1	C2	C3	C36	0.4(7)	C4	N4	C19	C20	-179.8(4)
C2	C1	C6	N1	-178.9(4)	C4	N4	C19	C24	0.3(4)
C2	C1	C6	C5	-0.8(7)	C4	C25	C26	O8	-137.0(3)
C2	C3	C36	C5	-0.7(7)	C4	C25	C26	C27	107.2(4)
C6	N1	C7	N2	0.4(5)	C19	N4	C4	N3	-0.2(4)
C6	N1	C7	C8	-179.2(4)	C19	N4	C4	C25	178.8(3)
C6	C1	C2	C3	0.4(7)	C19	C20	C21	C22	0.5(7)
C6	C5	C36	C3	0.3(7)	C20	C19	C24	N3	179.8(4)
C7	N1	C6	C1	-0.3(5)	C20	C19	C24	C23	-1.1(7)
C7	N1	C6	C5	-178.1(4)	C20	C21	C22	C23	-1.2(9)
C7	N2	C1	C2	179.0(5)	C21	C22	C23	C24	0.6(8)
C7	N2	C1	C6	0.1(5)	C22	C23	C24	N3	179.2(5)
C7	C8	C9	O2	-142.2(3)	C22	C23	C24	C19	0.5(7)
C7	C8	C9	C10	102.0(4)	C24	N3	C4	N4	0.1(4)
C8	O1	C14	O2	16.3(5)	C24	N3	C4	C25	-179.0(3)
C8	O1	C14	C13	133.1(4)	C24	C19	C20	C21	0.6(6)
C8	O1	C14	C15	-102.8(4)	C25	O6	C29	C28	68.2(4)
C8	O3	C12	C11	66.3(5)	C25	O7	C34	O8	23.5(4)
C8	C9	C10	O5	-88.5(4)	C25	O7	C34	C33	-96.2(4)
C8	C9	C10	C11	28.5(5)	C25	O7	C34	C35	138.8(3)
C9	O2	C14	O1	-32.0(4)	C25	C26	C27	O9	-88.7(4)
C9	O2	C14	C13	-148.4(4)	C25	C26	C27	C28	27.6(5)
C9	O2	C14	C15	86.2(4)	C26	O8	C34	O7	-35.5(4)

Table 6 Torsion Angles for 21.

A	B	C	D	Angle/°	A	B	C	D	Angle/°
C9	C10	C11	O4	-110.2(4)	C26	O8	C34	C33	83.1(4)
C9	C10	C11	C12	7.5(5)	C26	O8	C34	C35	-151.6(4)
C10	O5	C17	O4	-28.8(5)	C26	C27	C28	O10	-114.7(4)
C10	O5	C17	C16	88.4(5)	C26	C27	C28	C29	3.8(5)
C10	O5	C17	C18	-144.2(4)	C27	O9	C31	O10	-36.7(4)
C10	C11	C12	O3	-53.5(5)	C27	O9	C31	C30	-152.1(4)
C11	O4	C17	O5	35.5(4)	C27	O9	C31	C32	83.2(4)
C11	O4	C17	C16	-83.2(5)	C27	C28	C29	O6	-50.1(5)
C11	O4	C17	C18	151.2(5)	C28	O10	C31	O9	39.2(4)
C12	O3	C8	O1	87.6(4)	C28	O10	C31	C30	154.5(4)
C12	O3	C8	C7	-155.6(4)	C28	O10	C31	C32	-81.5(4)
C12	O3	C8	C9	-27.9(5)	C29	O6	C25	O7	82.0(4)
C14	O1	C8	O3	-118.8(4)	C29	O6	C25	C4	-159.7(3)
C14	O1	C8	C7	127.7(4)	C29	O6	C25	C26	-34.4(5)
C14	O1	C8	C9	4.2(4)	C31	O9	C27	C26	142.9(3)
C14	O2	C9	C8	34.2(4)	C31	O9	C27	C28	19.7(4)
C14	O2	C9	C10	157.1(3)	C31	O10	C28	C27	-26.4(4)
C17	O4	C11	C10	-27.5(4)	C31	O10	C28	C29	-147.2(3)
C17	O4	C11	C12	-148.0(4)	C34	O7	C25	O6	-127.5(3)
C17	O5	C10	C9	134.5(4)	C34	O7	C25	C4	117.7(3)
C17	O5	C10	C11	11.9(5)	C34	O7	C25	C26	-3.6(4)
C36	C5	C6	N1	178.1(4)	C34	O8	C26	C25	33.1(4)
C36	C5	C6	C1	0.5(6)	C34	O8	C26	C27	155.6(3)

Table 7 Hydrogen Atom Coordinates (Å×10^4) and Isotropic Displacement Parameters (Å^2×10^3) for 21.

Atom	*x*	*y*	*z*	U(eq)
H2	2542.29	4885.58	2452	40
H2A	423.92	5128.46	-99.03	48
H3A	-751.37	4535.24	-2122.71	51
H5	1509.78	2806.5	-755.21	44
H9	4712.4	2889.58	3952.14	35
H10	7477.74	2970.32	4982.15	38
H11	8628.09	3974.43	5025.62	41
H12A	6582.74	4454.06	5776.64	46
H12B	7166.28	4980.63	4756.42	46
H13A	4573.88	3552.95	8269.13	75
H13B	3298.69	4097.31	7667.9	75
H13C	4993.84	4241.59	7566.57	75
H15A	2665.16	2786.38	5051.75	81
H15B	1808.09	3222.7	6022.18	81

Table 7 Hydrogen Atom Coordinates (Å×10^4) and Isotropic Displacement Parameters (Å^2×10^3) for 21.

Atom	*x*	*y*	*z*	U(eq)
H15C	3031.04	2671.6	6713.12	81
H16A	9767.16	3136.29	3731.07	104
H16B	10171.2	3583.53	2491.57	104
H16C	9615.37	2814.83	2200.45	104
H18A	7354.36	3107.45	337.29	105
H18B	7908.02	3881.5	412.34	105
H18C	6267.5	3702.29	633.47	105
H36	-231.54	3396.21	-2423.71	46
H3	8018.19	5052.35	2221.98	36
H20	5845.69	7240.73	-245.76	45
H21	3744.78	6671.94	-1455.52	53
H22	3391.64	5522.91	-1143.07	61
H23	5188.49	4873.76	358.54	53
H26	10001.99	7007.9	3792.92	35
H27	11188.26	6859.27	6358.62	38
H28	11460.89	5818.4	7267.46	41
H29A	12120.89	5396.19	5236.66	41
H29B	11056.21	4842.38	5735.75	41
H30A	6414.15	6621.44	6680.09	80
H30B	6607.56	5838.46	7131.87	80
H30C	6572.16	6054.25	5543.63	80
H32A	10226.73	6581.77	8534.37	76
H32B	8872.8	6202.43	9018.27	76
H32C	8678.21	6971.4	8471	76
H33A	12218.07	6859.62	951.84	59
H33B	12614.59	7431.81	2139.3	59
H33C	10945.83	7142.73	1702.06	59
H35A	14161.18	5885.36	3881.83	64
H35B	14660.48	6617.02	3425.57	64
H35C	14141.99	6039.96	2267.76	64

8. References

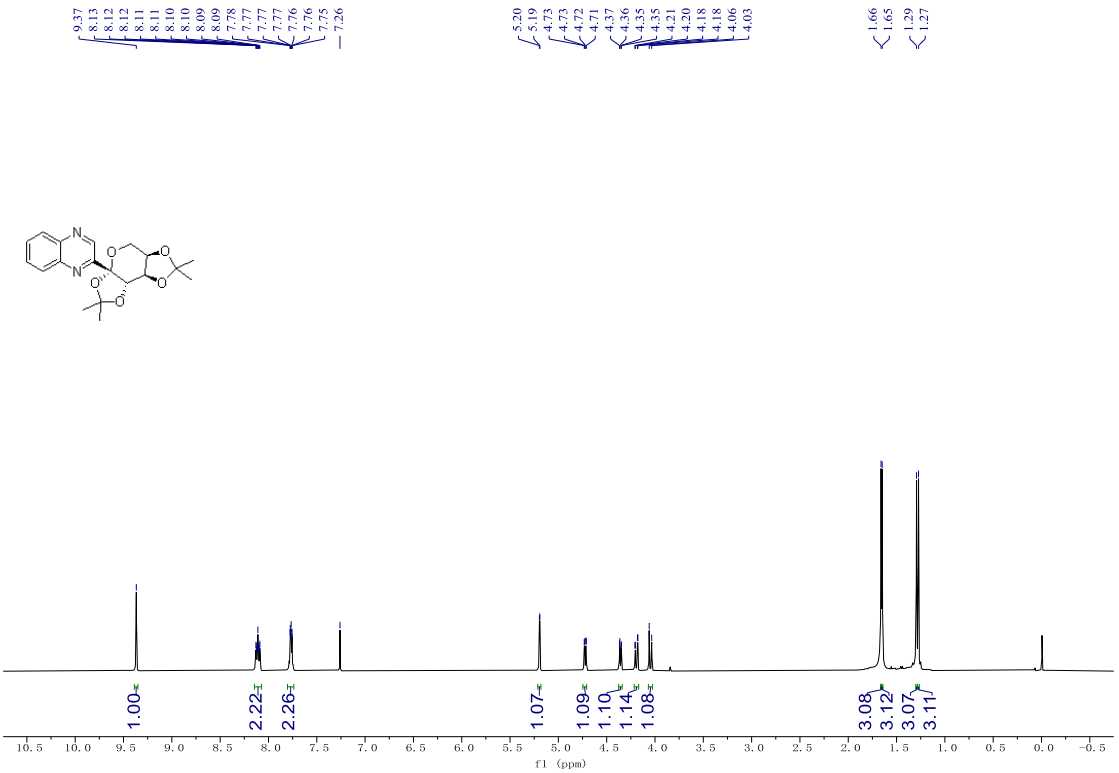
[1] Liu, D.-Y.; Wang, P.-F.; Ruan, Y.-J.; Wang, X.-L.; Hu,X.-Y.; Yang, Q.; Liu, J.; Wen, M.-M.; Zhang, C.-Z.; Xiao, Y.-H.; Liu, X.-G. *Org. Lett.*, **2024**, *26*, 5092-5097.

[2] Liu, D.-Y.; Ruan, Y.-J.; Wang, X.-L.; Hu, X.-Y.; Wang, P.-F.; Wen, M.-M.; Zhang, C.-Z.; Xiao, Y.-H.; Liu, X.-G. *Chem. Commun.*, **2024**, *60*, 10390-10393.

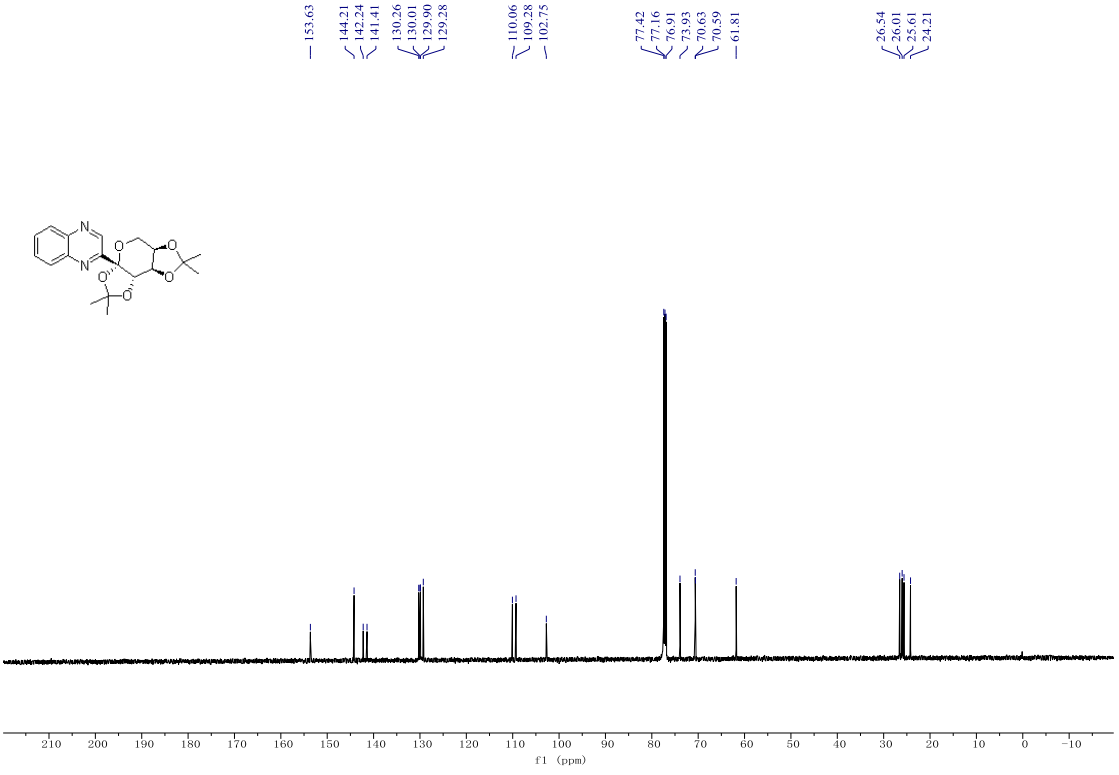
[3] (a) Pandit, R. P.; Kim, S. H.; Lee, Y. R. *Adv. Synth. Catal*. **2016**, *358*, 3586–3599. (b) Mangion, I. K.; Nwamba, I. K.; Shevlin, M.; Huffman, M. A. *Org. Lett*. **2009**, *11*, 3566–3569. (c)Tanwar, B.; Purohit, P.; Raju, B. N.; Kumar, D.; Kommi, D. N. Chakraborti, A. K. *RSC Adv*. **2015**, *5*, 11873–11883. (d) Xu, Y.; Huang, X.; Lv, G.; Lai, R.; Lv, S.; Li, J.; Hai, L; Wu, Y. *Eur. J. Org. Chem.* **2020**, *2022*, 4635-4638. (e) Song, J.-L.; Xiao, L.; Chen, S.-Y.; Zheng, Y.-C.; Liu, Y.-Z.; Zhang, S.-S.; Shu, B. *Adv. Synth. Catal*. **2023**, *365*, 1457-1464.

9. NMR Spectra of Substrates and Products

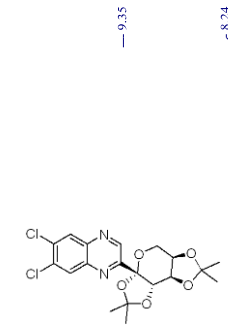
^{1}H NMR (500 MHz, $CDCl_3$) Spectra of compound 1



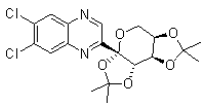
^{13}C NMR (126 MHz, $CDCl_3$) Spectra of compound 1

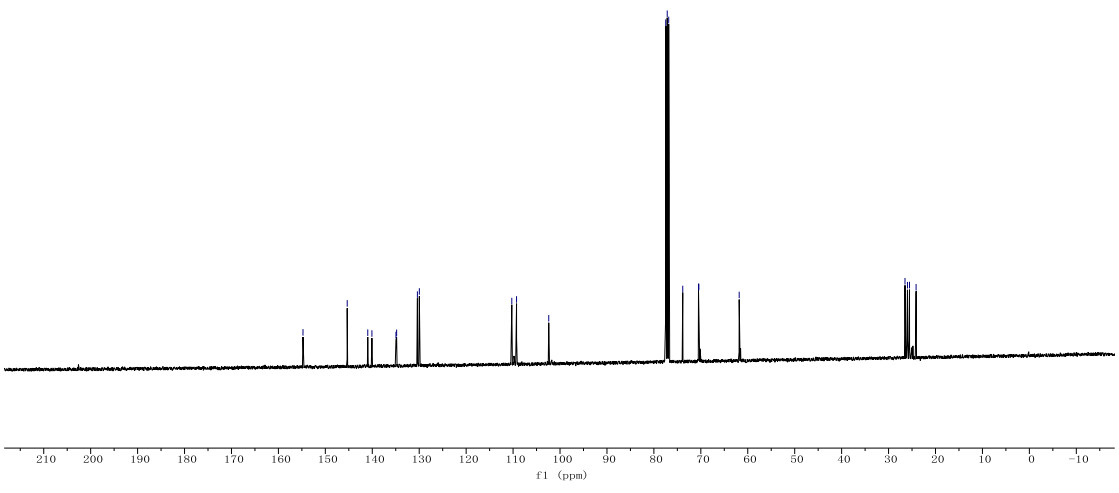


^{1}H NMR (300 MHz, $CDCl_3$) Spectra of compound 2

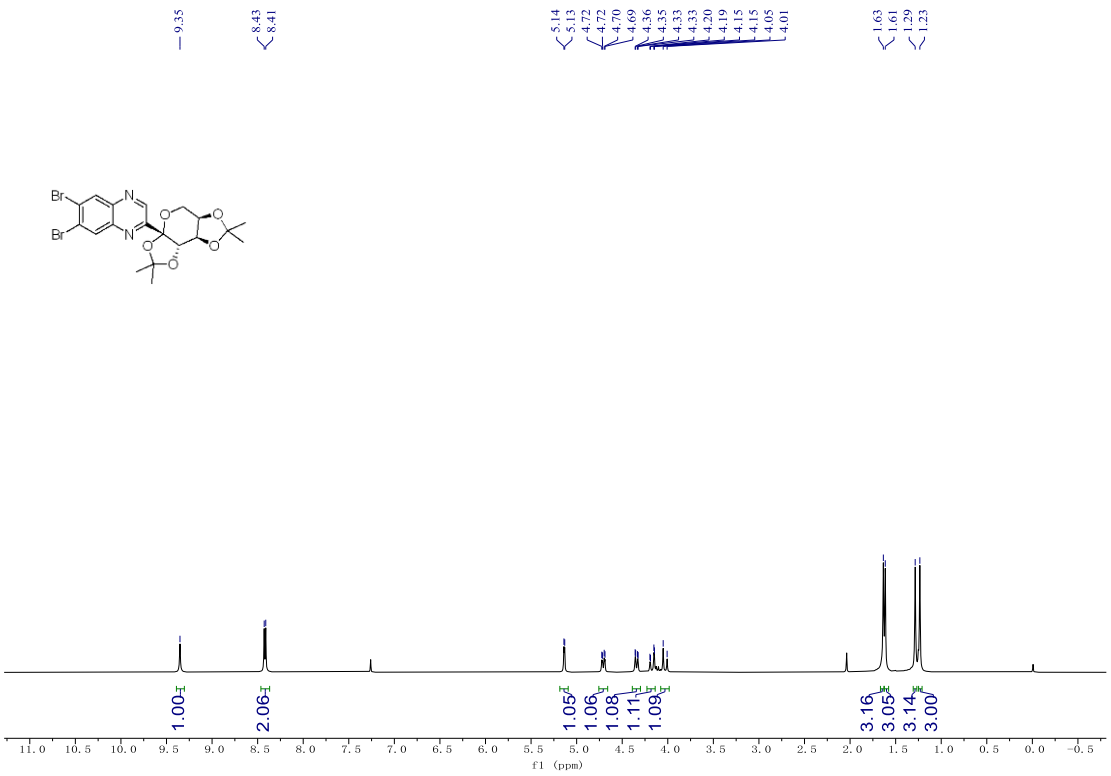


^{13}C NMR (101 MHz, $CDCl_3$) Spectra of compound 2

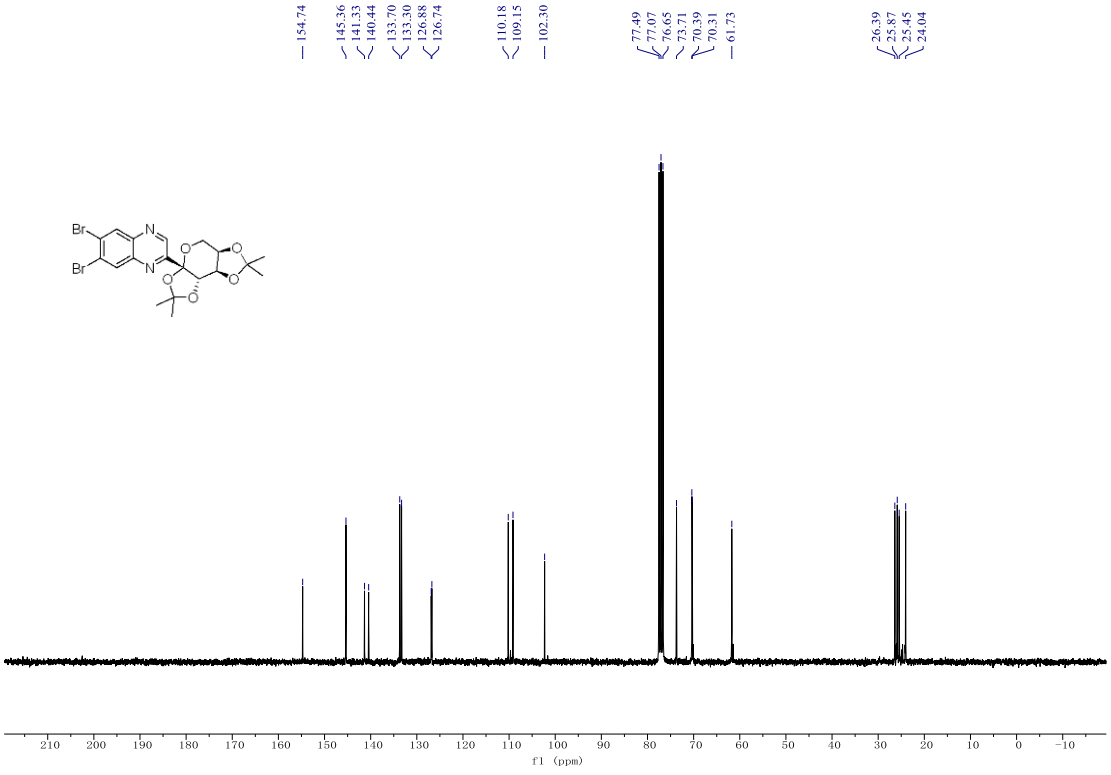




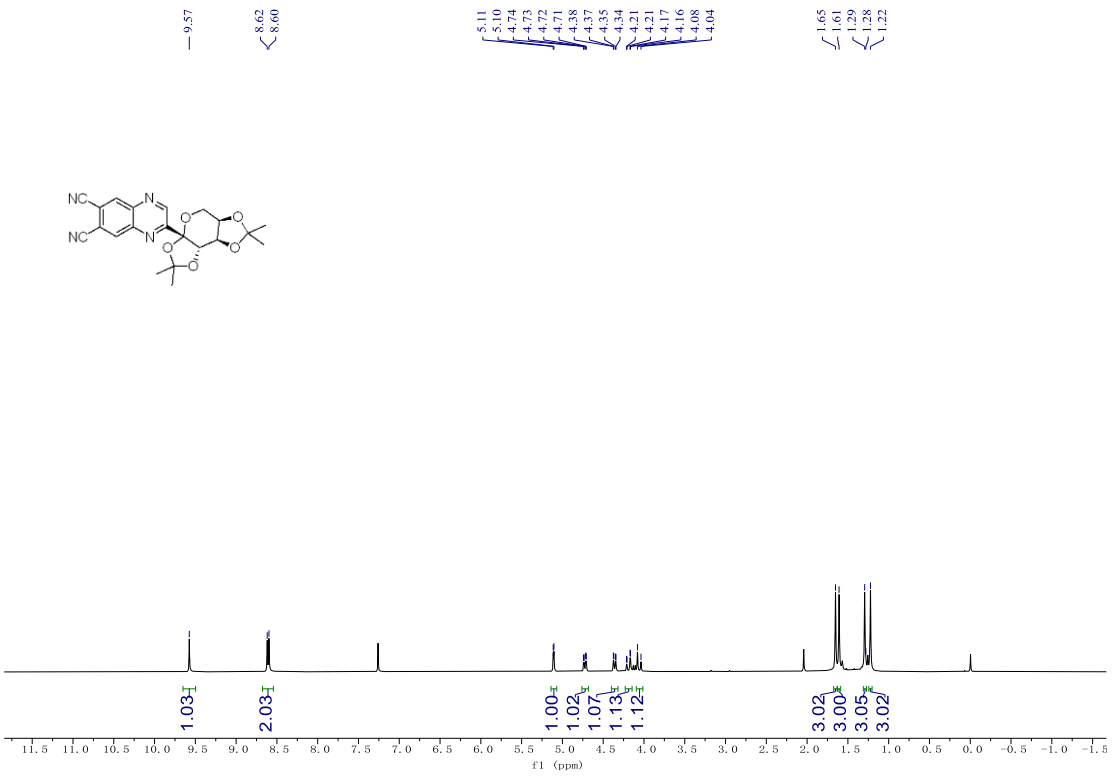
^{1}H NMR (300 MHz, $CDCl_3$) Spectra of compound 3



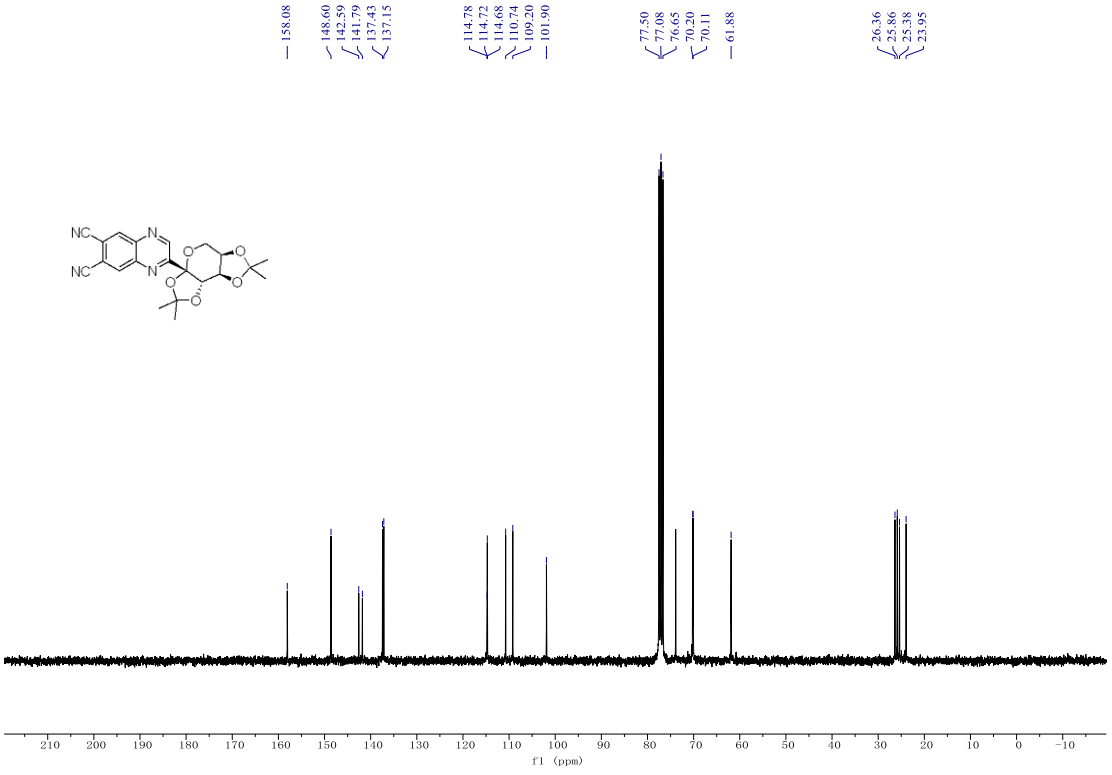
^{13}C NMR (75 MHz, $CDCl_3$) Spectra of compound 3



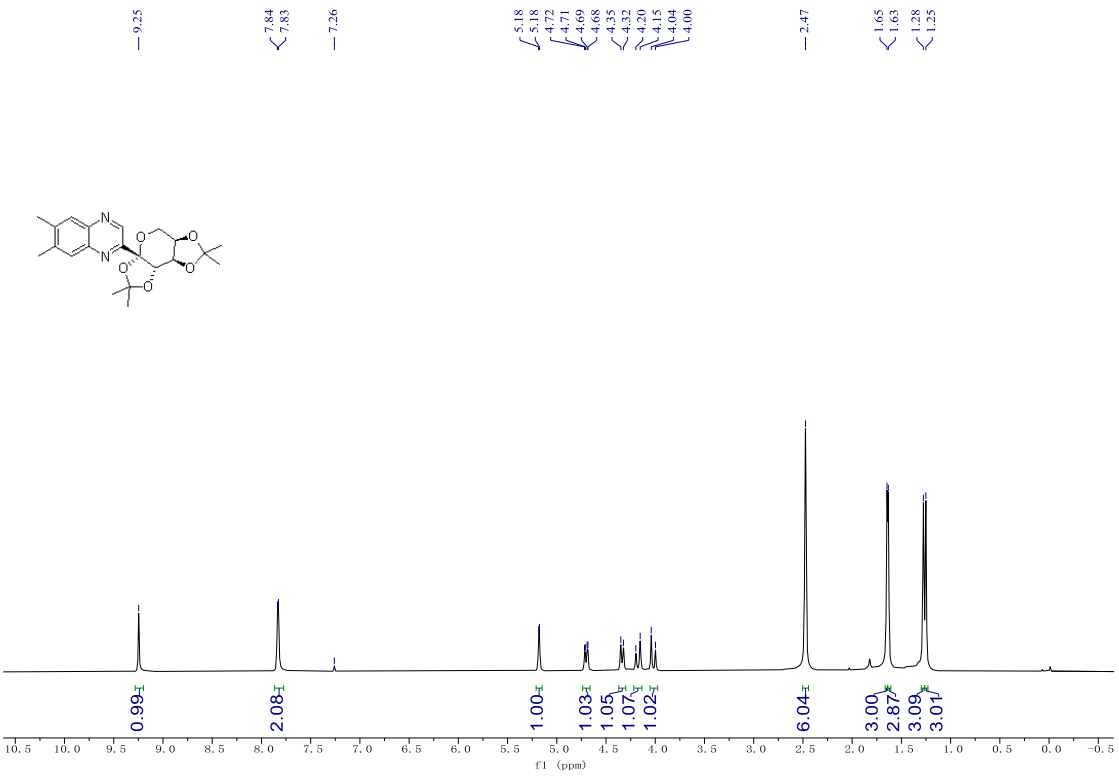
^{1}H NMR (300 MHz, $CDCl_3$) Spectra of compound 4



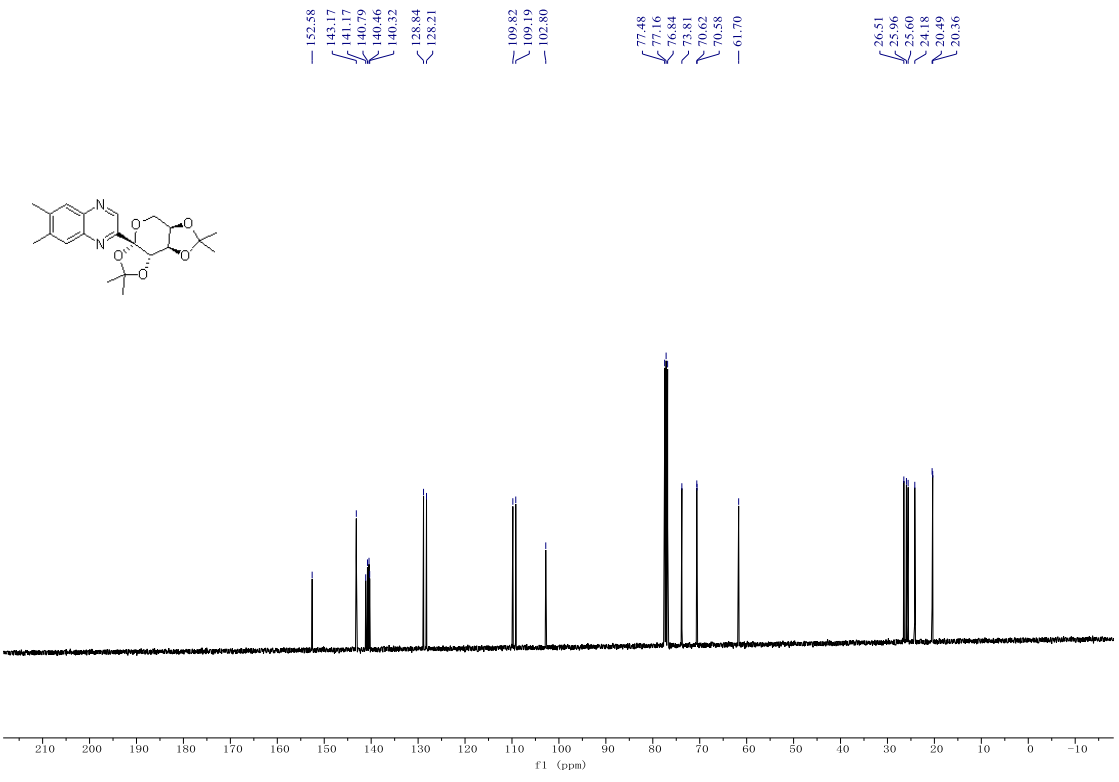
^{13}C NMR (75 MHz, $CDCl_3$) Spectra of compound 4



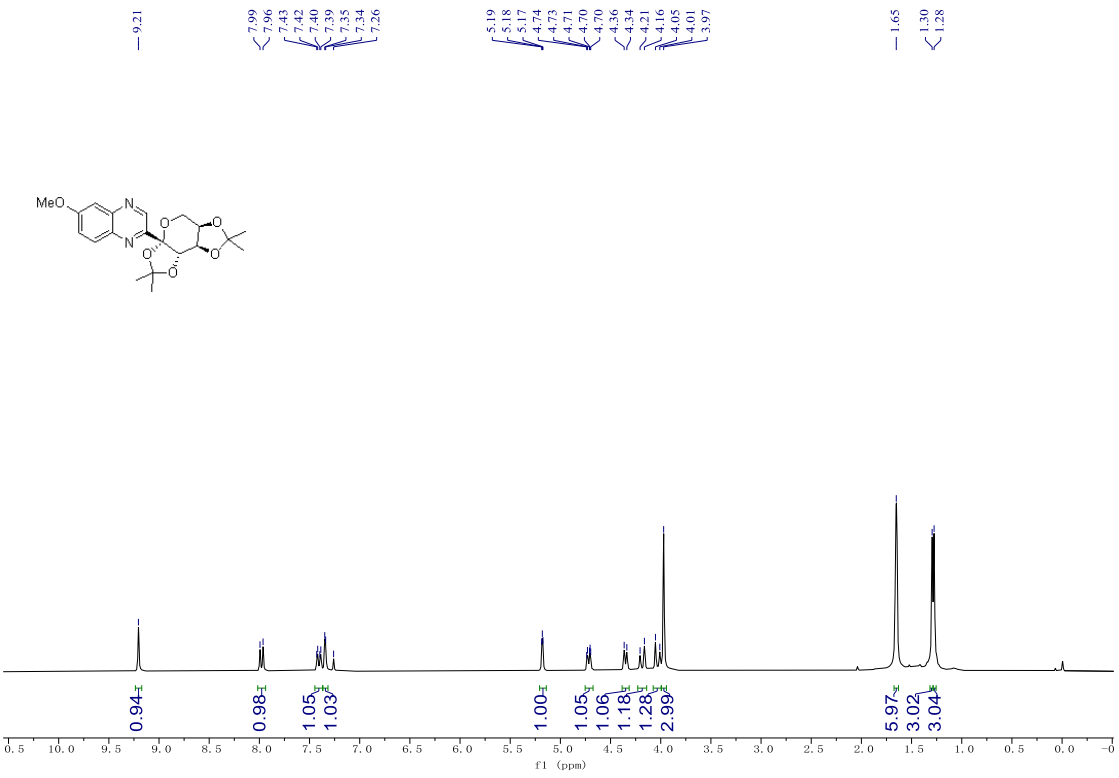
^{1}H NMR (300 MHz, $CDCl_3$) Spectra of compound 5



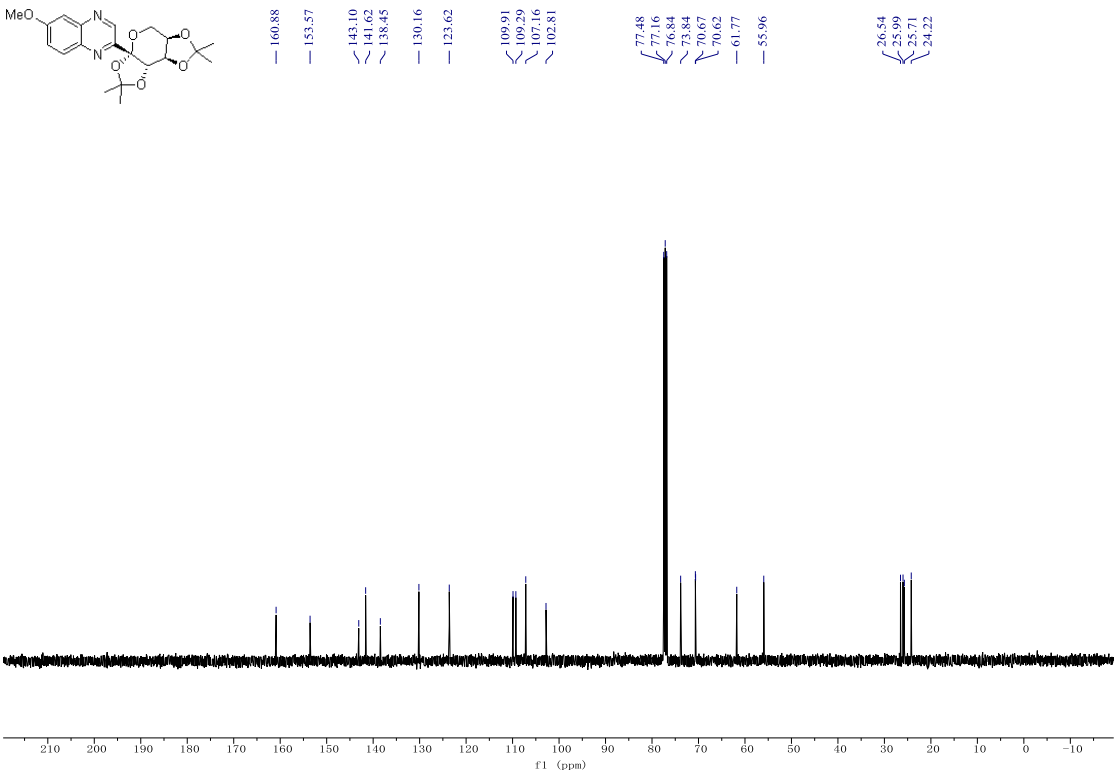
^{13}C NMR (101 MHz, $CDCl_3$) Spectra of compound 5



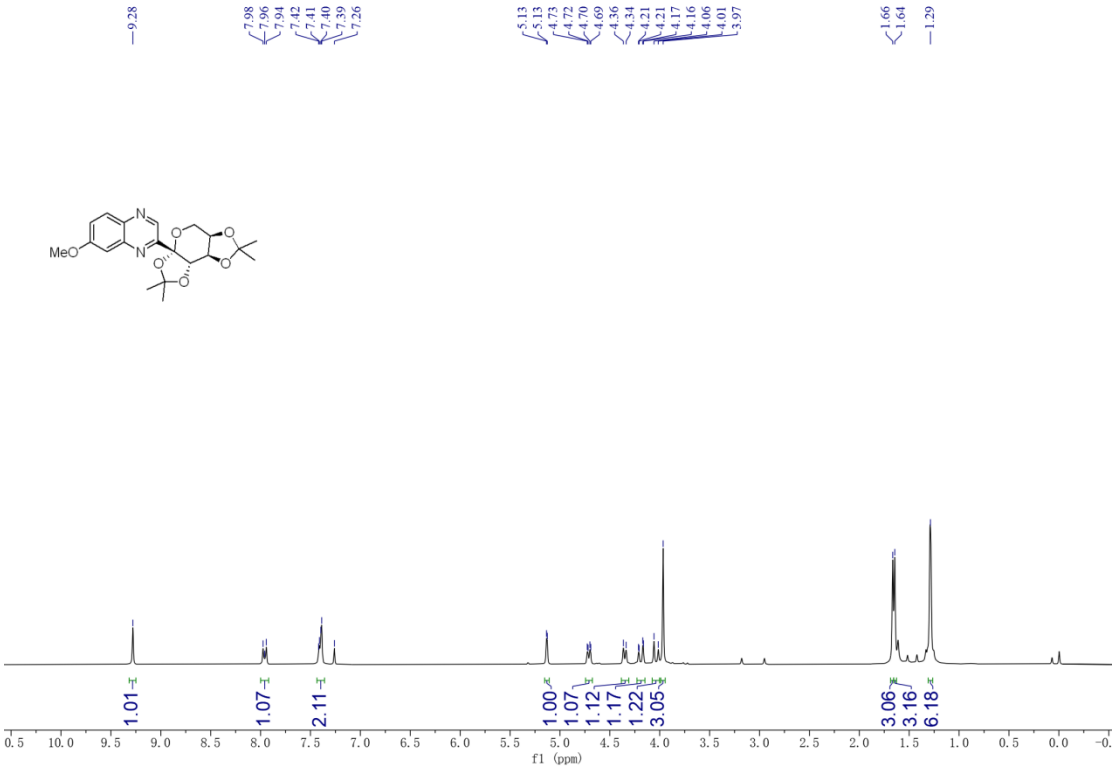
^{1}H NMR (300 MHz, $CDCl_3$) Spectra of compound 6a



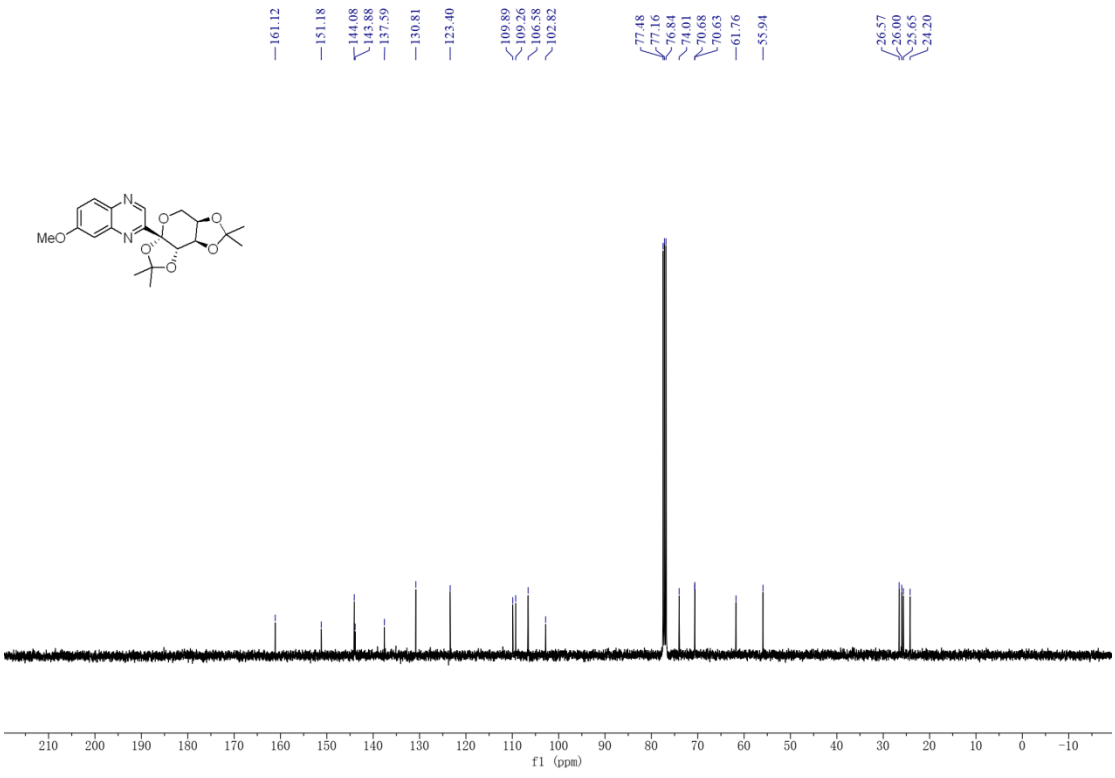
^{13}C NMR (101 MHz, $CDCl_3$) Spectra of compound 6a



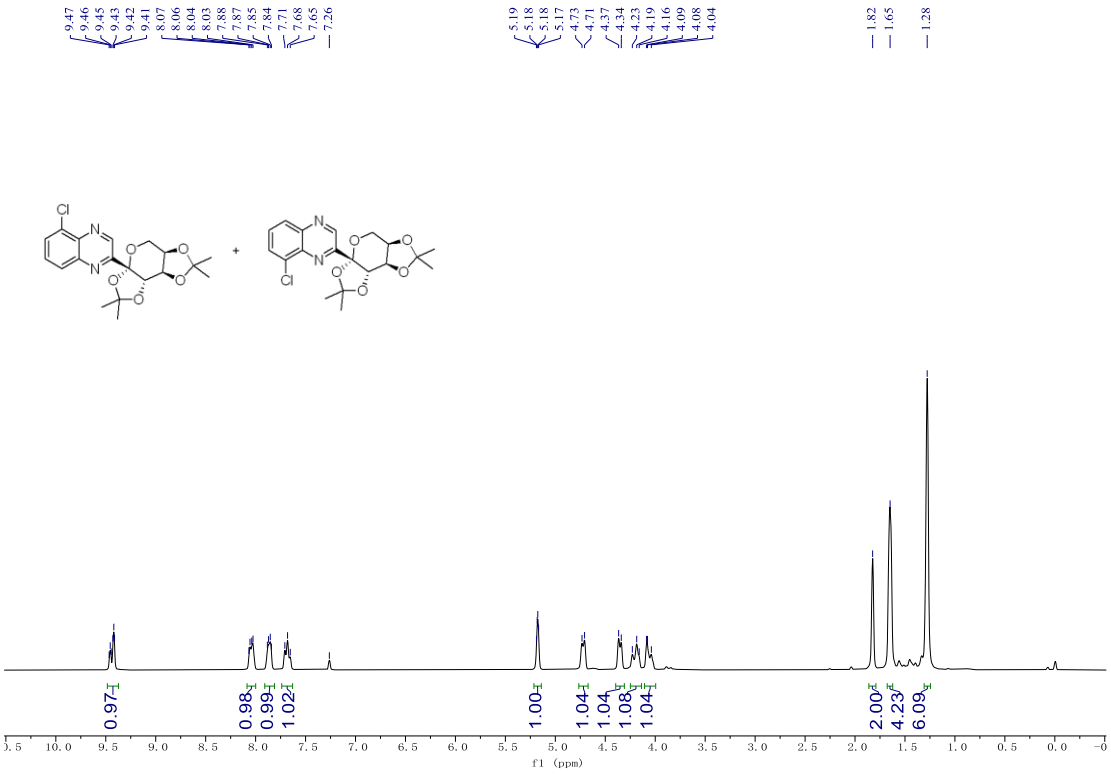
^{1}H NMR (300 MHz, $CDCl_3$) Spectra of compound 6b



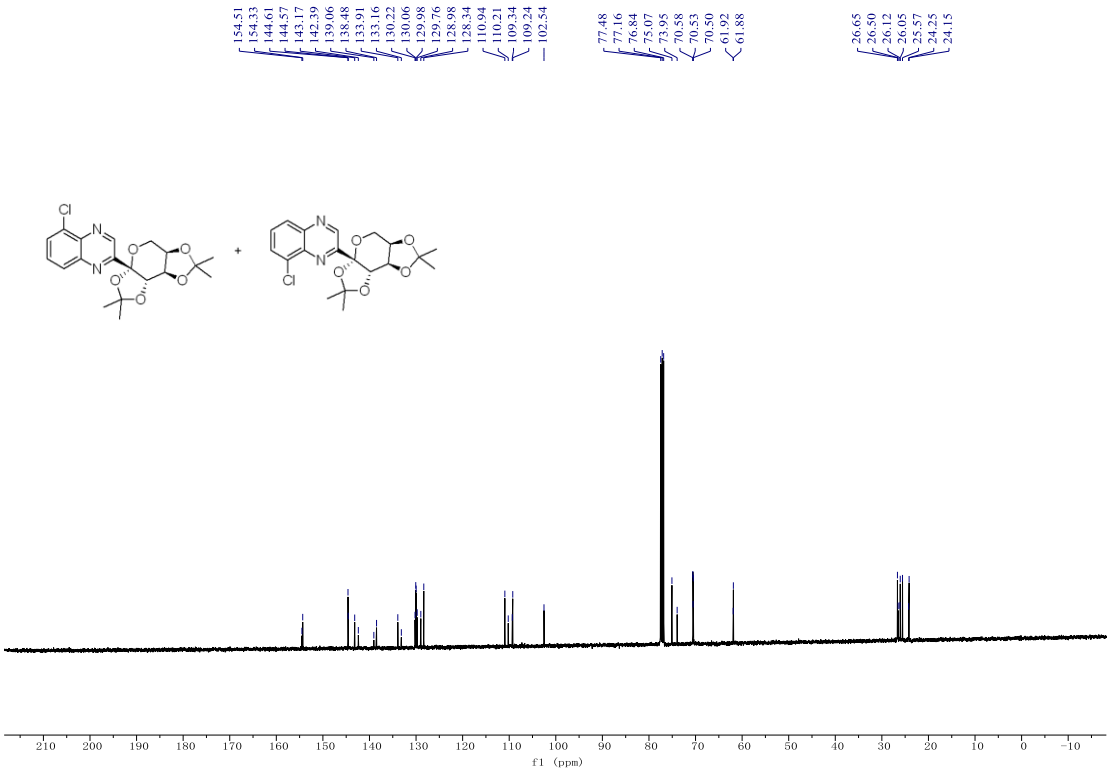
^{13}C NMR (101 MHz, $CDCl_3$) Spectra of compound 6b



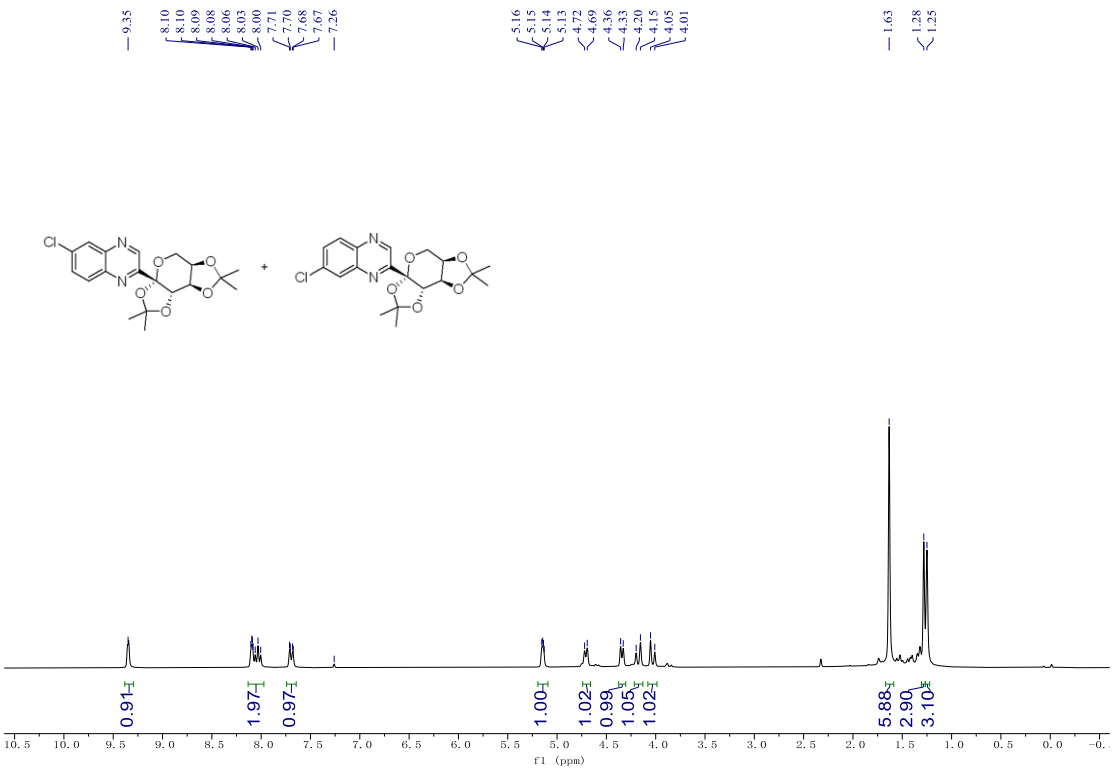
^{1}H NMR (300 MHz, $CDCl_3$) Spectra of compound 7



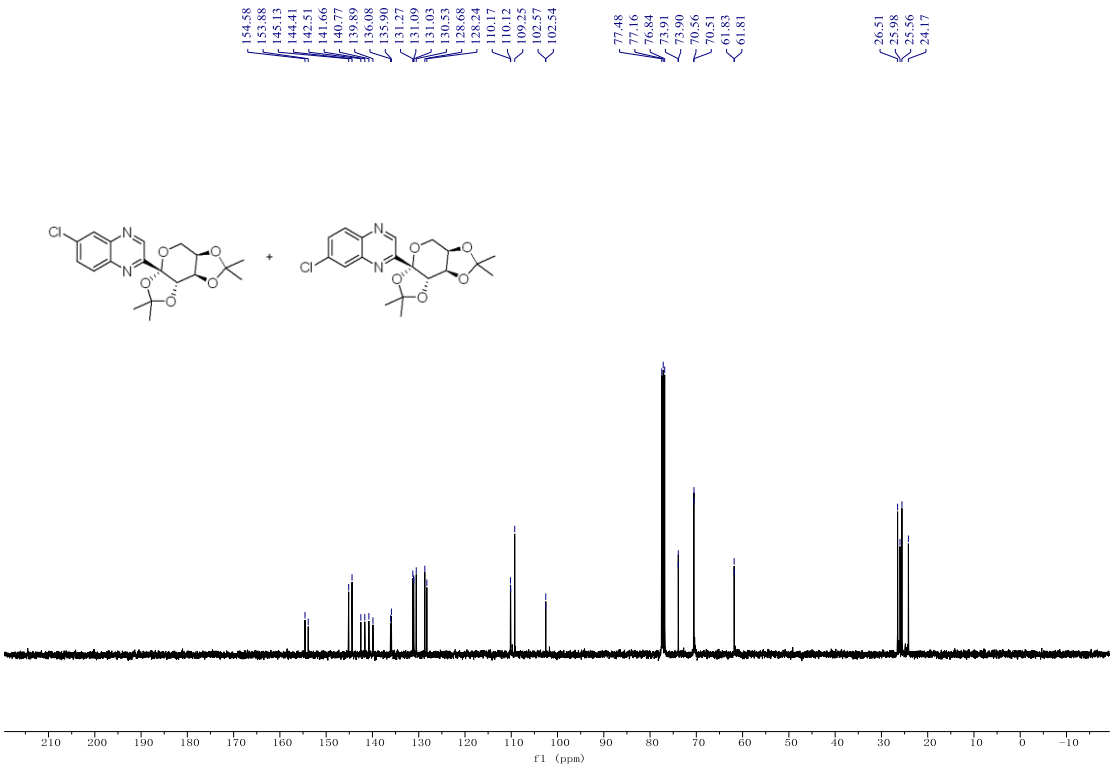
^{13}C NMR (101 MHz, $CDCl_3$) Spectra of compound 7



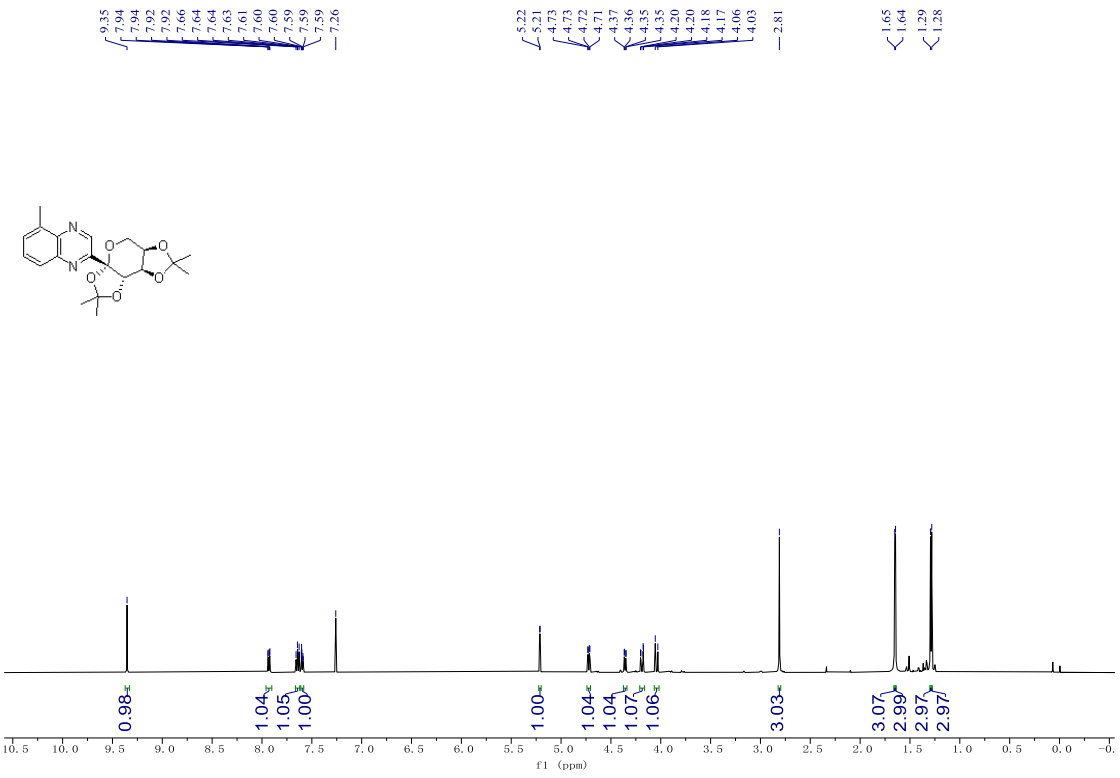
^{1}H NMR (300 MHz, $CDCl_3$) Spectra of compound 8



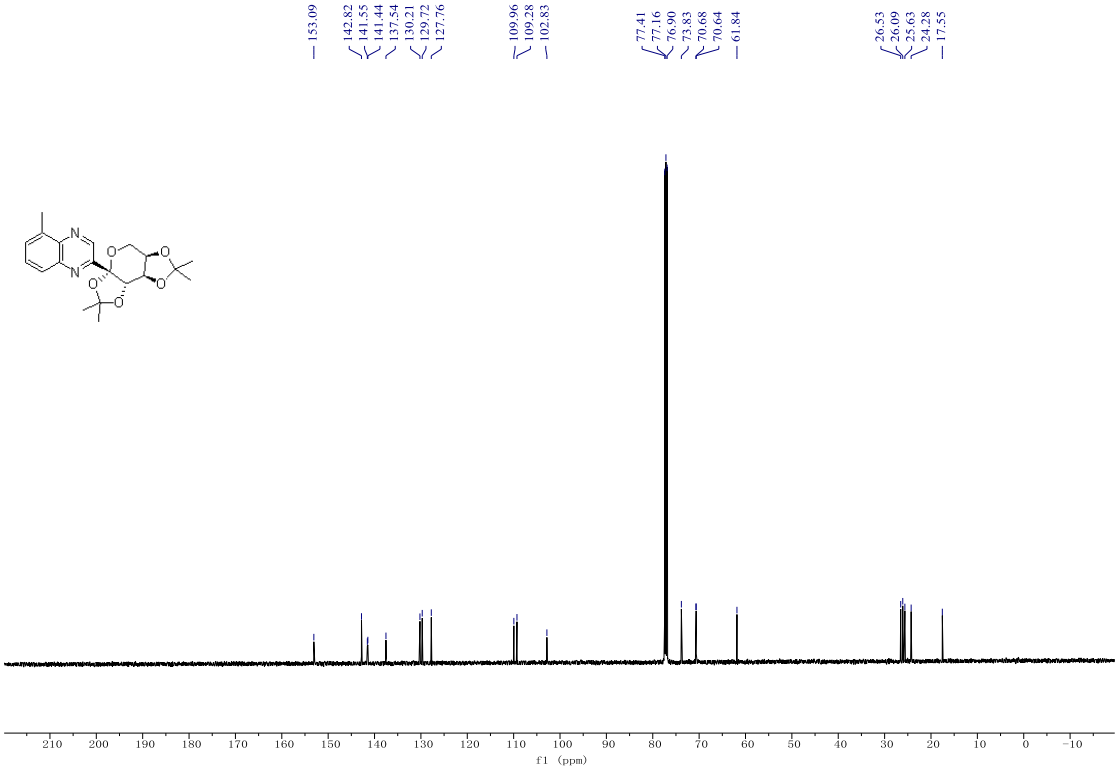
^{13}C NMR (101 MHz, $CDCl_3$) Spectra of compound 8



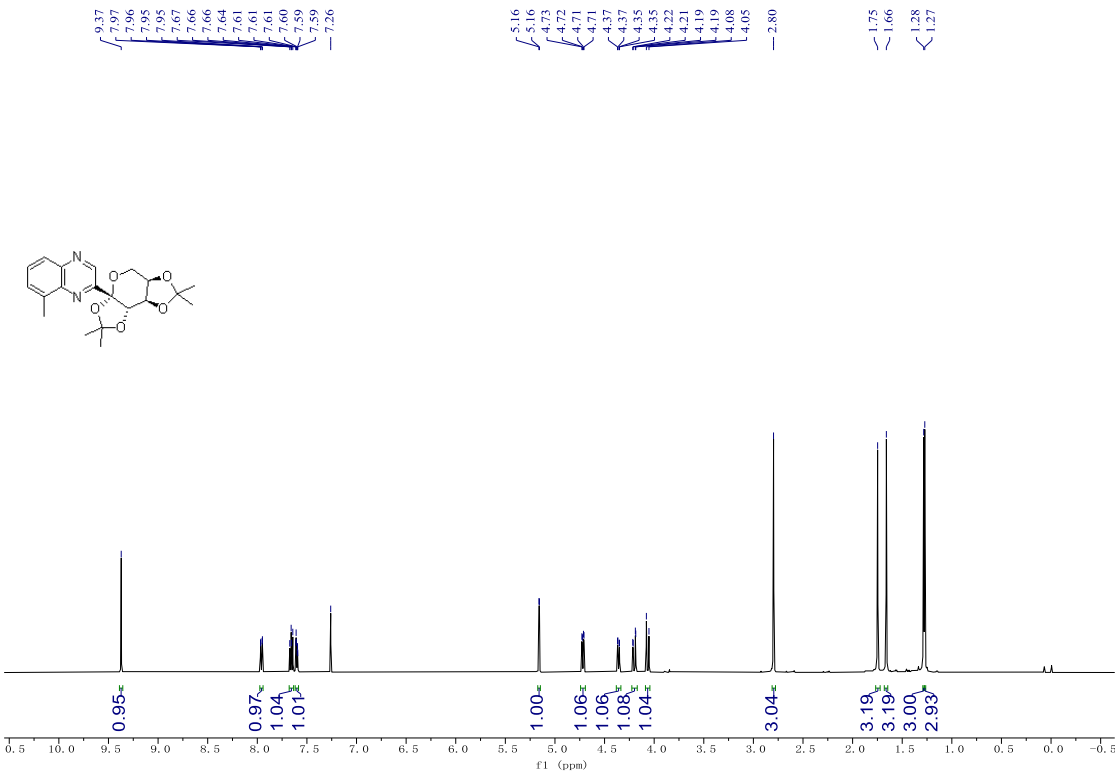
^{1}H NMR (500 MHz, $CDCl_3$) Spectra of compound 9a



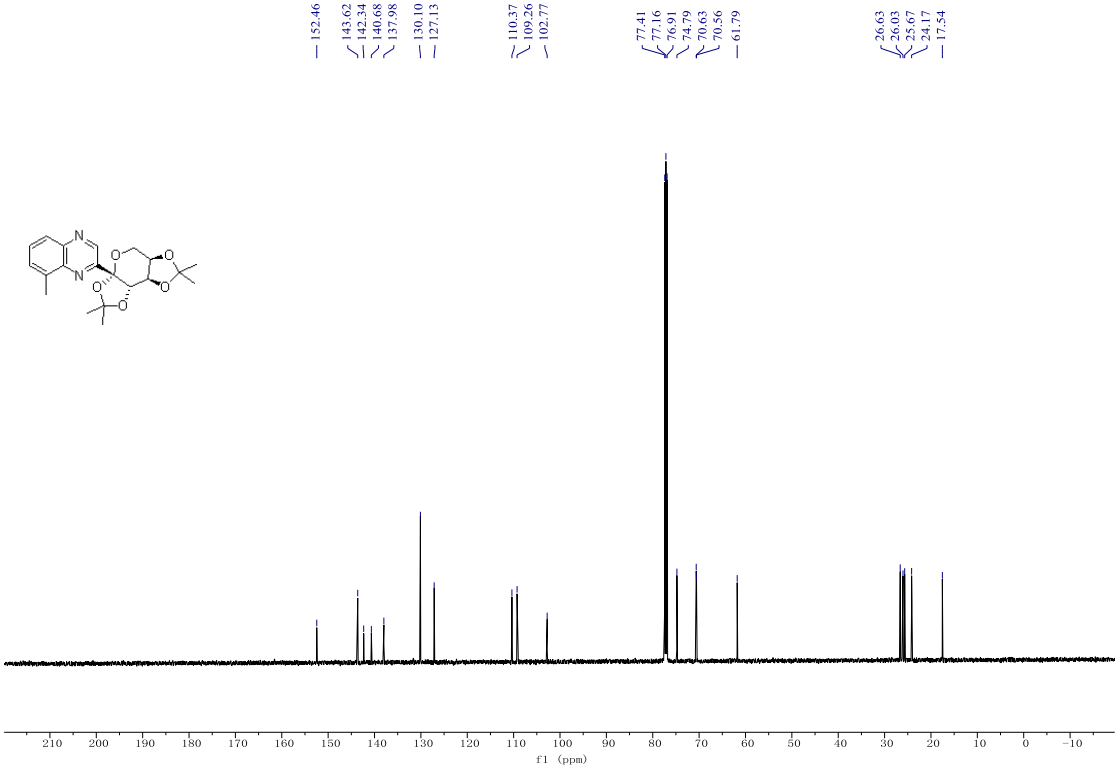
^{13}C NMR (126 MHz, $CDCl_3$) Spectra of compound 9a



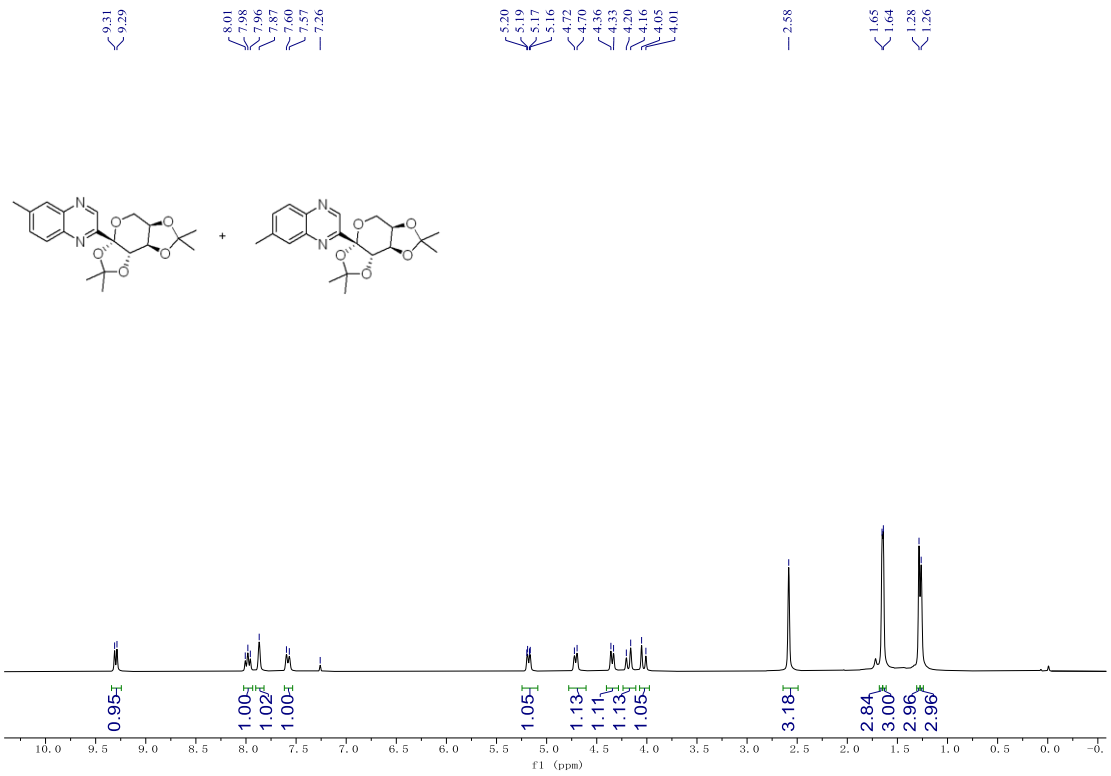
^{1}H NMR (500 MHz, $CDCl_3$) Spectra of compound 9b



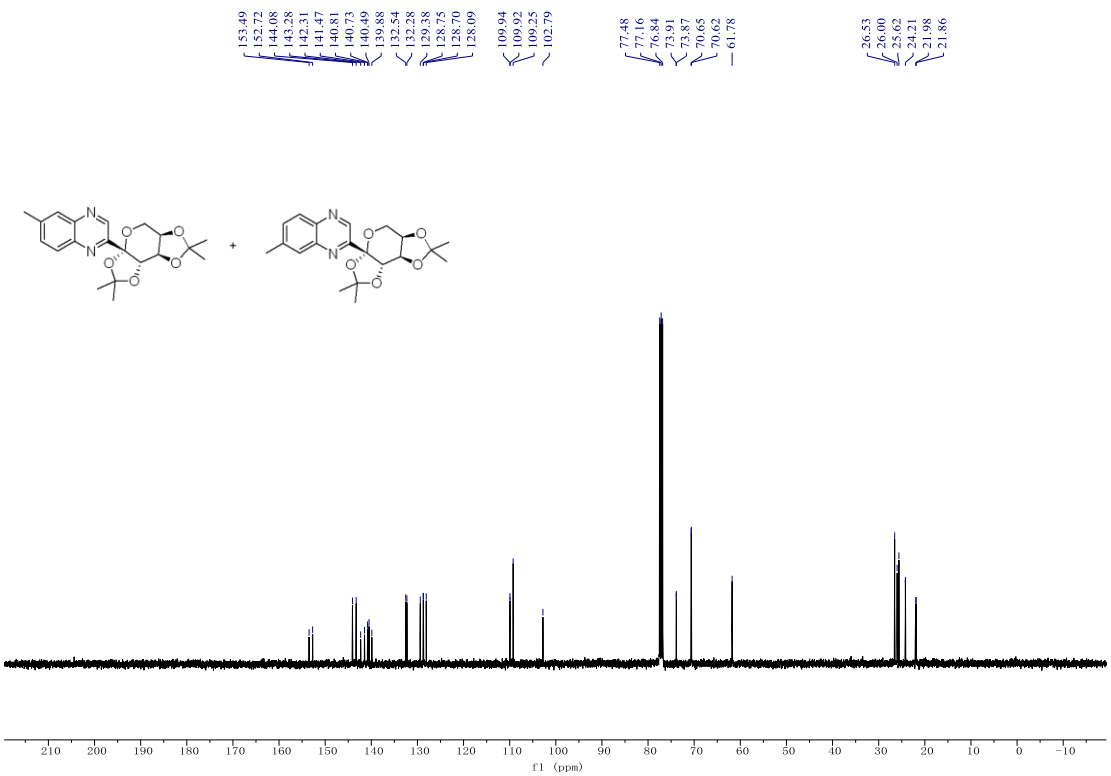
^{13}C NMR (126 MHz, $CDCl_3$) Spectra of compound 9b



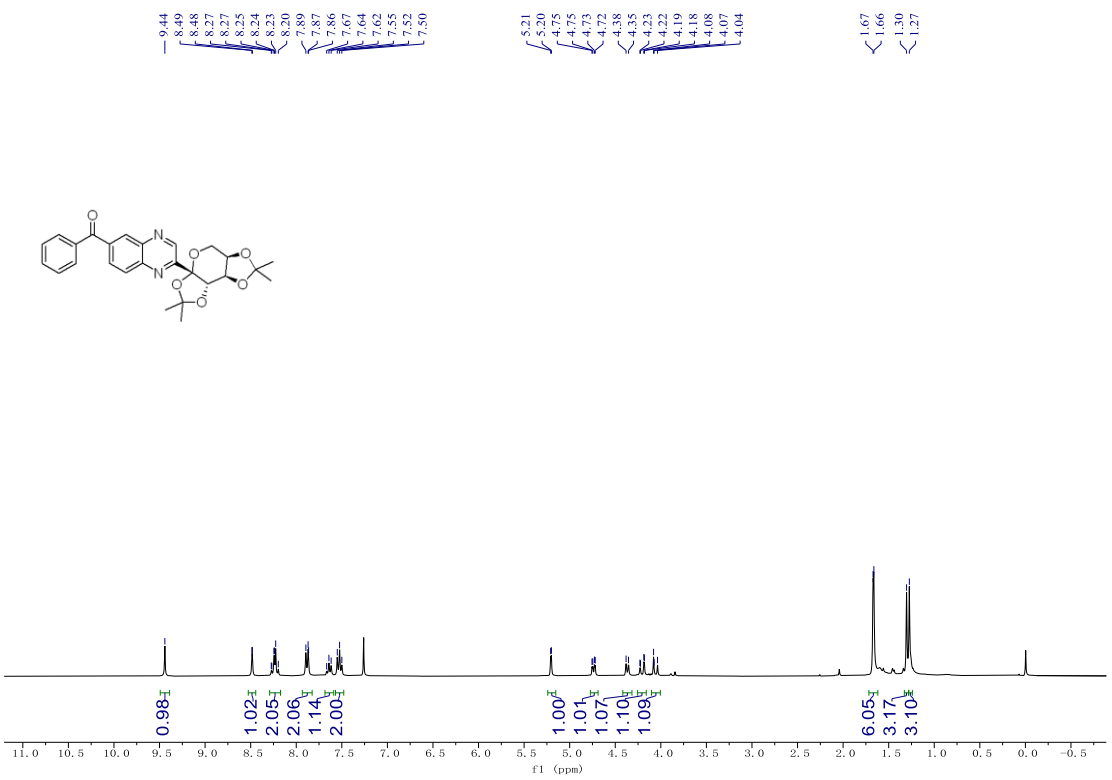
^{1}H NMR (300 MHz, $CDCl_3$) Spectra of compound 10



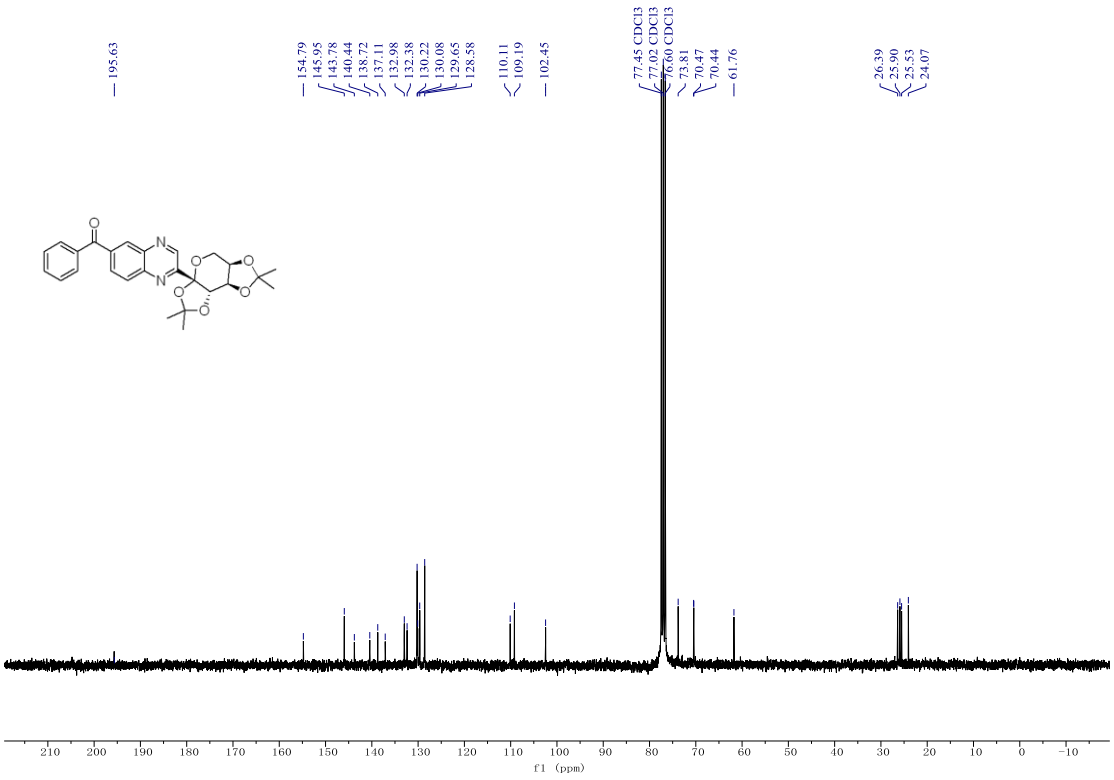
^{13}C NMR (101 MHz, $CDCl_3$) Spectra of compound 10



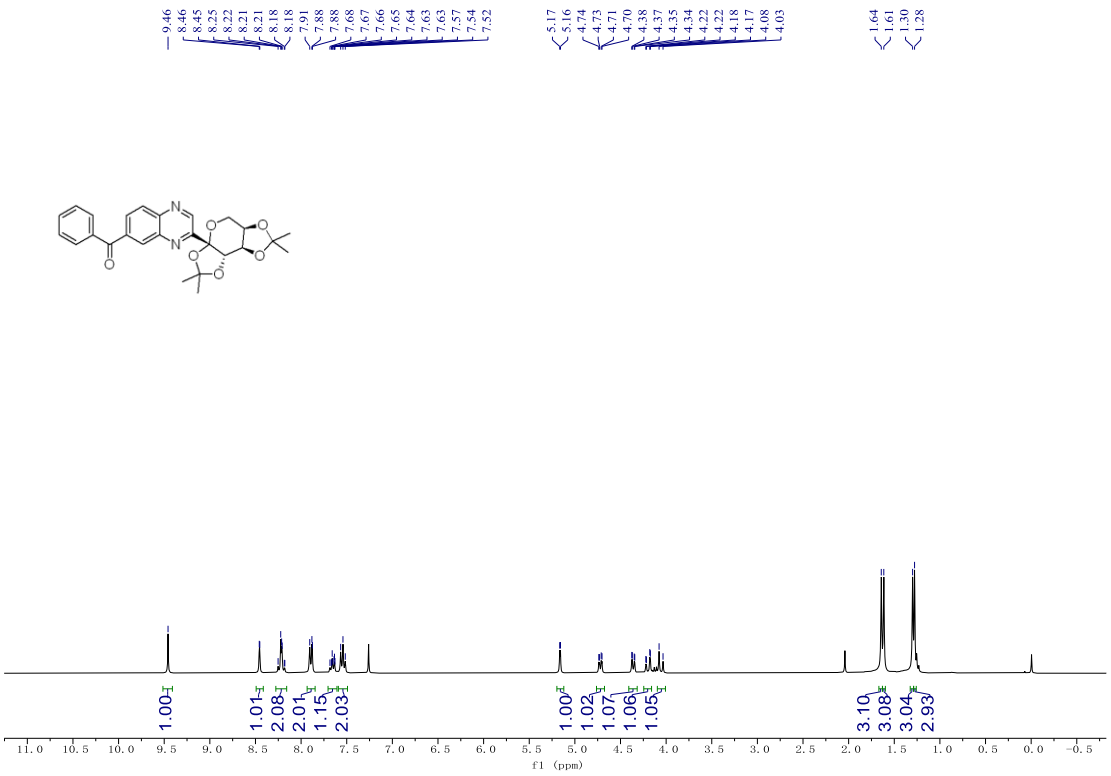
^{1}H NMR (300 MHz, $CDCl_3$) Spectra of compound 11a



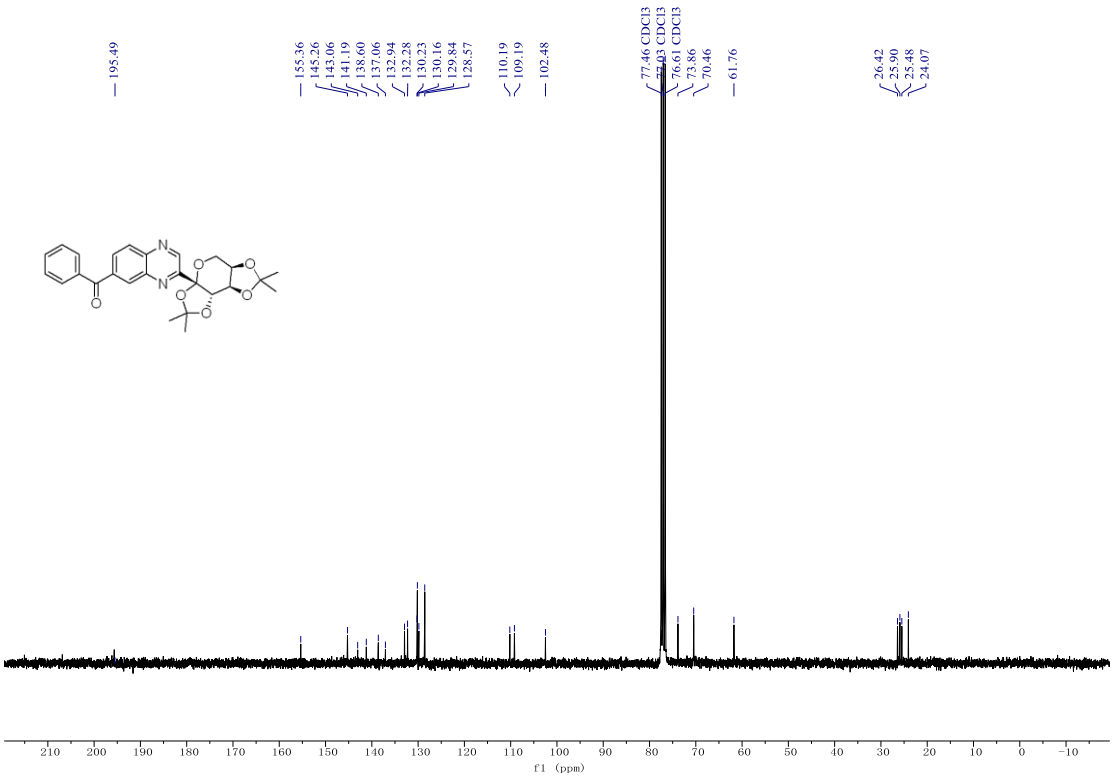
^{13}C NMR (75 MHz, $CDCl_3$) Spectra of compound 11a



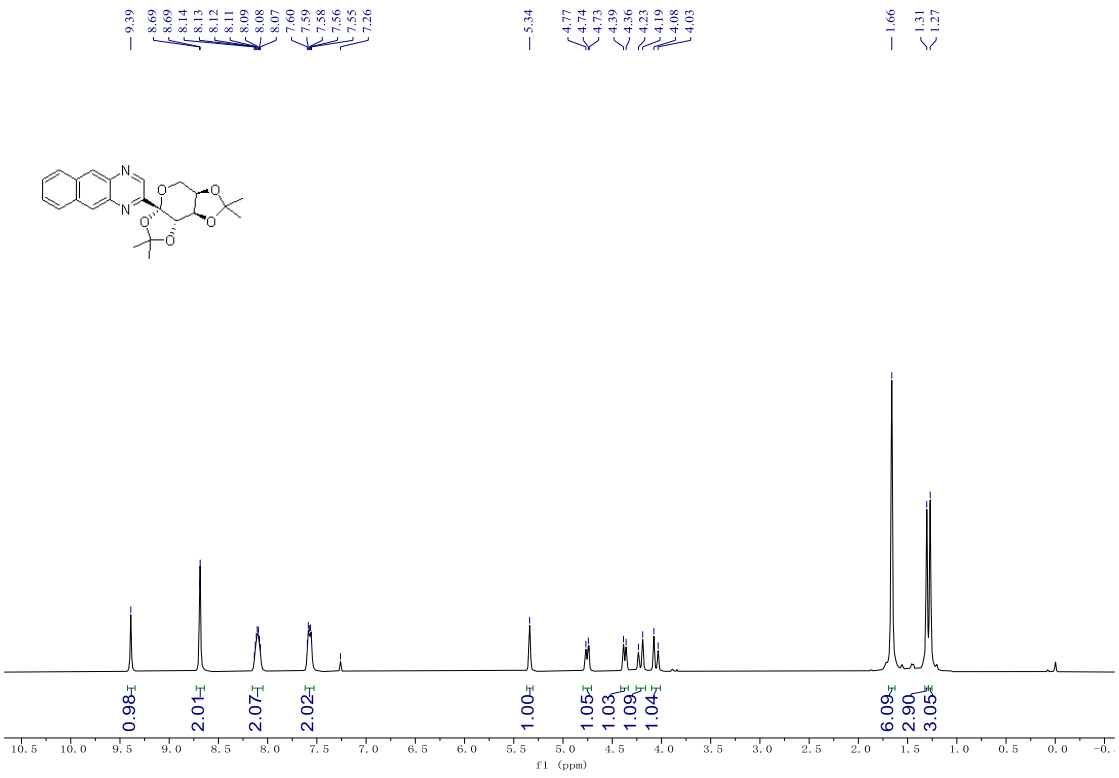
^{1}H NMR (300 MHz, $CDCl_3$) Spectra of compound 11b



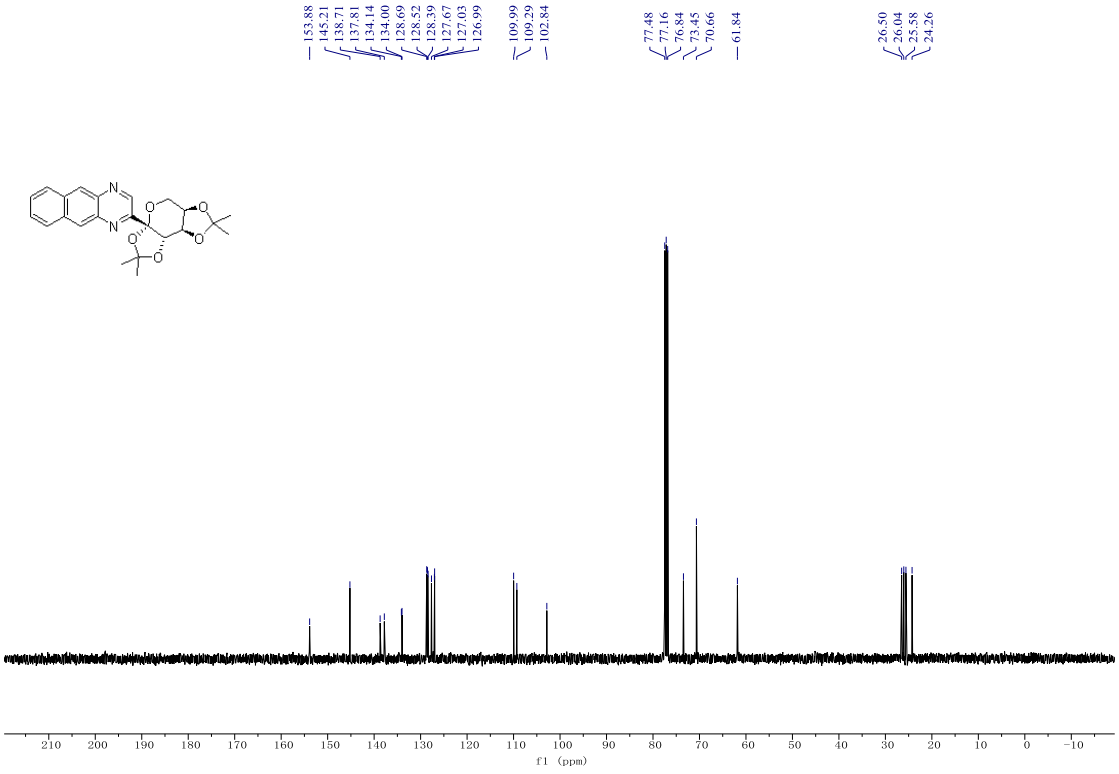
^{13}C NMR (75 MHz, $CDCl_3$) Spectra of compound 11b



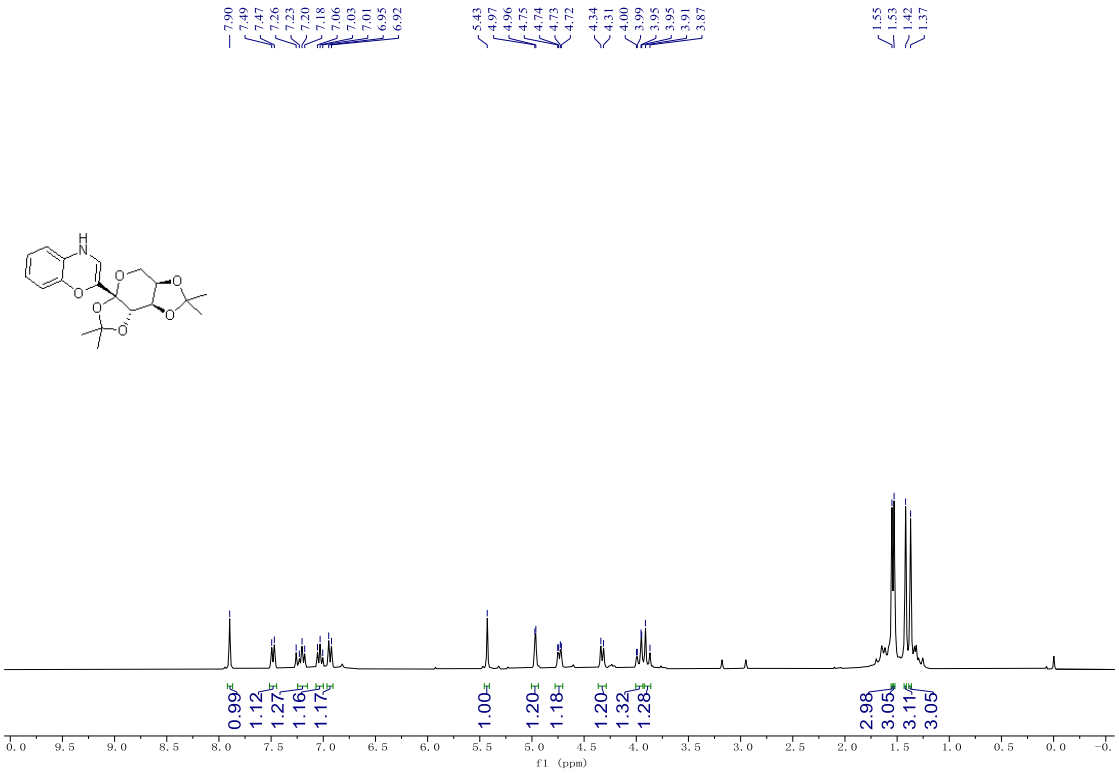
^{1}H NMR (300 MHz, $CDCl_3$) Spectra of compound 12



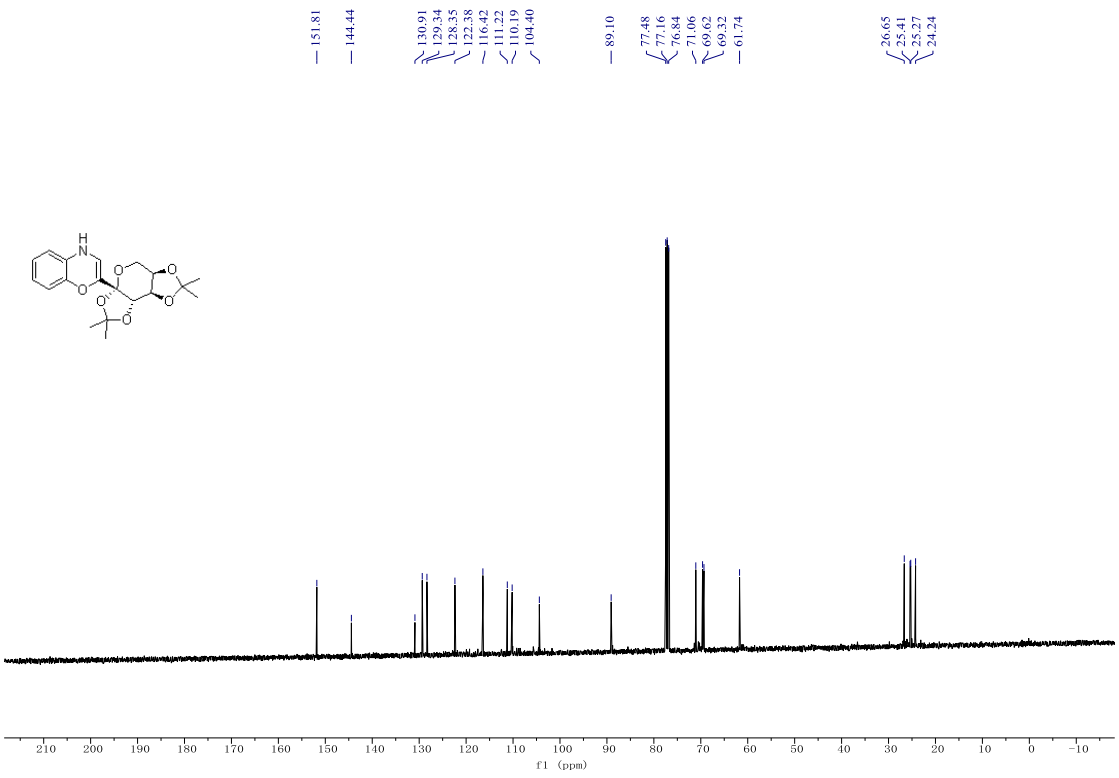
^{13}C NMR (101 MHz, $CDCl_3$) Spectra of compound 12



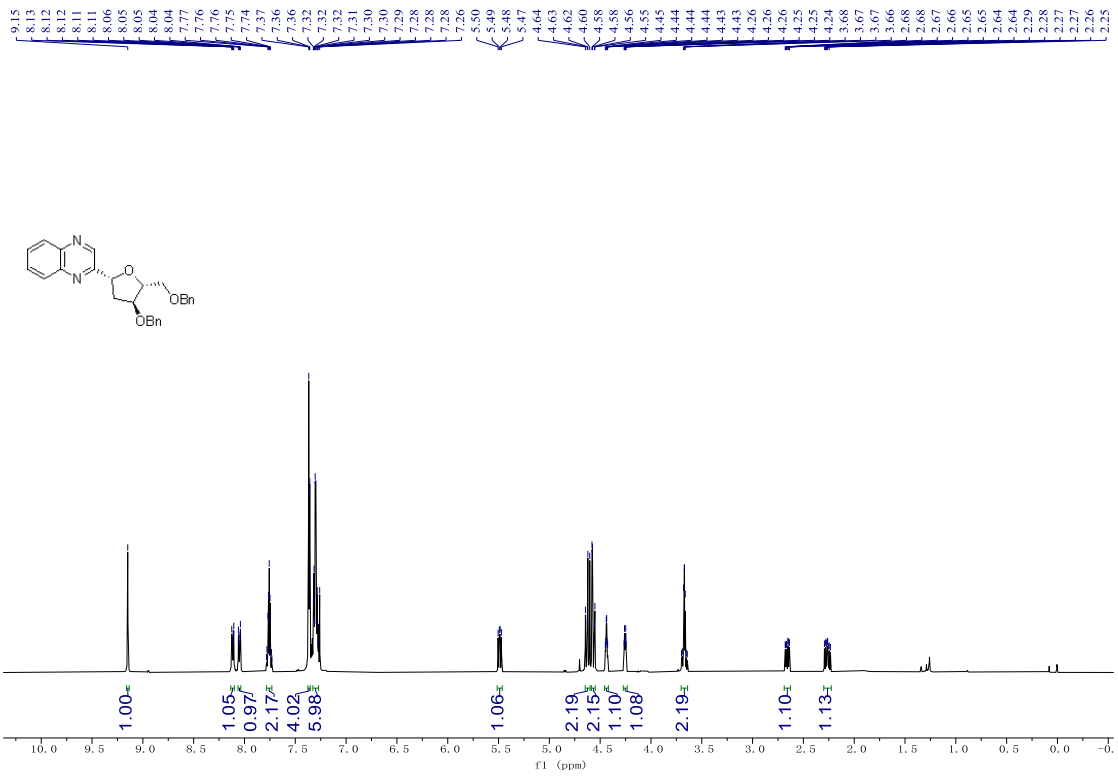
^{1}H NMR (300 MHz, $CDCl_3$) Spectra of compound 13



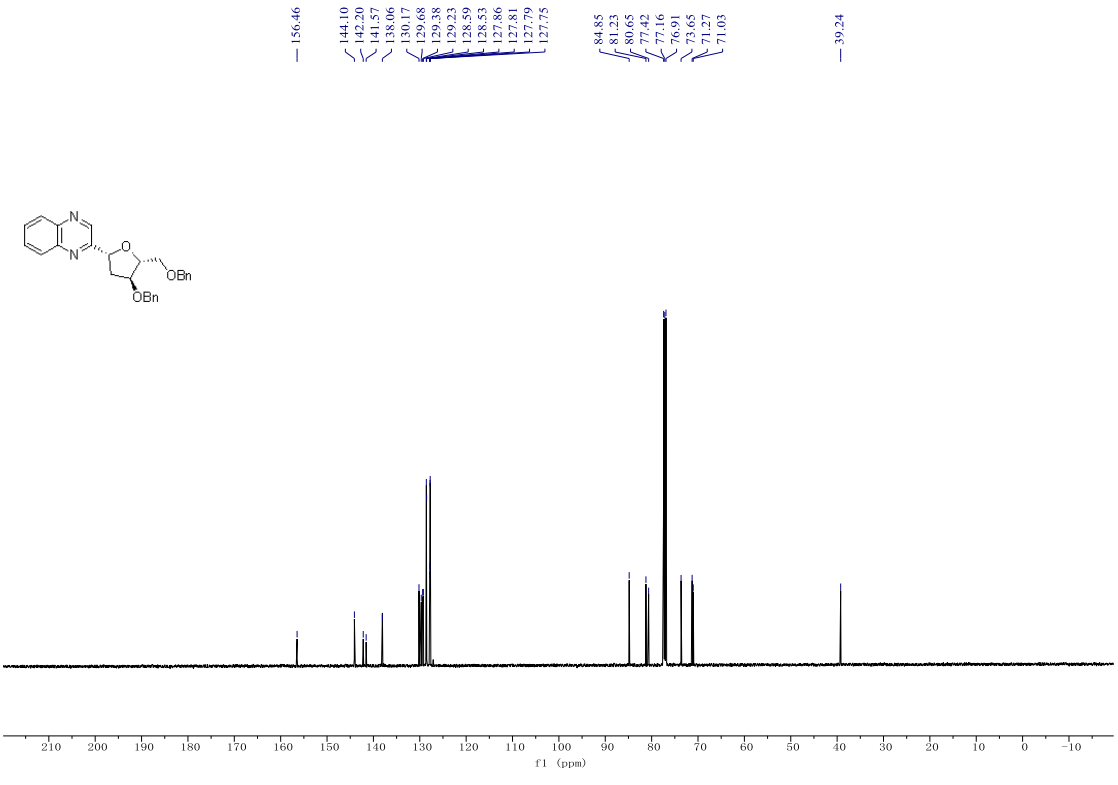
^{13}C NMR (101 MHz, $CDCl_3$) Spectra of compound 13



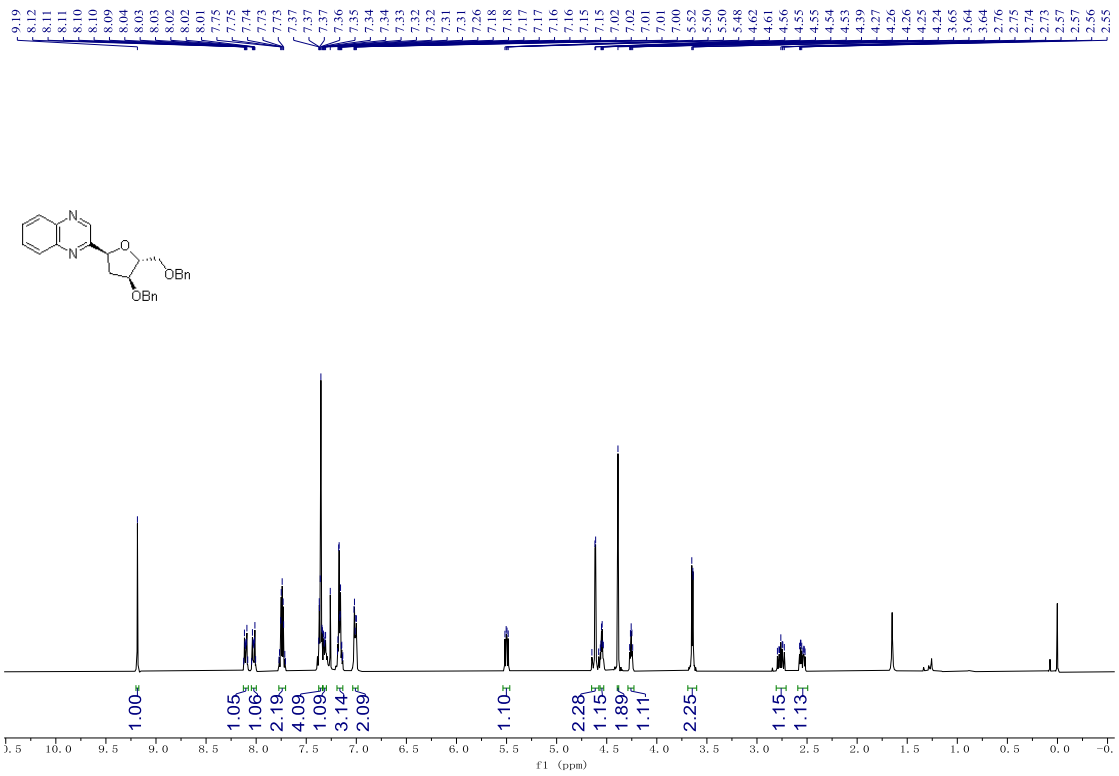
^{1}H NMR (500 MHz, $CDCl_3$) Spectra of compound 14



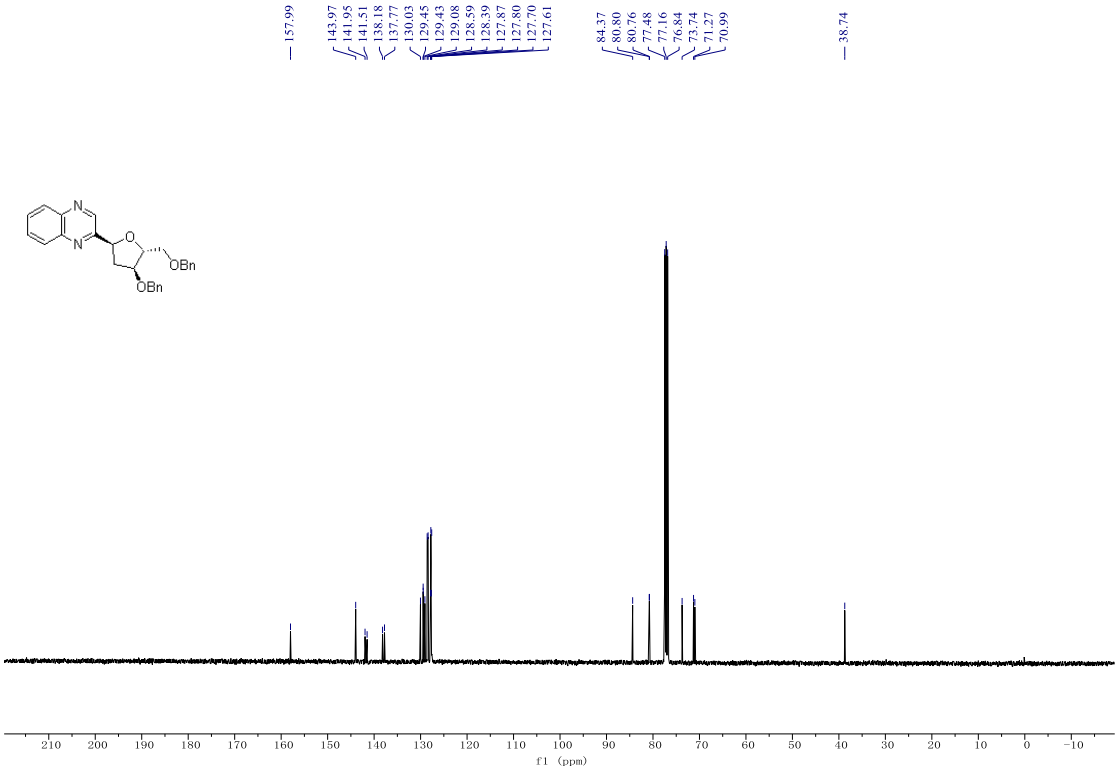
^{13}C NMR (126 MHz, $CDCl_3$) Spectra of compound 14



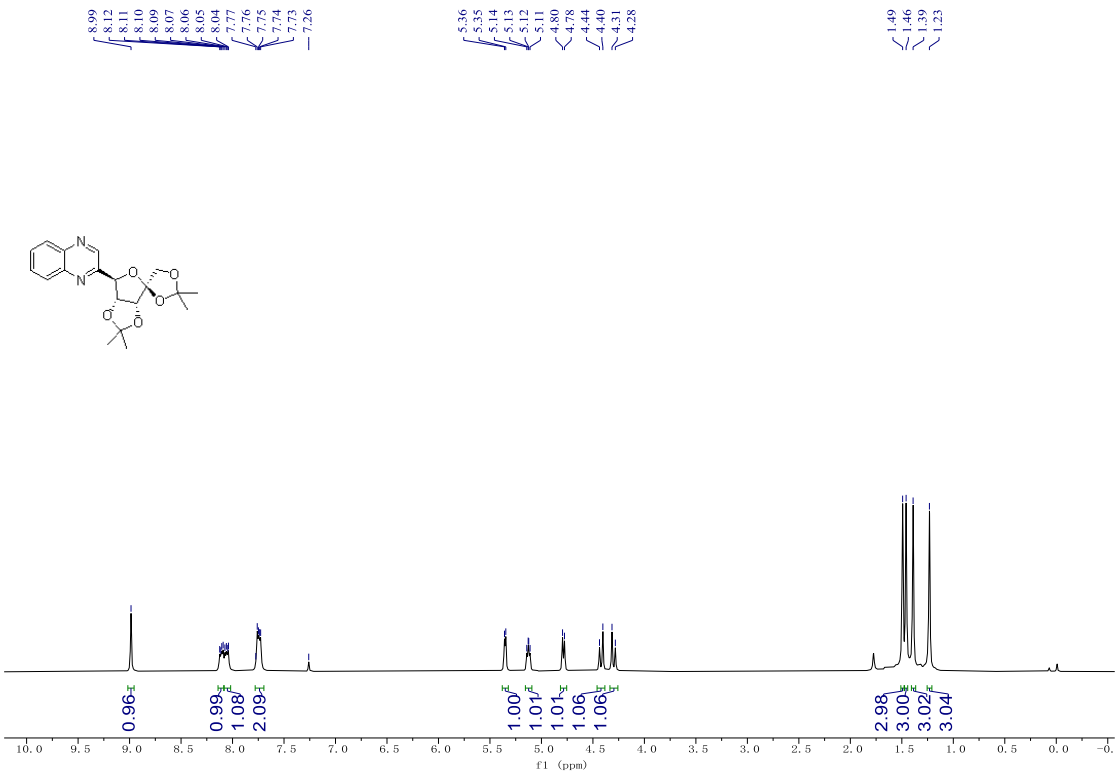
^{1}H NMR (400 MHz, $CDCl_3$) Spectra of compound 15



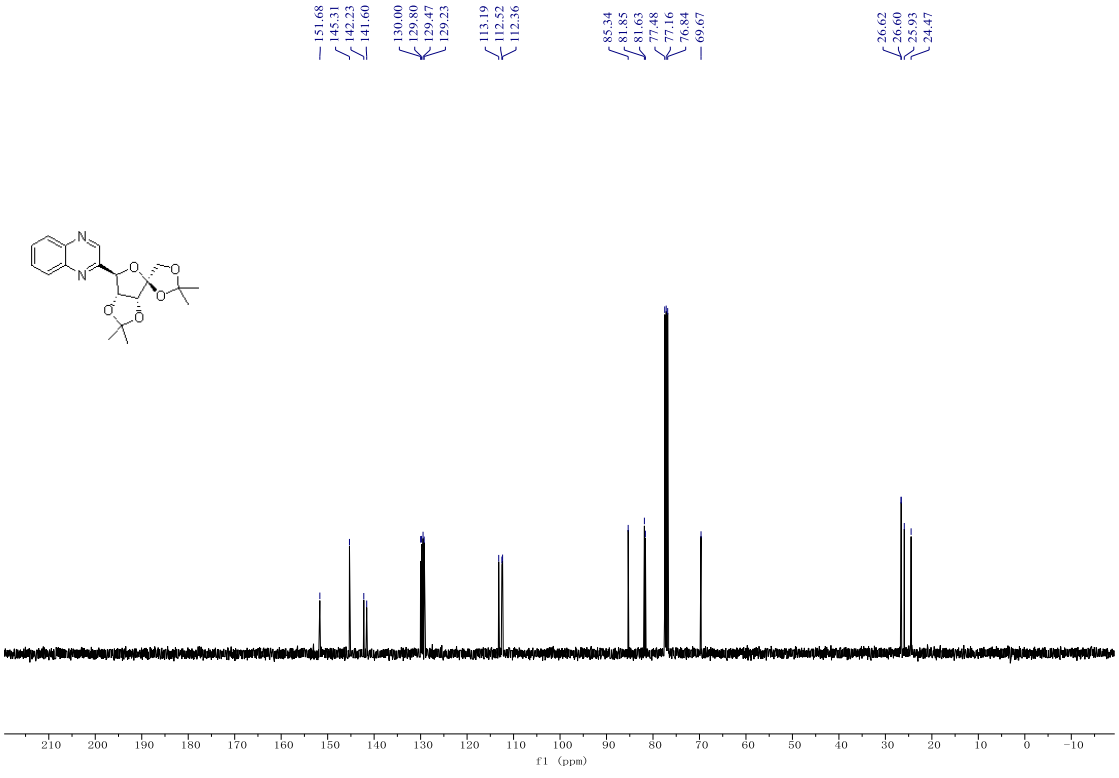
^{13}C NMR (101 MHz, $CDCl_3$) Spectra of compound 15



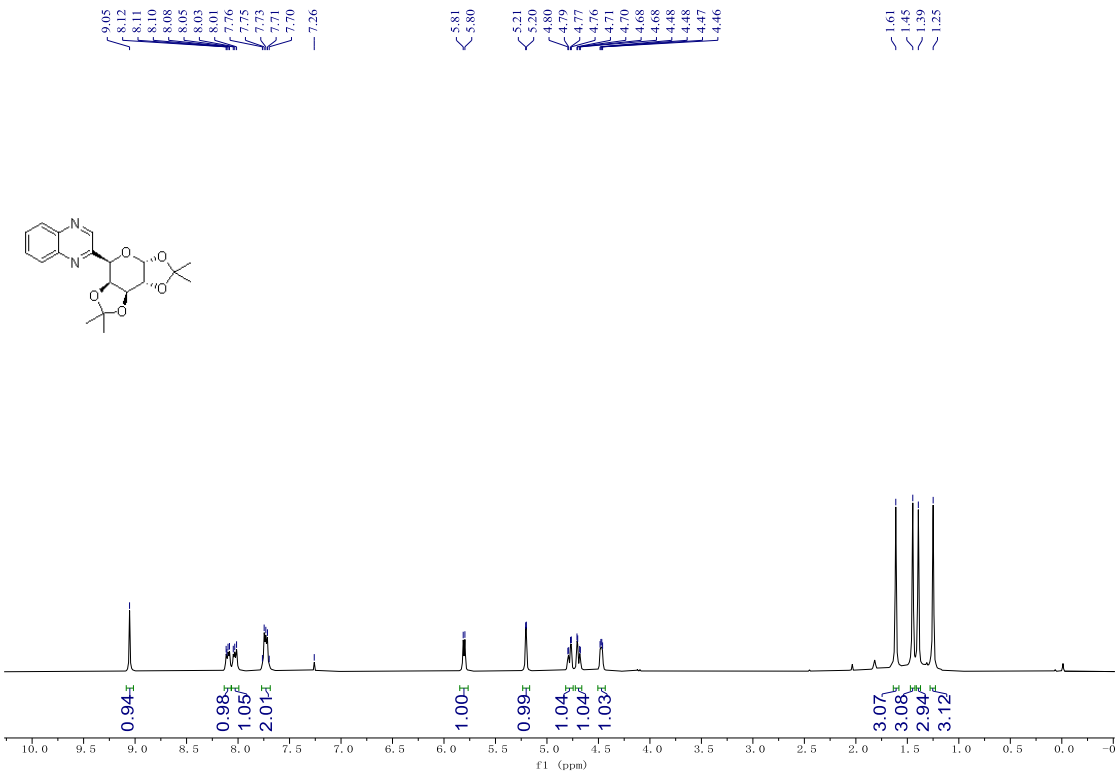
^{1}H NMR (300 MHz, $CDCl_3$) Spectra of compound 16



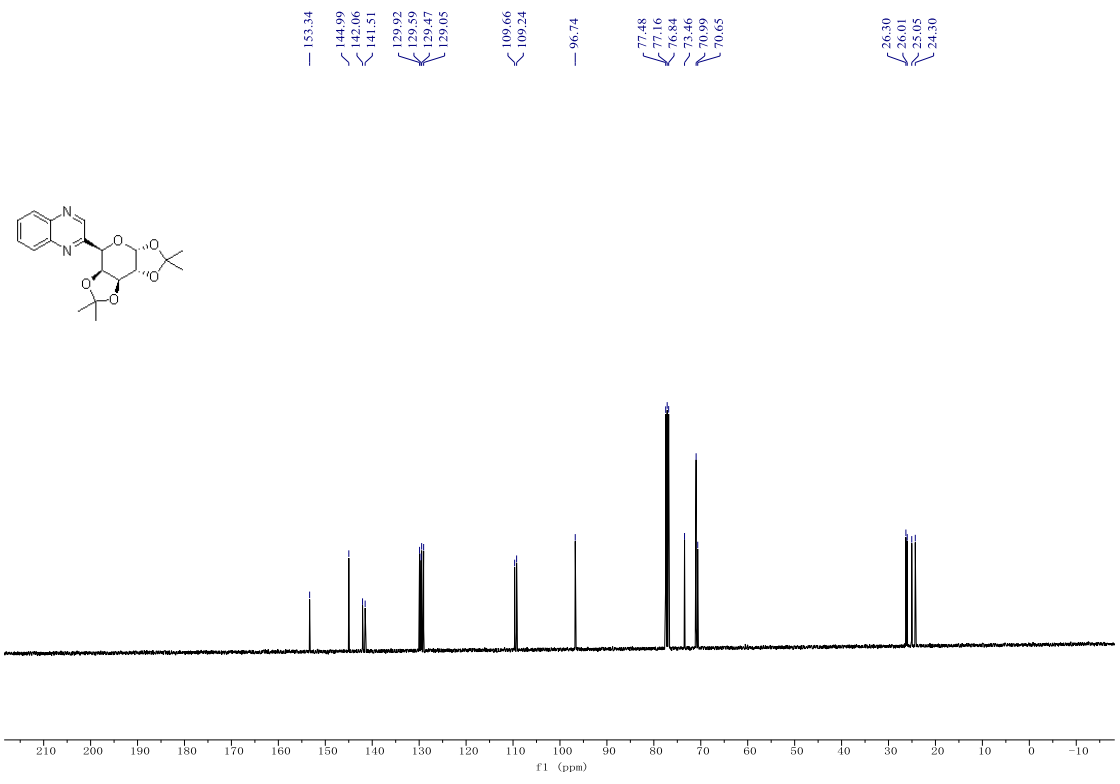
^{13}C NMR (101 MHz, $CDCl_3$) Spectra of compound 16



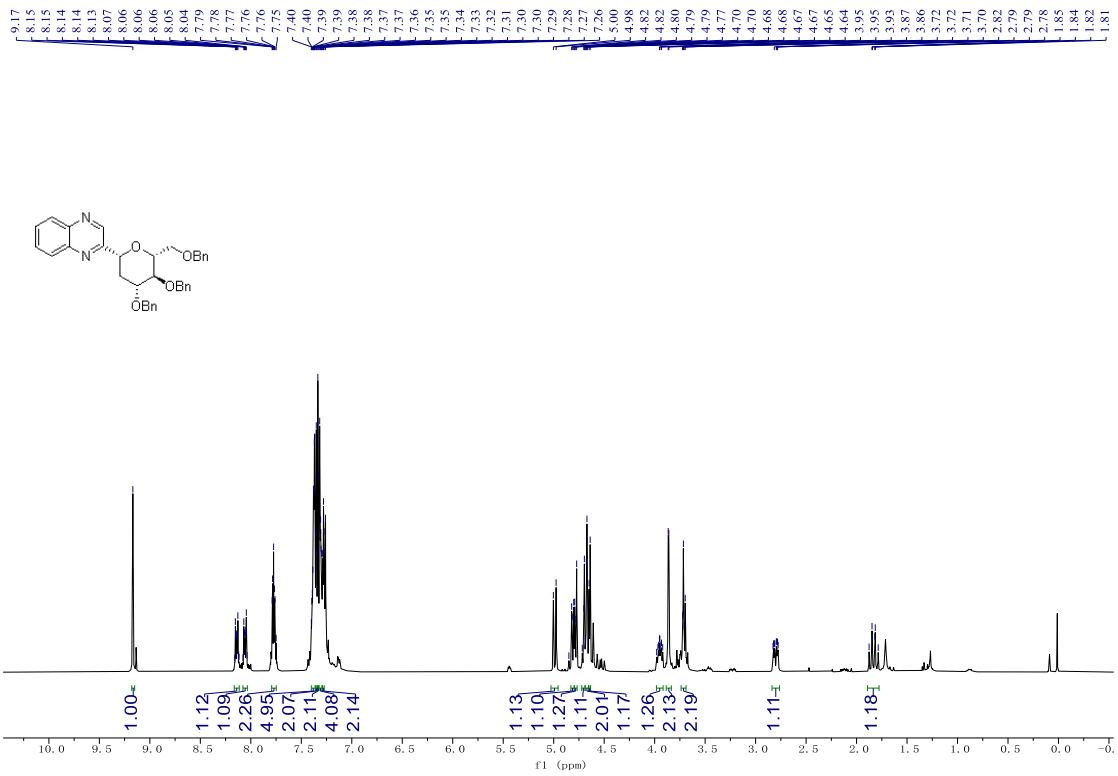
^{1}H NMR (300 MHz, $CDCl_3$) Spectra of compound 17



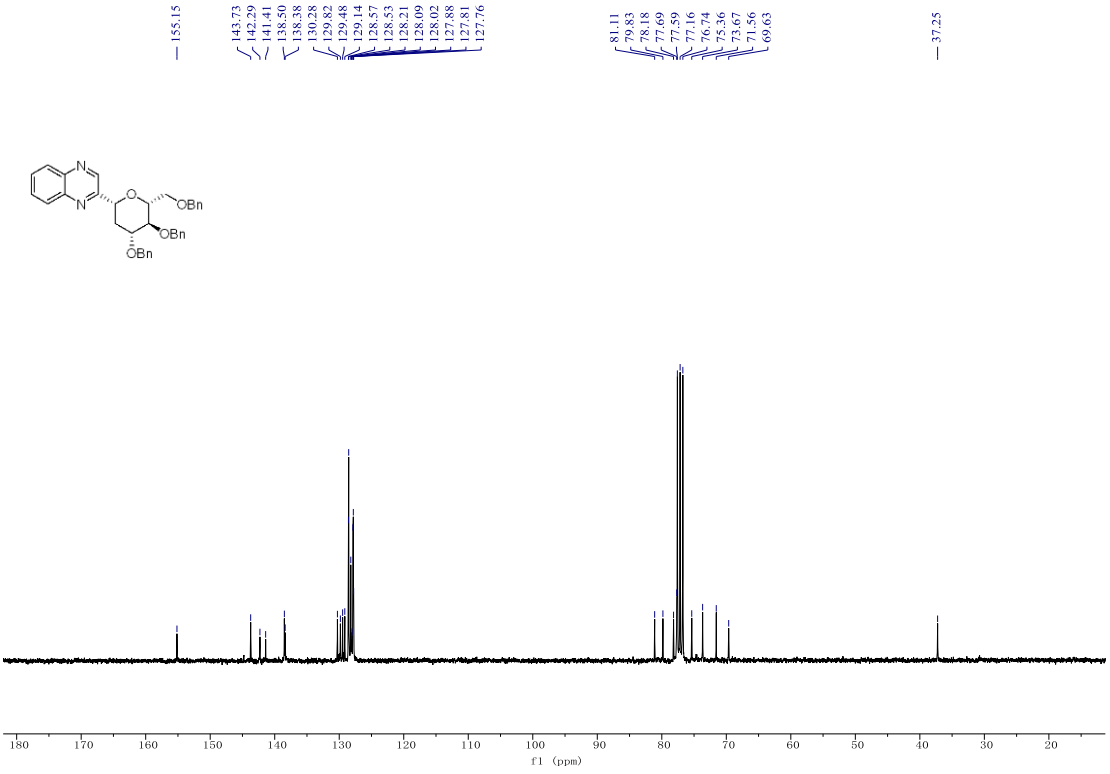
^{13}C NMR (101 MHz, $CDCl_3$) Spectra of compound 17



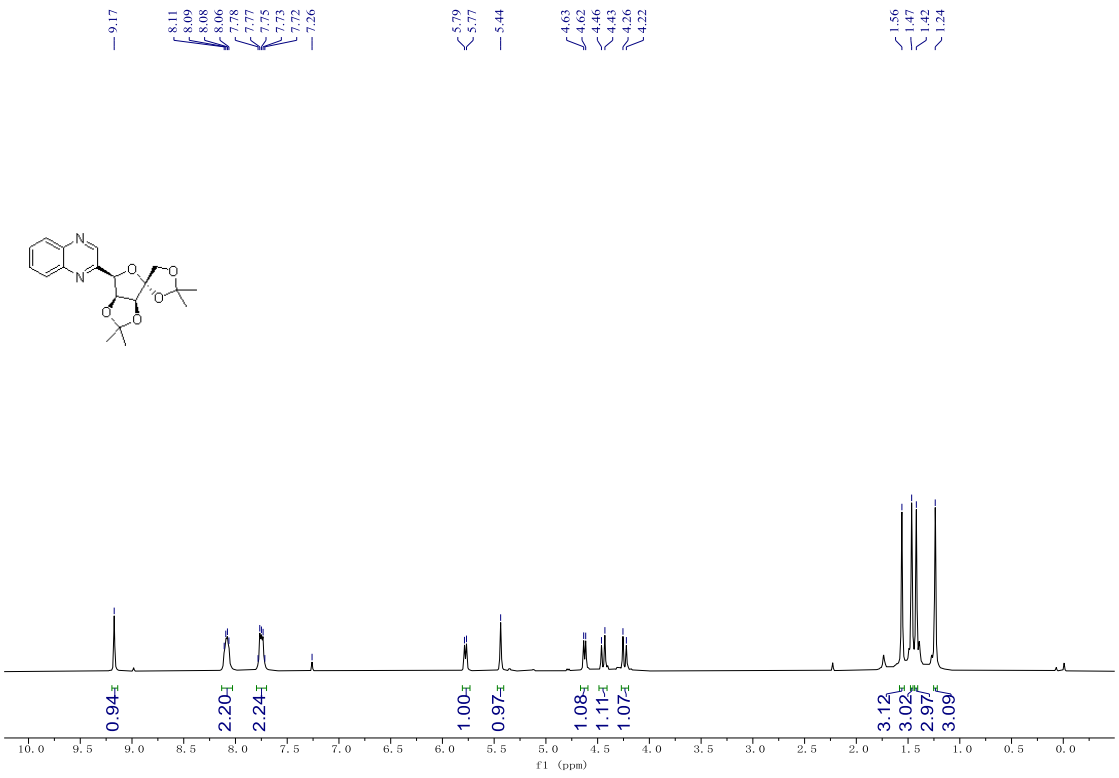
^{1}H NMR (400 MHz, $CDCl_3$) Spectra of compound 18



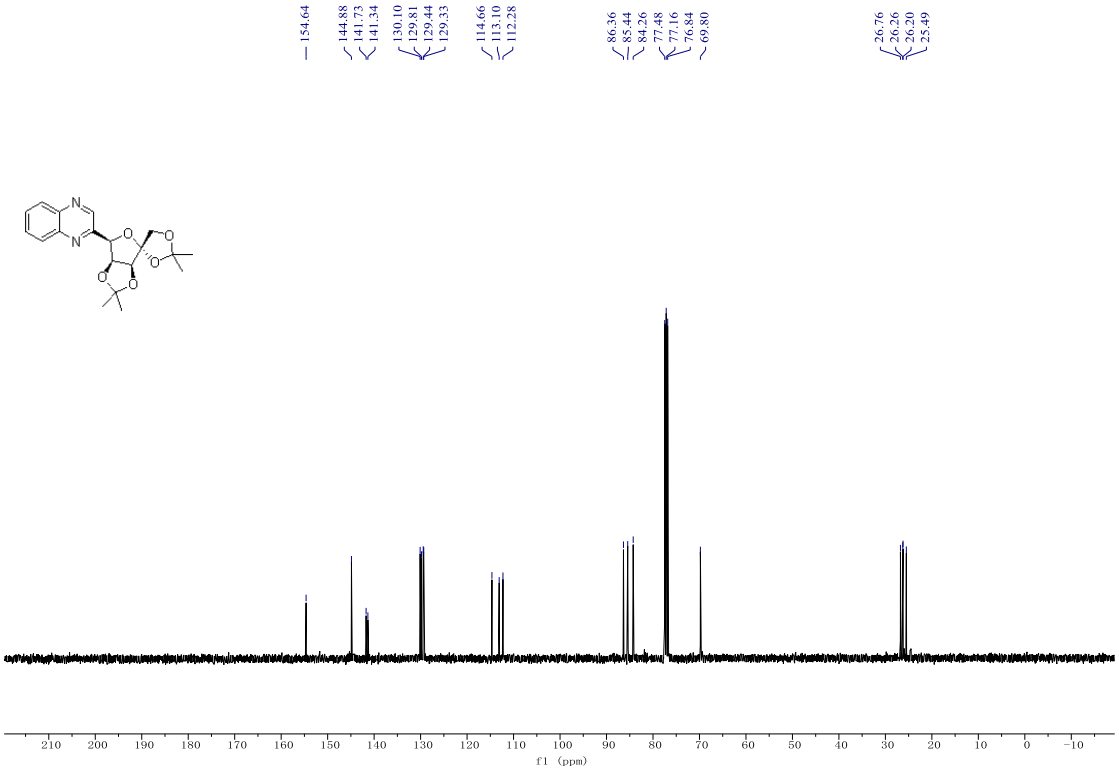
^{13}C NMR (75 MHz, $CDCl_3$) Spectra of compound 18



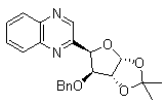
^{1}H NMR (300 MHz, $CDCl_3$) Spectra of compound 19

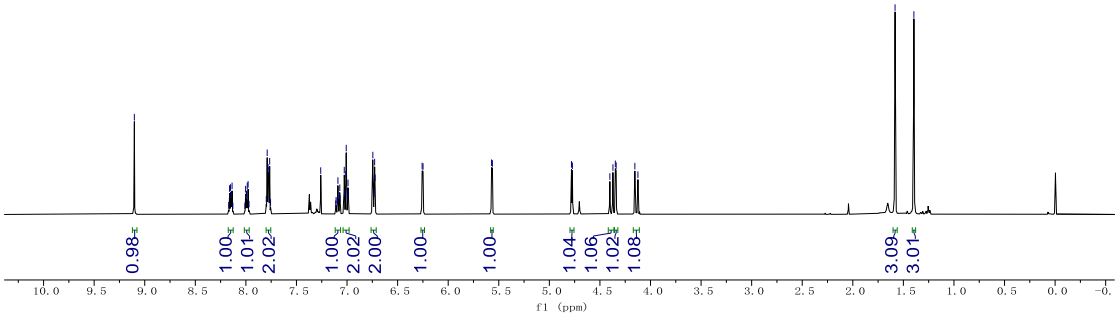


^{13}C NMR (101 MHz, $CDCl_3$) Spectra of compound 19

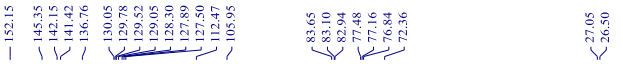


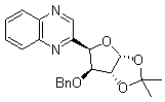
^{1}H NMR (400 MHz, $CDCl_3$) Spectra of compound 20

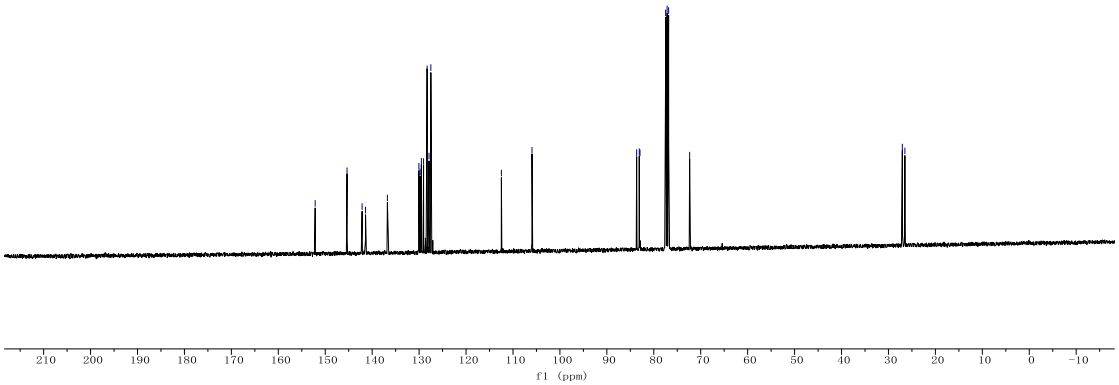




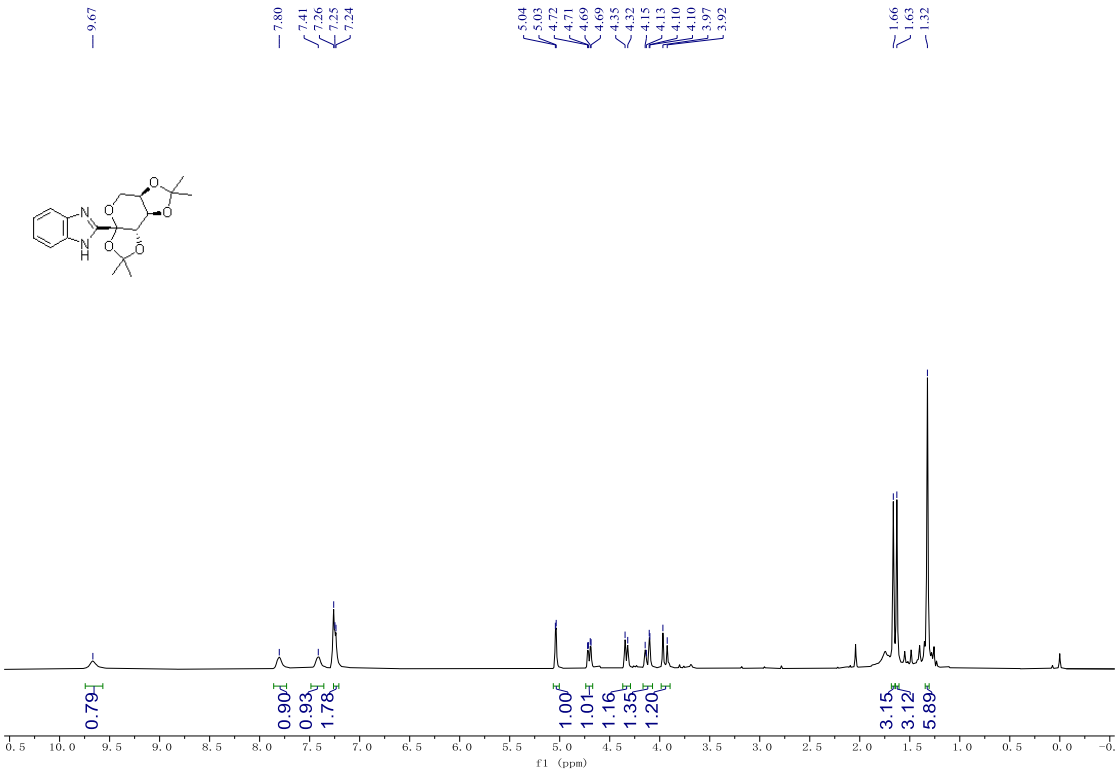
^{13}C NMR (101 MHz, $CDCl_3$) Spectra of compound 20



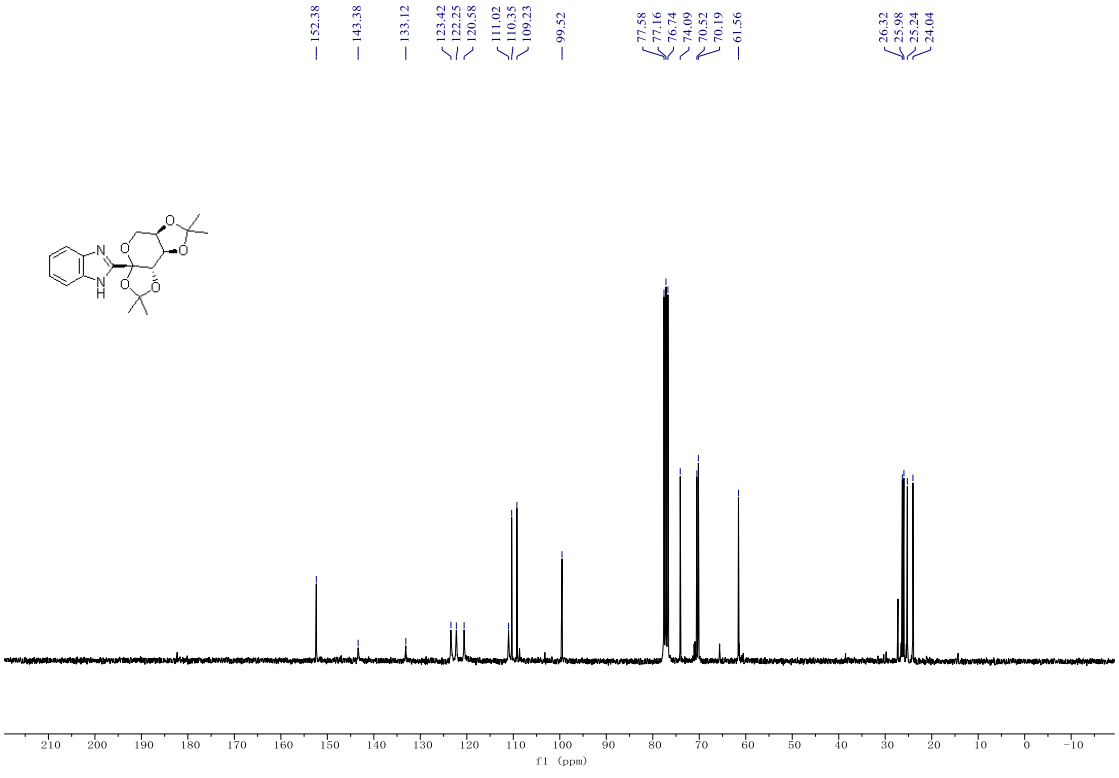




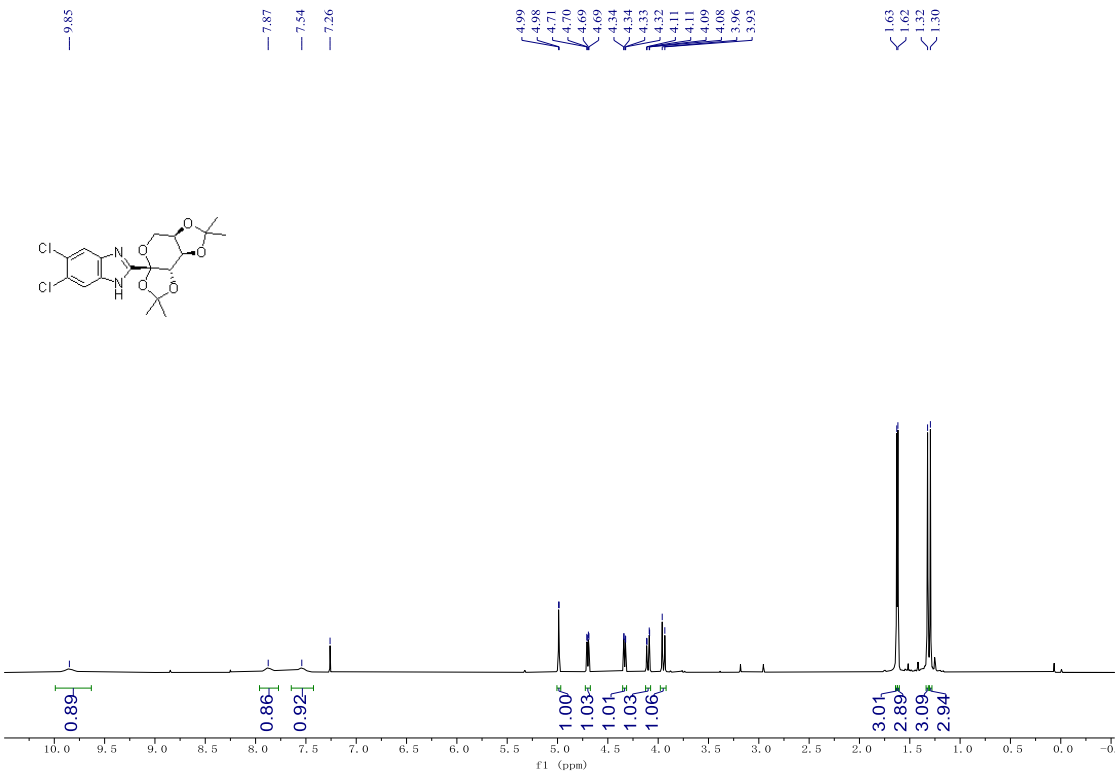
^{1}H NMR (300 MHz, $CDCl_3$) Spectra of compound 21



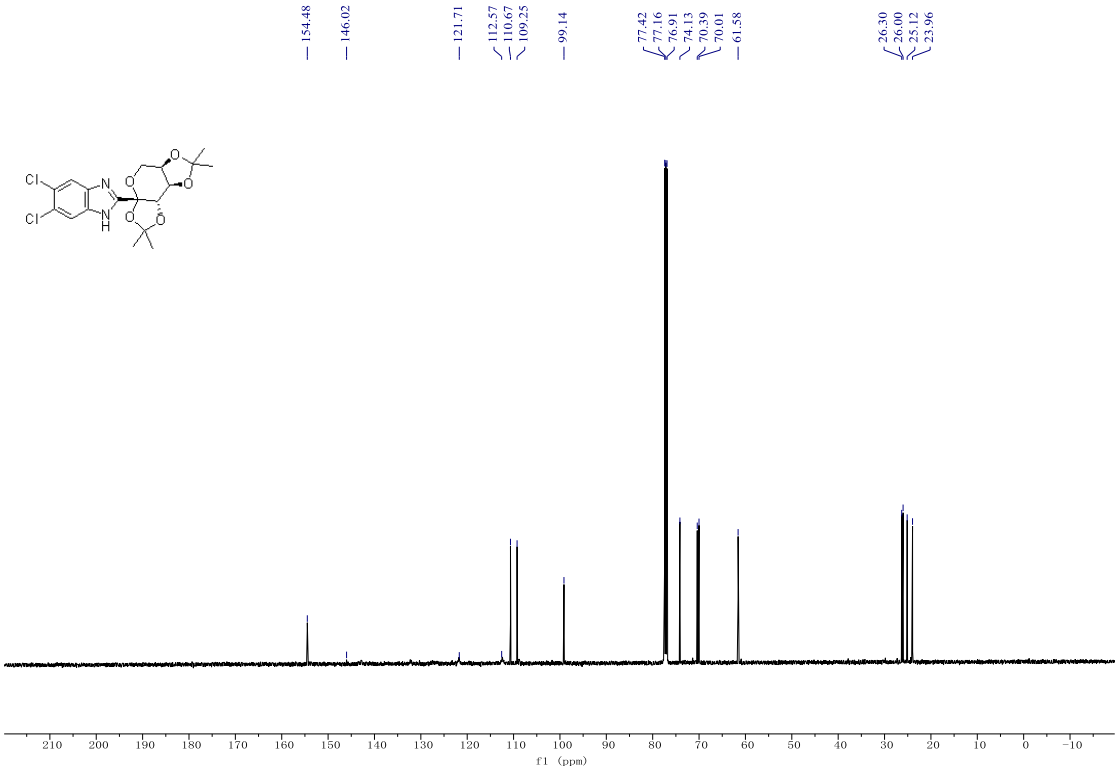
^{13}C NMR (75 MHz, $CDCl_3$) Spectra of compound 21



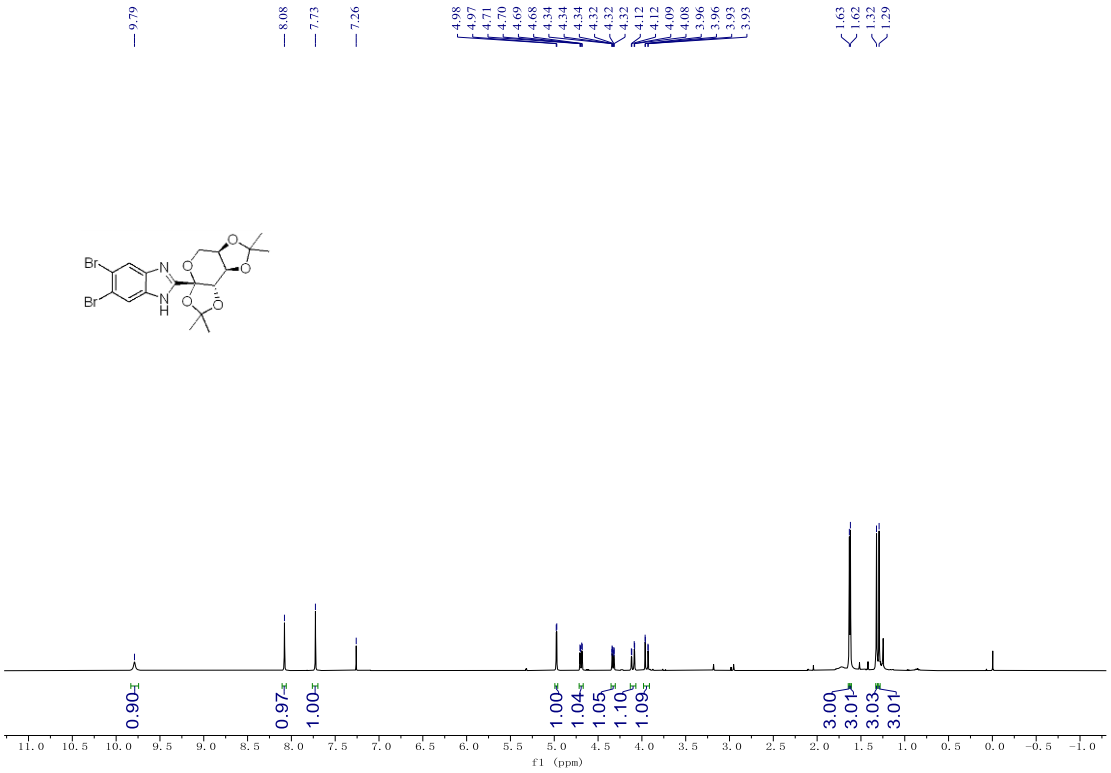
^{1}H NMR (500 MHz, $CDCl_3$) Spectra of compound 22



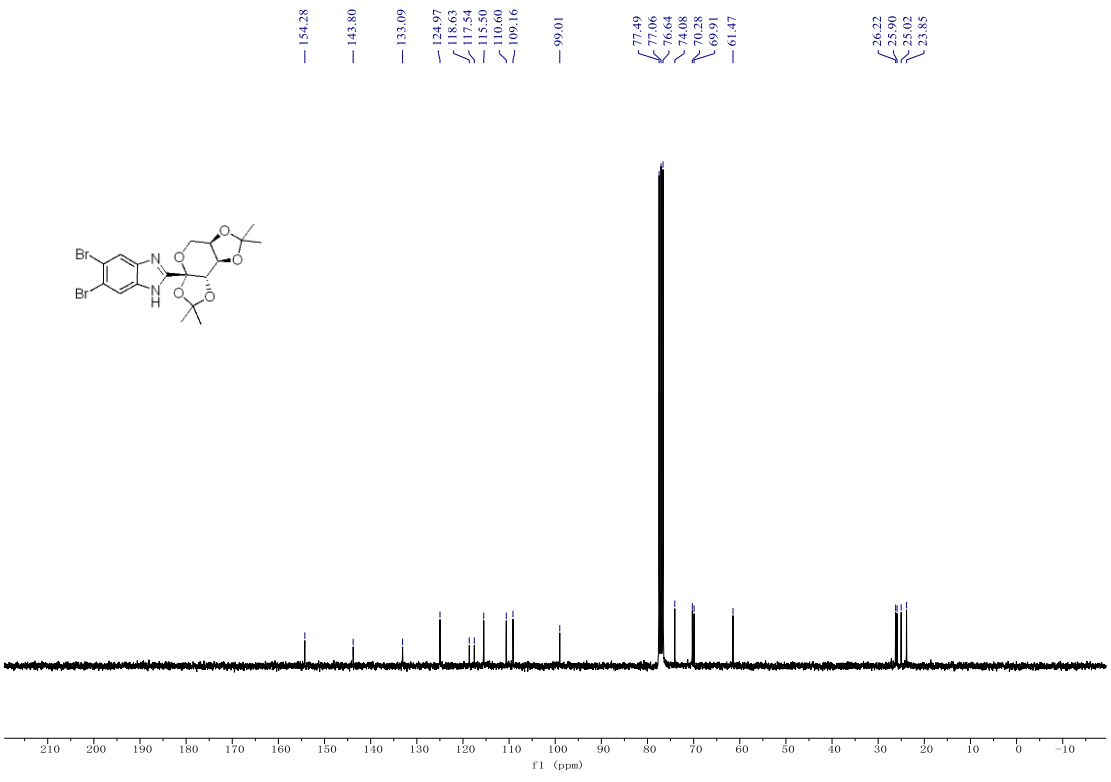
^{13}C NMR (126 MHz, $CDCl_3$) Spectra of compound 22



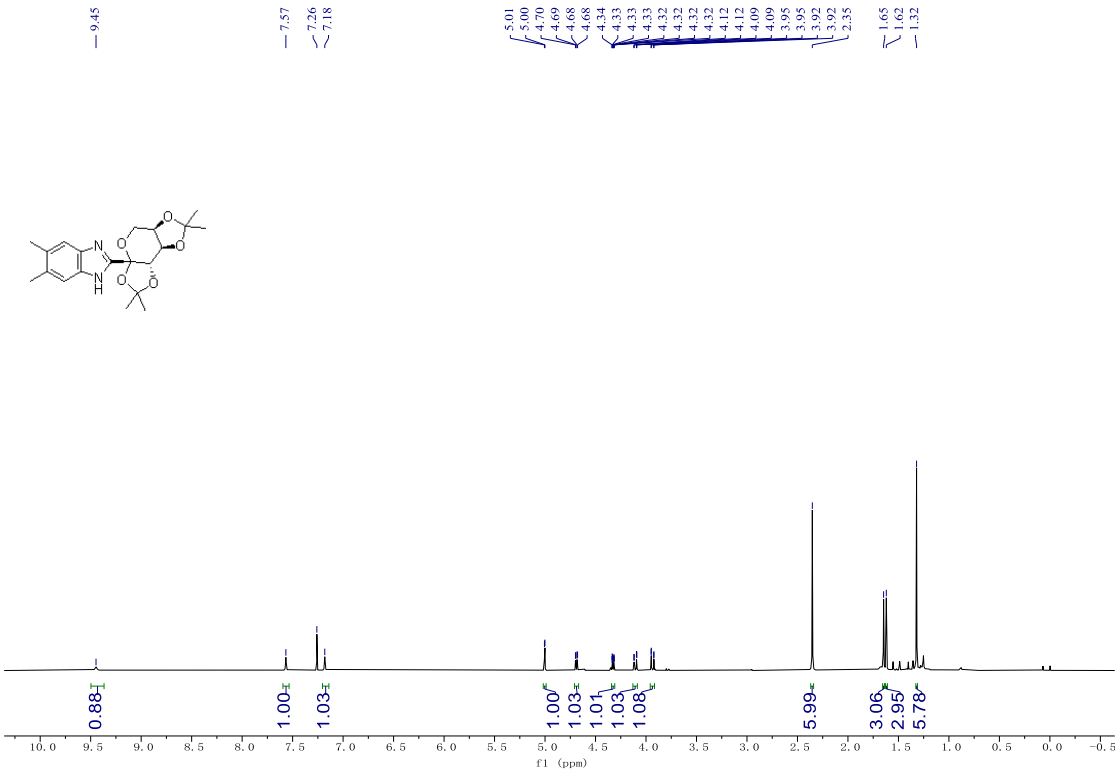
^{1}H NMR (400 MHz, $CDCl_3$) Spectra of compound 23



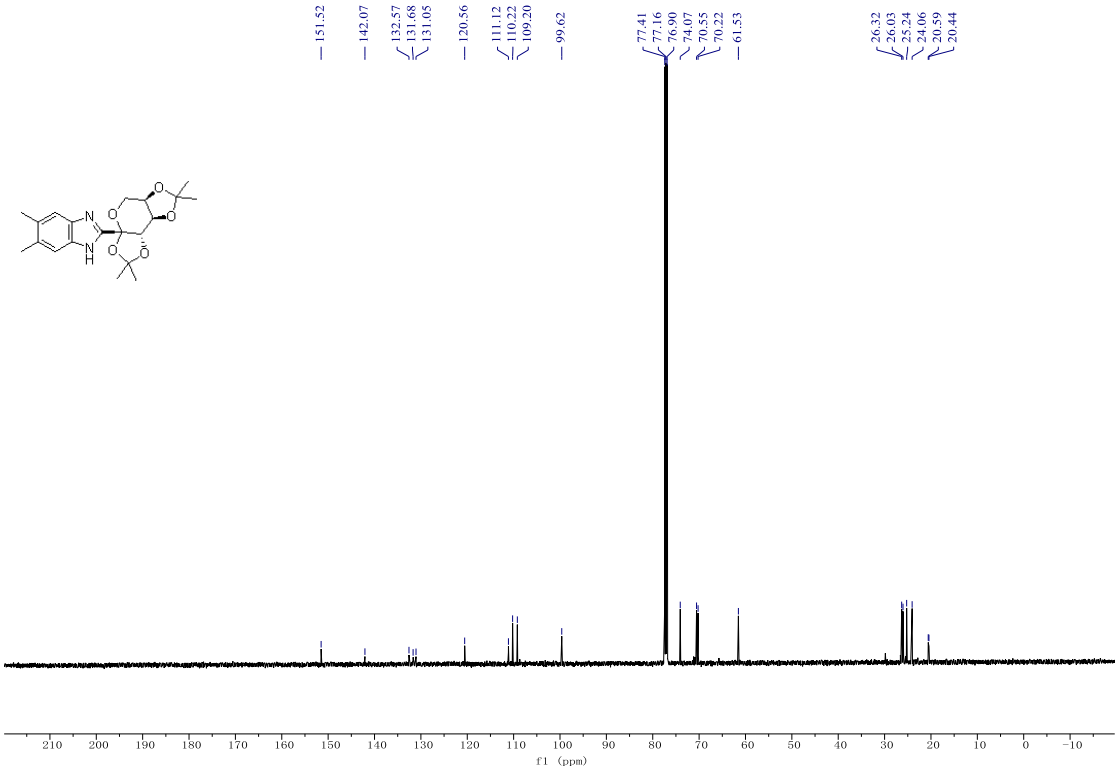
^{13}C NMR (75 MHz, $CDCl_3$) Spectra of compound 23



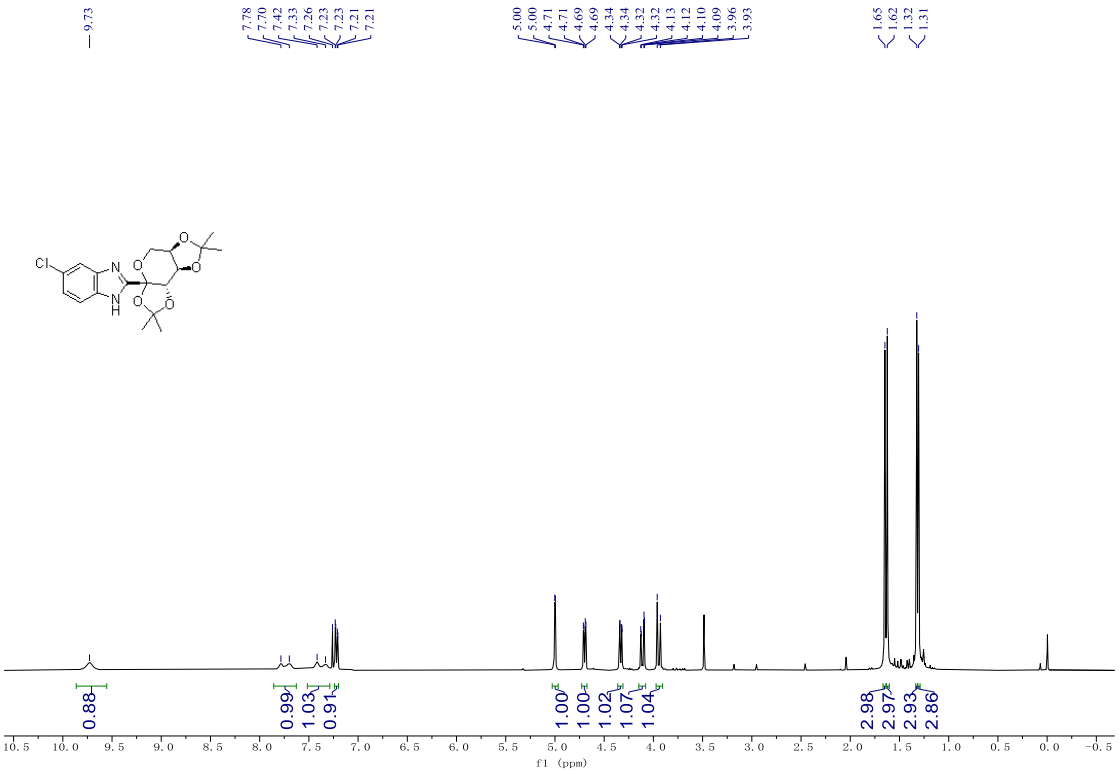
^{1}H NMR (500 MHz, $CDCl_3$) Spectra of compound 24



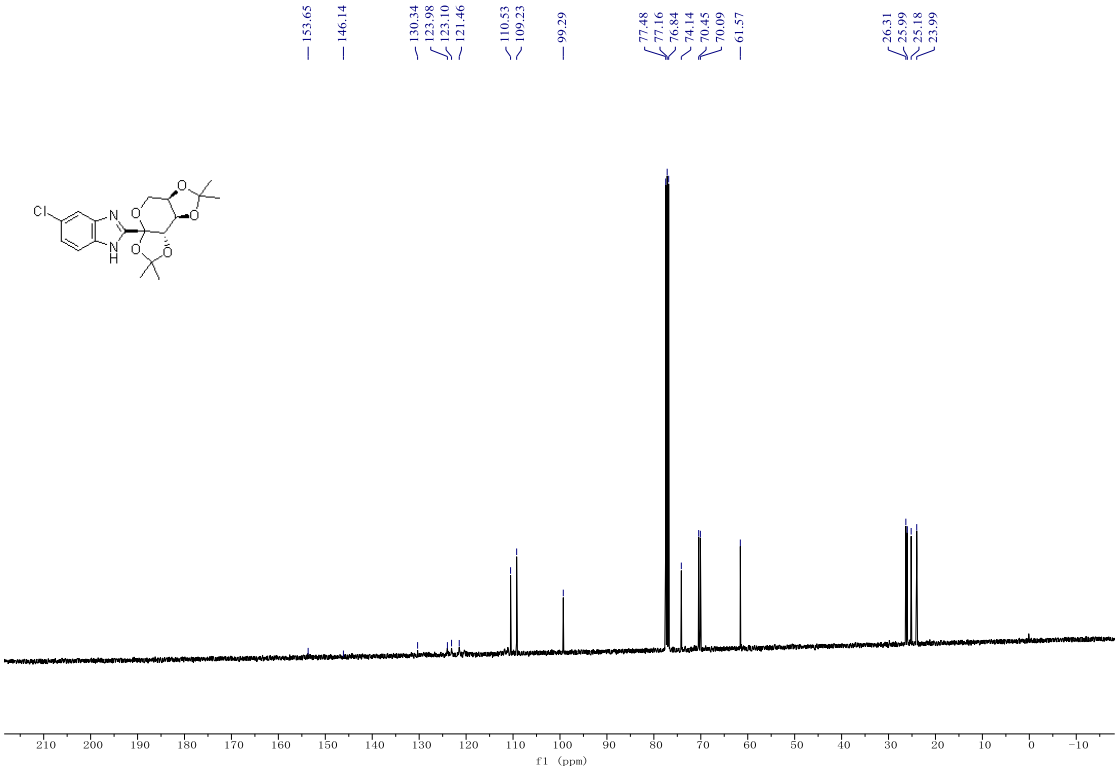
^{13}C NMR (126 MHz, $CDCl_3$) Spectra of compound 24



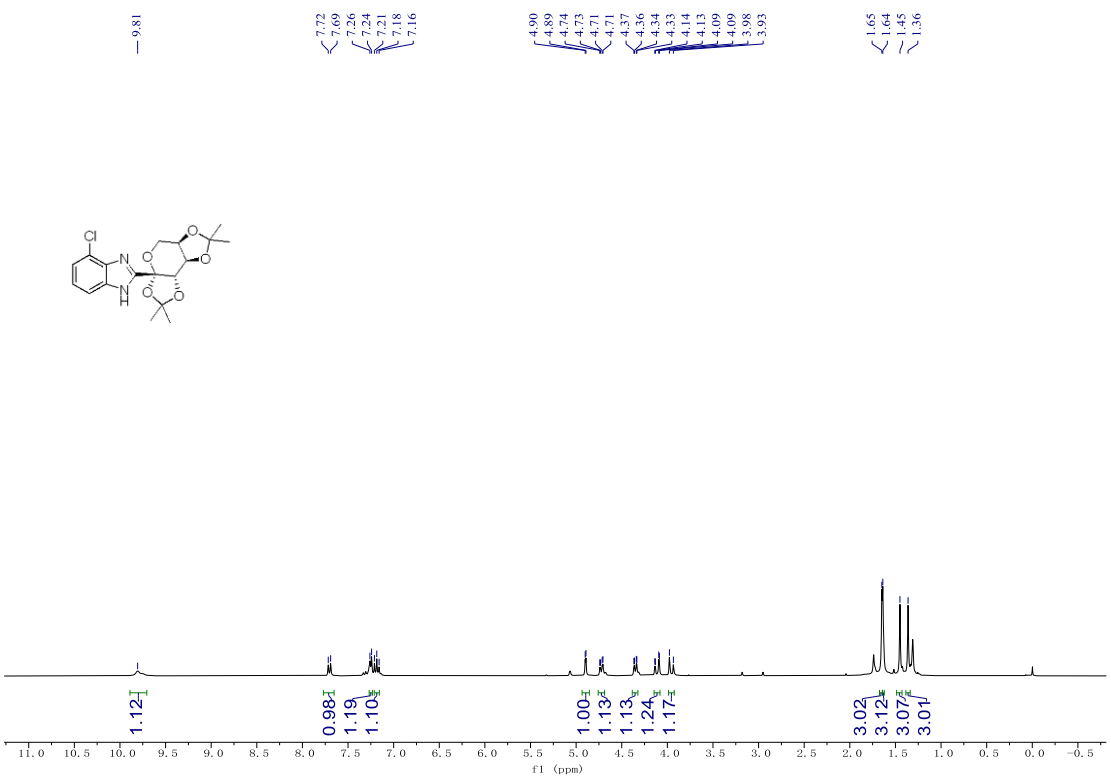
^{1}H NMR (400 MHz, $CDCl_3$) Spectra of compound 25



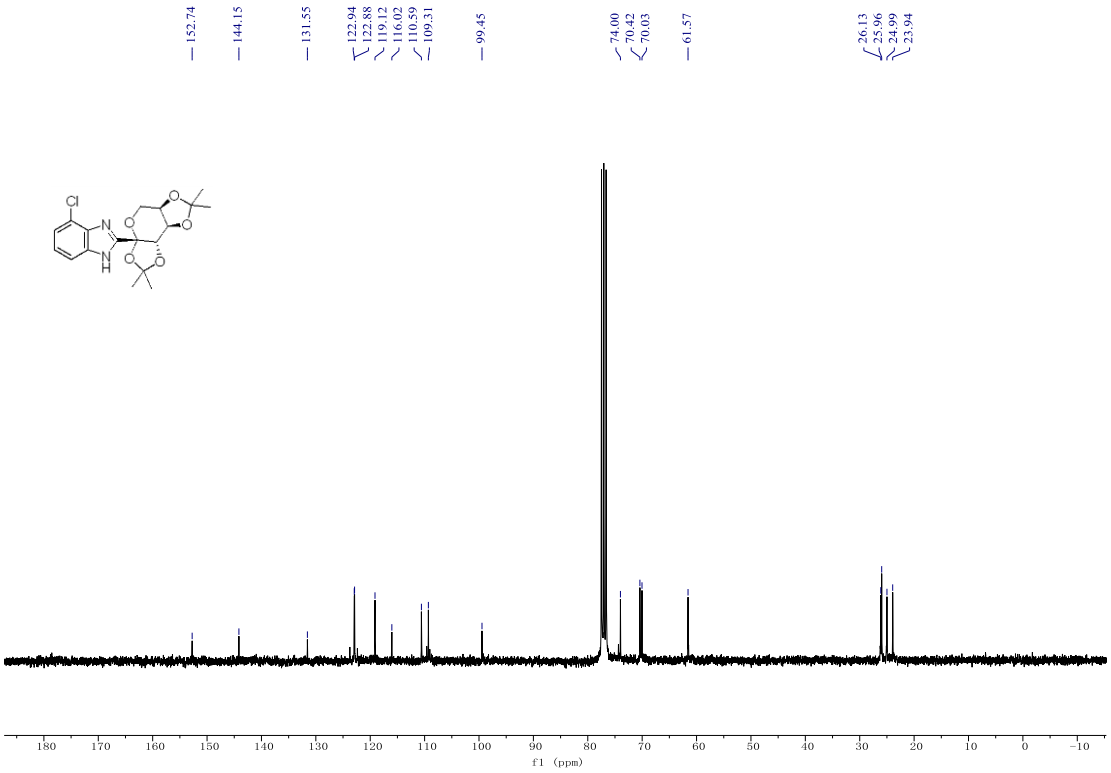
^{13}C NMR (101 MHz, $CDCl_3$) Spectra of compound 25



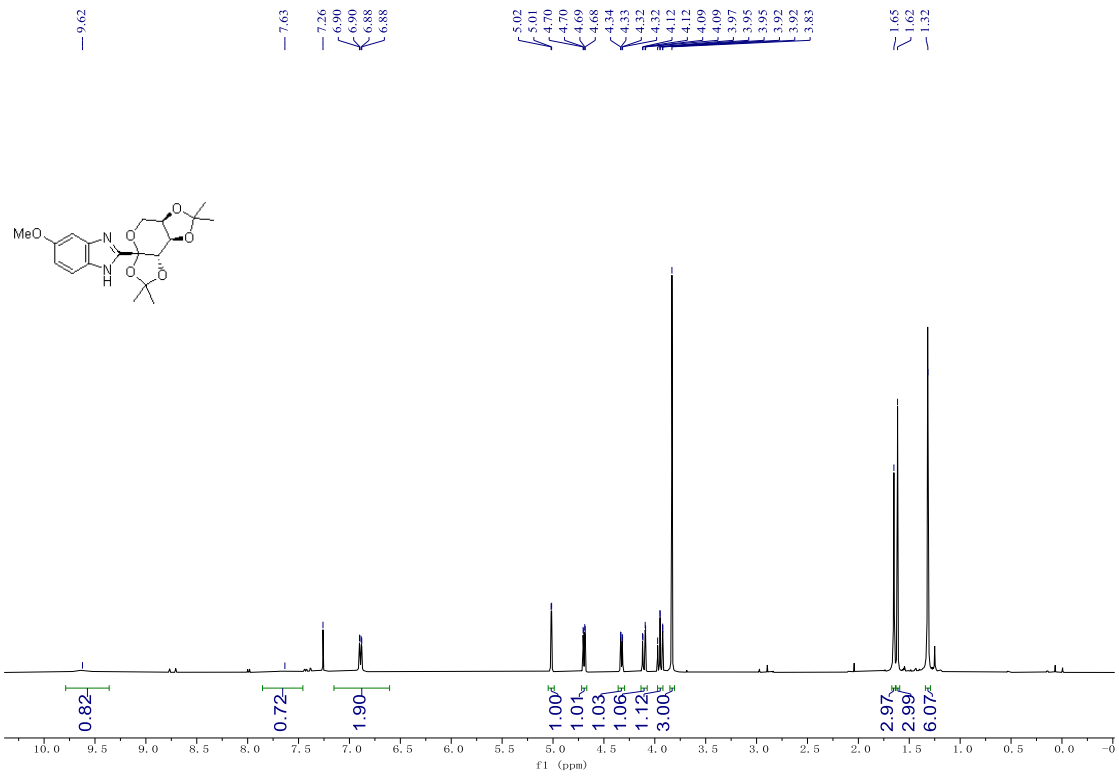
^{1}H NMR (300 MHz, $CDCl_3$) Spectra of compound 26



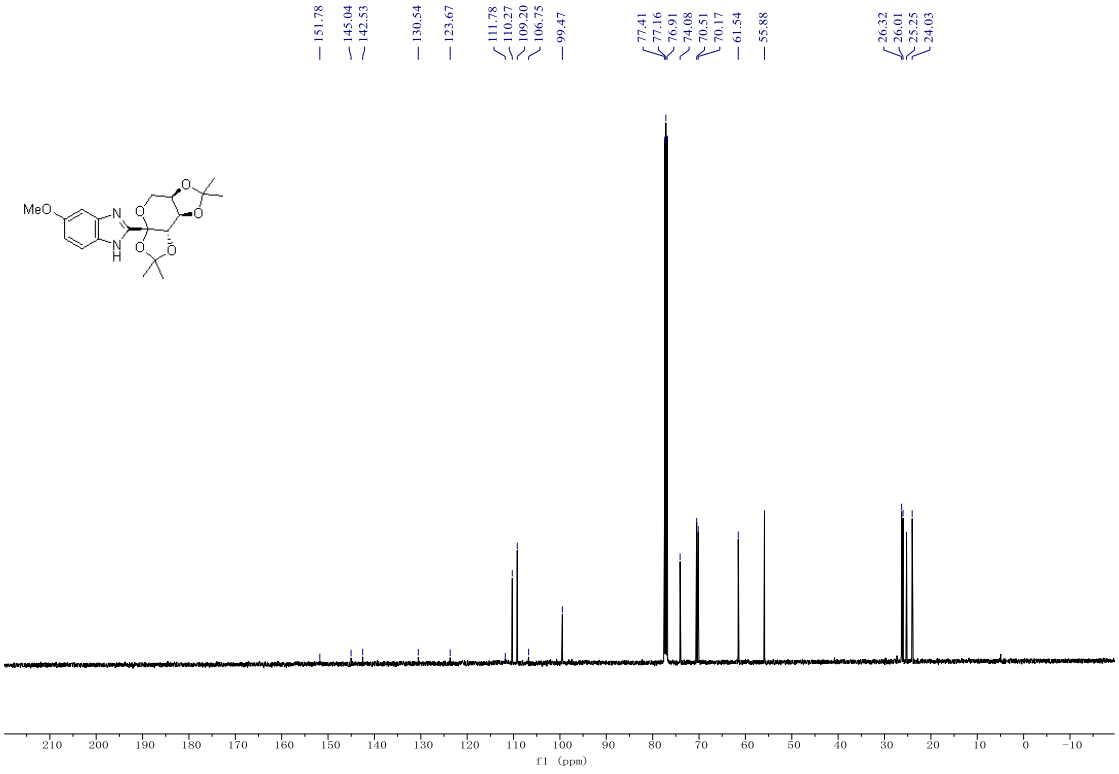
^{13}C NMR (75 MHz, $CDCl_3$) Spectra of compound 26



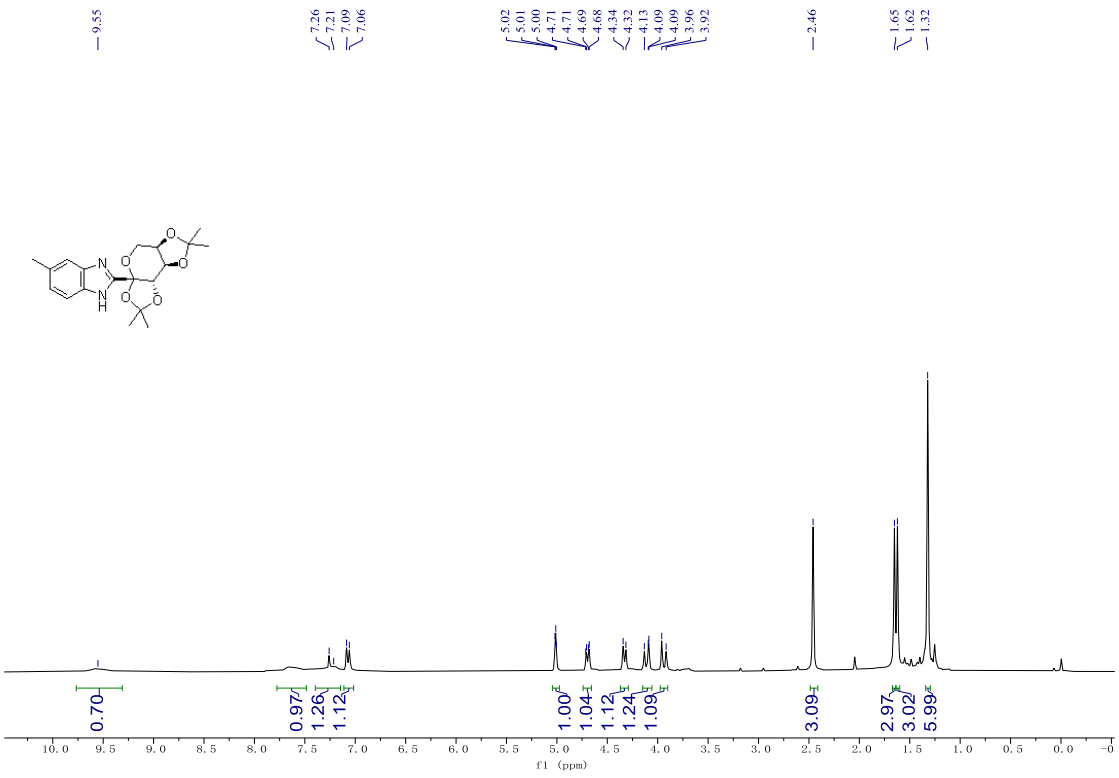
^{1}H NMR (500 MHz, $CDCl_3$) Spectra of compound 27



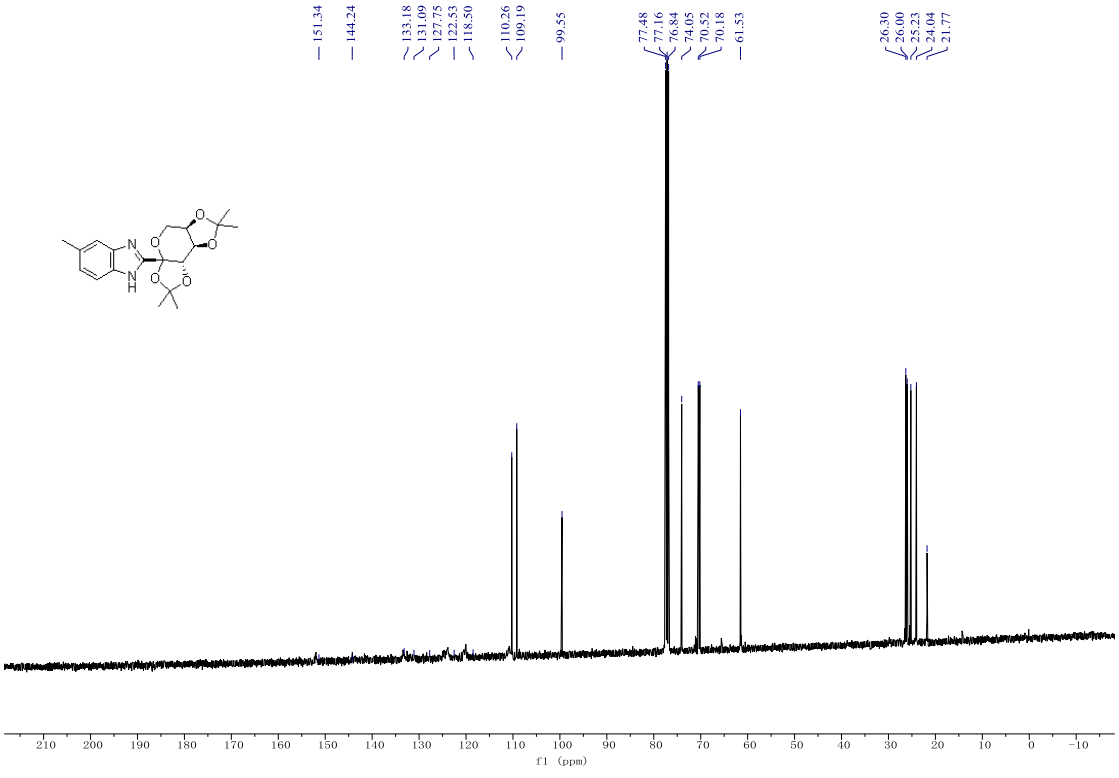
^{13}C NMR (126 MHz, $CDCl_3$) Spectra of compound 27



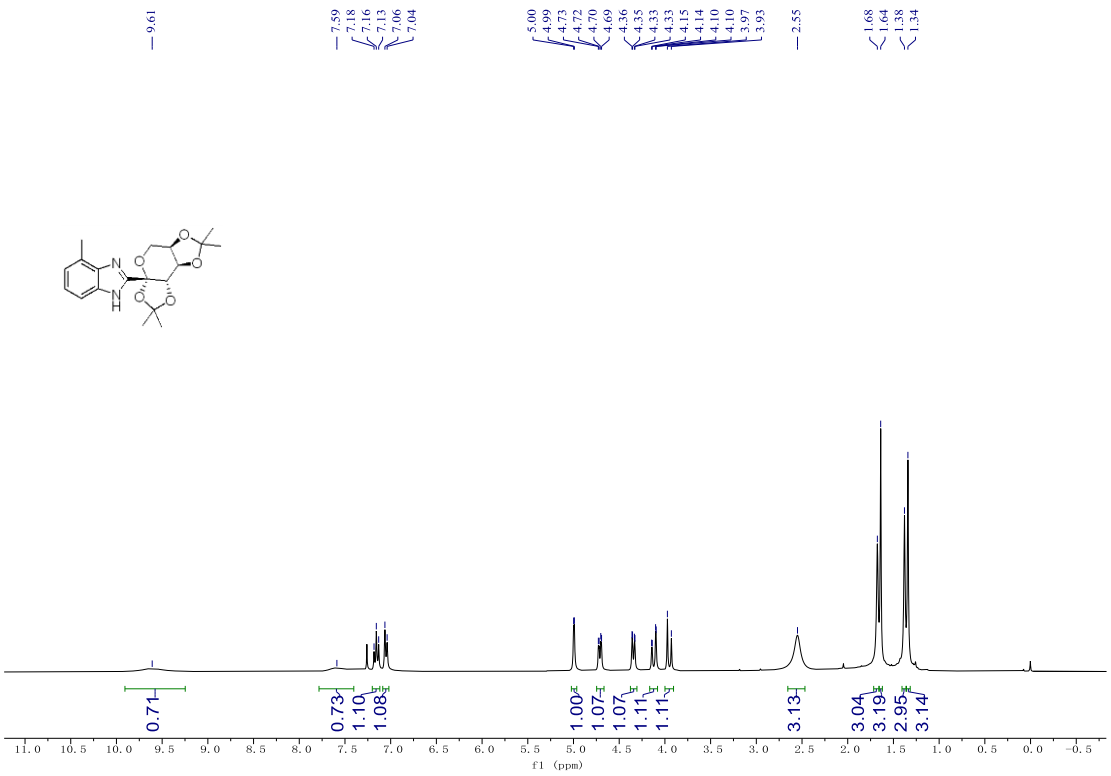
^{1}H NMR (300 MHz, $CDCl_3$) Spectra of compound 28



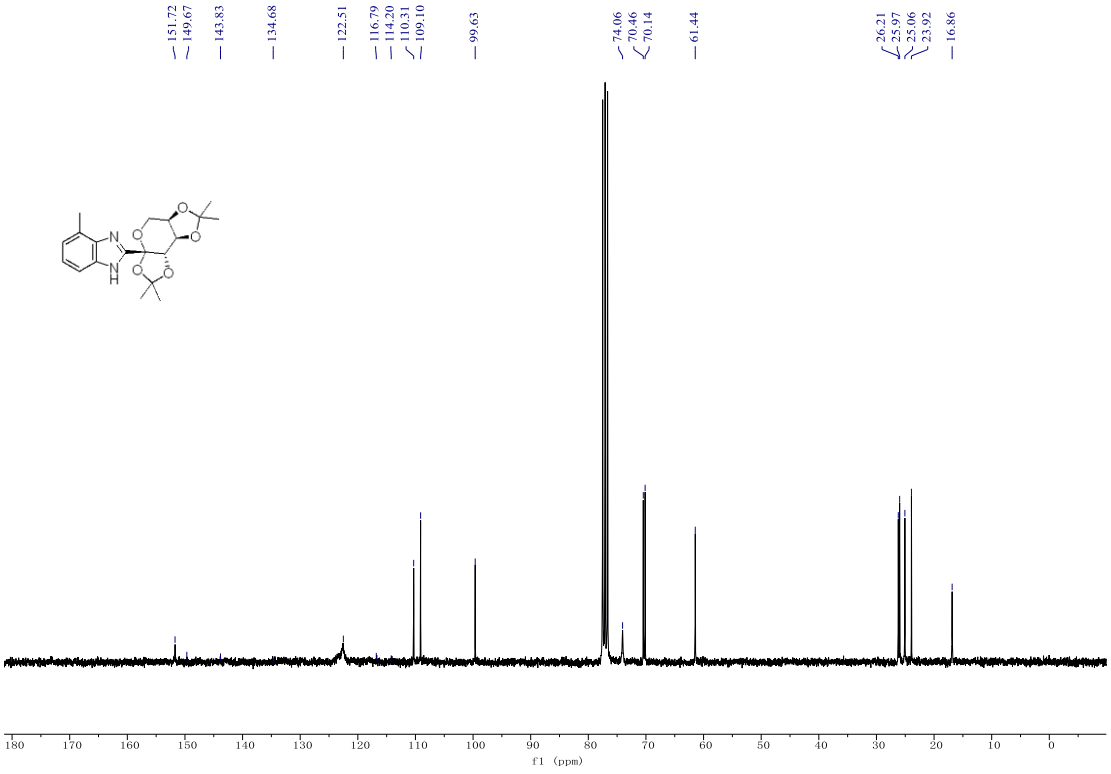
^{13}C NMR (101 MHz, $CDCl_3$) Spectra of compound 28



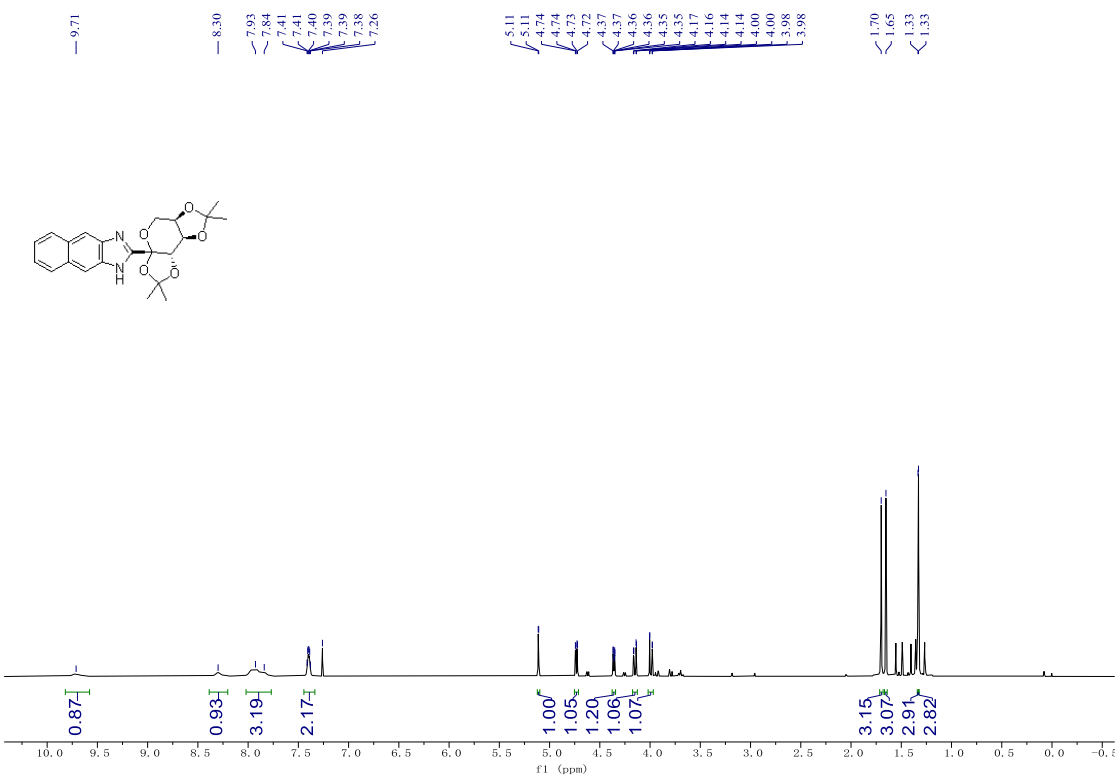
^{1}H NMR (300 MHz, $CDCl_3$) Spectra of compound 29



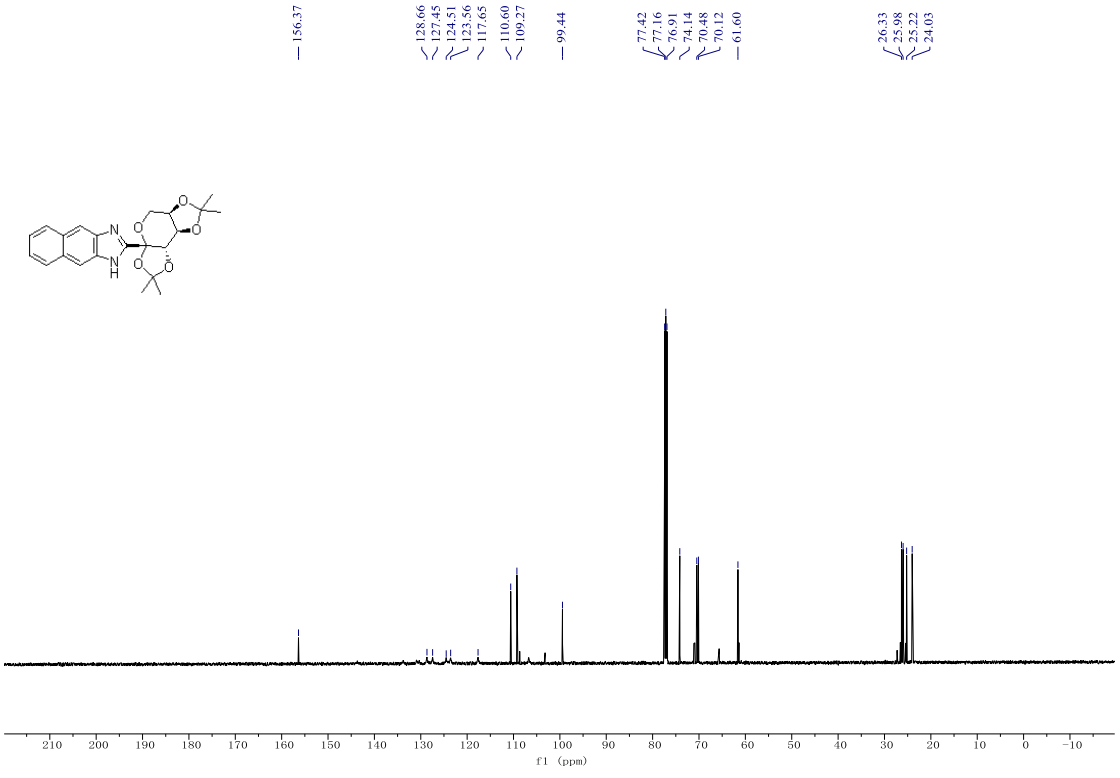
^{13}C NMR (75 MHz, $CDCl_3$) Spectra of compound 29



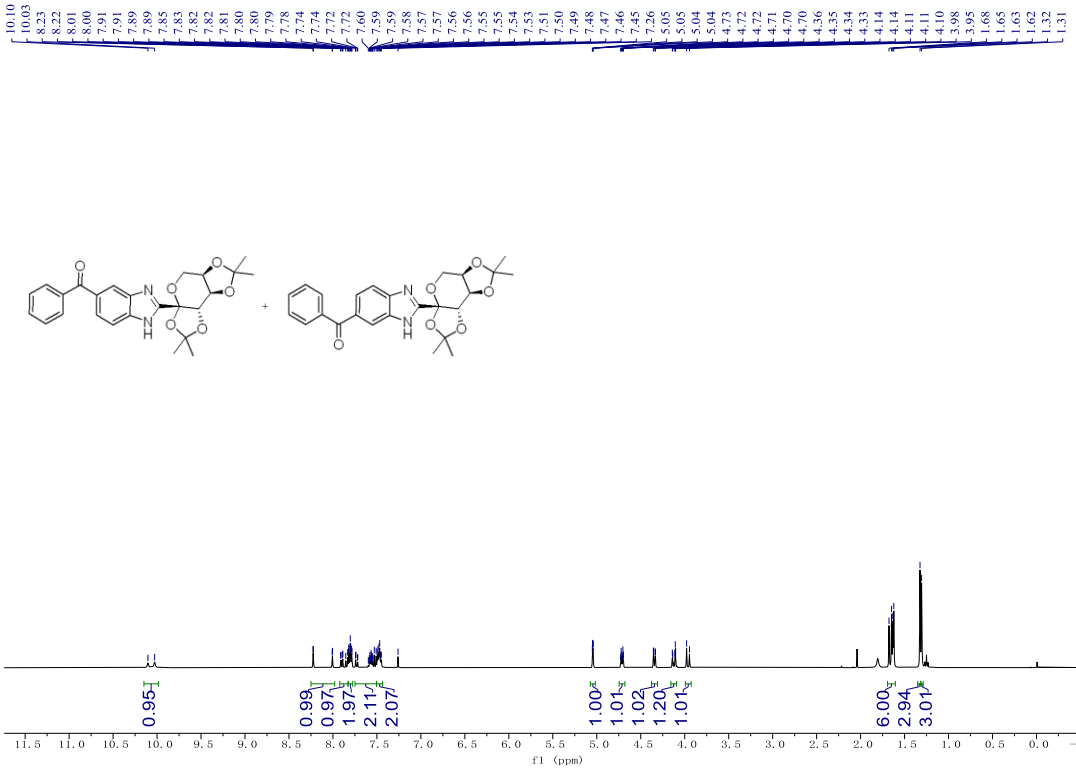
^{1}H NMR (500 MHz, $CDCl_3$) Spectra of compound 30



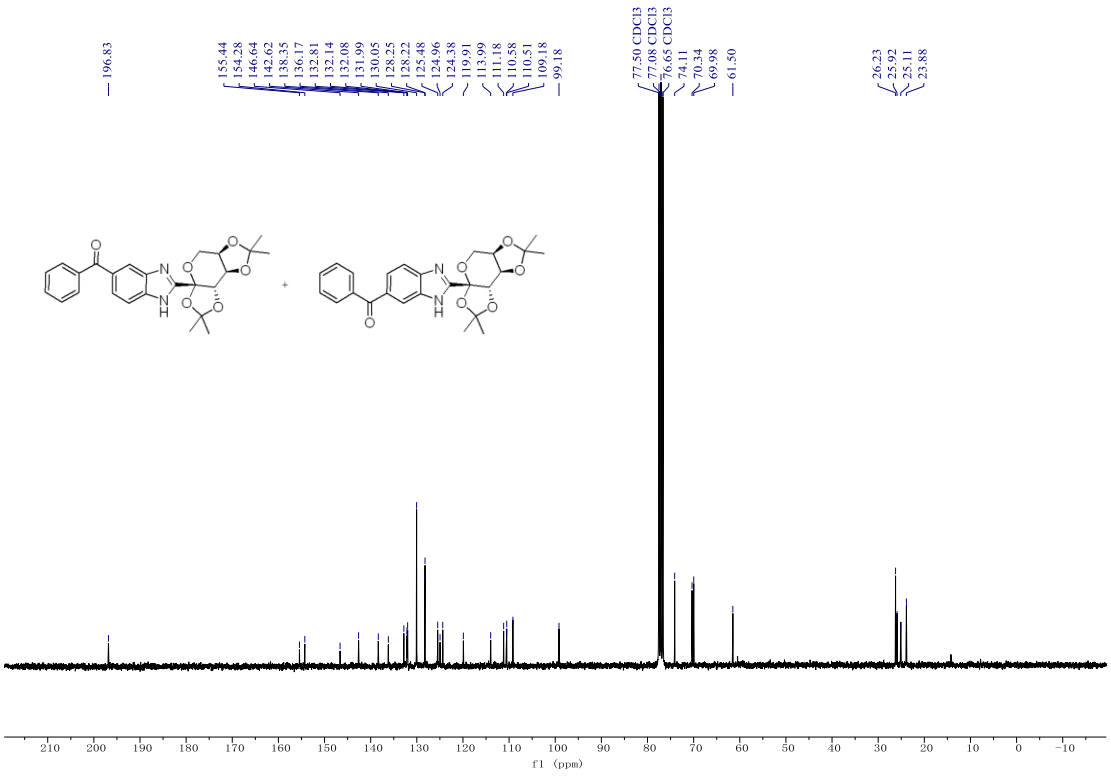
^{13}C NMR (126 MHz, $CDCl_3$) Spectra of compound 30



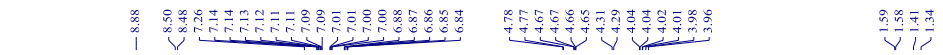
^{1}H NMR (300 MHz, $CDCl_3$) Spectra of compound 31

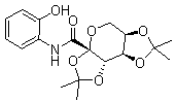


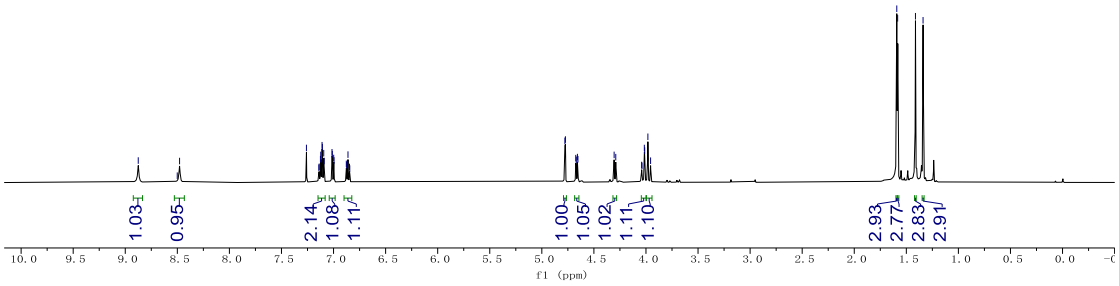
^{13}C NMR (75 MHz, $CDCl_3$) Spectra of compound 31



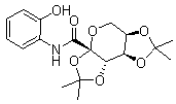
^{1}H NMR (500 MHz, $CDCl_3$) Spectra of compound 32

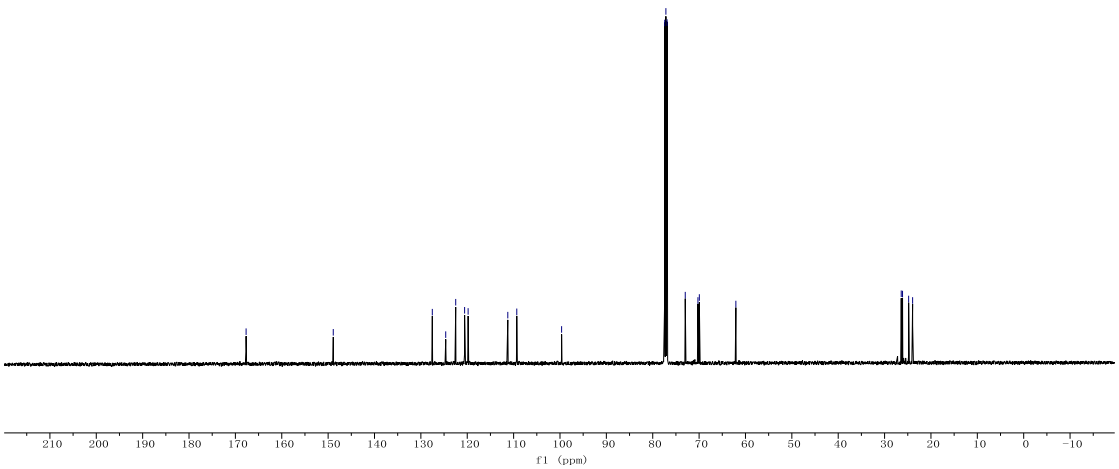




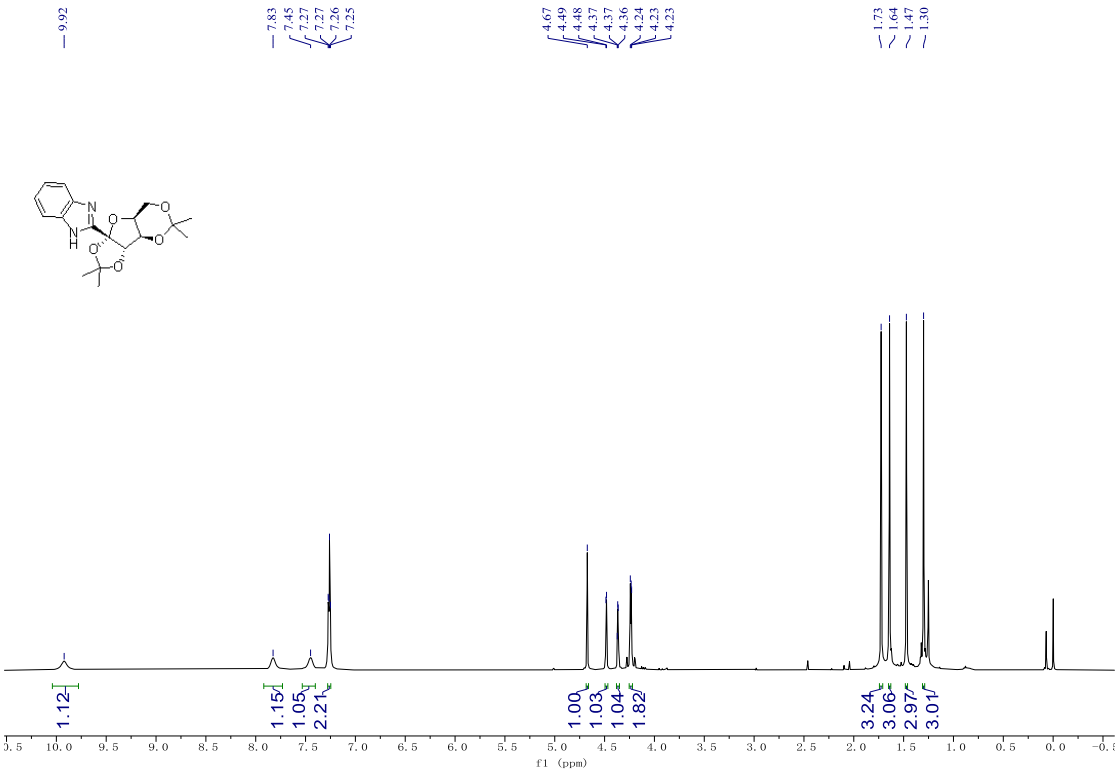


^{13}C NMR (126 MHz, $CDCl_3$) Spectra of compound 32

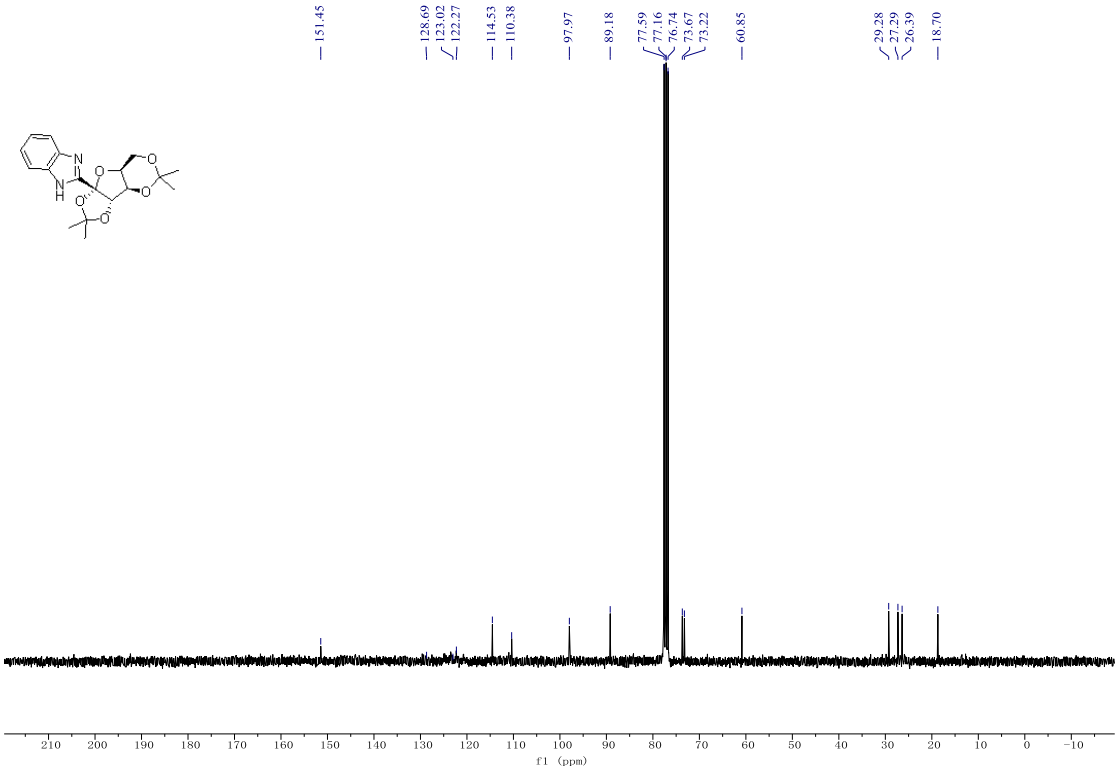




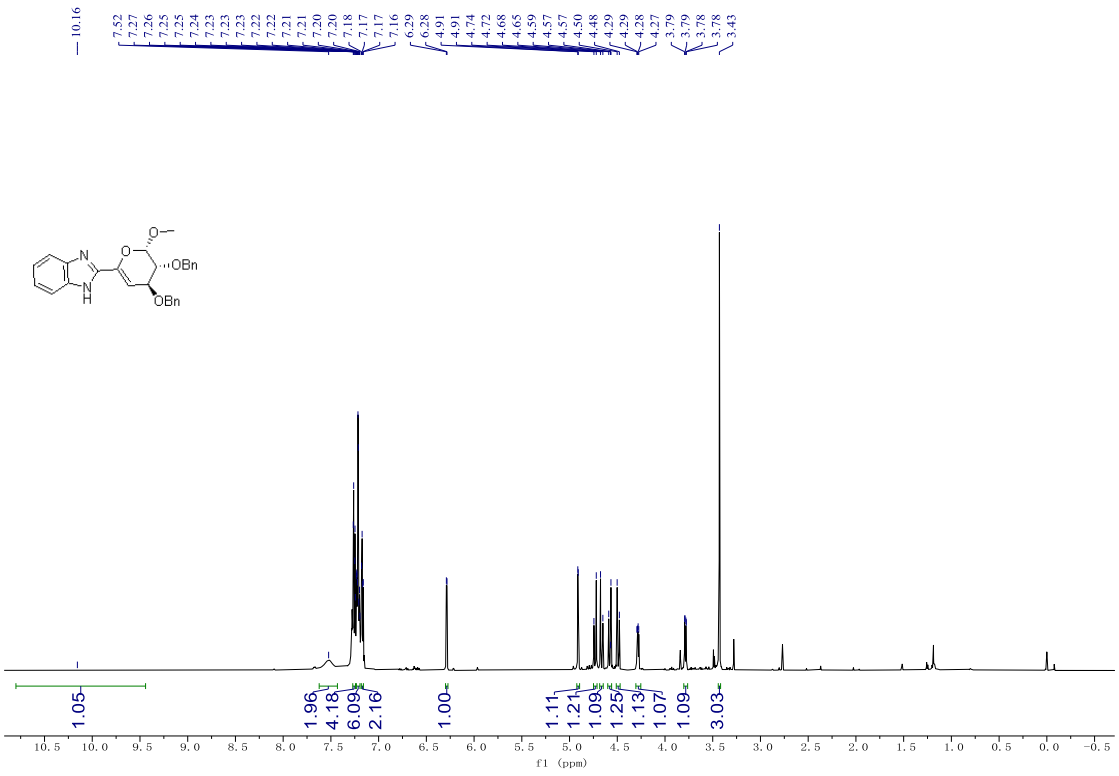
^{1}H NMR (400 MHz, $CDCl_3$) Spectra of compound 33



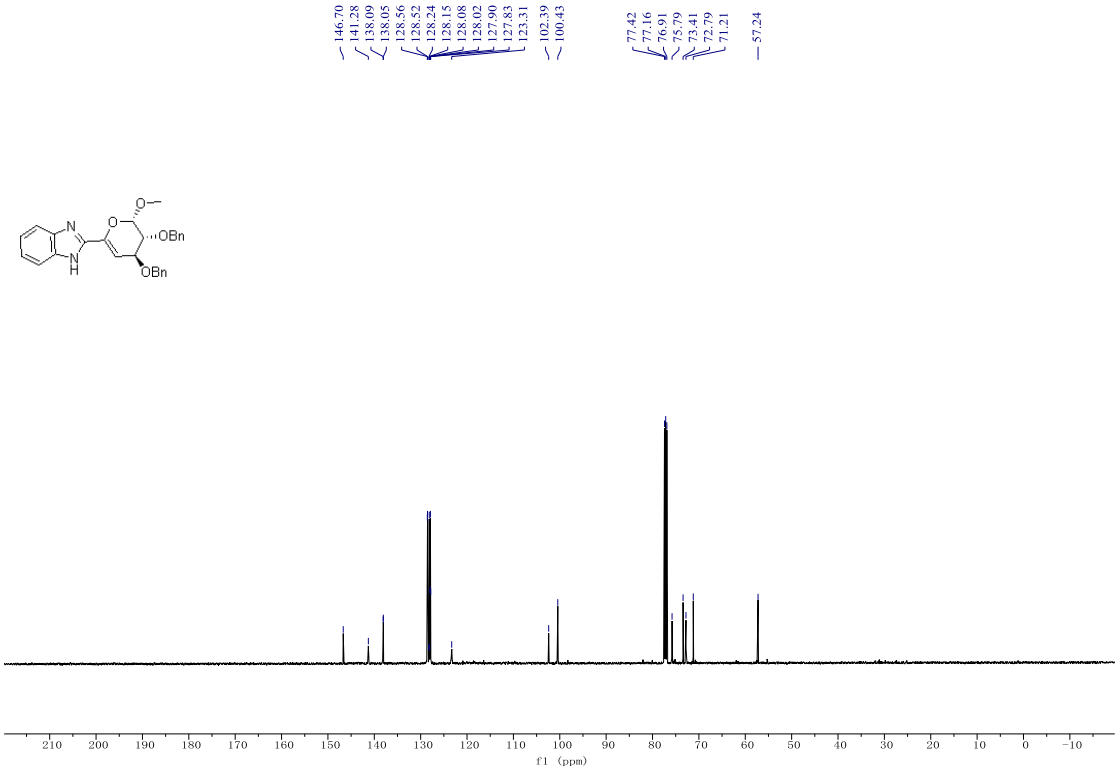
^{13}C NMR (75 MHz, $CDCl_3$) Spectra of compound 33



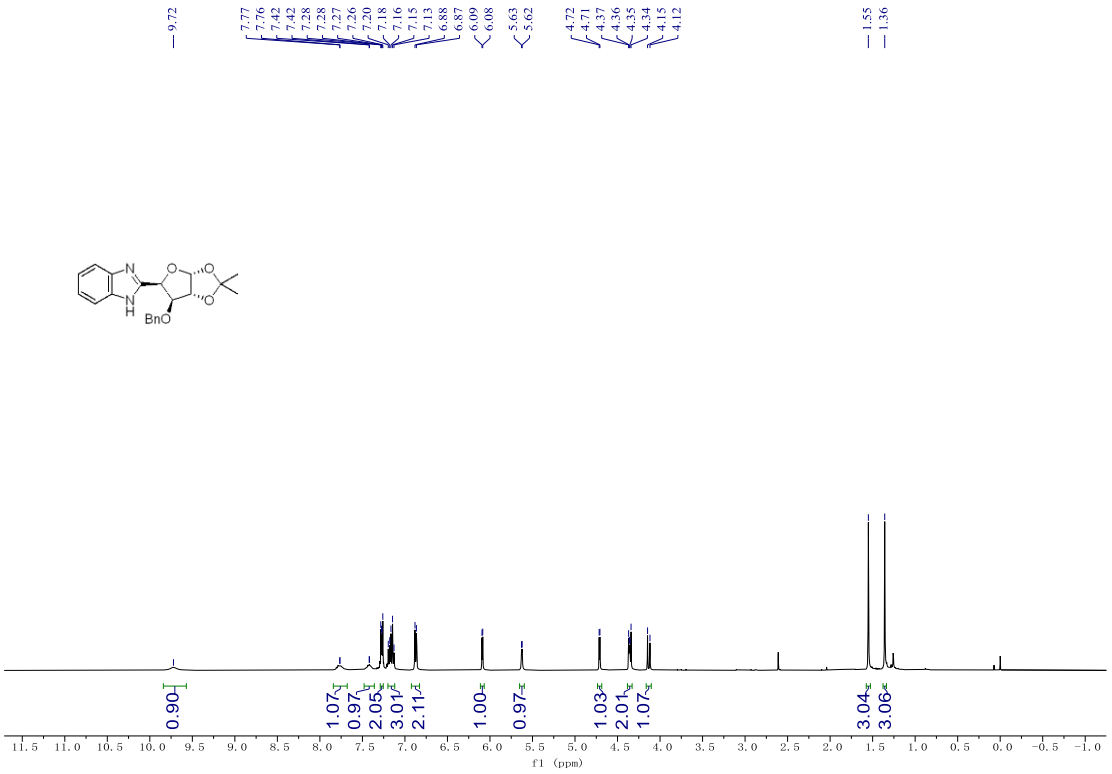
^{1}H NMR (500 MHz, $CDCl_3$) Spectra of compound 34



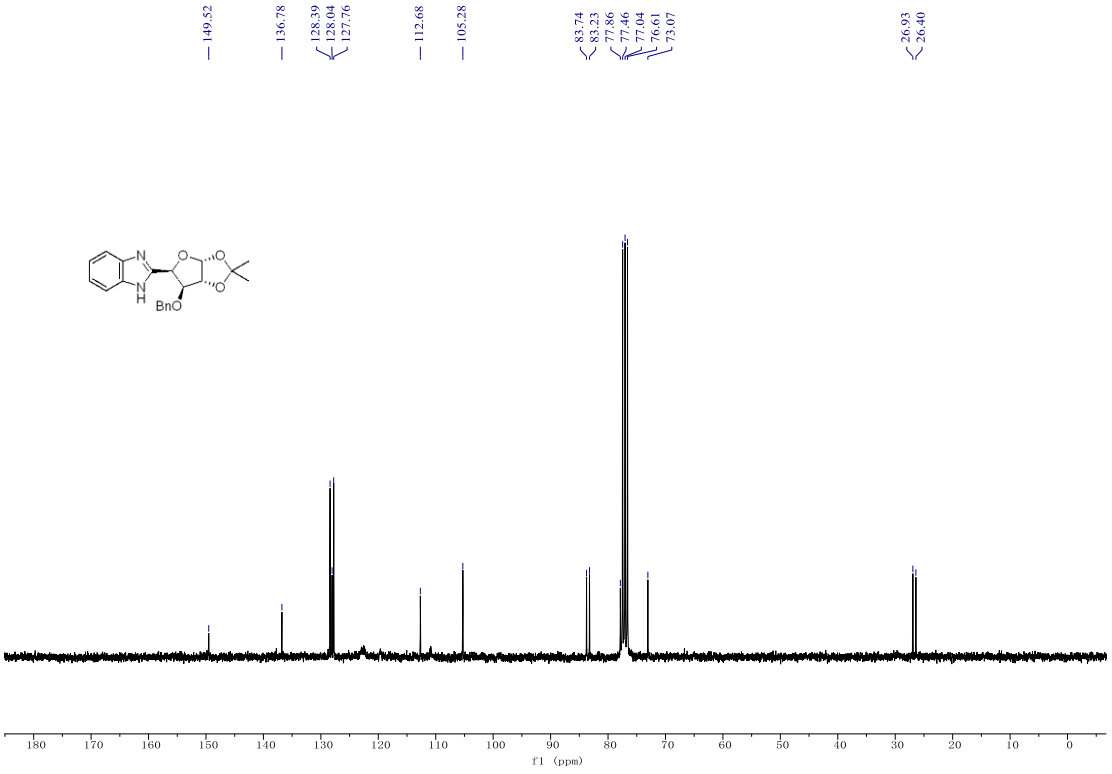
^{13}C NMR (126 MHz, $CDCl_3$) Spectra of compound 34



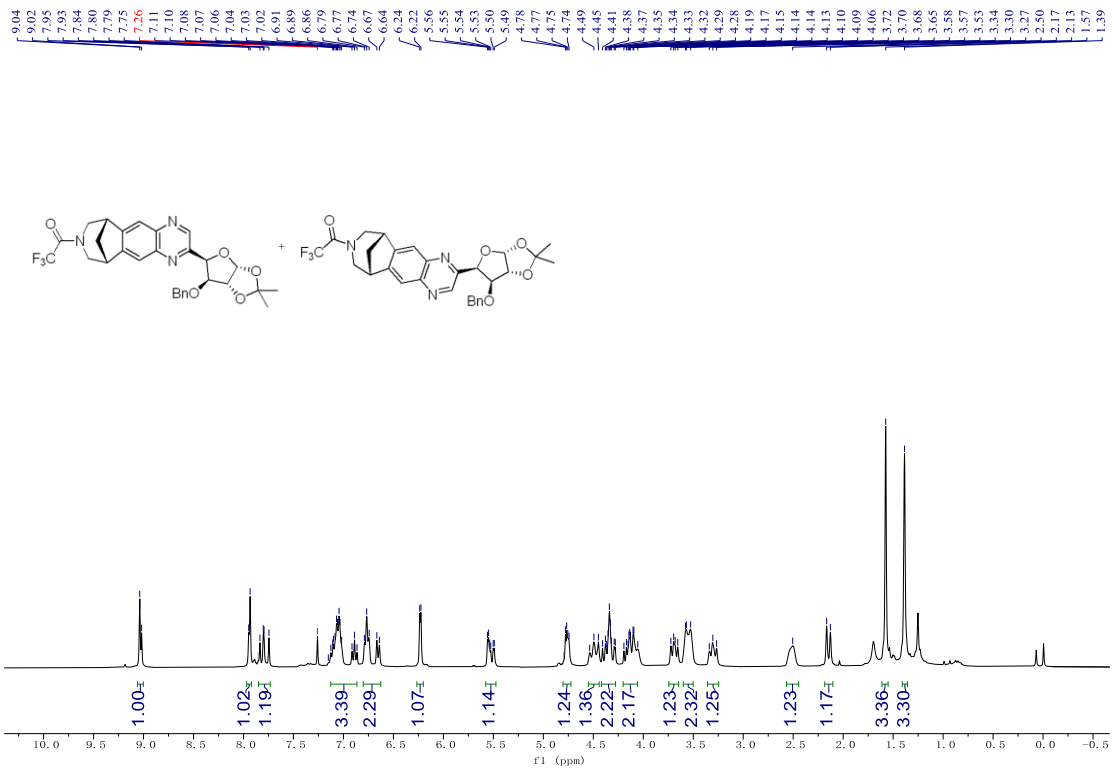
^{1}H NMR (400 MHz, $CDCl_3$) Spectra of compound 35



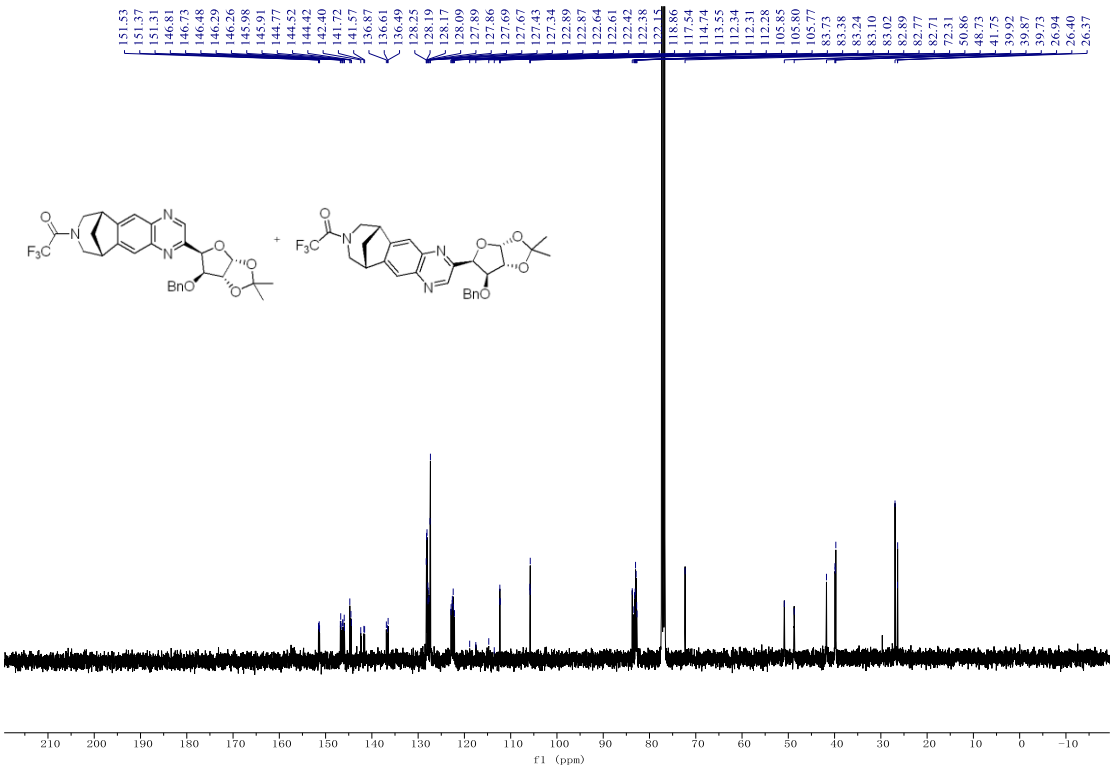
^{13}C NMR (75 MHz, $CDCl_3$) Spectra of compound 35



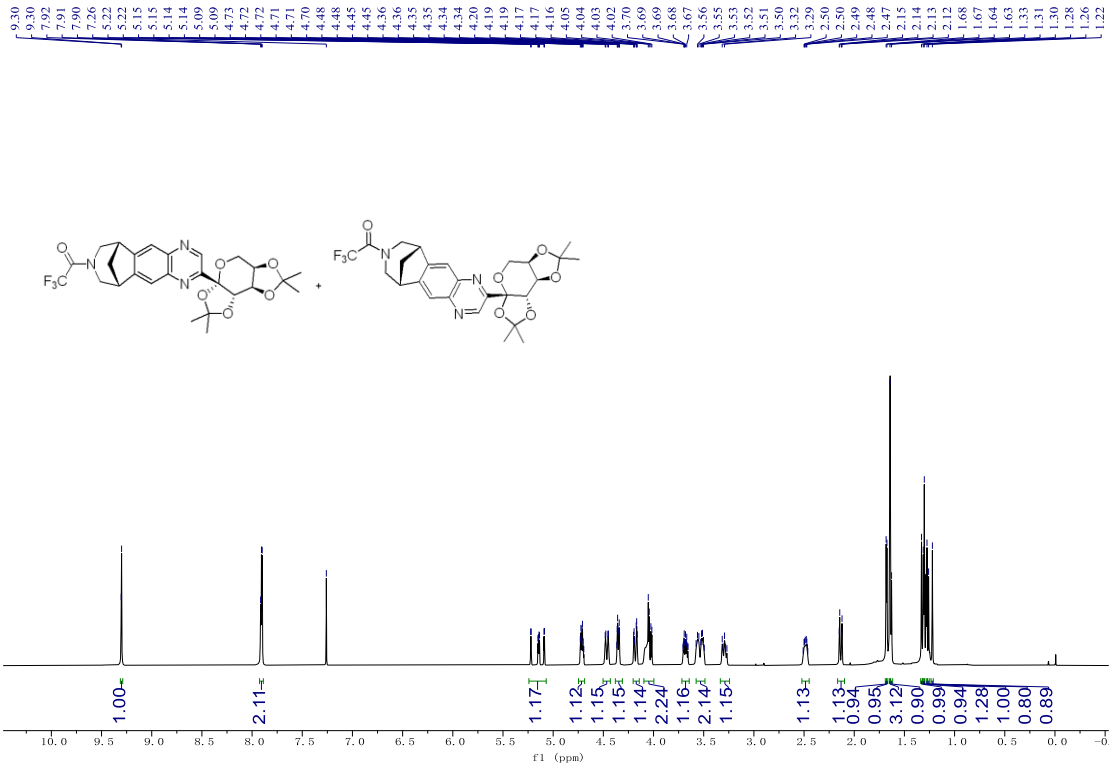
^{1}H NMR (300 MHz, $CDCl_3$) Spectra of compound 37



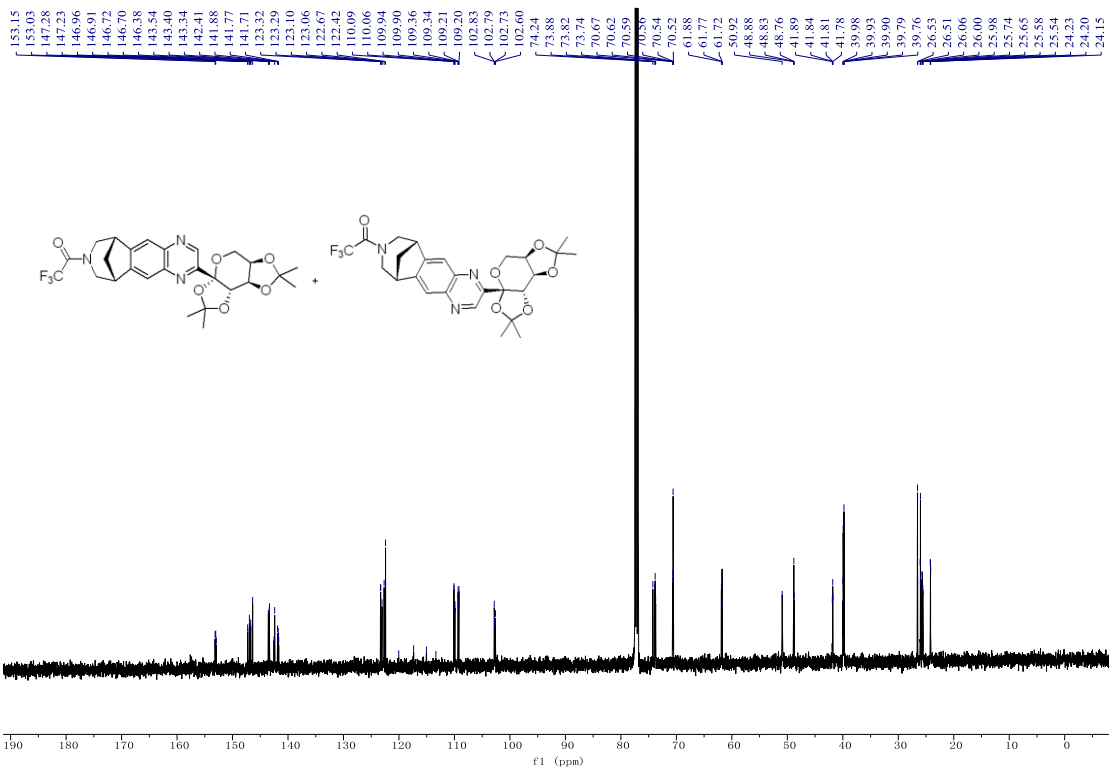
^{13}C NMR (101 MHz, $CDCl_3$) Spectra of compound 37



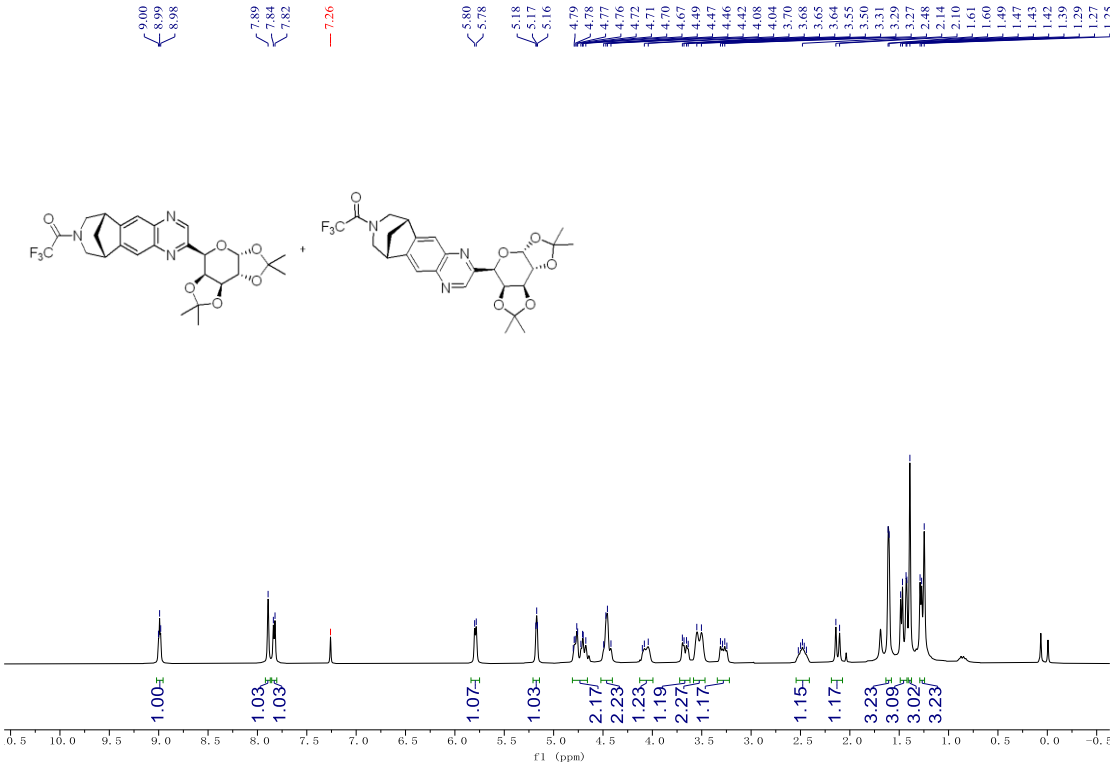
^{1}H NMR (500 MHz, $CDCl_3$) Spectra of compound 38



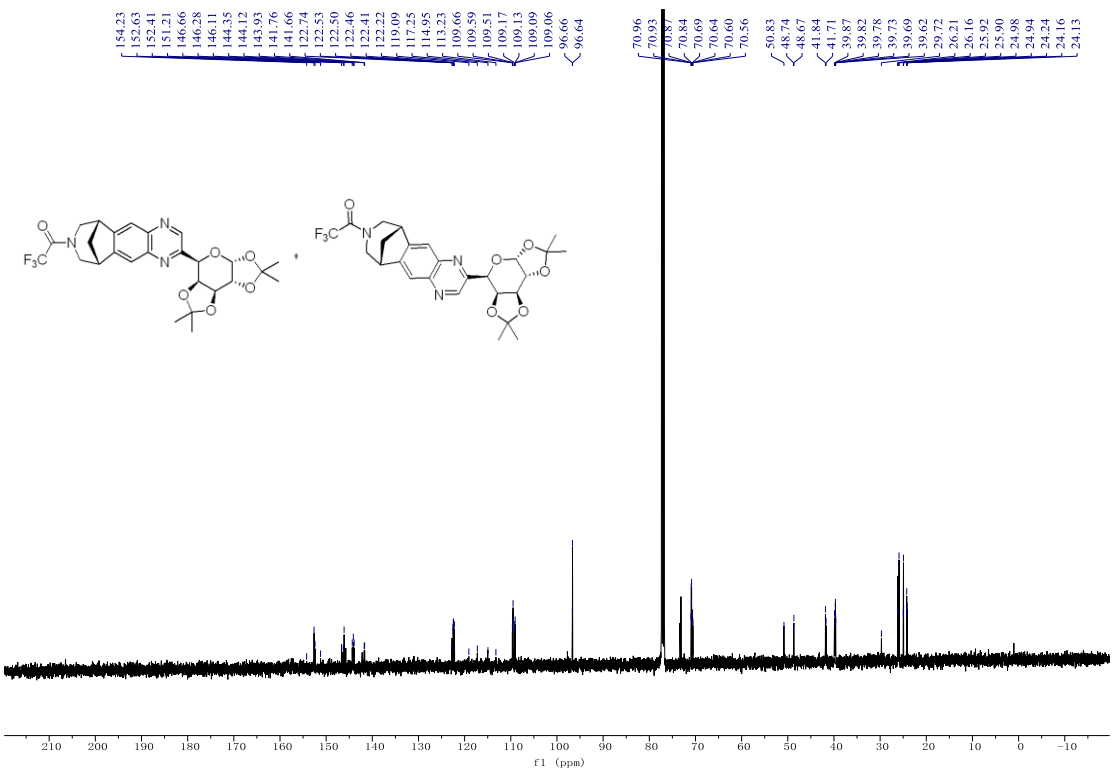
^{13}C NMR (126 MHz, $CDCl_3$) Spectra of compound 38



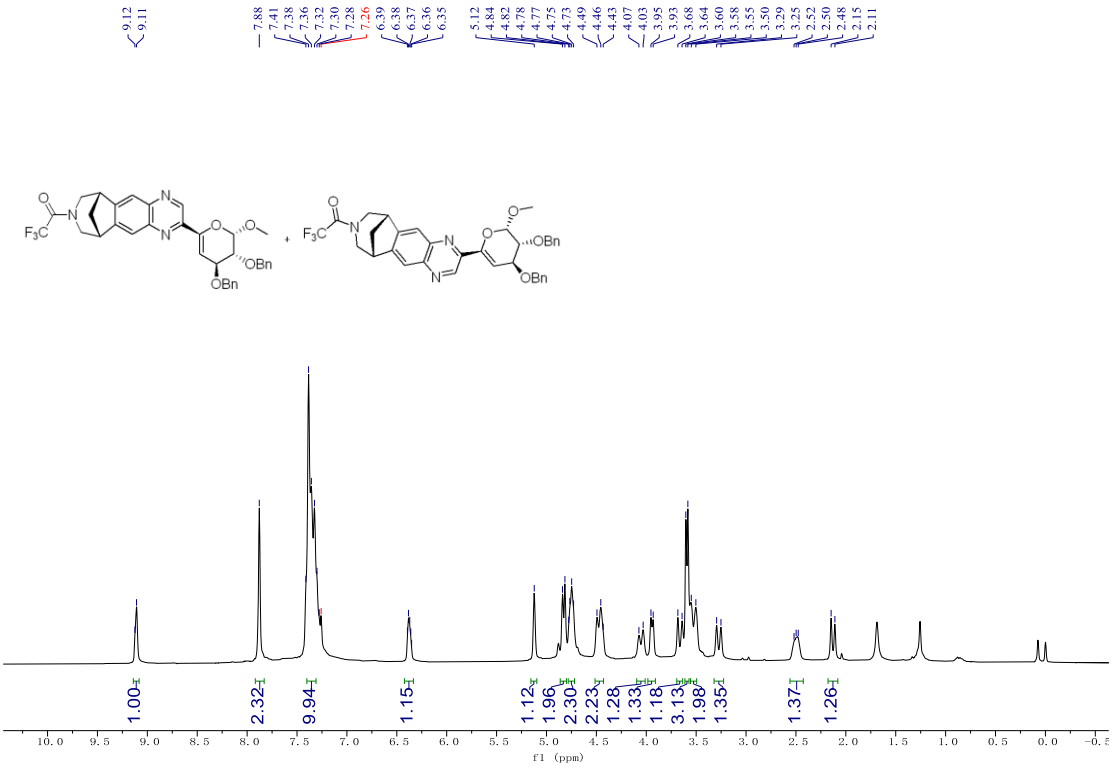
^{1}H NMR (300 MHz, $CDCl_3$) Spectra of compound 39



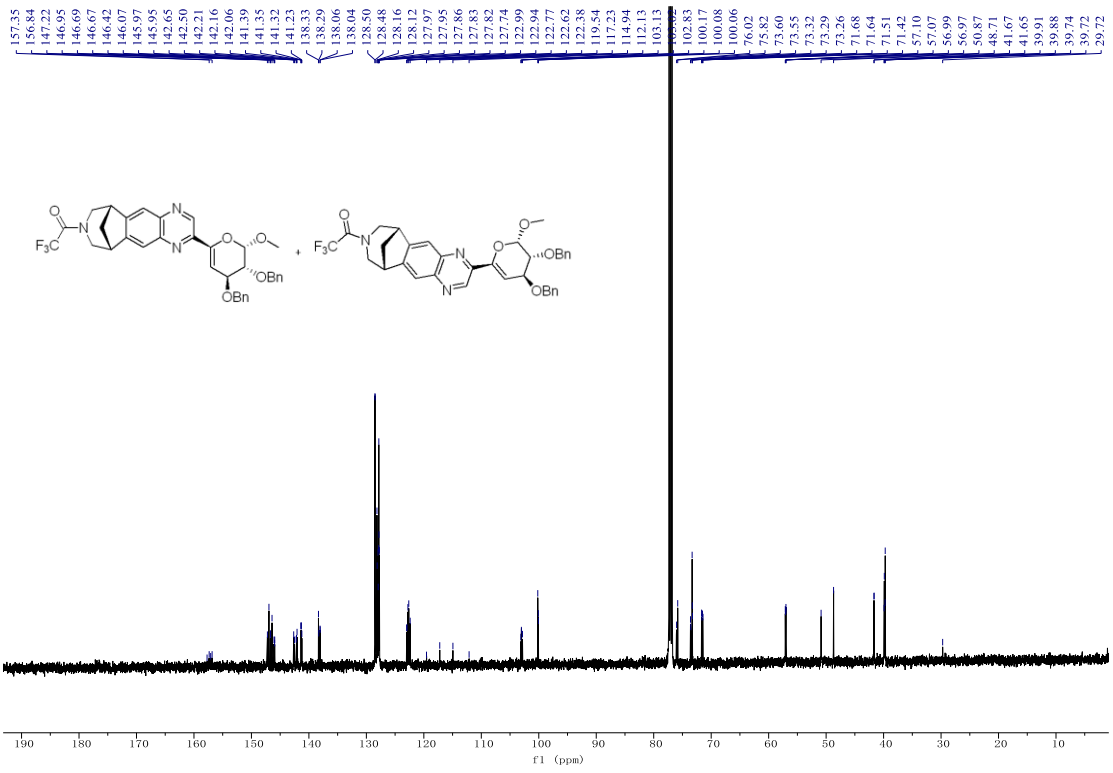
^{13}C NMR (126 MHz, $CDCl_3$) Spectra of compound 39



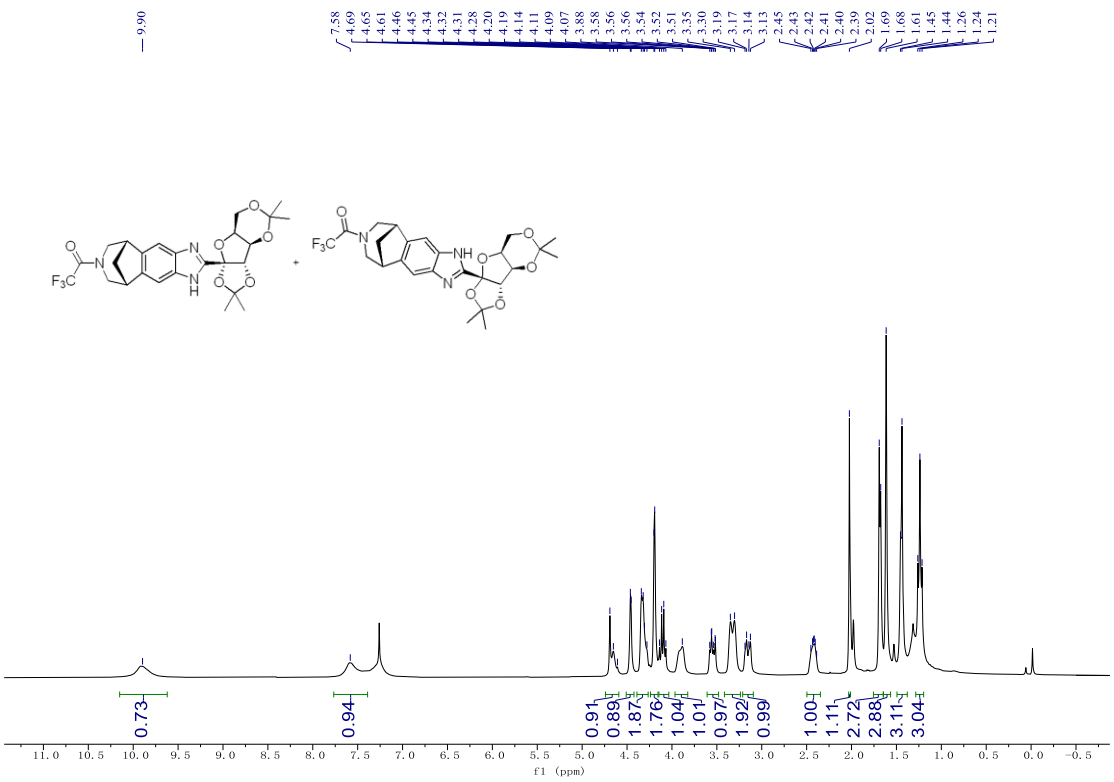
^{1}H NMR (300 MHz, $CDCl_3$) Spectra of compound 40



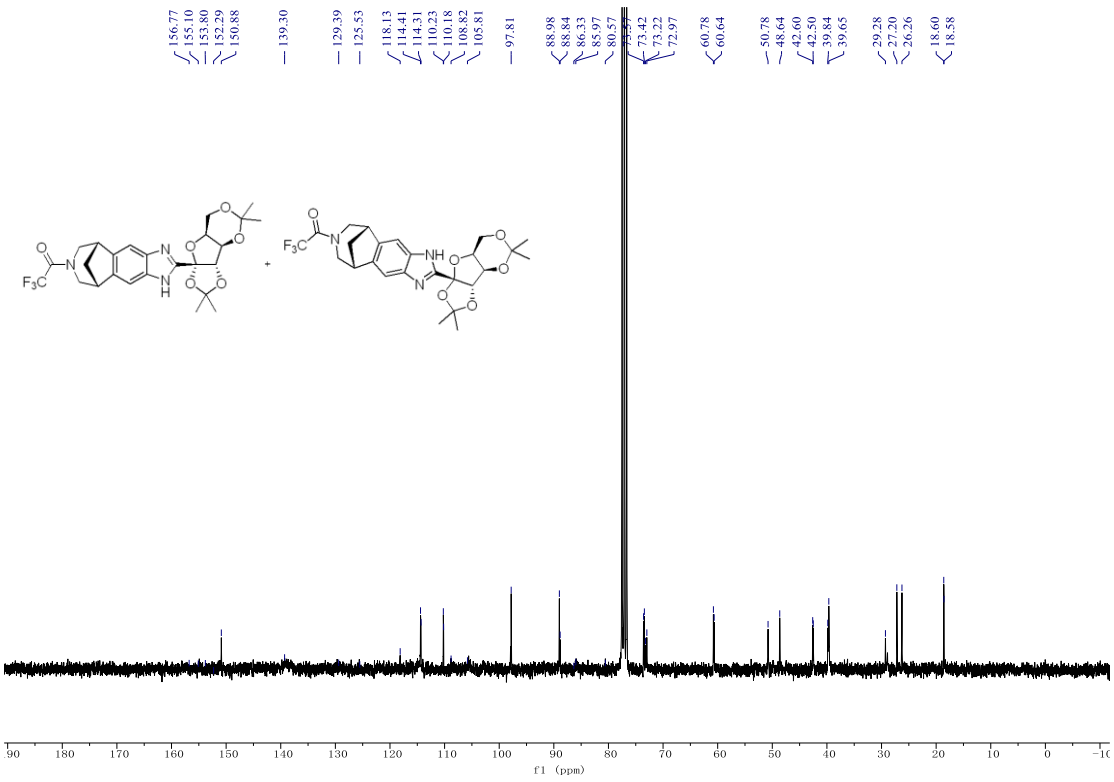
^{13}C NMR (126 MHz, $CDCl_3$) Spectra of compound 40



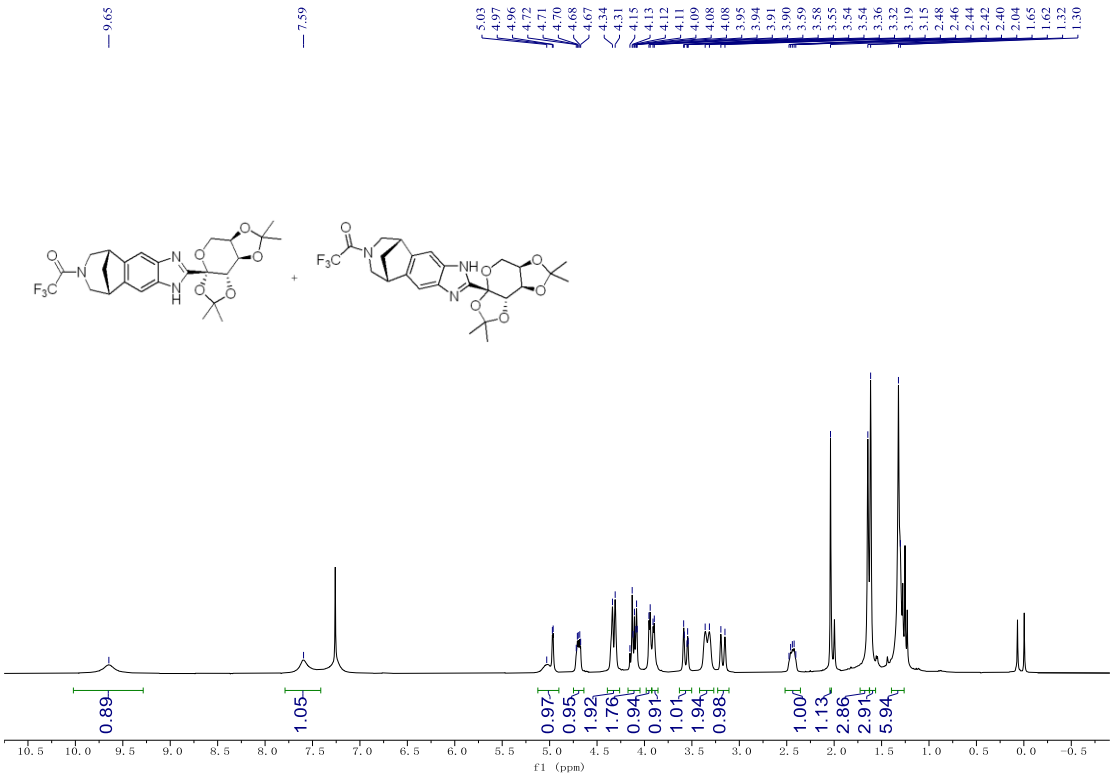
^{1}H NMR (300 MHz, $CDCl_3$) Spectra of compound 41



^{13}C NMR (75 MHz, $CDCl_3$) Spectra of compound 41



^{1}H NMR (300 MHz, $CDCl_3$) Spectra of compound 42



^{13}C NMR (75 MHz, $CDCl_3$) Spectra of compound 42