Supporting Information

N-Heterocyclic carbene-catalyzed enantioselective (dynamic) kinetic resolution for the assembly of inherently chiral macrocycles

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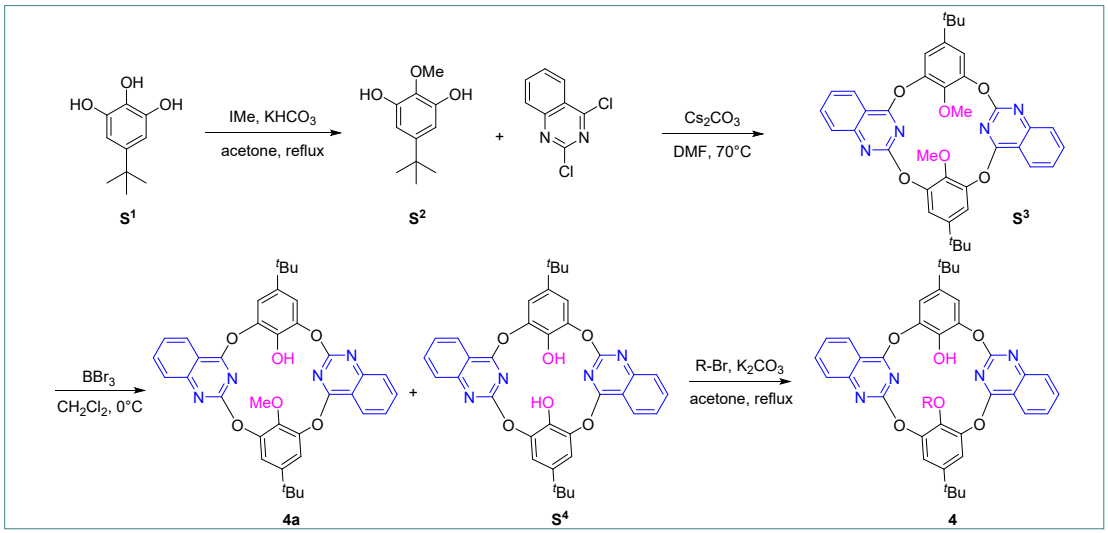
General information

Chemicals were purchased from commercial suppliers and used as received. Solvents were dried on alumina columns using a solvent dispensing system. Thin-layer chromatography (TLC) was conducted on plates (GF254) supplied by Yantai Chemicals (China) and visualized using a combination of UV, anisaldehyde, iodine, and potassium permanganate staining. ^{1}H NMR, ^{13}C NMR, spectra were recorded on a Bruker ACF400 (400 MHz) spectrometer. Chemical shifts were reported in parts per million (ppm), and the residual solvent peak was used as an internal reference: proton (chloroform δ 7.26), carbon (chloroform δ 77.16) or tetramethylsilane (TMS δ 0.00). Multiplicity was indicated as follows: s (singlet), d (doublet), t (triplet), q (quartet), m (multiplet), dd (doublet of doublet), bs (broad singlet). Coupling constants were reported in Hertz (Hz). All high resolution mass spectra were obtained from the Tsinghua University Mass Spectrometry Facility. High resolution mass spectra (HRMS) were performed on Agilent 6540 Q-TOF mass spectrometer (ESI). Flash chromatography separations were performed on Silica gel (300-400 mesh) supplied by Tsingdao Haiyang Chemicals (China). The enantiomeric excesses of products were determined on a Shimadzu LC-20AT Chiral HPLC. Optical rotations were recorded on Optical rotations were recorded on SGW-1 autopolarimeter. The melting point of the compoundswere determined on X-4 digital display micro-melting point tester purchased from Beijing Taki Instrument Co., Ltd. Single-crystal XRD experiments were carried out on a Rigaku XtaLAB Synergy-Custom instrument with CuKα radiation (λ = 1.54184 Å) at 191K, equipped with a rotating anode generator (FR-X: voltage,45 kV; current, 66 mA)

Preparation for substrates and products

(A) General procedure for the synthesis of substrates



Unless otherwise stated, the substrates **2** were used as supplied from commercial sources without further purification. The substrates **1** were prepared by following the literature report[1]; The substrates **4** were synthesized according to procedure as follows, **4b**, **4c**, **4d** were new compounds in which.

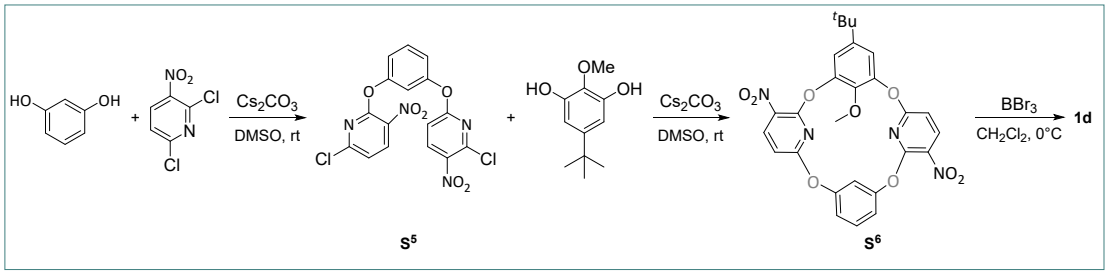
To a 1000 mL two-necked round bottom flask was added **S1** (7.28 g, 40.0mmol), $KHCO_3$ (5.0 g, 50 mmol, 1.25 equiv) and acetone (500 mL). And the reaction mixture was stirred reflux for 5 minutes. Subsequently, MeI (8.52 g, 60.0 mmol, 1.5 equiv) was added dropwisely. The reaction was reflux overnight. The reaction mixture was diluted with H_2O and extracted with EA. The organic layer was dried with Na_2SO_4, filtered, and concentrated under reduced pressure to give the crude product that was purified by silica column chromatography (PE / EtOAc from 20:1 to 10:1) to give the desired **S2** (3.2 g, 41% yield).

To a 500 mL two-necked round bottom flask was added 2,4-dichloroquinazoline (3.98 g, 20 mmol, 1.0 equiv), **S2** (3.92 g, 20 mmol, 1.0 equiv) and Cs_2CO_3 (19.54 g, 60 mmol, 3.0 equiv). The reaction system was then replaced with N_2 and dry DMF (250 mL) was added to the reaction system through a syringe. The reaction was heated at 70 °C overnight. The reaction was extracted with DCM (3 × 200 mL) and the combined organic layers were washed with brine (4 × 200 mL). The organic layer was dried with Na_2SO_4, filtered, and concentrated under reduced pressure to give the crude product that was purified by silica column chromatography (PE/DCM/EA = 20: 20: 1 to 8: 8: 1) to give **S3** (5.8 g, 45% yield).

To a 100 mL round bottom flask was added **S3** (3.86 g, 6.0 mmol) and dry DCM (80 mL). The reaction was cooled down to 0 °C and BBr_3 (15.0 g, 60 mmol, 10 equiv) was added. The reaction taken place at 0 °C for two days. The reaction was carefully

quenched with ice and neutralized with saturated $NaHCO_3$ and a minor quantity of MeOH was introduced into the reaction system to facilitate dissolution. The mixture was extracted with DCM (3 × 200 mL) and the combined organic layers were washed with H_2O and brine and dried over anhydrous Na_2SO_4. Solvents were removed in vacuo and the residue was purified by flash column chromatography on silica gel (PE/DCM/EA = 10: 10: 1 to 6: 6: 1) to give **4a** (557 mg, 15% yield) and (PE/DCM/EA = 1: 1: 1) to give **S[4]** (1.3 g, 35% yield).

The corresponding alkyl halides (1.1 equiv), **S[4]** (616 mg, 1.0 mmol) and K_2CO_3 (138 mg, 1.0 mmol, 1.0 equiv) were dissolved in acetone (20ml) and the reaction mixture was stirred reflux until **S[4]** was completely consumed. The reaction mixture was diluted with H_2O and extracted with EA. The organic layer was dried with Na_2SO_4, filtered, and concentrated under reduced pressure to give the crude product that was purified by silica column chromatography (PE / EtOAc from 20:1 to 8:1) to give **4b-4d**.



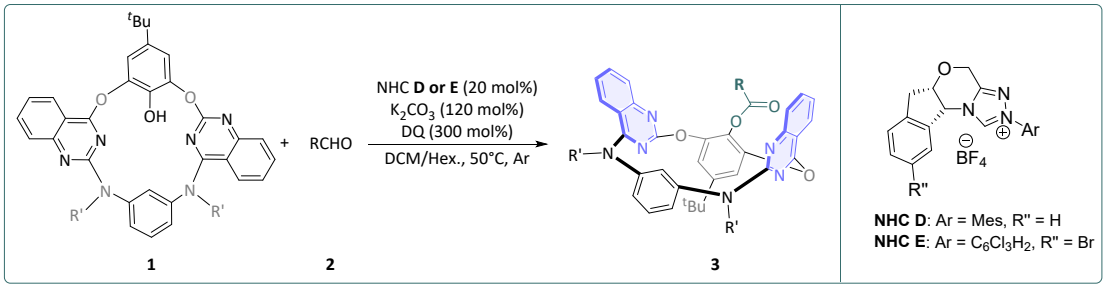
To a 500 mL two-necked round bottom flask was added 2,6-dichloro-3-nitropyridine (3.84 g, 20 mmol, 2.0 equiv), resorcinol (1.10 g, 10 mmol, 1.0 equiv) and Cs_2CO_3 (6.52 g, 20 mmol, 2.0 equiv). The reaction system was then replaced with N_2 and dry DMSO (500 mL) was added to the reaction system through a syringe. The reaction was heated at room temperature overnight. The reaction was extracted with DCM (3 × 200 mL) and the combined organic layers were washed with brine (4 × 300 mL). The organic layer was dried with Na_2SO_4, filtered, and concentrated under reduced pressure to give the crude product that was purified by silica column chromatography (PE/ EA = 20: 1 to 10: 1) to give **S[5]** (3.42 g, 81% yield).

To a 500 mL two-necked round bottom flask was added **S[5]** (2.11 g, 5 mmol, 1.0 equiv), **S[2]** (0.98 g, 5 mmol, 1.0 equiv) and Cs_2CO_3 (3.26 g, 10 mmol, 2.0 equiv). The reaction system was then replaced with N_2 and dry DMSO (250 mL) was added to the reaction system through a syringe. The reaction was heated at room temperature overnight. The reaction was extracted with DCM (3 × 200 mL) and the combined organic layers were washed with brine (4 × 200 mL). The organic layer was dried with Na_2SO_4, filtered, and concentrated under reduced pressure to give the crude product that was purified by silica column chromatography (PE/ EA = 15: 1 to 8: 1) to give **S[6]** (0.96 g, 35% yield).

To a 100 mL round bottom flask was added **S[6]** (0.61 g, 1.0 mmol) and dry DCM (50 mL). The reaction was cooled down to 0 °C and BBr_3 (1.25 g, 5 mmol, 5 equiv) was

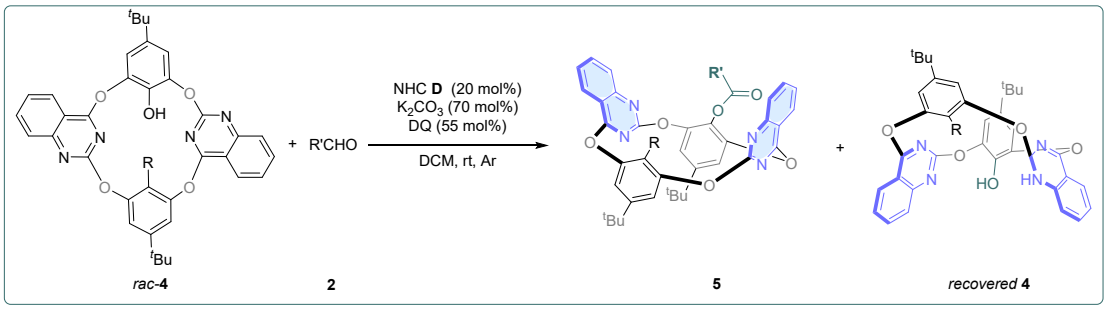
added. The reaction taken place at 0 °C overnight. The reaction was carefully quenched with ice and neutralized with saturated $NaHCO_3$ and a minor quantity of MeOH was introduced into the reaction system to facilitate dissolution. The mixture was extracted with DCM (3 × 200 mL) and the combined organic layers were washed with H_2O and brine and dried over anhydrous Na_2SO_4. Solvents were removed in vacuo and the residue was purified by flash column chromatography on silica gel (PE/DCM/EA = 10: 10: 1 to 4: 4: 1) to give **1d** (458 mg, 86% yield).

(B) General procedure for the synthesis of 3



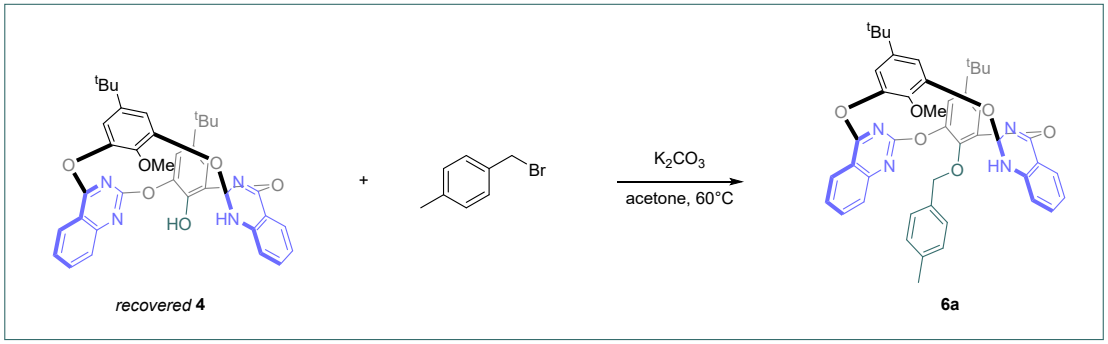
To a 15 mL tube sealing equipped with a magnetic stir bar, was added the pre-catalyst **D** or **E** (20 mol%), **1** (0.033 mmol, 1.0 equiv), **2** (0.1 mmol, 3.0 equiv), K_2CO_3 (0.04 mmol, 1.2 equiv) and DQ (0.1 mmol, 3.0 equiv). The tube was then brought into glove box. DCM (0.6 ml) and Hex. (0.6 ml) were added via a pipette. The tube sealing was heated at 50 °C for 36 hours. After completion of the reaction (monitored by TLC), the mixture was concentrated under reduced pressure. The resulting crude residue was purified via column chromatography on silica gel (40:1 to 8:1 hexanes/EtOAc) to afford the desired product **3**.

(C) General procedure for the synthesis of 5

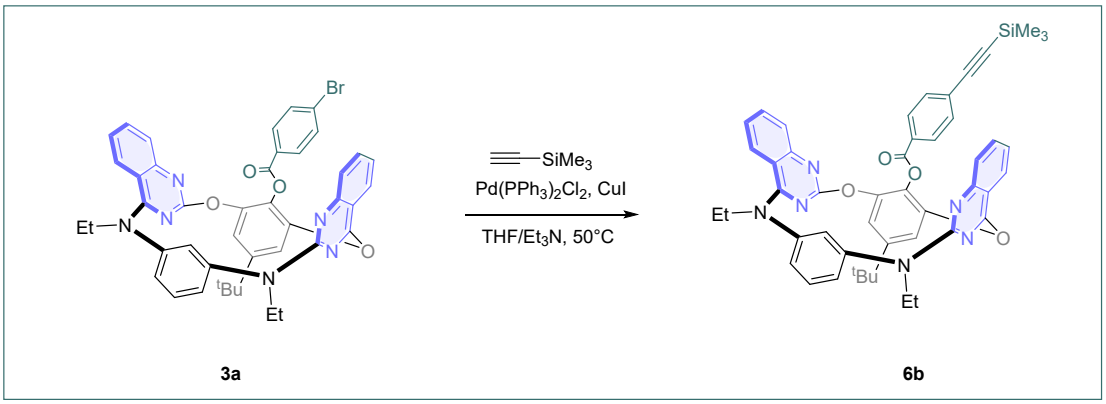


To a 15 mL reaction flask equipped with a magnetic stir bar, was added the pre-catalyst **D** (20 mol%), **4** (0.1 mmol, 1.0 equiv), **2** (0.08 mmol, 0.8 equiv), K_2CO_3 (0.07 mmol, 0.7 equiv) and DQ (0.055 mmol, 0.55 equiv). The tube was then brought into glove box, dry DCM (2.0 ml) and 4 Å MS (100 mg) were added. The flask was fixed by a metal holder and reacted in the glovebox until the corresponding **4** was completely consumed. After completion of the reaction (monitored by TLC), the mixture was concentrated under reduced pressure. The resulting crude residue was purified via column chromatography on silica gel to afford the desired product **5** and recovered **4**.

(D) Synthetic applications

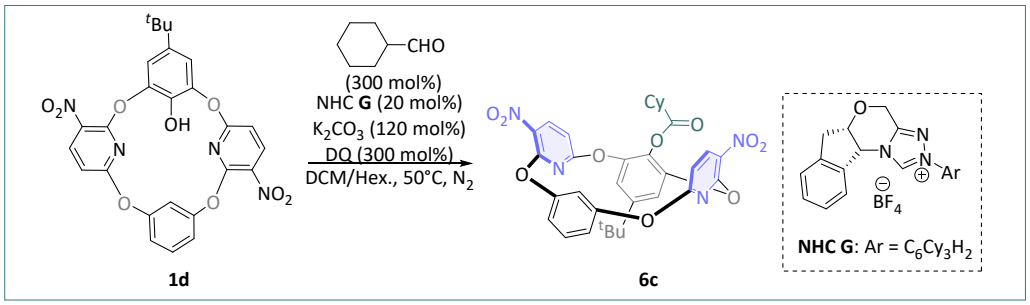


To a 15 mL tube sealing equipped with a magnetic stir bar, was added recovered **4** (0.06 mmol, 1.0 equiv), alkyl halides (0.09 mmol, 1.5 equiv), K_2CO_3 (0.09 mmol, 1.5 equiv). The tube was then brought into glove box. Then, acetone (1.2 ml) were added via a pipette. The tube sealing was heated at 60 °C for 6 hours. After completion of the reaction (monitored by TLC), the mixture was concentrated under reduced pressure. The resulting crude residue was purified via column chromatography on silica gel (40:1 to 8:1 hexanes/EtOAc) to afford the desired product **6a**.



To a 15 mL tube sealing equipped with a magnetic stir bar, was added **3a** (0.1 mmol, 1.0 equiv), $Pd(PPh_3)_2Cl_2$ (0.01 mmol, 0.1 equiv), CuI (0.01 mmol, 0.1 equiv). The tube was then brought into glove box. Then, THF (1.0 ml), Et_3N (1.0 ml) and TMS-acetylene (0.3 mmol, 3.0 equiv) were added via a pipette in sequence. The tube sealing was heated at 50 °C for 12 hours. After completion of the reaction (monitored by TLC), the mixture was concentrated under reduced pressure. The resulting crude residue was purified via column chromatography on silica gel (40:1 to 8:1 hexanes/EtOAc) to afford the desired product **6b**.

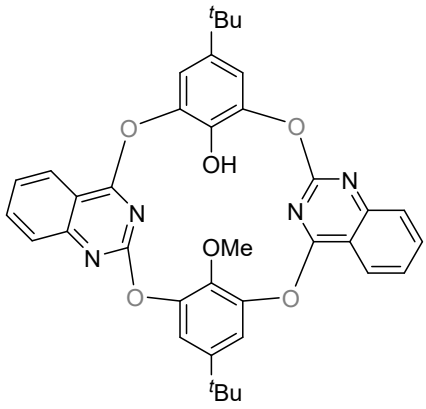
(E) General procedure for the synthesis of 6c



To a 15 mL tube sealing equipped with a magnetic stir bar, was added the pre-catalyst **G** (20 mol%), **1d** (0.1 mmol, 1.0 equiv), Cyclohexanecarboxaldehyde (0.3 mmol, 3.0 equiv), K_2CO_3 (0.12 mmol, 1.2 equiv) and DQ (0.3 mmol, 3.0 equiv). The tube was then brought into glove box. DCM (1.8 ml) and Hex. (1.8 ml) were added via a pipette. The tube sealing was heated at 50 °C for 24 hours. After completion of the reaction (monitored by TLC), the mixture was concentrated under reduced pressure. The resulting crude residue was purified via column chromatography on silica gel (40:1 to 6:1 hexanes/EtOAc) to afford the desired product **6c**.

Characterization data of substrates and products

3^5,7^5-di-tert-butyl-7^2-methoxy-2,4,6,8-tetraoxa-1(2,4),5(4,2)-diquinazolina-3,7(1,3)-dibenzenacyclooctaphan-3^2-ol (4a)



4a

4a: white solid. M.p. = 224 – 225 ℃

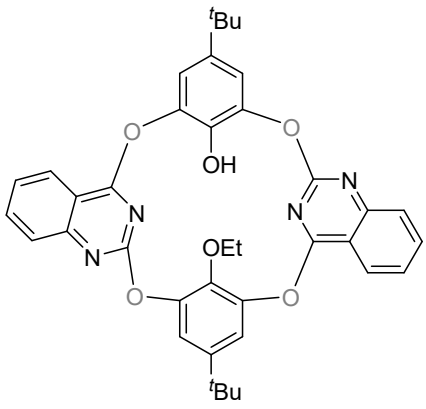
^{1}H NMR (400 MHz, $CDCl_3$) δ 8.31 (d, J = 8.1 Hz, 1H), 8.18 (d, J = 8.2 Hz, 1H), 7.95 – 7.81 (m, 2H), 7.82 – 7.65 (m, 2H), 7.54 – 7.46 (m, 1H), 7.42 (ddd, J = 8.2, 4.7, 3.3 Hz, 1H), 7.14 – 6.74 (m, 4H), 3.73 (s, 3H), 1.33 – 1.02 (m, 18H).

^{13}C NMR (100 MHz, $CDCl_3$) δ 168.9, 168.6, 160.9, 160.6, 153.3, 153.2, 148.0, 146.0, 145.1, 144.6, 143.1, 142.5, 141.8, 138.1, 134.8, 134.8, 126.3, 126.2, 125.2, 125.1, 124.4, 123.5, 118.0, 117.0, 116.6, 115.8, 113.1, 112.6, 61.5, 34.55, 34.3, 31.2, 31.1.

HRMS (ESI) m/z: $[M+H]^+$ Calcd for $C_{37}H_{35}N_4O_6$: 631.2551; Found: 631.2548.

HPLC (Chiralpak IA, *i*-propanol/hexane = 40/60, flow rate 1.0 mL/min, 30 ℃, λ = 254 nm): t_1 = 4.5 min, t_2 = 19.8 min. $[\alpha]^{25}_D$ = 73 (c = 2.2, $CHCl_3$) for 99:1 e.r..

3^5,7^5-di-tert-butyl-7^2-ethoxy-2,4,6,8-tetraoxa-1(2,4),5(4,2)-diquinazolina-3,7(1,3)-dibenzenacyclooctaphan-3^2-ol (4b)

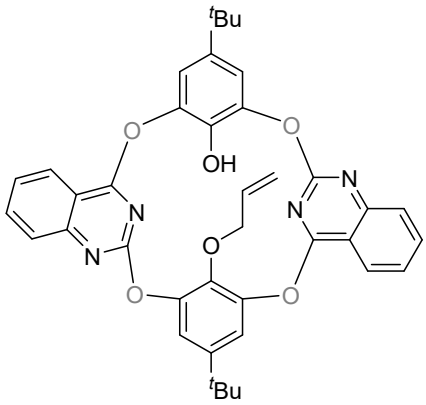


4b

4b: white solid. M.p. = 227 – 228 ℃

^{1}H NMR (400 MHz, $CDCl_3$) δ 8.26 – 8.18 (m, 1H), 8.10 (d, J = 8.2 Hz, 1H), 7.88 – 7.70 (m, 2H), 7.69 – 7.55 (m, 2H), 7.39 (ddd, J = 8.2, 6.7, 1.4 Hz, 1H), 7.32 (ddd, J = 8.1, 6.0, 2.0 Hz, 1H), 7.24 – 7.05 (m, 1H), 7.03 – 6.84 (m, 4H), 4.10 – 3.92 (m, 2H), 1.21 (s, 18H), 0.95 (t, J = 7.0 Hz, 3H).
^{13}C NMR (100 MHz, $CDCl_3$) δ 168.9, 168.6, 161.0, 160.8, 153.2, 153.0, 147.7, 146.3, 145.6, 143.9, 142. 9, 142.4, 140.4, 138.6, 134.6, 134.5, 126.1, 126.0, 125.0, 125.0, 124.3, 123.4, 118.0, 117.0, 116.4, 115.8, 113.1, 112.5, 69.7, 34.5, 34.2, 31.3, 31.2, 15.2.
HRMS (ESI) m/z: $[M+H]^+$ Calcd for $C_{38}H_{37}N_4O_6$: 645.2708; Found: 645.2711.
HPLC (Chiralpak IA, *i*-propanol/hexane = 30/70, flow rate 1.0 mL/min, 30 ℃, λ = 254 nm): t_1 = 5.2 min, t_2 = 25.8 min. $[\alpha]^{25}_D$ = 58 (*c* = 2.0, $CHCl_3$) for 97:3 e.r..

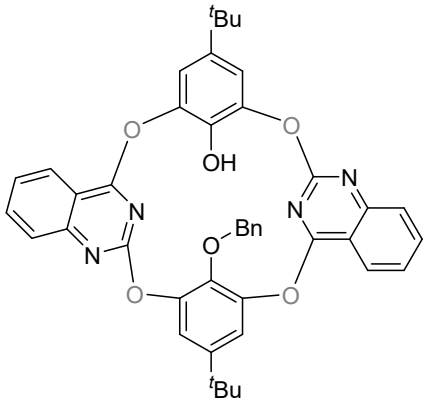
7^2-(allyloxy)-3^5,7^5-di-tert-butyl-2,4,6,8-tetraoxa-1(2,4),5(4,2)-diquinazolina-3,7(1,3)-dibenzenacyclooctaphan-3^2-ol (4c)



4c

4c: white solid. M.p. = 238 – 239℃
^{1}H NMR (400 MHz, $CDCl_3$) δ 8.22 (d, J = 8.2 Hz, 1H), 8.09 (d, J = 8.1 Hz, 1H), 7.82 – 7.71 (m, 2H), 7.68 – 7.54 (m, 2H), 7.40 (ddd, J = 8.2, 6.5, 1.5 Hz, 1H), 7.32 (ddd, J = 8.2, 6.4, 1.7 Hz, 1H), 7.05 – 6.83 (m, 4H), 5.80 – 5.60 (m, 1H), 5.01 – 4.76 (m, 2H), 4.58 – 4.38 (m, 2H), 1.29 – 1.13 (m, 18H).
^{13}C NMR (100 MHz, $CDCl_3$) δ 169.0, 168.7, 161.0, 160.8, 153.2, 152.9, 147.9, 146.2, 145.4, 143.6, 142.6, 142.1, 140.4, 138.8, 134.6, 133.1, 126.1, 126.0, 125.0, 124.9, 124.2, 123.4, 118.0, 118.0, 117.0, 116.5, 116.0, 113.1, 112.6, 74.6, 34.5, 34.2, 31.3, 31.2.
HRMS (ESI) m/z: $[M+H]^+$ Calcd for $C_{39}H_{37}N_4O_6$: 657.2708; Found: 645.2703.
HPLC (Chiralpak IA, *i*-propanol/hexane = 30/70, flow rate 1.0 mL/min, 30 ℃, λ = 254 nm): t_1 = 5.6 min, t_2 = 23.9 min. $[\alpha]^{25}_D$ = 53 (*c* = 2.0, $CHCl_3$) for 98:2 e.r.

7^2-(benzyloxy)-3^5,7^5-di-tert-butyl-2,4,6,8-tetraoxa-1(2,4),5(4,2)-diquinazolina-3,7(1,3)-dibenzenacyclooctaphan-3^2-ol (4d)



4d

4d: white solid. M.p. = 279 – 281℃

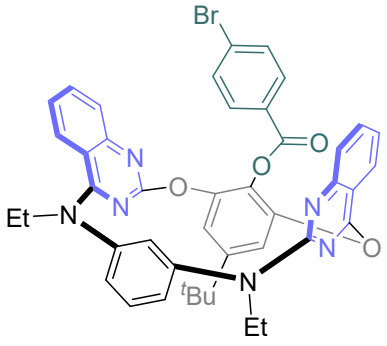
^{1}H NMR (400 MHz, $CDCl_3$) δ 8.23 (dd, J = 8.2, 1.3 Hz, 1H), 7.97 (dd, J = 8.3, 1.4 Hz, 1H), 7.83 – 7.70 (m, 2H), 7.68 – 7.61 (m, 1H), 7.53 (ddd, J = 8.4, 6.9, 1.4 Hz, 1H), 7.42 (ddd, J = 8.2, 6.5, 1.5 Hz, 1H), 7.29 (ddd, J = 8.0, 6.2, 1.1 Hz, 1H), 7.12 – 6.62 (m, 9H), 5.19 – 4.61 (m, 2H), 1.21 (s, 18H).

^{13}C NMR (100 MHz, $CDCl_3$) δ 171.1, 168.9, 168.7, 161.0, 160.7, 153.2, 153.0, 147.9, 146.1, 145.2, 144.2, 143.0, 142.4, 140.5, 138.5, 136.4, 134.7, 128.0, 127.7, 127. 6, 126.2, 125.9, 125.1, 124.9, 124.2, 123.6, 118.1, 117.0, 116.5, 115.9, 113.1, 112.5, 75.5, 34.5, 34.2, 31.3, 31.2.

HRMS (ESI) m/z: $[M+H]^+$ Calcd for $C_{43}H_{39}N_4O_6$: 707.2864; Found: 707.2868.

HPLC (Chiralpak IA, *i*-propanol/hexane = 30/70, flow rate 1.0 mL/min, 30 ℃, λ = 254 nm): t_1 = 5.7 min, t_2 = 18.7 min. $[\alpha]^{25}_D$ = 95 (c = 1.5, $CHCl_3$) for 98:2 e.r.

3^5-(tert-butyl)-6,8-diethyl-2,4-dioxa-6,8-diaza-1(2,4),5(4,2)-diquinazolina-3,7(1,3)-dibenzenacyclooctaphane-3^2-yl 4-bromobenzoate (*S*-3a)



3a

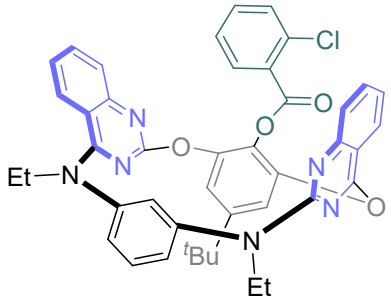
3a: 23.5 mg, 91% yield, white solid. M.p. = 219 – 221 ℃

^{1}H NMR (400 MHz, $CDCl_3$) δ 8.03 (d, J = 8.4 Hz, 1H), 7.93 (d, J = 8.2 Hz, 1H), 7.84 – 7.41 (m, 4H), 7.41 – 7.24 (m, 4H), 7.20 – 7.02 (m, 3H), 7.02 – 6.66 (m, 5H), 4.38 – 3.77 (m, 4H), 1.60 – 1.39 (m, 3H), 1.39 – 0.99 (m, 12H).

^{13}C NMR (100 MHz, $CDCl_3$) δ 166.6, 166.1, 162.7, 161.1, 158.1, 154.7, 149.5, 145.7, 145.5, 145.2, 145.0, 133.9, 133.4, 133.0, 131.2, 131.2, 129.9, 128.9, 128.2, 127.7, 127.5,

127.3, 125.5, 125.0, 124.6, 123.7, 123.2, 122.3, 118.0, 117.1, 113.2, 110.8, 49.6, 44.6, 34.6, 31.2, 14.3, 13.2.
HRMS (ESI) m/z: $[M+H]^+$ Calcd for $C_{43}H_{38}BrN_6O_4$: 781.2132; Found: 781.2129.
HPLC (Chiralpak IB, *i*-propanol/hexane = 15/85, flow rate 1.0 mL/min, 30 °C, λ = 254 nm): t_R (major) = 5.7 min, t_R (minor) = 7.8 min, 96:4 e.r.; $[\alpha]^{25}_D$ = -87 (*c* = 1.5, $CHCl_3$).

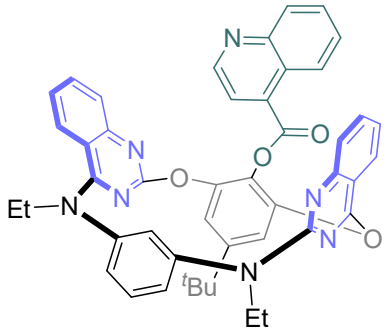
3^5-(tert-butyl)-6,8-diethyl-2,4-dioxa-6,8-diaza-1(2,4),5(4,2)-diquinazolina-3,7(1,3)-dibenzenacyclooctaphane-3^2-yl 2-chlorobenzoate (*S*-3b)



3b

3b: 22.4 mg, 92% yield, white solid. M.p. = 217 – 218 °C
^{1}H NMR (400 MHz, $CDCl_3$) δ 8.06 (d, J = 8.1 Hz, 1H), 8.01 (d, J = 8.1 Hz, 1H), 7.83 – 7.75 (m, 1H), 7.75 – 7.53 (m, 3H), 7.38 – 7.20 (m, 3H), 7.21 – 7.06 (m, 3H), 7.02 – 6.98 (m, 1H), 6.98 – 6.90 (m, 2H), 6.89 (d, J = 2.3 Hz, 1H), 6.87 – 6.68 (m, 2H), 4.36 – 3.98 (m, 4H), 1.47 – 1.40 (m, 3H), 1.34 – 1.23 (m, 13H).
^{13}C NMR (100 MHz, $CDCl_3$) δ 166.6, 166.0, 162.5, 161.3, 154.7, 149.5, 145.7, 145.3, 145.3, 145.0, 133.9, 133.5, 133.3, 133.0, 132.3, 131.5, 130.5, 129.8, 129.2, 128.9, 127.7, 127.2, 126.1, 125.6, 124.9, 124.7, 123.9, 123.1, 122.2, 118.1, 117.3, 113.2, 110.9, 49.5, 44.6, 34.6, 31.2, 14.2, 13.2.
HRMS (ESI) m/z: $[M+H]^+$ Calcd for $C_{43}H_{38}ClN_6O_4$: 737.2638; Found: 737.2643.
HPLC (Chiralpak IB, *i*-propanol/hexane = 15/85, flow rate 1.0 mL/min, 30 °C, λ = 254 nm): t_R (major) = 6.7 min, t_R (minor) = 7.6 min, 97:3 e.r.; $[\alpha]^{25}_D$ = -65 (*c* = 1.5, $CHCl_3$).

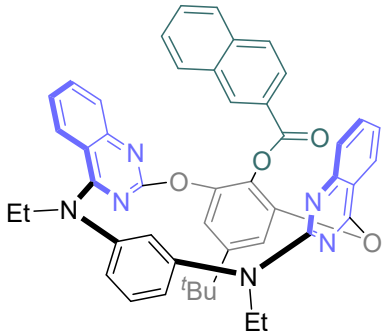
3^5-(tert-butyl)-6,8-diethyl-2,4-dioxa-6,8-diaza-1(2,4),5(4,2)-diquinazolina-3,7(1,3)-dibenzenacyclooctaphane-3^2-yl quinoline-4-carboxylate (*S*-3c)



3c

3c: 21.4 mg, 86% yield, Colorless oil.
^{1}H NMR (400 MHz, $CDCl_3$) δ 8.51 (d, J = 4.4 Hz, 1H), 8.31 (d, J = 8.5 Hz, 1H), 8.06 (d, J = 8.1 Hz, 1H), 8.02 – 7.87 (m, 2H), 7.83 – 7.50 (m, 5H), 7.38 – 7.15 (m, 5H), 7.08 – 7.02 (m, 1H), 7.02 – 6.86 (m, 3H), 6.84 – 6.74 (m, 1H), 4.32 – 3.92 (m, 4H), 1.46 – 1.38 (m, 3H), 1.34 – 1.23 (m, 12H).
^{13}C NMR (100 MHz, $CDCl_3$) δ 166.5, 166.0, 163.3, 161.1, 154.6, 150.0, 149.3, 148.6, 145.7, 145.4, 145.2, 144.8, 134.3, 134.1, 133.3, 133.2, 130.0, 129.6, 129.6, 128.8, 127.8, 127.6, 127.3, 125.6, 125.4, 125.1, 124.7, 124.5, 123.6, 123.3, 122.5, 121.8, 118.3, 117.3, 113.2, 110.6, 49.6, 44.7, 34.7, 31.3, 14.2, 13.2.
HRMS (ESI) m/z: $[M+H]^+$ Calcd for $C_{46}H_{40}N_7O_4$: 754.3136; Found: 754.3133.
HPLC (Chiralpak IB, *i*-propanol/hexane = 20/80, flow rate 1.0 mL/min, 30 °C, λ = 254 nm): t_R (major) = 52.3 min, t_R (minor) = 26.0 min, 97:3 e.r.; $[\alpha]^{25}_D$ = -93 (*c* = 1.3, $CHCl_3$).

3^5-(tert-butyl)-6,8-diethyl-2,4-dioxa-6,8-diaza-1(2,4),5(4,2)-diquinazolina-3,7(1,3)-dibenzenacyclooctaphane-3^2-yl 2-naphthoate (*S*-3d)

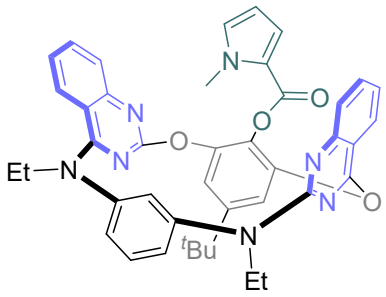


3d

3d: 18.1 mg, 73% yield, white solid. M.p. = 223 – 224 °C
^{1}H NMR (400 MHz, $CDCl_3$) δ 8.06 (d, J = 8.5 Hz, 1H), 7.95 (d, J = 8.1 Hz, 1H), 7.84 (s, 1H), 7.72 – 7.40 (m, 8H), 7.40 – 7.26 (m, 4H), 7.15 – 6.81 (m, 6H), 4.38 – 3.93 (m, 4H), 1.55 – 1.42 (m, 3H), 1.38 – 1.25 (m, 12H).
^{13}C NMR (100 MHz, $CDCl_3$) δ 166.7, 166.2, 163.6, 161.2, 158.2, 154.7, 153.9, 149.3, 145.8, 145.7, 145.3, 145.2, 135.4, 133.8, 133.7, 132.9, 131.9, 131.6, 129.9, 129.2, 129.0,

128.1, 127.8, 127.7, 127.4, 127.2, 126.2, 126.0, 125.4, 125.2, 124.9, 124.6, 123.7, 123.1, 122.2, 117.9, 117.1, 113.3, 110.9, 77.4, 49.6, 44.7, 34.6, 31.3, 14.3, 13.3.
HRMS (ESI) m/z: $[M+H]^+$ Calcd for $C_{47}H_{41}N_6O_4$: 753.3184; Found: 753.3188.
HPLC (Chiralpak IB, *i*-propanol/hexane = 15/85, flow rate 1.0 mL/min, 30 °C, λ = 254 nm): t_R (major) = 6.9 min, t_R (minor) = 9.1 min, 92:8 e.r.; $[\alpha]^{25}_D$ = -67 (*c* = 1.0, $CHCl_3$).

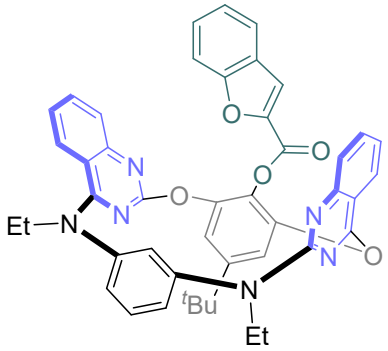
3^5-(tert-butyl)-6,8-diethyl-2,4-dioxa-6,8-diaza-1(2,4),5(4,2)-diquinazolina-3,7(1,3)-dibenzenacyclooctaphane-3^2-yl 1-methyl-1H-pyrrole-2-carboxylate (*S*-3e)



3e

3e: 21.2 mg, 91% yield, Colorless oil.
^{1}H NMR (400 MHz, $CDCl_3$) δ 8.03 (d, *J* = 8.4 Hz, 1H), 7.98 (d, *J* = 8.1 Hz, 1H), 7.87 – 7.47 (m, 4H), 7.39 – 7.30 (m, 1H), 7.26 – 7.20 (m, 1H), 7.17 – 7.08 (m, 1H), 7.04 – 6.75 (m, 5H), 6.59 – 6.38 (m, 1H), 6.11 (dd, *J* = 4.0, 1.8 Hz, 1H), 5.63 (dd, *J* = 4.1, 2.5 Hz, 1H), 4.28 – 3.97 (m, 4H), 3.70 (s, 3H), 1.52 – 1.41 (m, 3H), 1.34 – 1.23 (m, 12H).
^{13}C NMR (100 MHz, $CDCl_3$) δ 166.6, 166.1, 161.2, 158.2, 157.7, 154.7, 153.8, 148.9, 145.8, 145.8, 145.4, 145.3, 133.8, 133.4, 132.9, 129.9, 129.8, 128.7, 127.7, 127.3, 125.5, 124.9, 124.6, 123.8, 123.0, 122.1, 120.7, 118.9, 117.8, 116.9, 113.2, 111.0, 107.6, 49.5, 44.5, 36.4, 34.6, 31.3, 14.2, 13.3.
HRMS (ESI) m/z: $[M+H]^+$ Calcd for $C_{42}H_{40}N_7O_4$: 706.3136; Found: 706.3133.
HPLC (Chiralpak IB, *i*-propanol/hexane = 20/80, flow rate 1.0 mL/min, 30 °C, λ = 254 nm): t_R (major) = 5.9 min, t_R (minor) = 6.9 min, 97:3 e.r.; $[\alpha]^{25}_D$ = -77 (*c* = 1.3, $CHCl_3$).

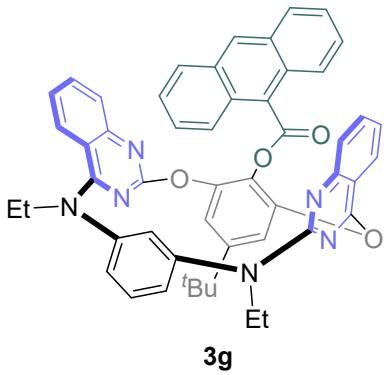
3^5-(tert-butyl)-6,8-diethyl-2,4-dioxa-6,8-diaza-1(2,4),5(4,2)-diquinazolina-3,7(1,3)-dibenzenacyclooctaphane-3^2-yl benzofuran-2-carboxylate (*S*-3f)



3f

3f: 18.9 mg, 77% yield, colorless oil.
^{1}H NMR (400 MHz, $CDCl_3$) δ 8.05 (d, J = 8.4 Hz, 1H), 7.97 (d, J = 8.1 Hz, 1H), 7.85 – 7.43 (m, 4H), 7.39 – 7.22 (m, 5H), 7.18 – 7.03 (m, 2H), 7.03 – 6.84 (m, 5H), 6.75 (s, 1H), 4.37 – 3.90 (m, 4H), 1.51 – 1.44 (m, 3H), 1.28 (s, 12H).
^{13}C NMR (100 MHz, $CDCl_3$) δ 166.6, 166.1, 161.2, 156.5, 156.1, 155.8, 154.7, 149.7, 145.7, 145.6, 145.2, 145.1, 143.7, 133.9, 133.0, 132.9, 131.9, 129.9, 129.0, 128.1, 127.8, 127.6, 127.2, 126.4, 125.5, 124.6, 123.7, 123.4, 123.1, 122.6, 122.3, 118.1, 117.2, 115.1, 113.3, 112.2, 110.8, 49.6, 44.8, 34.6, 31.2, 14.3, 13.2.
HRMS (ESI) m/z: $[M+H]^+$ Calcd for $C_{45}H_{39}N_6O_5$: 743.2976; Found: 743.2975.
HPLC (Chiralpak IB, *i*-propanol/hexane = 15/85, flow rate 1.0 mL/min, 30 ℃, λ = 254 nm): t_R (major) = 7.0 min, t_R (minor) = 9.3 min, 92:8 e.r.; $[\alpha]^{25}_D$ = -48 (*c* = 1.1, $CHCl_3$).

3^5-(tert-butyl)-6,8-diethyl-2,4-dioxa-6,8-diaza-1(2,4),5(4,2)-diquinazolina-3,7(1,3)-dibenzenacyclooctaphane-3^2-yl anthracene-9-carboxylate (*S*-3g)

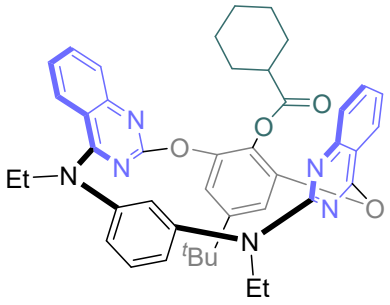


3g

3g: 23.3 mg, 88% yield, white solid. M.p. = 224 – 226 ℃.
^{1}H NMR (400 MHz, $CDCl_3$) δ 8.43 (d, J = 7.9 Hz, 1H), 8.23 – 8.10 (m, 2H), 8.00 – 7.60 (m, 6H), 7.52 – 7.16 (m, 5H), 7.11 – 6.73 (m, 8H), 6.71 – 6.59 (m, 1H), 4.07 – 3.70 (m, 4H), 1.32 (s, 9H), 1.27 – 1.18 (m, 3H), 1.15 – 1.06 (m, 3H).
^{13}C NMR (100 MHz, $CDCl_3$) δ 167.4, 166.7, 165.9, 161.0, 158.1, 154.7, 149.9, 145.8, 145.4, 145.1, 145.0, 134.3, 134.0, 133.0, 130.2, 130.1, 129.9, 128.8, 128.7, 128.5, 128.4, 128.1, 128.1, 127.7, 127.6, 127.2, 127.0, 126.7, 126.6, 126.1, 125.2, 125.1, 125.1, 125.0, 124.7, 124.1, 123.0, 122.4, 118.6, 117.6, 113.3, 111.0, 49.3, 44.4, 34.7, 31.3, 14.0, 13.1.

HRMS (ESI) m/z: $[M+H]^+$ Calcd for $C_{51}H_{43}N_6O_4$: 803.3340; Found: 803.3337.
HPLC (Chiralpak IC, *i*-propanol/hexane = 20/80, flow rate 1.0 mL/min, 30 °C, λ = 254 nm): t_R (major) = 18.4 min, t_R (minor) = 15.9 min, 86:14 e.r.; $[\alpha]^{25}_D$ = -71 (*c* = 1.1, $CHCl_3$).

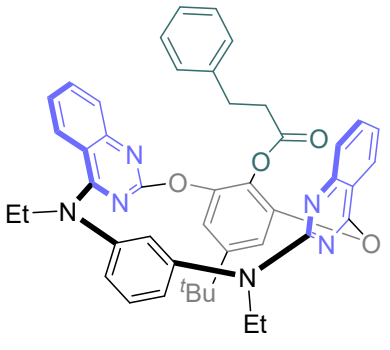
3^5-(tert-butyl)-6,8-diethyl-2,4-dioxa-6,8-diaza-1(2,4),5(4,2)-diquinazolina-3,7(1,3)-dibenzenacyclooctaphane-3^2-yl cyclohexanecarboxylate (*S*-3h)



3h

3h: 22.4 mg, 96% yield, colorless oil.
^{1}H NMR (400 MHz, $CDCl_3$) δ 8.10 – 7.95 (m, 2H), 7.82 (dd, *J* = 8.5, 1.3 Hz, 1H), 7.80 – 7.56 (m, 3H), 7.35 (m, *J* = 8.3, 6.9, 1.4 Hz, 1H), 7.26 – 7.13 (m, 2H), 7.03 – 6.86 (m, 3H), 6.86 – 6.68 (m, 2H), 4.22 – 3.98 (m, 4H), 2.07 – 2.02 (m, 1H), 1.47 – 1.25 (m, 20H), 1.01 – 0.85 (m, 5H).
^{13}C NMR (100 MHz, $CDCl_3$) δ 172.5, 166.5, 166.0, 161.2, 154.7, 149.0, 145.8, 145.3, 145.1, 144.8, 134.1, 133.5, 133.0, 129.8, 128.8, 128.8, 127.6, 127.2, 127.2, 125.5, 124.8, 124.7, 123.8, 123.1, 122.4, 117.9, 116.9, 113.2, 110.8, 49.5, 44.7, 42.1, 34.5, 31.2, 28.4, 28.3, 25.4, 24.9, 24.8, 14.2, 13.3.
HRMS (ESI) m/z: $[M+H]^+$ Calcd for $C_{43}H_{45}N_6O_4$: 709.3497; Found: 709.3501.
HPLC (Chiralpak IB, *i*-propanol/hexane = 10/90, flow rate 1.0 mL/min, 30 °C, λ = 254 nm): t_R (major) = 6.1 min, t_R (minor) = 6.9 min, 98:2 e.r.; $[\alpha]^{25}_D$ = -47 (*c* = 1.3, $CHCl_3$).

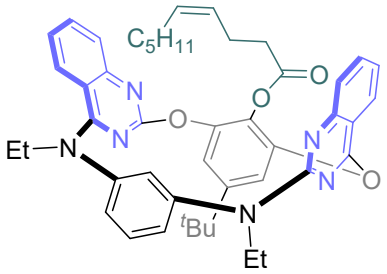
3^5-(tert-butyl)-6,8-diethyl-2,4-dioxa-6,8-diaza-1(2,4),5(4,2)-diquinazolina-3,7(1,3)-dibenzenacyclooctaphane-3^2-yl 3-phenylpropanoate (*S*-3i)



3i

3i: 22.9 mg, 95% yield, colorless oil.
^{1}H NMR (400 MHz, $CDCl_3$) δ 8.13 – 7.91 (m, 2H), 7.88 – 7.78 (m, 1H), 7.78 – 7.47 (m, 3H), 7.36 (ddd, J = 8.4, 6.9, 1.4 Hz, 1H), 7.22 (dd, J = 8.4, 7.3 Hz, 2H), 7.14 – 6.99 (m, 3H), 6.99 – 6.87 (m, 3H), 6.86 – 6.82 (m, 1H), 6.82 – 6.55 (m, 3H), 4.19 – 3.98 (m, 4H), 2.68 – 2.51 (m, 2H), 2.48 – 2.28 (m, 2H), 1.49 – 1.41 (m, 3H), 1.32 – 1.24 (m, 12H).
^{13}C NMR (100 MHz, $CDCl_3$) δ 169.7, 166.5, 166.0, 161.3, 158.2, 154.8, 149.2, 145.7, 145.3, 145.2, 144.9, 140.1, 134.0, 133.4, 133.0, 129.8, 128.9, 128.5, 128.2, 127.9, 127.7, 127.3, 125.9, 125.4, 125.1, 124.7, 123.7, 123.1, 122.4, 118.0, 117.1, 113.3, 110.8, 49.5, 44.6, 34.6, 34.6, 31.2, 30.3, 14.2, 13.2.
HRMS (ESI) m/z: $[M+H]^+$ Calcd for $C_{45}H_{43}N_6O_4$: 731.3340; Found: 731.3341.
HPLC (Chiralpak IB, *i*-propanol/hexane = 5/95, flow rate 1.0 mL/min, 30 °C, λ = 254 nm): t_R (major) = 10.9 min, t_R (minor) = 13.5 min, 99:1 e.r.; $[\alpha]^{25}_D$ = -101 (*c* = 1.2, $CHCl_3$).

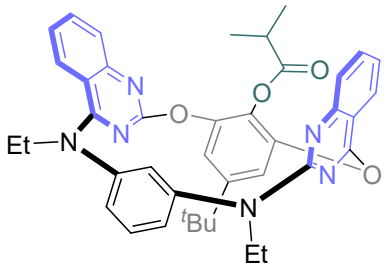
3^5-(tert-butyl)-6,8-diethyl-2,4-dioxa-6,8-diaza-1(2,4),5(4,2)-diquinazolina-3,7(1,3)-dibenzenacyclooctaphane-3^2-yl (*Z*)-dec-4-enoate (*S*-3j)



3j

3j: 21.0 mg, 85% yield, colorless oil.
^{1}H NMR (400 MHz, $CDCl_3$) δ 8.11 – 7.95 (m, 2H), 7.88 – 7.52 (m, 4H), 7.35 (ddd, J = 8.4, 6.9, 1.4 Hz, 1H), 7.27 – 7.08 (m, 2H), 7.02 – 6.87 (m, 3H), 6.87 – 6.62 (m, 2H), 5.18 – 5.06 (m, 1H), 5.04 – 4.84 (m, 1H), 4.23 – 3.88 (m, 4H), 2.17 – 1.94 (m, 4H), 1.75 – 1.66 (m, 2H), 1.48 – 1.40 (m, 3H), 1.31 – 1.23 (m, 13H), 1.18 – 1.10 (m, 4H), 0.91 – 0.84 (m, 4H).
^{13}C NMR (100 MHz, $CDCl_3$) δ 169.9, 166.5, 166.0, 161.2, 158.1, 154.8, 149.1, 145.8, 145.2, 144.9, 134.0, 133.5, 133.0, 131.5, 131.2, 129.8, 128.8, 127.7, 127.5, 127.3, 126.9, 125.5, 125.1, 124.7, 123.7, 123.1, 122.3, 118.1, 117.0, 113.2, 110.8, 49.5, 44.6, 34.5, 33.5, 31.3, 31.2, 29.1, 26.8, 22.5, 22.4, 14.2, 14.0, 13.2.
HRMS (ESI) m/z: $[M+H]^+$ Calcd for $C_{46}H_{51}N_6O_4$: 751.3966; Found: 751.3962.
HPLC (Chiralpak IB, *i*-propanol/hexane = 5/95, flow rate 1.0 mL/min, 30 °C, λ = 254 nm): t_R (major) = 7.2 min, t_R (minor) = 8.6 min, 99:1 e.r.; $[\alpha]^{25}_D$ = -89 (*c* = 1.2, $CHCl_3$).

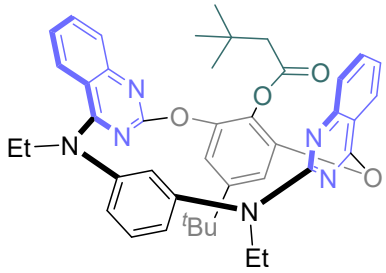
3^5-(tert-butyl)-6,8-diethyl-2,4-dioxa-6,8-diaza-1(2,4),5(4,2)-diquinazolina-3,7(1,3)-dibenzenacyclooctaphane-3^2-yl isobutyrate (*S*-3k)



3k

3k: 18.1 mg, 82% yield, colorless oil.
^{1}H NMR (400 MHz, $CDCl_3$) δ 8.11 – 7.94 (m, 2H), 7.85 – 7.77 (m, 1H), 7.77 – 7.50 (m, 3H), 7.35 (ddd, J = 8.4, 6.8, 1.4 Hz, 1H), 7.27 – 7.13 (m, 2H), 7.04 – 6.86 (m, 3H), 6.87 – 6.66 (m, 2H), 4.24 – 3.83 (m, 4H), 2.29 (p, J = 7.0 Hz, 1H), 1.43 (t, J = 7.0 Hz, 3H), 1.32 – 1.22 (m, 12H), 0.80 (d, J = 7.0 Hz, 3H), 0.69 (d, J = 7.0 Hz, 3H).
^{13}C NMR (100 MHz, $CDCl_3$) δ 173.5, 166.4, 166.0, 161.2, 154.8, 149.0, 145.8, 145.3, 145.2, 144.8, 134.0, 133.5, 133.0, 129.8, 128.7, 128.7, 127.7, 127.3, 127.1, 125.5, 125.0, 124.7, 123.7, 123.0, 122.3, 117.9, 116.9, 113.2, 110.8, 49.5, 44.5, 34.5, 33.4, 31.2, 18.5, 18.5, 14.2, 13.2.
HRMS (ESI) m/z: $[M+H]^+$ Calcd for $C_{40}H_{41}N_6O_4$: 669.3184; Found: 669.3187.
HPLC (Chiralpak IB, *i*-propanol/hexane = 10/90, flow rate 1.0 mL/min, 30 ℃, λ = 254 nm): t_R (major) = 6.1 min, t_R (minor) = 6.7 min, 97:3 e.r.; $[\alpha]^{25}_D$ = -73 (*c* = 1.1, $CHCl_3$).

3^5-(tert-butyl)-6,8-diethyl-2,4-dioxa-6,8-diaza-1(2,4),5(4,2)-diquinazolina-3,7(1,3)-dibenzenacyclooctaphane-3^2-yl 3,3-dimethylbutanoate (*S*-3l)

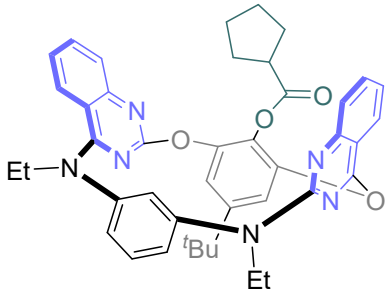


3l

3l: 18.6 mg, 81% yield, white solid. M.p. = 209 – 210 ℃.
^{1}H NMR (400 MHz, $CDCl_3$) δ 8.23 – 7.89 (m, 2H), 7.89 – 7.77 (m, 1H), 7.78 – 7.43 (m, 3H), 7.36 (ddd, J = 8.4, 6.8, 1.3 Hz, 1H), 7.21 (t, J = 7.8 Hz, 2H), 7.08 – 6.85 (m, 3H), 6.85 – 6.60 (m, 2H), 4.34 – 3.89 (m, 4H), 2.07 – 1.91 (m, 2H), 1.60 – 1.37 (m, 3H), 1.33 – 1.19 (m, 12H), 0.70 (s, 9H).
^{13}C NMR (100 MHz, $CDCl_3$) δ 168.9, 166.5, 166.1, 161.2, 154.8, 149.0, 145.8, 145.3, 145.2, 144.9, 134.0, 133.5, 133.0, 129.8, 129.1, 128.67 127.7, 127.4, 127.2, 125.6, 125.0, 124.7, 123.9, 123.0, 122.2, 118.0, 117.0, 113.3, 110.9, 49.5, 46.7, 44.5, 34.5, 31.2, 30.2, 29.1, 14.2, 13.2.
HRMS (ESI) m/z: $[M+H]^+$ Calcd for $C_{42}H_{45}N_6O_4$:697.3497; Found: 697.3499.

HPLC (Chiralpak IB, *i*-propanol/hexane = 10/90, flow rate 1.0 mL/min, 30 °C, λ = 254 nm): t_R (major) = 7.6 min, t_R (minor) = 8.7 min, 99:1 e.r.; $[\alpha]^{25}_D$ = -85 (*c* = 1.4, $CHCl_3$).

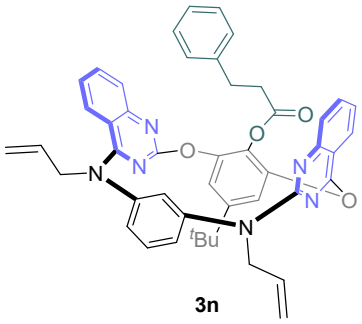
3^5-(tert-butyl)-6,8-diethyl-2,4-dioxa-6,8-diaza-1(2,4),5(4,2)-diquinazolina-3,7(1,3)-dibenzenacyclooctaphane-3^2-yl cyclopentanecarboxylate (*S*-3m)



3m

3m: 19.9 mg, 87% yield, colorless oil.
^{1}H NMR (400 MHz, $CDCl_3$) δ 8.12 – 7.95 (m, 2H), 7.81 (dd, *J* = 8.5, 1.3 Hz, 1H), 7.76 – 7.45 (m, 3H), 7.35 (ddd, *J* = 8.3, 6.8, 1.4 Hz, 1H), 7.26 – 7.12 (m, 2H), 7.06 – 6.86 (m, 3H), 6.86 – 6.60 (m, 2H), 4.26 – 3.98 (m, 4H), 2.59 – 2.37 (m, 1H), 1.52 – 0.84 (m, 25H).
^{13}C NMR (100 MHz, $CDCl_3$) δ 173.2, 166.4, 166.1, 161.3, 154.8, 148.9, 145.8, 145.3, 145.2, 144.9, 134.0, 133.5, 133.0, 129.8, 128.7, 128.5, 127.7, 127.2, 125.4, 125.0, 124.8, 124.7, 123.8, 123.0, 122.3, 117.9, 116.9, 113.2, 110.8, 49.5, 44.5, 43.0, 34.5, 31.2, 29.7, 29.4, 25.4, 14.2, 13.3.
HRMS (ESI) m/z: $[M+H]^+$ Calcd for $C_{42}H_{43}N_6O_4$: 695.3340; Found: 695.3338.
HPLC (Chiralpak IB, *i*-propanol/hexane = 5/95, flow rate 1.0 mL/min, 30 °C, λ = 254 nm): t_R (major) = 9.5 min, t_R (minor) = 11.4 min, 99:1 e.r.; $[\alpha]^{25}_D$ = -66 (*c* = 1.0, $CHCl_3$).

6,8-diallyl-3^5-(tert-butyl)-2,4-dioxa-6,8-diaza-1(2,4),5(4,2)-diquinazolina-3,7(1,3)-dibenzenacyclooctaphane-3^2-yl 3-phenylpropanoate (*S*-3n)



3n

3n: 20.9 mg, 84% yield, colorless oil.
^{1}H NMR (400 MHz, $CDCl_3$) δ 8.32 – 8.12 (m, 1H), 8.04 (d, *J* = 8.2 Hz, 1H), 7.91 – 7.78 (m, 1H), 7.77 – 7.62 (m, 3H), 7.42 – 7.31 (m, 1H), 7.26 – 7.22 (m, 1H), 7.19 (t, 1H), 7.12 –

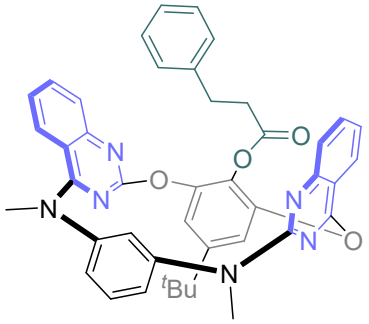
7.01 (m, 3H), 7.03 – 6.73 (m, 7H), 6.20 – 5.86 (m, 2H), 5.55 – 5.43 (m, 1H), 5.36 (dd, *J* = 10.5, 1.6 Hz, 1H), 5.24 – 5.00 (m, 1H), 4.85 – 4.63 (m, 3H), 4.48 (s, 1H), 2.76 – 2.50 (m, 2H), 2.47 – 2.22 (m, 2H), 1.26 (s, 9H).

^{13}C NMR (100 MHz, $CDCl_3$) δ 169.7, 166.7, 166.7, 161.2, 154.7, 149.2, 146.1, 145.2, 145.1, 144.9, 140.0, 134.1, 133.4, 133.3, 133.1, 129.7, 129.0, 128.2, 127.9, 127.6, 127.1, 125.9, 125.2, 125.0, 123.7, 123.3, 122.6, 118.2, 118.1, 117.5, 117.1, 113.4, 110.9, 57.4, 52.9, 34.6, 34.6, 31.2, 30.3.

HRMS (ESI) m/z: $[M+H]^+$ Calcd for $C_{47}H_{43}N_6O_4$: 755.3340; Found: 755.3347.

HPLC (Chiralpak IB, *i*-propanol/hexane = 10/90, flow rate 1.0 mL/min, 30 °C, λ = 254 nm): t_R (major) = 6.9 min, t_R (minor) = 8.1 min, 99:1 e.r.; $[\alpha]^{25}_D$ = -108 (*c* = 1.0, $CHCl_3$).

3^5-(tert-butyl)-6,8-dimethyl-2,4-dioxa-6,8-diaza-1(2,4),5(4,2)-diquinazolina-3,7(1,3)-dibenzenacyclooctaphane-3^2-yl 3-phenylpropanoate (*S*-3o)



3o

3o: 20.6 mg, 89% yield, colorless oil.

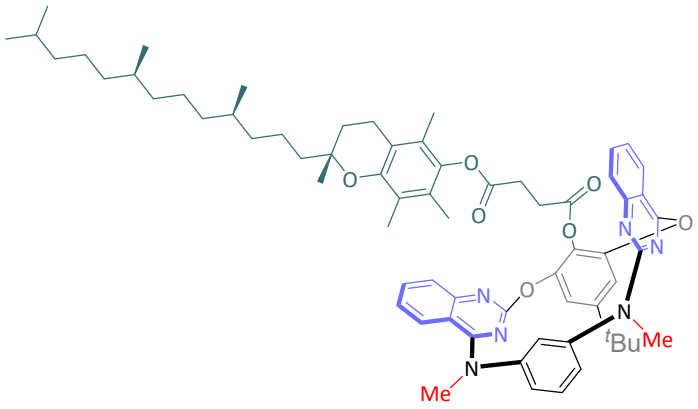
^{1}H NMR (400 MHz, $CDCl_3$) δ 8.22 (d, *J* = 7.9 Hz, 1H), 8.04 (d, *J* = 8.1 Hz, 1H), 7.90 – 7.78 (m, 1H), 7.81 – 7.56 (m, 3H), 7.42 – 7.33 (m, 1H), 7.37 – 7.13 (m, 2H), 7.16 – 7.01 (m, 3H), 7.02 – 6.88 (m, 3H), 6.91 – 6.71 (m, 4H), 3.81 (s, 3H), 3.57 (s, 3H), 2.68 – 2.49 (m, 2H), 2.50 – 2.14 (m, 2H), 1.25 (s, 9H).

^{13}C NMR (100 MHz, $CDCl_3$) δ ^{13}C NMR (101 MHz, $CDCl_3$) δ 169.6, 166.5, 166.1, 161.2, 158.5, 155.0, 153.4, 149.3, 148.3, 147.1, 145.3, 144.9, 140.0, 134.3, 133.4, 133.1, 130.1, 128.2, 127.9, 127.5, 126.9, 126.1, 125.9, 125.7, 124.9, 124.5, 123.7, 122.9, 122.7, 118.2, 117.0, 113.4, 110.8, 44.3, 38.5, 34.6, 34.6, 31.2, 30.3.

HRMS (ESI) m/z: $[M+H]^+$ Calcd for $C_{43}H_{39}N_6O_4$: 703.3027; Found: 703.3033.

HPLC (Chiralpak IB, *i*-propanol/hexane = 10/90, flow rate 1.0 mL/min, 30 °C, λ = 254 nm): t_R (major) = 9.5 min, t_R (minor) = 10.9min, 99:1 e.r.; $[\alpha]^{25}_D$ = -95 (*c* = 1.2, $CHCl_3$).

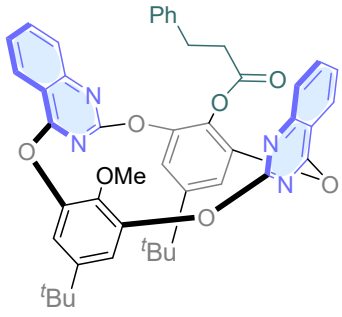
3^5-(tert-butyl)-6,8-dimethyl-2,4-dioxa-6,8-diaza-1(2,4),5(4,2)-diquinazolina-3,7(1,3)-dibenzenacyclooctaphane-3^2-yl((R)-2,5,7,8-tetramethyl-2-((4R,8R)-4,8,12-trimethyltridecyl)chroman-6-yl) succinate(3p)



3p

3p: 21.0 mg, 58% yield, colorless oil.
^{1}H NMR (400 MHz, $CDCl_3$) δ 8.22 (d, J = 8.4 Hz, 1H), 8.16 – 7.45 (m, 5H), 7.42 – 7.33 (m, 1H), 7.28 – 7.19 (m, 1H), 7.21 – 7.09 (m, 1H), 7.09 – 6.76 (m, 5H), 3.83 (s, 3H), 3.64 (s, 3H), 2.82 – 2.36 (m, 6H), 2.24 – 1.69 (m, 12H), 1.61 – 1.51 (m, 3H), 1.29 – 1.21 (m, 14H), 1.20 – 1.03 (m, 6H), 1.03 – 0.62 (m, 12H).
^{13}C NMR (100 MHz, $CDCl_3$) δ 170.2, 169.2, 166.8, 166.1, 161.0, 157.6, 154.7, 149.5, 149.4, 148.4, 146.6, 145.3, 144.7, 143.2, 140.4, 134.8, 133.2, 130.3, 128.2, 127.8, 127.4, 126.7, 126.7, 125.8, 125.6, 124.9, 124.0, 123.8, 123.1, 122.9, 118.4, 118.3, 117.3, 117.0, 113.3, 110.5, 75.0, 44.4, 39.4, 37.5, 37.5, 37.4, 37.3, 34.6, 32.8, 32.7, 31.2, 28.6, 28.5, 28.0, 24.8, 24.5, 22.7, 22.6, 21.0, 20.6, 19.8, 19.7, 12.9, 12.1, 11.8.
HRMS (ESI) m/z: $[M+H]^+$ Calcd for $C_{68}H_{87}N_6O_7$: 1099.6631; Found: 1099.6627.

3^5,7^5-di-tert-butyl-7^2-methoxy-2,4,6,8-tetraoxa-1(2,4),5(4,2)-diquinazolina-3,7(1,3)-dibenzenacyclooctaphane-3$_2$-yl 3-phenylpropanoate (*S*-5a)

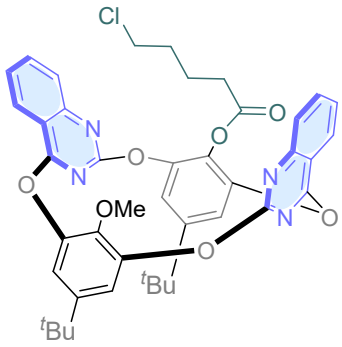


5a

5a: 32.0 mg, 42% yield, 12h, white solid, m.p. = 270-271 °C
^{1}H NMR (400 MHz, $CDCl_3$) δ 8.30 (d, J = 7.9 Hz, 1H), 8.20 (d, J = 8.1 Hz, 1H), 7.96 – 7.81 (m, 4H), 7.58 – 7.44 (m, 2H), 7.14 – 7.09 (m, 1H), 7.06 – 6.87 (m, 6H), 6.63 – 6.44 (m, 2H), 3.56 (s, 3H), 2.28 – 2.09 (m, 4H), 1.27 (s, 9H), 1.25 (s, 9H).
^{13}C NMR (100 MHz, $CDCl_3$) δ 169.1, 169.0, 168.5, 161.2, 160.9, 153.6, 150.3, 147.3, 146.1, 145.2, 144.4, 141.9, 139.8, 134.9, 134.8, 133.0, 128.2, 127.6, 126.7, 126.5, 126.0, 125.4, 125.4, 123.9, 123.8, 117.7, 117.7, 116.7, 116.6, 113.0, 112.7, 61.0, 35.1, 34.7, 34.5, 31.2, 31.2, 30.0.

HRMS (ESI) m/z: $[M+H]^+$ Calcd for $C_{46}H_{43}N_4O_7$: 763.3126; Found: 763.3128.
HPLC (Chiralpak IB, *i*-propanol/hexane = 15/85, flow rate 1.0 mL/min, 30 °C, λ = 254 nm): t_R (major) = 10.0 min, t_R (minor) = 9.2 min, 97:3 e.r.; $[\alpha]^{25}_D$ = -122 (*c* = 1.2, $CHCl_3$).

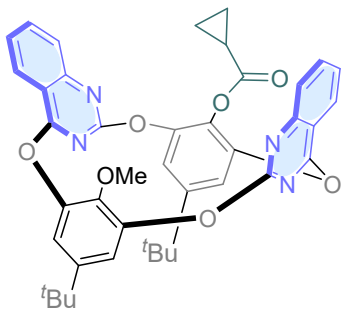
3^5,7^5-di-tert-butyl-7^2-methoxy-2,4,6,8-tetraoxa-1(2,4),5(4,2)-diquinazolina-3,7(1,3)-dibenzenacyclooctaphane-3^2-yl 5-chloropentanoate (*S*-5b)



5b

5b: 32.9 mg, 44% yield, 12h, white solid, m.p. = 262-263 °C
^{1}H NMR (400 MHz, $CDCl_3$) δ 8.30 (d, *J* = 8.2 Hz, 1H), 8.21 (d, *J* = 8.7 Hz, 1H), 7.94 – 7.81 (m, 4H), 7.57 – 7.46 (m, 2H), 7.11 – 7.06 (m, 1H), 7.04 – 6.95 (m, 2H), 6.95 – 6.89 (m, 1H), 3.64 (s, 3H), 2.97 – 2.79 (m, 2H), 1.92 – 1.79 (m, 2H), 1.29 – 1.14 (m, 22H).
^{13}C NMR (100 MHz, $CDCl_3$) δ 169.3, 169.0, 168.4, 161.1, 160.9, 153.5, 150.3, 147.3, 146.0, 145.2, 144.3, 142.0, 135.0, 134.9, 133.0, 126.6, 126.6, 125.4, 123.8, 117.8, 117.7, 116.7, 116.7, 113.0, 112.6, 61.0, 43.7, 34.7, 34.4, 32.7, 31.2, 31.2, 31.1, 21.4.
HRMS (ESI) m/z: $[M+H]^+$ Calcd for $C_{42}H_{42}ClN_4O_7$: 749.2737; Found: 749.2740.
HPLC (Chiralpak IB, *i*-propanol/hexane = 10/90, flow rate 1.0 mL/min, 30 °C, λ = 254 nm): t_R (major) = 7.0min, t_R (minor) = 6.3 min, 95:5 e.r.; $[\alpha]^{25}_D$ = -107 (*c* = 1.0, $CHCl_3$).

3^5,7^5-di-tert-butyl-7^2-methoxy-2,4,6,8-tetraoxa-1(2,4),5(4,2)-diquinazolina-3,7(1,3)-dibenzenacyclooctaphane-3^2-yl cyclopropanecarboxylate (*S*-5c)

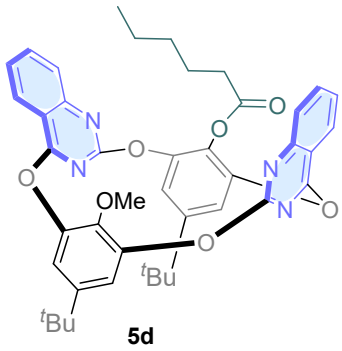


5c

5c: 29.3 mg, 42% yield, 12h, colorless oil.

^{1}H NMR (400 MHz, $CDCl_3$) δ 8.29 (d, J = 8.0 Hz, 1H), 8.22 (d, J = 8.0 Hz, 1H), 7.95 – 7.77 (m, 4H), 7.55 – 7.40 (m, 2H), 7.09 – 7.03 (m, 1H), 7.01 (dd, J = 4.2, 2.3 Hz, 2H), 6.97 – 6.89 (m, 1H), 3.64 (s, 3H), 1.24 (s, 9H), 1.23 (s, 9H), 1.14 – 1.07 (m, 1H), 0.43 – 0.06 (m, 4H).
^{13}C NMR (100 MHz, $CDCl_3$) δ 170.5, 168.9, 168.5, 161.1, 160.9, 153.6, 153.5, 150.0, 147.4, 146.2, 145.3, 145.2, 144.4, 141.8, 134.9, 134.7, 132.7, 126.7, 126.4, 125.3, 125.3, 124.0, 123.7, 117.7, 117.6, 116.6, 116.5, 112.9, 112.7, 60.7, 34.7, 34.4, 31.2, 31.2, 12.7, 7.9, 7.8.
HRMS (ESI) m/z: $[M+H]^+$ Calcd for $C_{41}H_{39}N_4O_7$: 699.2813; Found: 699.2810.
HPLC (Chiralpak IA, *i*-propanol/hexane = 20/80, flow rate 1.0 mL/min, 30 ℃, λ = 254 nm): t_R (major) = 9.3 min, t_R (minor) = 12.2 min, 90:10 e.r.; $[\alpha]^{25}_D$ = -86 (*c* = 1.1, $CHCl_3$).

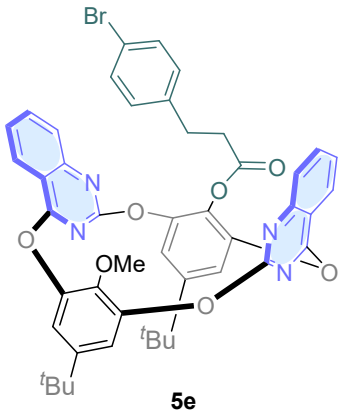
3^5,7^5-di-tert-butyl-7^2-methoxy-2,4,6,8-tetraoxa-1(2,4),5(4,2)-diquinazolina-3,7(1,3)-dibenzenacyclooctaphane-3^2-yl hexanoate (*S*-5d)



5d

5d: 26.9 mg, 37% yield, 16h, colorless oil.
^{1}H NMR (400 MHz, $CDCl_3$) δ 8.29 (d, J = 8.2 Hz, 1H), 8.21 (d, J = 7.9 Hz, 1H), 7.96 – 7.77 (m, 4H), 7.56 – 7.43 (m, 2H), 7.10 – 7.05 (m, 1H), 7.00 (t, J = 2.7 Hz, 2H), 6.96 – 6.88 (m, 1H), 3.63 (s, 3H), 1.87 – 1.74 (m, 2H), 1.24 (s, 9H), 1.23 (s, 9H), 0.97 – 0.66 (m, 7H), 0.50 – 0.47 (m, 2H).
^{13}C NMR (100 MHz, $CDCl_3$) δ 169.9, 169.0, 168.5, 161.1, 160.9, 153.5, 153.4, 150.1, 147.2, 146.0, 145.2, 145.1, 144.4, 141.9, 134.9, 134.7, 133.2, 126.7, 126.4, 125.3, 125.3, 123.9, 123.7, 117.7, 117.7, 116.7, 116.6, 113.0, 112.7, 60.8, 34.7, 34.4, 33.7, 31.2, 31.2, 30.8, 23.9, 21.7, 13.4.
HRMS (ESI) m/z: $[M+H]^+$ Calcd for $C_{43}H_{45}N_4O_7$: 729.3283; Found: 729.3279.
HPLC (Chiralpak IB, *i*-propanol/hexane = 5/95, flow rate 1.0 mL/min, 30 ℃, λ = 254 nm): t_R (major) = 7.6 min, t_R (minor) = 6.8 min, 92:8 e.r.; $[\alpha]^{25}_D$ = -82 (*c* = 1.0, $CHCl_3$).

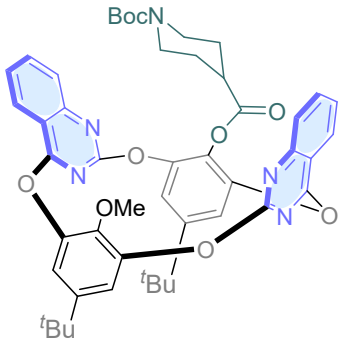
3^5,7^5-di-tert-butyl-7^2-methoxy-2,4,6,8-tetraoxa-1(2,4),5(4,2)-diquinazolina-3,7(1,3)-dibenzenacyclooctaphane-3^2-yl 3-(4-bromophenyl)propanoate (*S*-5e)



5e

5e: 34.4 mg, 41% yield, 12h, white solid, m.p. = 291-292 °C
^{1}H NMR (400 MHz, $CDCl_3$) δ8.30 (d, J = 8.1 Hz, 1H), 8.15 (d, J = 8.1 Hz, 1H), 8.02 – 7.81 (m, 4H), 7.56 – 7.45 (m, 2H), 7.14 – 6.94 (m, 6H), 6.52 – 6.30 (m, 2H), 3.56 (s, 3H), 2.36 – 2.04 (m, 4H), 1.25 (s, 9H), 1.24 (s, 9H).
^{13}C NMR (100 MHz, $CDCl_3$) δ 169.1, 168.7, 168.4, 161.1, 160.9, 153.5, 153.4, 150.4, 147.4, 146.1, 145.2, 145.2, 144.4, 141.9, 138.7, 135.1, 134.9, 133.0, 131.3, 129.3, 126.7, 126.4, 125.5, 125.5, 123.8, 123.8, 119.8, 117.8, 117.7, 116.8, 116.7, 113.0, 112.6, 61.0, 34.7, 34.7, 34.5, 31.2, 31.2, 29.2.
HRMS (ESI) m/z: $[M+H]^+$ Calcd for $C_{46}H_{42}BrN_4O_7$: 841.2231; Found: 841.2235.
HPLC (Chiralpak IB, *i*-propanol/hexane = 10/90, flow rate 1.0 mL/min, 30 °C, λ = 254 nm): t_R (major) = 7.2 min, t_R (minor) = 6.5 min, 98:2 e.r.; $[\alpha]^{25}_D$ = -130 (*c* = 1.3, $CHCl_3$).

1-(tert-butyl)4-(3^5,7^5-di-tert-butyl-7^2-methoxy-2,4,6,8-tetraoxa-1(2,4),5(4,2)-diquinazolina-3,7(1,3)-dibenzenacyclooctaphane-3^2-yl) piperidine-1,4-dicarboxylate (*S*-5f)

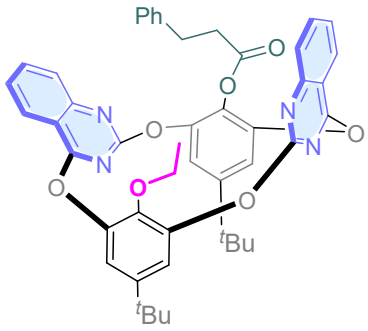


5f

5f: 37.9 mg, 45% yield, 24h, white solid, m.p. > 300 °C
^{1}H NMR (400 MHz, $CDCl_3$) δ 8.28 (d, J = 8.2 Hz, 1H), 8.17 (d, J = 8.2 Hz, 1H), 7.95 – 7.74 (m, 4H), 7.62 – 7.33 (m, 2H), 7.14 – 7.07 (m, 1H), 7.01 (d, J = 2.3 Hz, 2H), 6.97 – 6.89 (m, 1H), 3.60 (s, 3H), 3.43 – 3.11 (m, 2H), 2.46 – 2.25 (m, 2H), 1.95 (dq, J = 10.2, 5.1, 4.0 Hz, 1H), 1.30 (s, 9H), 1.24 (s, 9H), 1.22 (s, 9H), 1.14 – 0.77 (m, 4H).

^{13}C NMR (100 MHz, $CDCl_3$) δ 170.5, 169.0, 168.3, 161.0, 160.8, 154.0, 153.5, 153.4, 150.3, 147.5, 146.2, 145.3, 145.1, 144.2, 141.8, 135.0, 134.9, 132.7, 126.5, 126.5, 125.5, 125.4, 123.7, 123.6, 117.7, 117.6, 116.7, 116.6, 112.9, 112.6, 79.2, 60.9, 42.5, 40.7, 34.7, 34.5, 31.3, 31.2, 31.2, 28.4, 28.3, 26.8.
HRMS (ESI) m/z: $[M+H]^+$ Calcd for $C_{48}H_{52}N_5O_9$: 842.3760; Found: 842.3763.
HPLC (Chiralpak IB, *i*-propanol/hexane = 10/90, flow rate 1.0 mL/min, 30 °C, λ = 254 nm): t_R (major) = 5.3 min, t_R (minor) = 4.7 min, 75:25 e.r.; $[\alpha]^{25}_D$ = -48 (*c* = 1.2, $CHCl_3$).

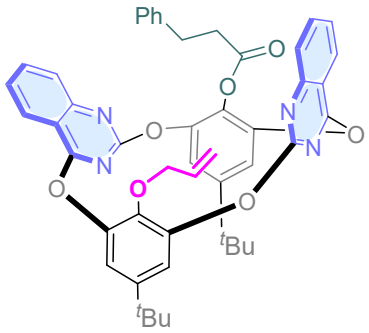
3^5,7^5-di-tert-butyl-72-ethoxy-2,4,6,8-tetraoxa-1(2,4),5(4,2)-diquinazolina-3,7(1,3)-dibenzenacyclooctaphane-3^2-yl 3-phenylpropanoate (*S*-5g)



5g

5g: 37.5 mg, 49% yield, 24h, white solid, m.p. = 268-269 °C
^{1}H NMR (400 MHz, $CDCl_3$) δ 8.28 (d, *J* = 8.2 Hz, 1H), 8.20 (d, *J* = 8.2 Hz, 1H), 7.97 – 7.75 (m, 4H), 7.61 – 7.42 (m, 2H), 7.12 (d, *J* = 2.2 Hz, 1H), 7.08 – 6.88 (m, 6H), 6.61 – 6.44 (m, 2H), 3.97 – 3.74 (m, 2H), 2.35 – 2.22 (m, 2H), 2.17 – 2.02 (m, 2H), 1.26 (s, 9H), 1.25 (s, 9H), 0.80 – 0.63 (m, 3H).
^{13}C NMR (100 MHz, $CDCl_3$) δ 169.1, 169.0, 168.5, 161.1, 161.0, 153.5, 153.4, 150.2, 147.2, 146.5, 145.7, 145.3, 144.4, 140.7, 139.6, 135.0, 134.8, 132.9, 128.2, 127.6, 126.7, 126.4, 126.0, 125.4, 125.4, 123.9, 123.7, 117.6, 117.6, 116.7, 116.6, 113.0, 112.6, 69.2, 34.9, 34.7, 34.5, 31.3, 31.2, 30.1, 15.3.
HRMS (ESI) m/z: $[M+H]^+$ Calcd for $C_{47}H_{45}N_4O_7$: 777.3283; Found: 777.3278.
HPLC (Chiralpak IB, *i*-propanol/hexane = 10/80, flow rate 1.0 mL/min, 30 °C, λ = 254 nm): t_R (major) = 12.4 min, t_R (minor) = 11.6 min, 94:6 e.r.; $[\alpha]^{25}_D$ = -113 (*c* = 1.3, $CHCl_3$).

3^5,7^5-di-tert-butyl-72-ethoxy-2,4,6,8-tetraoxa-1(2,4),5(4,2)-diquinazolina-3,7(1,3)-dibenzenacyclooctaphane-3^2-yl 3-phenylpropanoate (*S*-5h)



5h

5h: 30.7 mg, 39% yield, 16h, white solid, m.p. = 279-281 °C

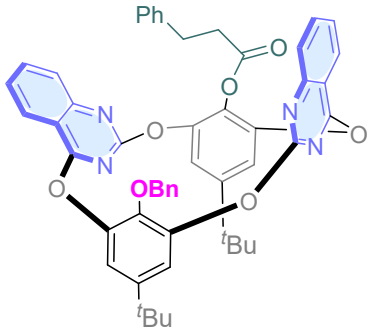
^{1}H NMR (400 MHz, $CDCl_3$) δ 8.27 (d, J = 8.0 Hz, 1H), 8.20 (d, J = 7.9 Hz, 1H), 7.97 – 7.79 (m, 4H), 7.57 – 7.42 (m, 2H), 7.14 – 7.07 (m, 1H), 7.07 – 6.96 (m, 5H), 6.98 – 6.88 (m, 1H), 6.71 – 6.39 (m, 2H), 5.42 (ddt, J = 17.2, 10.4, 5.7 Hz, 1H), 4.70 (dd, J = 17.1, 1.7 Hz, 1H), 4.52 (dd, J = 10.4, 1.6 Hz, 1H), 4.39 – 4.19 (m, 2H), 2.30 (t, J = 8.3 Hz, 2H), 2.18 – 1.98 (m, 2H), 1.26 (s, 9H), 1.25 (s, 9H).

^{13}C NMR (100 MHz, $CDCl_3$) δ 169.1, 169.1, 168.5, 161.1, 160.9, 153.5, 153.4, 150.3, 147.5, 146.4, 145.5, 145.3, 144.4, 140.5, 139.7, 135.0, 134.8, 133.1, 133.0, 128.2, 127.6, 126.7, 126.4, 126.0, 125.5, 125.4, 123.9, 123.8, 117.7, 117.6, 117.3, 116.7, 116.6, 113.0, 112.7, 74.0, 34.8, 34.7, 34.5, 31.2, 31.2, 30.1.

HRMS (ESI) m/z: $[M+H]^+$ Calcd for $C_{48}H_{45}N_4O_7$: 789.3283; Found: 789.3288.

HPLC (Chiralpak IA, *i*-propanol/hexane = 15/85, flow rate 1.0 mL/min, 30 ℃, λ = 254 nm): t_R (major) = 14.9 min, t_R (minor) = 32.2 min, 90:10 e.r.; $[\alpha]^{25}_D$ = -87 (c = 1.3, $CHCl_3$).

7^2-(benzyloxy)-3^5,7^5-di-tert-butyl-2,4,6,8-tetraoxa-1(2,4),5(4,2)-diquinazolina-3,7(1,3)-dibenzenacyclooctaphane-3^2-yl 3-phenylpropanoate (*S*-5i)



5i

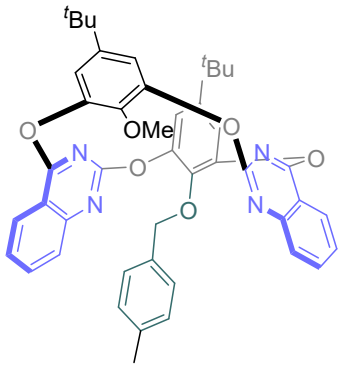
5i: 42.8 mg, 51% yield, 24h, white solid, m.p. > 300 °C

^{1}H NMR (400 MHz, $CDCl_3$) δ 8.17 (t, J = 7.5 Hz, 2H), 8.05 – 7.66 (m, 4H), 7.59 – 7.36 (m, 2H), 7.23 – 6.81 (m, 7H), 6.81 – 6.02 (m, 7H), 4.98 – 4.57 (m, 2H), 2.37 – 2.15 (m, 2H), 1.87 – 1.67 (m, 1H), 1.66 – 1.54 (m, 1H), 1.41 – 0.96 (m, 18H).

^{13}C NMR (100 MHz, $CDCl_3$) δ 169.34 168.9, 168.6, 161.1, 161.0, 153.5, 153.4, 150.2, 147.7, 146.5, 145.6, 145.3, 144.5, 140.5, 139.7, 136.5, 134.9, 134.7, 133.0, 128.2, 127.9,

127.6, 127.6, 127.5, 126.6, 126.5, 125.9, 125.5, 125.3, 123.9, 123.8, 117.7, 117.6, 116.7, 116.5, 113.0, 112.7, 75.0, 34.7, 34.5, 34.1, 31.3, 31.2, 29.9.
HRMS (ESI) m/z: $[M+H]^+$ Calcd for $C_{52}H_{47}N_4O_7$: 839.3439; Found: 839.3442.
HPLC (Chiralpak IA, *i*-propanol/hexane = 15/85, flow rate 1.0 mL/min, 30 ℃, λ = 254 nm): t_R (major) = 13.2 min, t_R (minor) = 26.8 min, 89:11 e.r.; $[\alpha]^{25}_D$ = -82 (*c* = 1.5, $CHCl_3$).

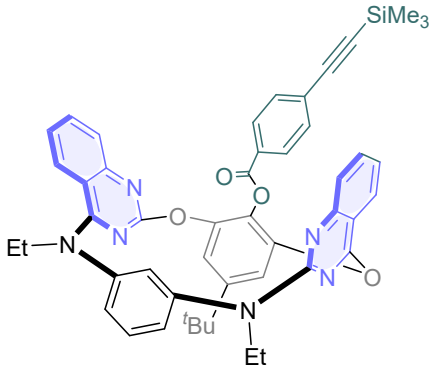
3^2-(benzyloxy)-3^5,7^5-di-tert-butyl-7^2-methoxy-2,4,6,8-tetraoxa-1(2,4),5(4,2)-diquinazolina-3,7(1,3)-dibenzenacyclooctaphane (*R*-6a)



6a

6a: 37.4 mg, 85% yield, white solid, m.p. > 300 °C
^{1}H NMR (400 MHz, $CDCl_3$) δ 8.27 (d, *J* = 8.2 Hz, 1H), 8.07 (dd, *J* = 8.3, 1.3 Hz, 1H), 7.92 – 7.74 (m, 4H), 7.49 (ddd, *J* = 8.3, 5.4, 2.8 Hz, 1H), 7.41 (ddd, *J* = 8.2, 6.6, 1.4 Hz, 1H), 6.99 (dd, *J* = 9.6, 2.4 Hz, 2H), 6.93 – 6.84 (m, 2H), 6.71 – 6.51 (m, 4H), 4.88 (d, *J* = 11.4 Hz, 1H), 4.78 (d, *J* = 11.4 Hz, 1H), 3.54 (s, 3H), 2.09 (s, 3H), 1.30 – 1.20 (m, 18H).
^{13}C NMR (100 MHz, $CDCl_3$) δ 169.2, 169.2, 161.4, 161.3, 153.4, 153.3, 146.9, 146.8, 146.0, 145.9, 145.1, 145.0, 141.9, 140.8, 136.6, 134.5, 134.5, 134.1, 128.2, 128.2, 126.8, 126.6, 126.3, 125.1, 124.9, 123.9, 123.7, 117.9, 117.7, 116.7, 116.5, 113.1, 76.7, 60.7, 34.4, 34.4, 31.3, 20.9.
HRMS (ESI) m/z: $[M+H]^+$ Calcd for $C_{45}H_{43}N_4O_6$: 735.3177; Found: 735.3179.
HPLC (Chiralpak IA, *i*-propanol/hexane = 15/85, flow rate 1.0 mL/min, 30 ℃, λ = 254 nm): t_R (major) = 9.2 min, t_R (minor) = 12.6 min, 97:3 e.r.; $[\alpha]^{25}_D$ = +195 (*c* = 1.3, $CHCl_3$).

3^5-(tert-butyl)-6,8-diethyl-2,4-dioxa-6,8-diaza-1(2,4),5(4,2)-diquinazolina-3,7(1,3)-dibenzenacyclooctaphane-3^2-yl 4-((trimethylsilyl)ethynyl)benzoate(*S*-6b)



6b

6b: 71.0 mg, 89% yield, colorless oil.

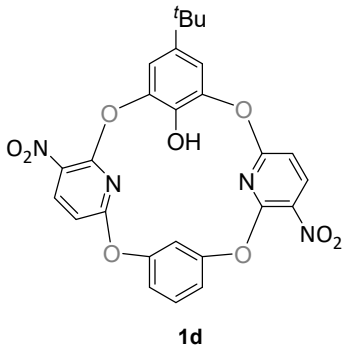
^{1}H NMR (400 MHz, $CDCl_3$) δ 8.03 (d, J = 8.5 Hz, 1H), 7.93 (d, J = 8.1 Hz, 1H), 7.71 – 7.63 (m, 2H), 7.63 – 7.53 (m, 2H), 7.42 – 7.33 (m, 3H), 7.25 (t, J = 7.9 Hz, 1H), 7.16 – 7.03 (m, 3H), 7.03 – 6.91 (m, 3H), 6.88 (d, J = 2.2 Hz, 2H), 4.32 – 3.98 (m, 4H), 1.45 (t, J = 7.0 Hz, 3H), 1.33 – 1.27 (m, 12H), 0.23 (s, 9H).

^{13}C NMR (100 MHz, $CDCl_3$) δ 186.6, 166.6, 166.1, 162.8, 161.1, 158.1, 154.7, 153.7, 151.5, 149.4, 145.8, 145.5, 145.3, 145.1, 133.9, 133.6, 133.0, 131.4, 129.9, 129.5, 128.8, 128.2, 127.8, 127.7, 127.3, 125.5, 125.0, 124.6, 123.6, 123.2, 122.2, 118.0, 117.1, 113.2, 110.8, 104.0, 97.6, 49.5, 44.6, 34.6, 31.3, 14.3, 13.3, -0.2.

HRMS (ESI) m/z: $[M+H]^+$ Calcd for $C_{48}H_{47}N_6O_4Si$: 799.3423; Found: 799.3427.

HPLC (Chiralpak IB, *i*-propanol/hexane = 15/85, flow rate 1.0 mL/min, 30 °C, λ = 254 nm): t_R (major) = 4.6 min, t_R (minor) = 5.8 min, 96:4 e.r.; $[\alpha]^{25}_D$ = -99 (*c* = 1.5, $CHCl_3$)

3^5-(tert-butyl)-1^3,5^5-dinitro-2,4,6,8-tetraoxa-1,5(2,6)-dipyridina-3,7(1,3)-dibenzenacyclooctaphan-3^2-ol (1d)



1d

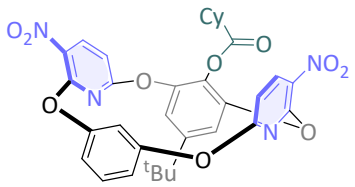
1d: yellow solid. M.p. = 209 – 210°C

^{1}H NMR (400 MHz, $CDCl_3$) δ 8.49 (dd, J = 8.7, 1.5 Hz, 2H), 7.18 (t, J = 8.2 Hz, 1H), 6.95 – 6.66 (m, 6H), 6.68 – 6.44 (m, 1H), 1.18 (s, 9H).

^{13}C NMR (100 MHz, $CDCl_3$) δ 164.7, 164.6, 164.1, 156.4, 156.0, 155.9, 153.3, 153.1, 152.9, 143.7, 143.6, 140.6, 140.3, 140.2, 139.7, 139.7, 137.8, 130.0, 129.9, 127.7, 127.5, 127.5, 119.8, 119.4, 119.3, 117.4, 117.4, 117.3, 117.1, 117.0, 105.1, 104.8, 104.5, 34.2, 31.2.

HRMS (ESI) m/z: $[M+H]^+$ Calcd for $C_{26}H_{21}N_4O_9$: 533.1303; Found: 533.1309.

3^5-(tert-butyl)-1^3,5^5-dinitro-2,4,6,8-tetraoxa-1,5(2,6)-dipyridina-3,7(1,3)-dibenzenacyclooctaphane-3^2-yl cyclohexanecarboxylate (*S*-6c)

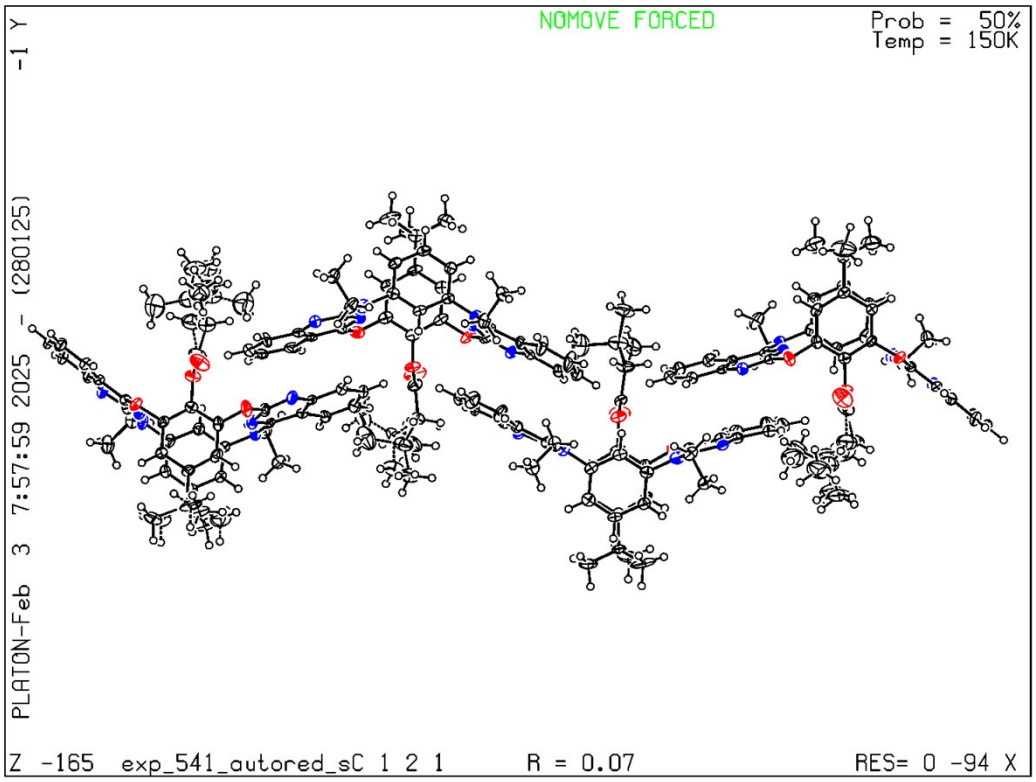


6c

6c: 44.3 mg, 69% yield, colorless oil.
^{1}H NMR (400 MHz, $CDCl_3$) δ 8.53 (t, J = 9.0 Hz, 2H), 7.26 – 7.15 (m, 1H), 7.03 – 6.69 (m, 6H), 6.67 – 6.51 (m, 1H), 2.29 – 2.17 (m, 1H), 1.70 – 1.48 (m, 5H), 1.34 – 1.04 (m, 14H).
^{13}C NMR (100 MHz, $CDCl_3$) δ 172.1, 164.4, 163.9, 156.3, 155.7, 153.2, 152.9, 150.1, 144.7, 144.4, 139.8, 139.5, 133.1, 130.0, 127.8, 127.4, 119.6, 119.4, 118.2, 117.9, 117.0, 104.8, 104.0, 42.3, 34.7, 31.1, 28.6, 28.5, 25.4, 24.9, 24.9.
HRMS (ESI) m/z: $[M+H]^+$ Calcd for $C_{33}H_{31}N_4O_{10}$: 643.2035; Found: 643.2037.
HPLC (Chiralpak IA, *i*-propanol/hexane = 10/90, flow rate 1.0 mL/min, 30 ℃, λ = 254 nm): t_R (major) = 30.5 min, t_R (minor) = 13.4 min, 91:9 e.r.; $[\alpha]^{25}_D$ = -91 (*c* = 1.4, $CHCl_3$).

X-ray Crystal Structure Data for Compound (3l) (CCDC: 2421502)

A colorless needle like crystal of 3l was obtained by vaporization of its diethyl ether / petroleum ether solution.



Crystal data and structure refinement for exp_541_autored_sq.

Identification code	exp_541_autored_sq
Empirical formula	$C_{42}H_{44}N_6O_4$
Formula weight	696.83
Temperature/K	150
Crystal system	monoclinic
Space group	C2
a/Å	72.2732(7)
b/Å	9.21670(10)
c/Å	24.9319(2)
α/°	90
β/°	92.5770(10)

γ/°	90
Volume/Å^3	16590.8(3)
Z	16
ρ_{calc}g/cm^3	1.116
μ/mm^{-1}	0.584
F(000)	5920.0
Crystal size/mm^3	? × ? × ?
Radiation	Cu Kα (λ = 1.54184)
2Θ range for data collection/°	7.346 to 148.708
Index ranges	$0 \leq h \leq 89$, $-10 \leq k \leq 11$, $-29 \leq l \leq 30$
Reflections collected	127549
Independent reflections	27135 [R_{int} = 0.0517, R_{sigma} = 0.0603]
Data/restraints/parameters	27135/437/2078
Goodness-of-fit on F^2	1.037
Final R indexes [I>=2σ (I)]	R_1 = 0.0710, wR_2 = 0.1787
Final R indexes [all data]	R_1 = 0.0975, wR_2 = 0.1936
Largest diff. peak/hole / e Å^{-3}	0.41/-0.29
Flack parameter	0.1(2)

Computational information

Computational methods

DFT calculations were performed with the Gaussian 16 revision C.01 suite of program. Geometry optimizations and vibrational analysis were performed using the Minnesota hybrid meta generalized gradient approximation exchange-correlation functional (M06-2X) in conjunction with Pople's polarized double-ζ 6-31G(d) basis set for all atoms. The implicit universal Solvation Model Based on Solute Electron Density (SMD) in toluene was used throughout to account for solvation effects. Transition structures were verified to process only one vibrational mode with imaginary frequency while minima have none. High level single point electronic energies were calculated at SMD(DCM)-M06-2X/def2-TZVP level of theory. All energies mentioned in the text are solvated Gibbs free energies. Structures are rendered using CYLview 20. Sacn were conducted at SMD(DCM)-M06-2X/6-31G(d) level of theory.

(1) Calculated energy profile of the of TS-(S_p)-**1a** and TS-(R_p)-**1a**

Species	**TS1**	**TS2**
Optimization Level	SMD(DCM)-M06-2X/6-31G(d)	
Electronic Energy Level	SMD(DCM)-M06-2X/def2-TZVP	
G Correction (au)	0.897375	0.897392
Electronic Energy (au)	-9751.673293	-9751.658633
Imaginaries	1	1
G_{sol}(au) at 1atm	-9750.775918	-9750.761241

TS1

C	6.293082	-0.775375	-0.288277
C	5.892724	-0.390037	-1.566504
C	5.241529	0.829139	-1.753962
C	4.942993	1.676737	-0.693574
C	5.310919	1.247526	0.576652
C	6.006260	0.054702	0.790175
C	5.057615	1.933127	1.886771
C	6.126908	1.288889	2.822365
C	6.338538	-0.123163	2.249650
N	3.727372	1.627262	2.484374
C	3.564295	1.860331	3.827660
C	4.802188	2.165220	4.609445
O	5.764388	1.214438	4.189906
C	2.542739	1.227358	2.010344
N	1.708670	1.254207	3.055075
N	2.339906	1.632910	4.197914
C	0.323459	0.908579	3.108992

C	-0.651089	1.790425	2.642105
C	-1.995283	1.455930	2.721192
C	-2.346354	0.249138	3.310709
C	-1.400194	-0.629055	3.831428
C	-0.060725	-0.288391	3.719990
Cl	1.141385	-1.346308	4.381741
Cl	-0.209548	3.323585	1.981829
Cl	-4.024821	-0.172032	3.424524
Br	4.684664	1.308533	-3.498878
H	6.823177	-1.712428	-0.147303
H	6.091210	-1.032410	-2.418450
H	4.420314	2.615142	-0.852881
H	5.118274	3.022557	1.849144
H	7.034443	1.893505	2.707873
H	7.353634	-0.489606	2.417829
H	5.644190	-0.819083	2.736424
H	5.131339	3.196160	4.428213
H	4.622258	2.020398	5.674377
H	-2.748736	2.136791	2.341864
H	-1.698099	-1.551473	4.318072
C	2.605550	-1.549635	-2.110094
C	2.868518	-2.683130	-1.353055
C	2.897471	-2.657270	0.055725
C	2.680528	-1.469562	0.709848
C	2.403799	-0.289626	-0.034056
C	2.340853	-0.355177	-1.451658
C	2.167182	0.948494	0.584199
Br	3.265161	-4.303057	-2.218435
O	1.785868	2.038468	-0.035679
H	2.607771	-1.588218	-3.194165
H	3.102773	-3.564965	0.611562
H	2.712892	-1.442293	1.796106
H	2.221712	0.563371	-2.017859
C	-3.336748	-3.588971	2.476802
N	-4.441906	-3.161958	1.802103
C	-4.226033	-2.409807	0.739543
N	-3.006584	-1.999775	0.271412
C	-1.960401	-2.422515	0.908292
C	-2.022825	-3.266221	2.060626
C	-0.894216	-3.741885	2.758294
C	-1.068763	-4.508234	3.888064
C	-2.376334	-4.815283	4.331997
C	-3.486092	-4.375772	3.646189
C	-1.172607	4.714671	-1.469159

N	-0.294725	3.716240	-1.795772
C	-0.855404	2.566059	-2.039947
N	-2.127646	2.189433	-1.887387
C	-2.982670	3.101221	-1.438006
C	-2.565890	4.488782	-1.321331
C	-3.421779	5.605307	-1.165522
C	-2.907290	6.877275	-1.056316
C	-1.512956	7.083671	-1.099731
C	-0.662329	6.025273	-1.312349
O	-0.728266	-2.076404	0.483688
C	-0.638976	-1.545981	-0.801890
C	-0.406392	-0.151787	-0.938290
C	-0.298985	0.283241	-2.292954
C	-0.440543	-0.552791	-3.387138
C	-0.638208	-1.923212	-3.204970
C	-0.721110	-2.397845	-1.881471
O	0.015803	1.612742	-2.496536
C	-0.800673	-2.900352	-4.368910
O	-0.243435	0.661386	0.047914
C	-5.164851	-0.942250	-0.963984
C	-5.567103	-1.174145	-2.278546
C	-5.492219	-0.147979	-3.218291
C	-5.028785	1.111822	-2.851672
C	-4.627766	1.338655	-1.535366
C	-4.690048	0.316836	-0.593668
C	0.303572	-3.965352	-4.299702
C	-2.175521	-3.582339	-4.264905
C	-0.709953	-2.195440	-5.724884
N	-5.299476	-1.979811	0.007428
C	-7.179034	-1.424359	1.533812
C	-6.658677	-2.334649	0.427874
N	-4.235041	2.661651	-1.130288
C	-6.446371	3.741745	-0.741980
C	-5.126458	3.284958	-0.137322
H	0.097488	-3.490017	2.394858
H	-0.210169	-4.877167	4.439716
H	-2.504760	-5.415872	5.227833
H	-4.491242	-4.617488	3.977210
H	-4.496367	5.474596	-1.169882
H	-3.578157	7.723007	-0.947298
H	-1.113841	8.088200	-0.996088
H	0.410759	6.162842	-1.400035
H	-0.370630	-0.108755	-4.374026
H	-0.878458	-3.454869	-1.681925

H	-5.932059	-2.158246	-2.557765
H	-5.804432	-0.331050	-4.241593
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H	-0.825976	-2.932391	-6.526432
H	-1.498016	-1.443813	-5.842318
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H	-6.580555	-1.549368	2.440816
H	-7.295379	-2.264973	-0.457634
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H	-6.294286	4.472961	-1.541530
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TS2

O	-0.186023	-0.001066	-0.842372
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C	0.086287	0.456731	0.382031
C	-0.271324	1.752463	0.789798
C	-0.075464	2.209457	2.080436
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C	6.362557	-2.657528	1.046800
C	6.775029	-3.922764	1.397407
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C	4.514301	-4.535688	1.984557
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N	2.712230	-3.018036	1.605554
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O	1.008793	-1.654025	1.029993

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C	1.014741	0.741435	5.457207
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H	1.171096	-0.658256	3.397792
H	-0.362450	3.231859	2.309692
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H	7.816868	-4.202181	1.279638
H	6.183171	-5.853769	2.177783
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H	5.501681	-0.368336	-2.117720
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H	3.728553	3.282072	-3.549006
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H	0.293723	-0.084180	5.459602

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H	-1.524566	1.602043	5.044424
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Cl	0.018000	-4.749178	-0.437064
Cl	0.399183	-0.555485	-3.844075
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H	-4.811397	-3.922691	-0.373887
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H	-3.458295	-5.230776	-4.159752
H	3.143535	-1.190298	-3.436940
H	2.824151	-4.583177	-0.793147
C	-2.873753	0.162711	2.563980
C	-2.569759	-1.048294	3.179053
C	-2.229949	-2.188982	2.447063
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C	-2.776802	0.251344	1.182851
C	-2.084678	-0.678560	-0.968373
Br	-2.593102	-1.149194	5.062854
O	-2.258969	0.445760	-1.607072
H	-3.154068	1.031517	3.150232
H	-2.004848	-3.121489	2.951806
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(2) Scan plot of Sub **1a** and **3a**

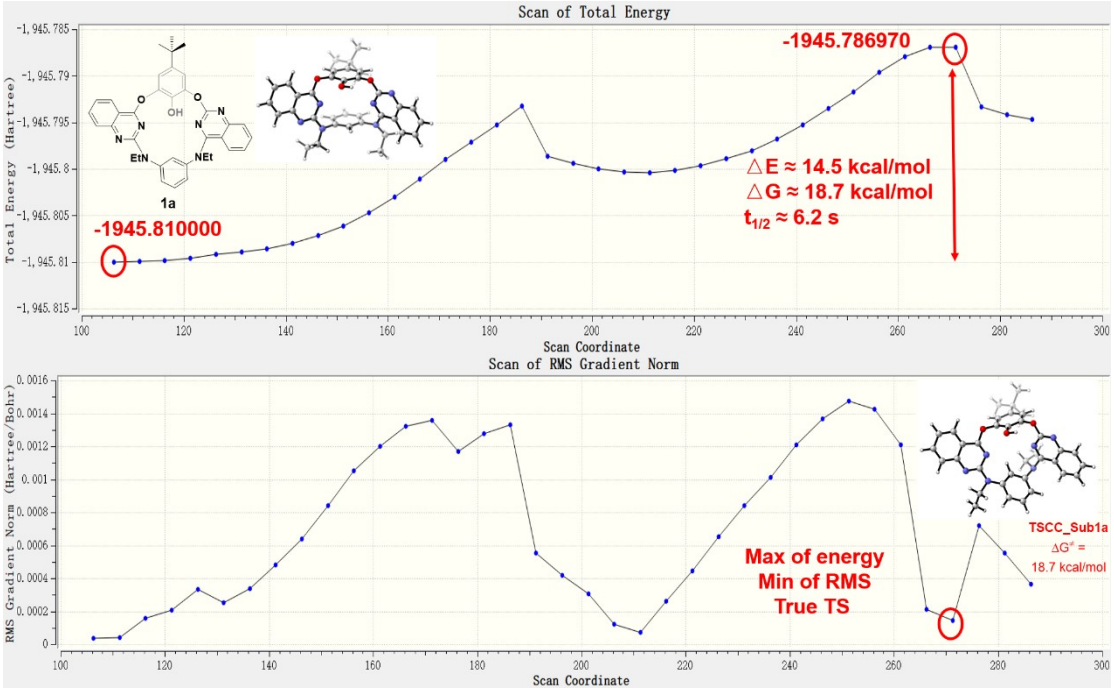

Figure SIx. Scan plot of Sub **1a** and the △E, △G and $t_{1/2}$ of isomerization.

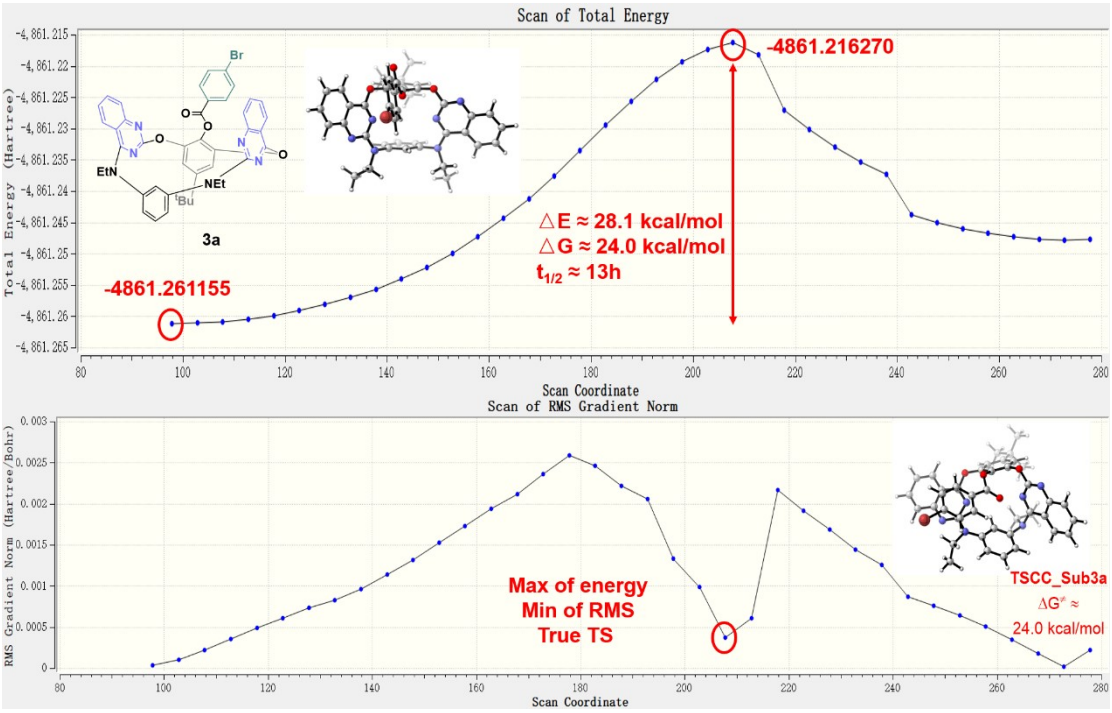

Figure SIy. Scan plot of Sub **3a** and the △E, △G and $t_{1/2}$ of isomerization.

Species	**TSCC_Sub1a**	**TSCC_Sub3a**
Optimization Level	SMD(DCM)-M06-2X/6-31G(d)	
Electronic Energy Level	SMD(DCM)-M06-2X/def2-TZVP	
G Correction (au)	0.582788	0.654179
Electronic Energy (au)	-1946.505517	-4864.491872
Imaginaries	1	1
G_{sol}(au) at 1atm	-1945.922729	-4863.837693

TSCC_Sub3a

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N	3.210428	1.083688	1.921427
C	2.128642	0.501922	1.449252
N	1.184809	1.103209	0.650465
C	1.459387	2.315619	0.261826
C	2.629811	3.044967	0.638172
C	2.927647	4.359703	0.218262
C	4.067581	4.972087	0.683679
C	4.926198	4.289188	1.577582
C	4.646391	3.009044	1.993921
C	-4.279916	-2.783474	-1.249879
N	-3.804931	-1.850119	-2.130529
C	-3.235077	-0.817833	-1.584377
N	-3.026316	-0.572935	-0.276447
C	-3.371147	-1.499815	0.571306

C	-4.093977	-2.657480	0.152295
C	-4.645302	-3.616911	1.033263
C	-5.335721	-4.690996	0.526784
C	-5.490784	-4.839750	-0.872562
C	-4.980300	-3.909463	-1.746124
O	0.655793	3.001086	-0.576715
C	-0.657037	2.653654	-0.825919
C	-0.968385	1.505798	-1.550937
C	-2.318473	1.281738	-1.828903
C	-3.284727	2.203508	-1.451562
C	-2.962299	3.373670	-0.758989
C	-1.621202	3.573990	-0.435052
O	-2.734573	0.116832	-2.444641
C	-4.065250	4.357830	-0.365874
O	0.096002	0.773188	-2.028551
C	0.829235	-1.622952	1.826689
C	0.938327	-3.016259	2.010992
C	-0.188056	-3.807602	2.189877
C	-1.457699	-3.252105	2.198276
C	-1.587955	-1.878472	2.004276
C	-0.463522	-1.064967	1.824293
C	-5.051660	3.652928	0.579253
C	-3.502200	5.590032	0.347619
C	-4.808281	4.820608	-1.629264
N	2.020303	-0.862929	1.698709
C	3.525476	-1.726360	3.506673
C	3.295786	-1.537107	2.013802
N	-2.934758	-1.344210	1.925026
C	-4.581982	0.344603	2.596922
C	-3.102977	0.025635	2.439743
H	2.254128	4.870024	-0.461831
H	4.311015	5.982104	0.370842
H	5.821017	4.787560	1.938553
H	5.298123	2.473148	2.676586
H	-4.530806	-3.470210	2.102500
H	-5.770882	-5.425845	1.196230
H	-6.033048	-5.697805	-1.258536
H	-5.106026	-4.004130	-2.819960
H	-4.315877	1.965086	-1.697575
H	-1.282443	4.450625	0.105003
H	1.898494	-3.509632	2.041861
H	-0.060571	-4.875299	2.340689
H	-2.337670	-3.865765	2.350566
H	-0.595896	-0.006522	1.644840

H	-5.849179	4.345183	0.872163
H	-5.517368	2.784256	0.102311
H	-4.540895	3.313312	1.486986
H	-2.993455	5.321281	1.279747
H	-4.322992	6.269407	0.599389
H	-2.796462	6.136844	-0.287308
H	-5.600157	5.527236	-1.356875
H	-4.124897	5.322172	-2.323069
H	-5.274316	3.981909	-2.156111
H	2.716127	-2.298231	3.970642
H	4.463613	-2.264488	3.675033
H	3.589961	-0.753073	4.000849
H	3.318663	-2.487016	1.478019
H	4.092481	-0.931219	1.588542
H	-5.073789	-0.411241	3.216996
H	-4.710062	1.321429	3.072046
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C	0.321069	-0.515914	-1.639340
O	-0.540417	-1.264649	-1.268179
C	1.758863	-0.879948	-1.741563
C	2.106699	-2.196463	-1.432188
C	2.749535	0.062105	-2.026602
C	3.442487	-2.575453	-1.392429
H	1.324634	-2.912949	-1.201958
C	4.090086	-0.304817	-1.982726
H	2.477965	1.086061	-2.261172
C	4.417624	-1.617670	-1.655889
H	3.723037	-3.593243	-1.144259
H	4.868443	0.422428	-2.184674
Br	6.242752	-2.109945	-1.535474

TSCC_Sub1a

C	4.948042	-0.998538	-0.101598
N	4.107733	-2.041429	0.130184
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N	2.224318	-0.655794	-0.370307
C	3.035980	0.334045	-0.612760
C	4.462570	0.253590	-0.524466
C	5.344984	1.326290	-0.777095
C	6.696947	1.141550	-0.604436
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C	6.343613	-1.163211	0.077230

C	-4.654483	-0.454453	-1.353444
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C	-2.921433	-0.558296	0.314836
C	-4.214596	-0.982762	-0.109640
C	-5.056306	-1.843155	0.634879
C	-6.280181	-2.204203	0.128417
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C	-5.914057	-0.856387	-1.860063
O	2.605339	1.549808	-0.996447
C	1.316170	2.022116	-0.821034
C	0.269783	1.577468	-1.620484
C	-0.958917	2.221471	-1.448705
C	-1.132821	3.271441	-0.568522
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O	-2.039528	1.722251	-2.171953
C	-0.278530	4.897760	1.183428
O	0.452400	0.573396	-2.501440
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C	0.064241	-4.388618	0.333276
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C	-1.469083	-2.219594	1.100202
C	-0.136573	-2.021410	0.720132
C	-1.308192	4.481422	2.246266
C	1.018984	5.294373	1.892919
C	-0.806900	6.118829	0.414227
N	2.036451	-3.007531	-0.006856
C	3.150940	-4.953285	1.113808
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N	-2.307602	-1.099517	1.480398
C	-2.675836	0.866370	2.908381
C	-1.643171	-0.080371	2.315858
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H	7.387662	1.956417	-0.794842
H	8.262691	-0.240719	-0.036603
H	6.710438	-2.130390	0.406044
H	-4.725736	-2.182657	1.610611
H	-6.934977	-2.857395	0.695876
H	-7.668902	-2.017703	-1.522402
H	-6.234691	-0.457355	-2.816951
H	-2.124821	3.707594	-0.487497

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H	-1.681219	-5.564337	0.688527
H	-3.074845	-3.620575	1.399775
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H	3.825443	-4.314384	1.690255
H	2.192293	-4.917789	-0.842080
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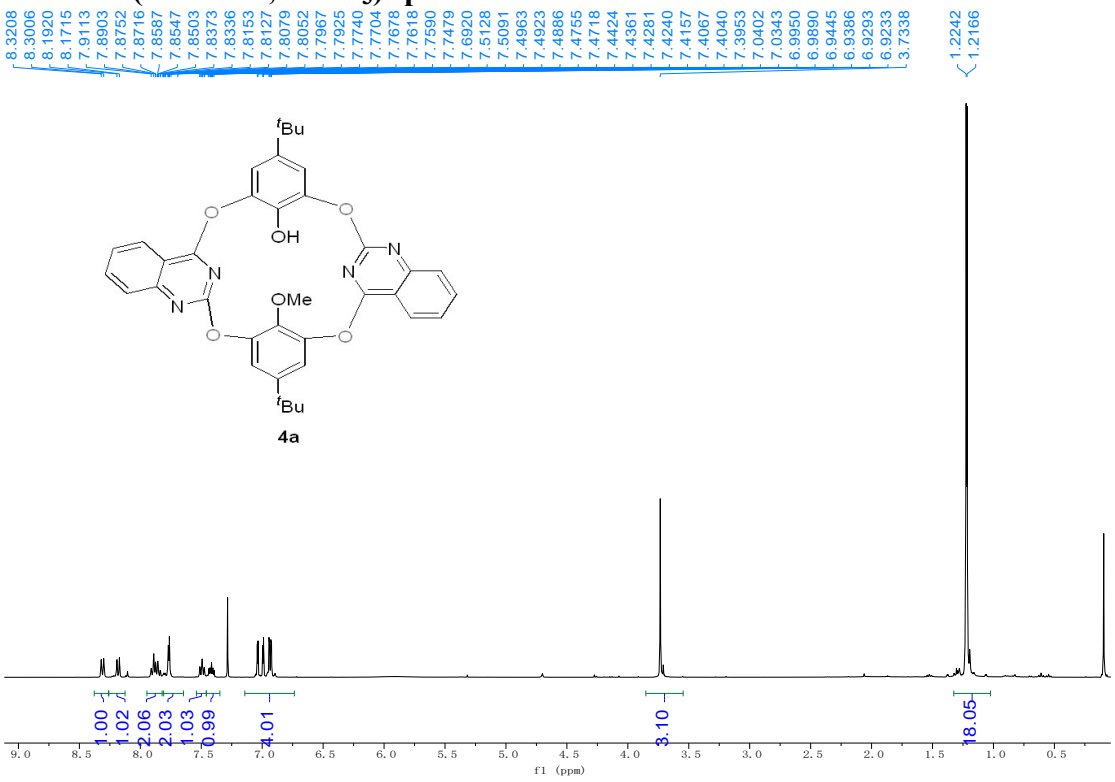
H	-3.455784	0.305414	3.432674
H	-2.198608	1.546329	3.619686
H	-3.148960	1.474658	2.129983
H	-1.129445	-0.628845	3.110182
H	-0.891399	0.488537	1.753713

References

1 Q.-L. Lu, X.-D. Wang, S. Tong, J. Zhu and M.-X. Wang, *ACS. Catal*. 2024, **14**, 5140-5146.

^{1}H NMR , ^{13}C NMR spectra of substrates and products

^{1}H NMR (400 MHz, $CDCl_3$) spectra of 4a



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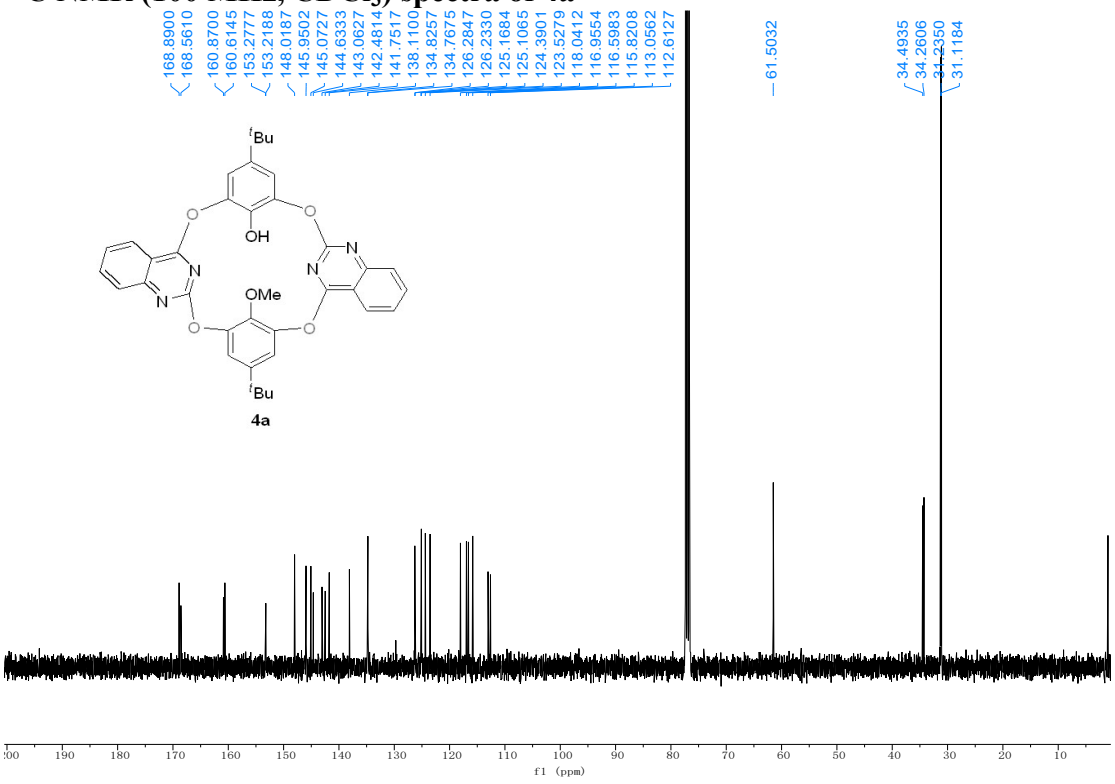

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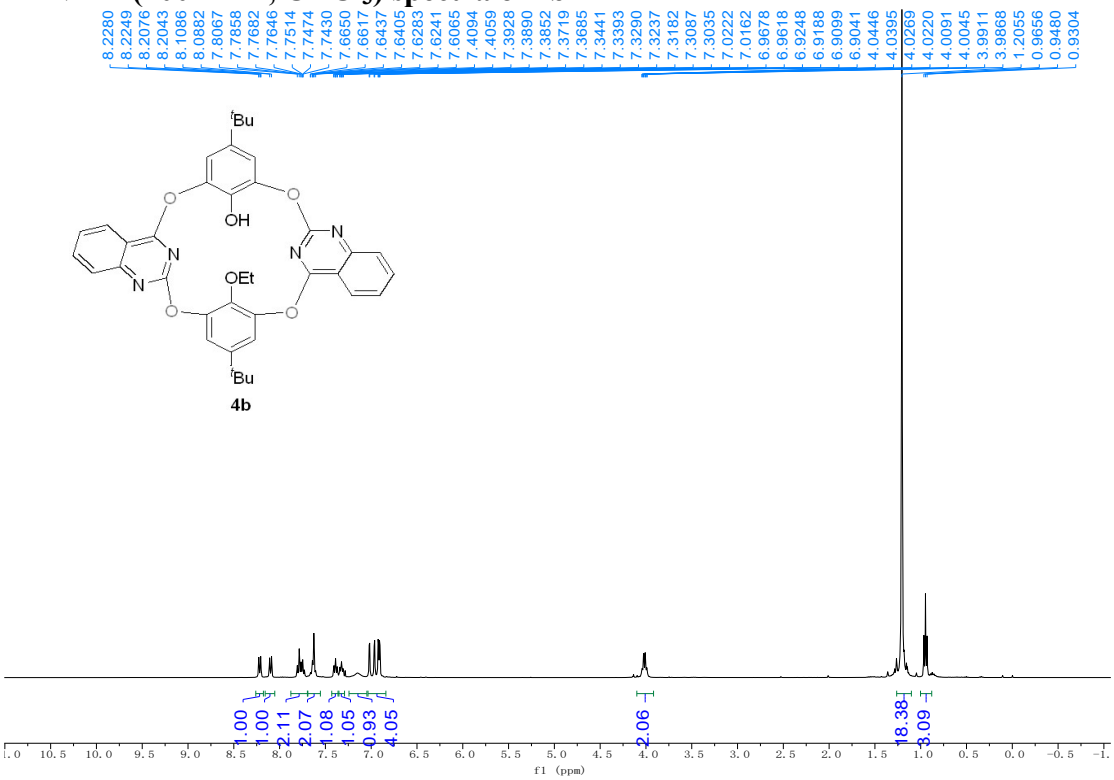
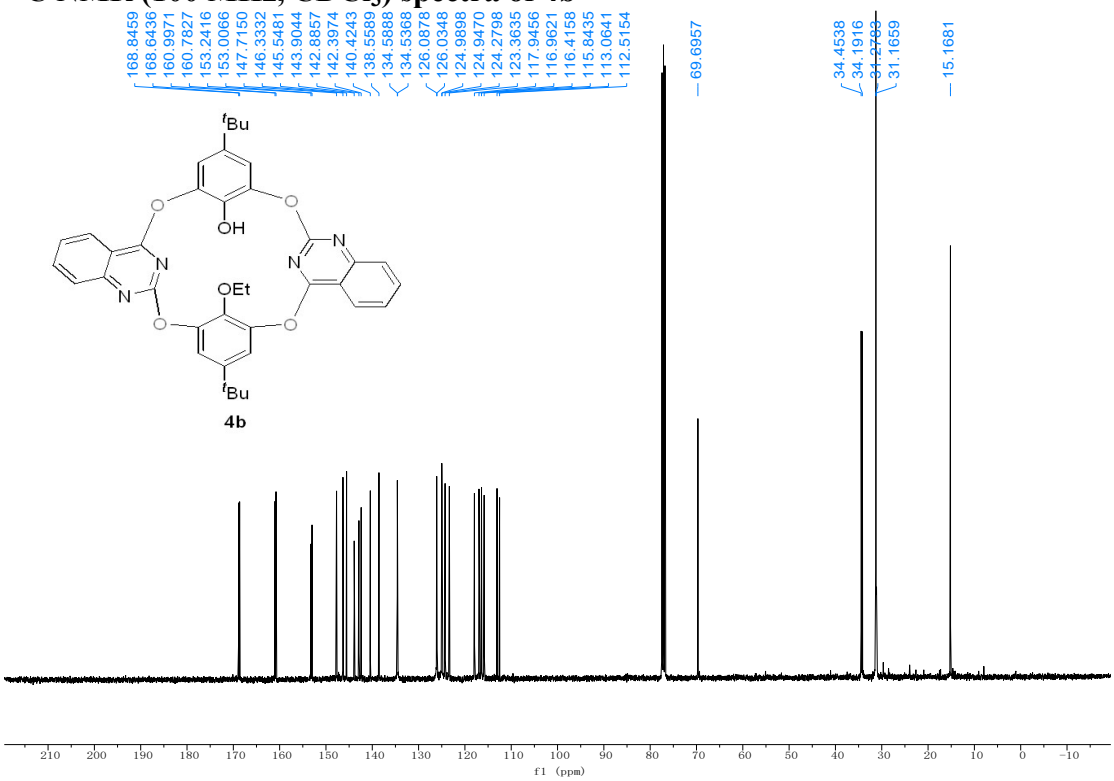
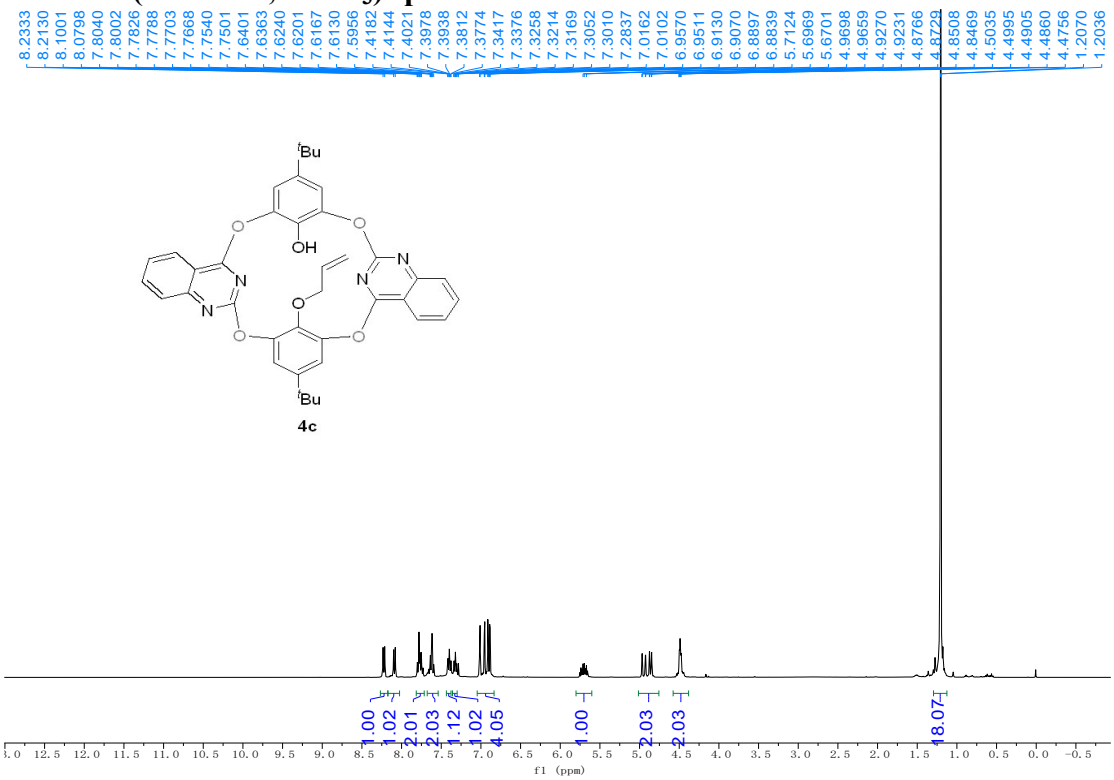


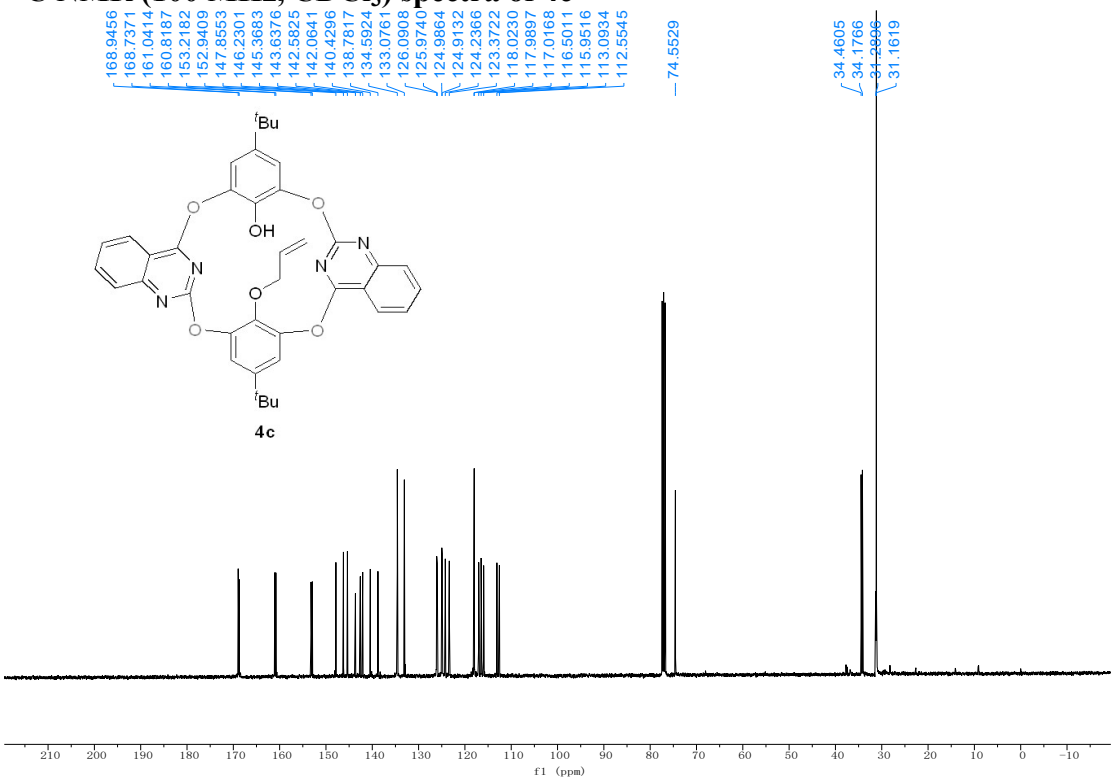
^{13}C NMR (100 MHz, $CDCl_3$) spectra of 4b



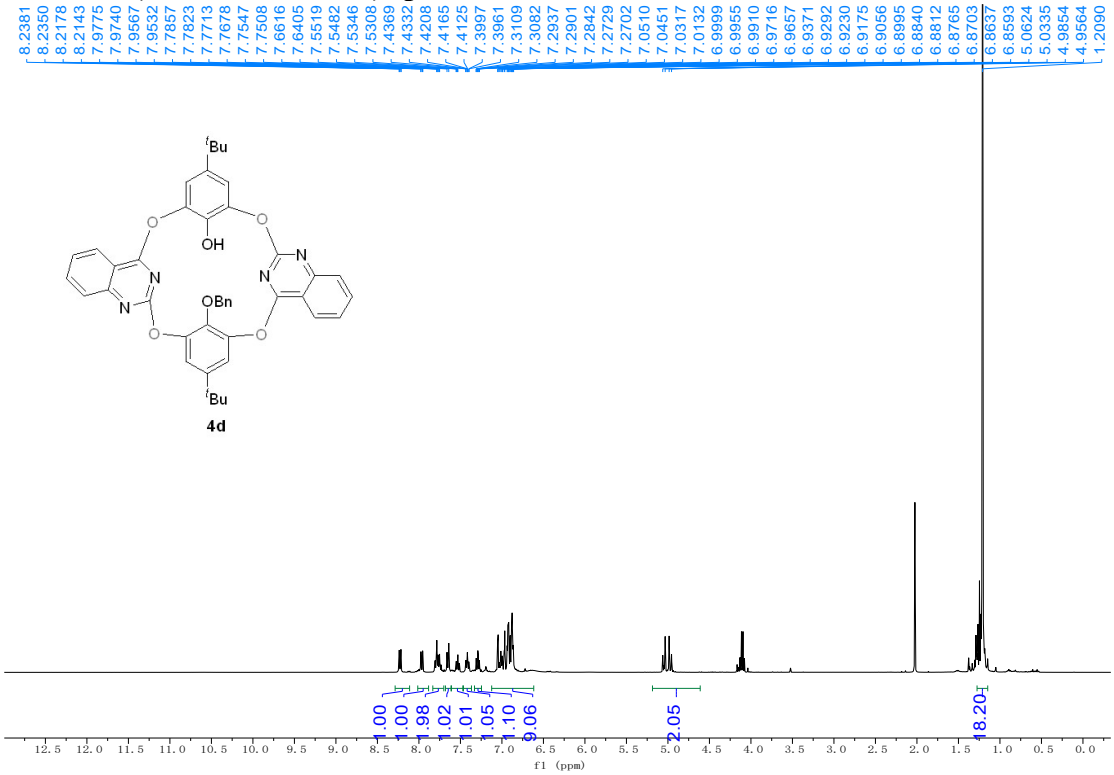
^{1}H NMR (400 MHz, $CDCl_3$) spectra of 4c



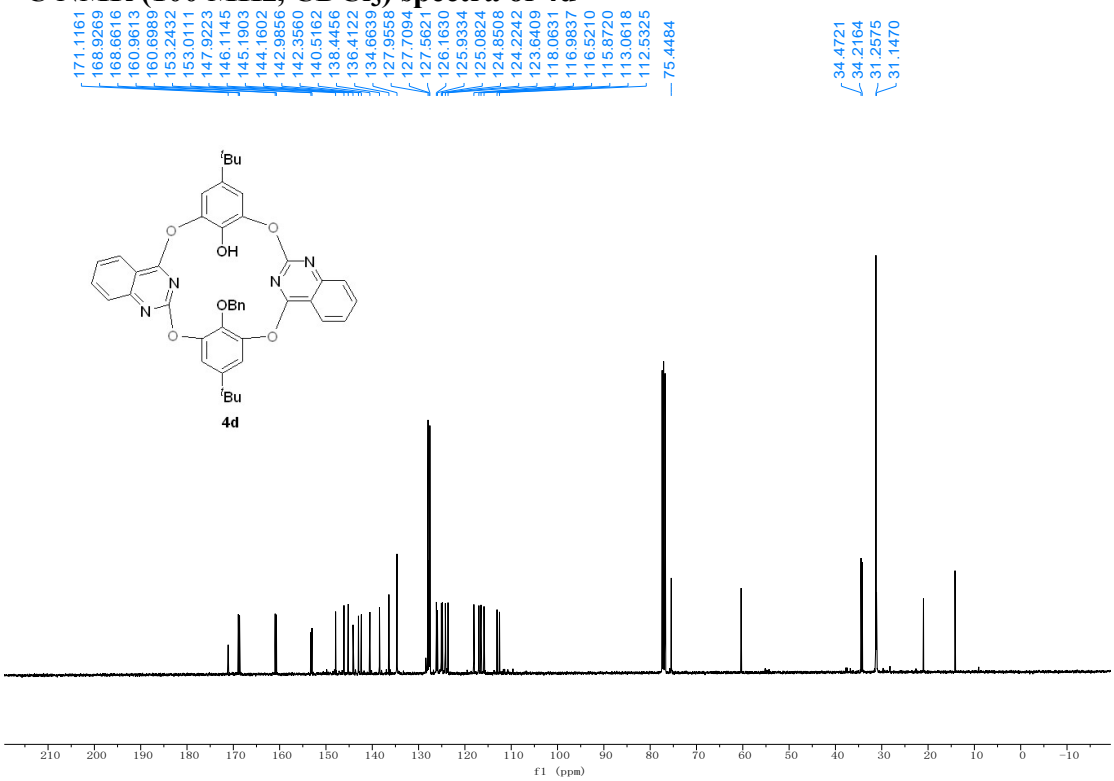
^{13}C NMR (100 MHz, $CDCl_3$) spectra of 4c



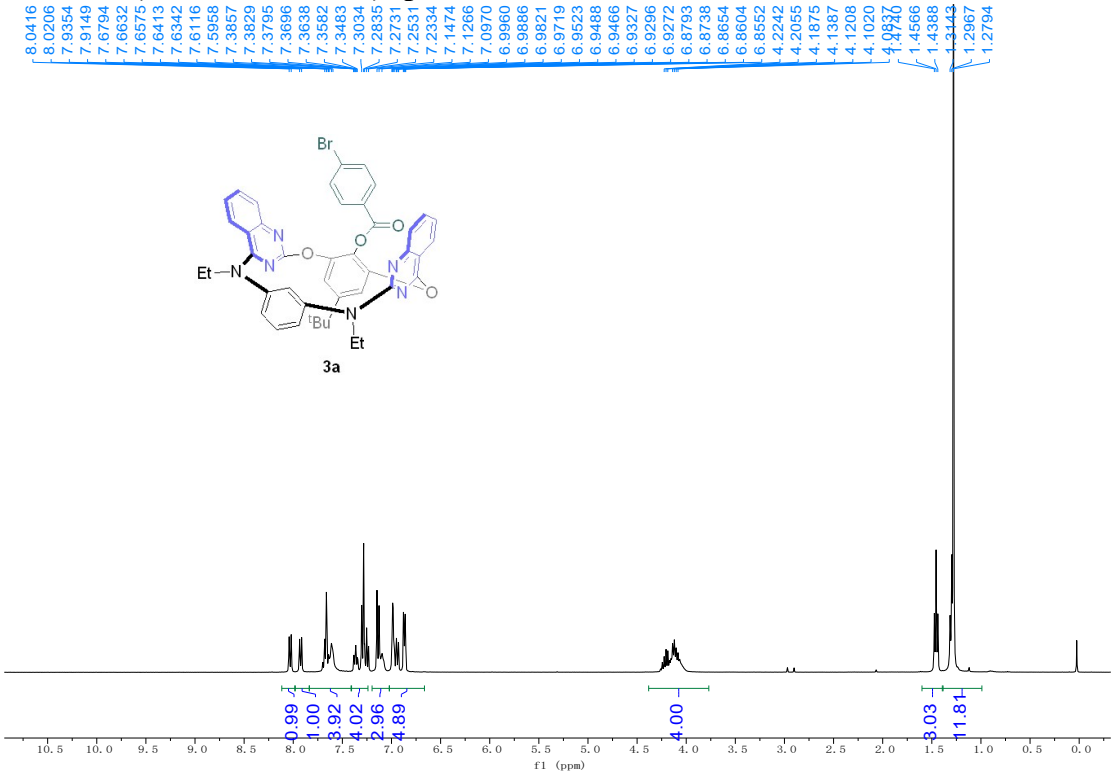
^{1}H NMR (400 MHz, $CDCl_3$) spectra of 4d



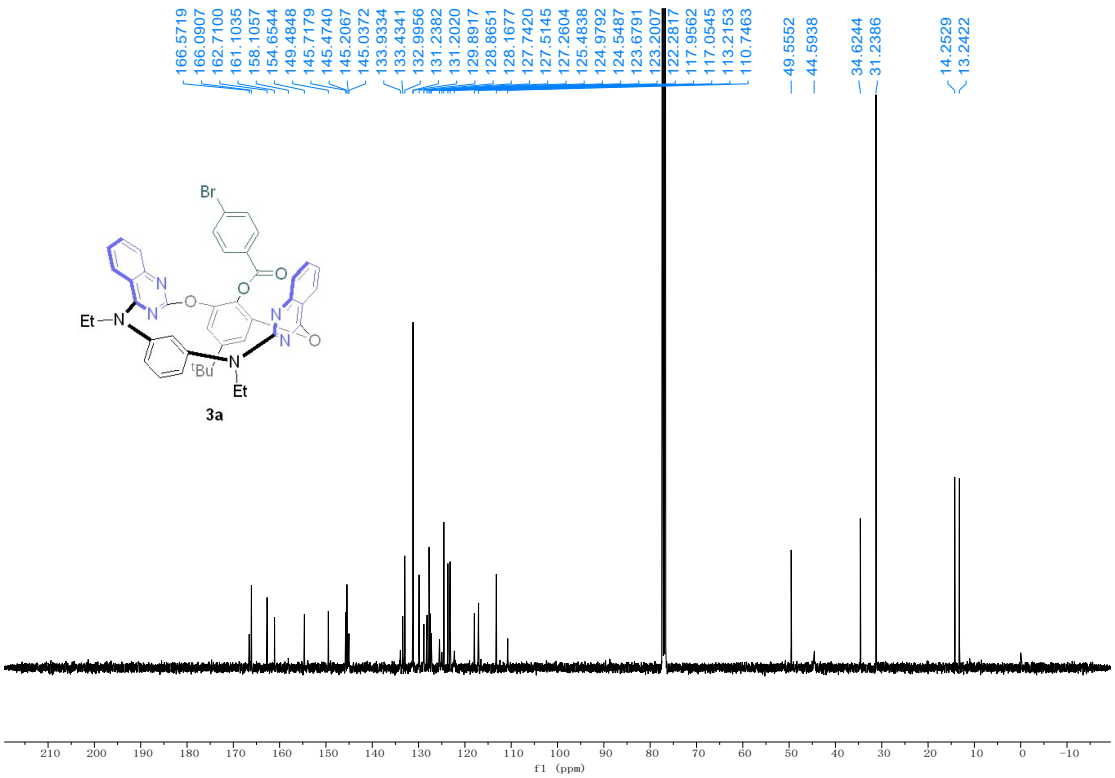
^{13}C NMR (100 MHz, $CDCl_3$) spectra of 4d



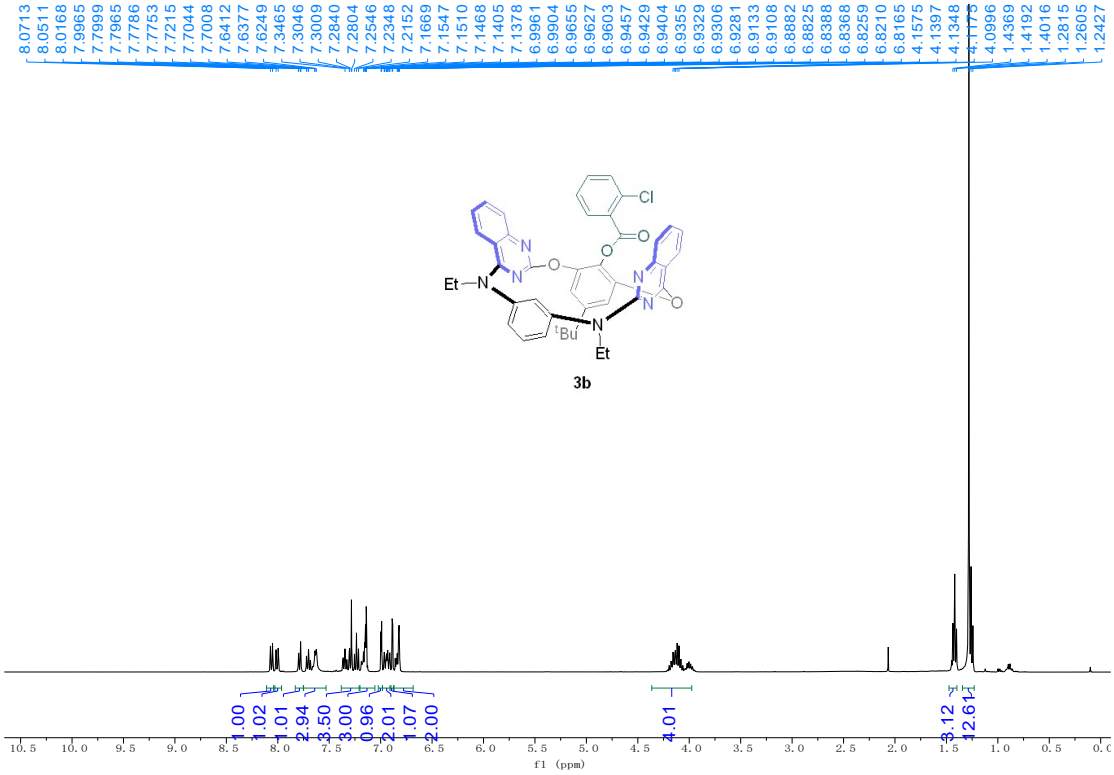
^{1}H NMR (400 MHz, $CDCl_3$) spectra of 3a



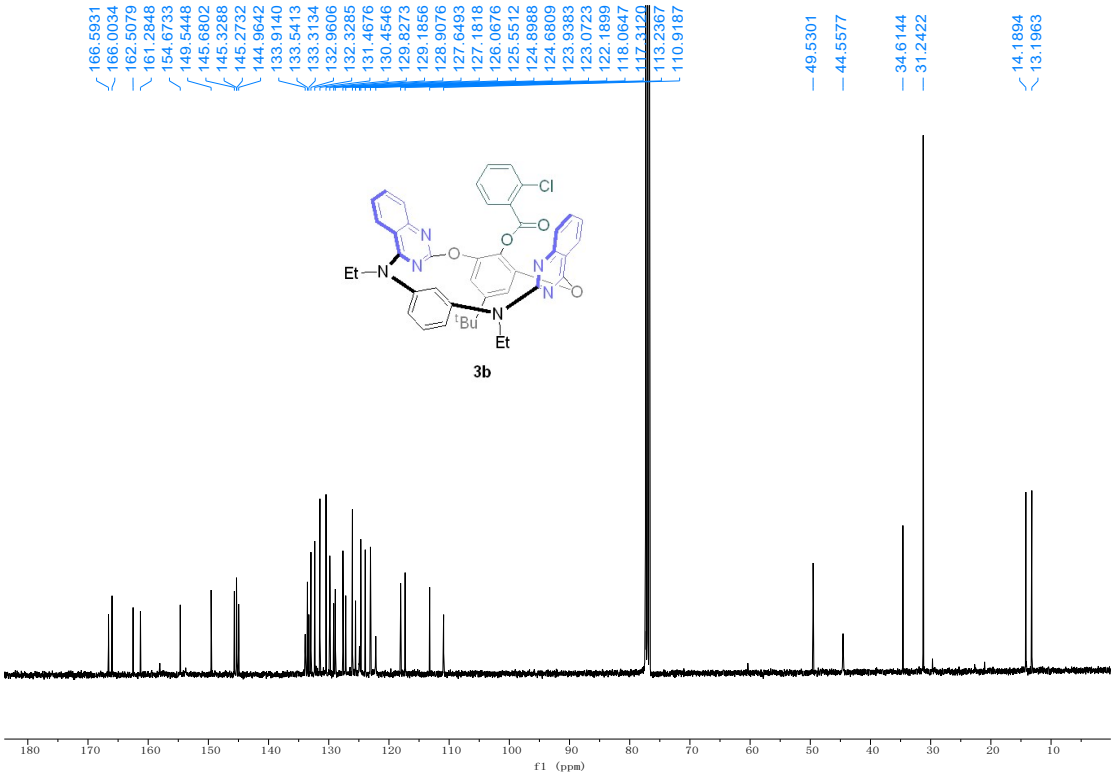
^{13}C NMR (100 MHz, $CDCl_3$) spectra of 3a



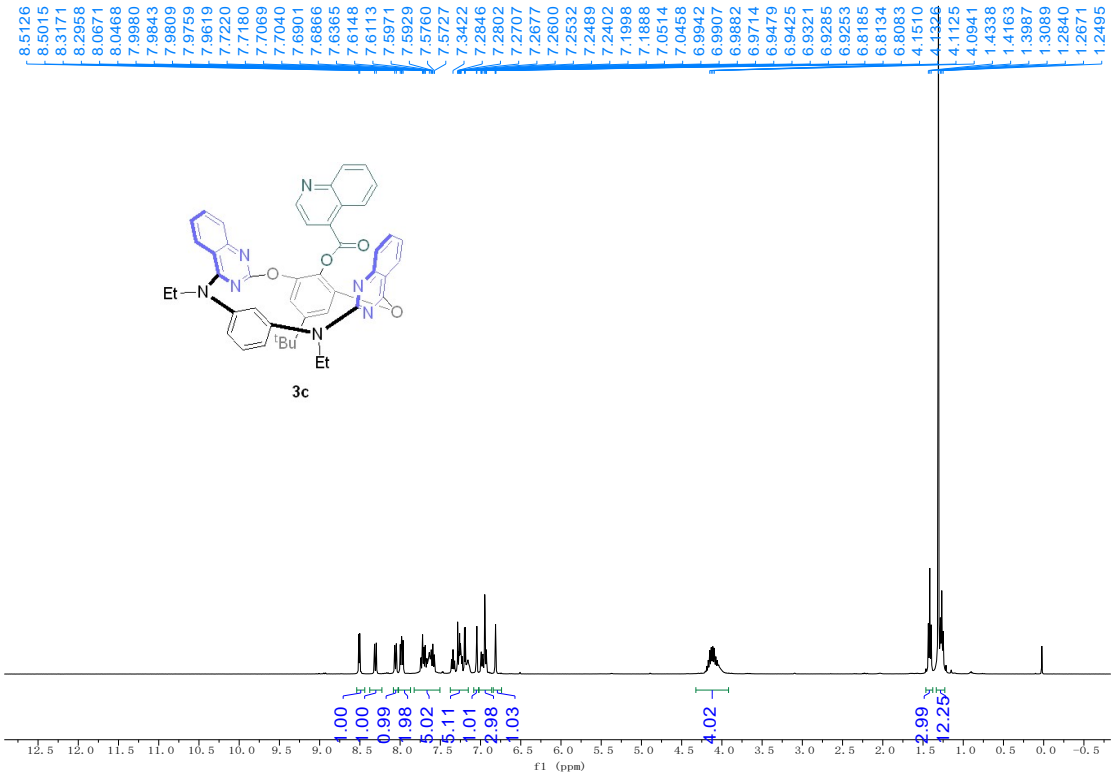
^{1}H NMR (400 MHz, $CDCl_3$) spectra of 3b



^{13}C NMR (100 MHz, $CDCl_3$) spectra of 3b

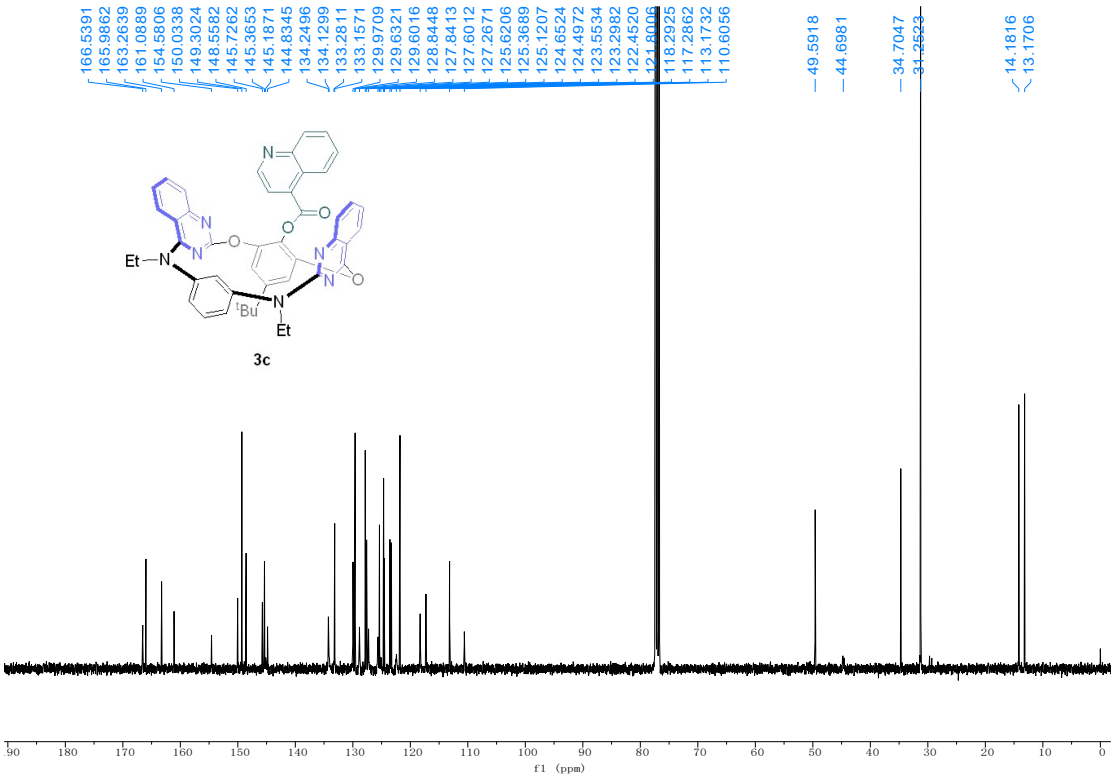


^{1}H NMR (400 MHz, $CDCl_3$) spectra of 3c



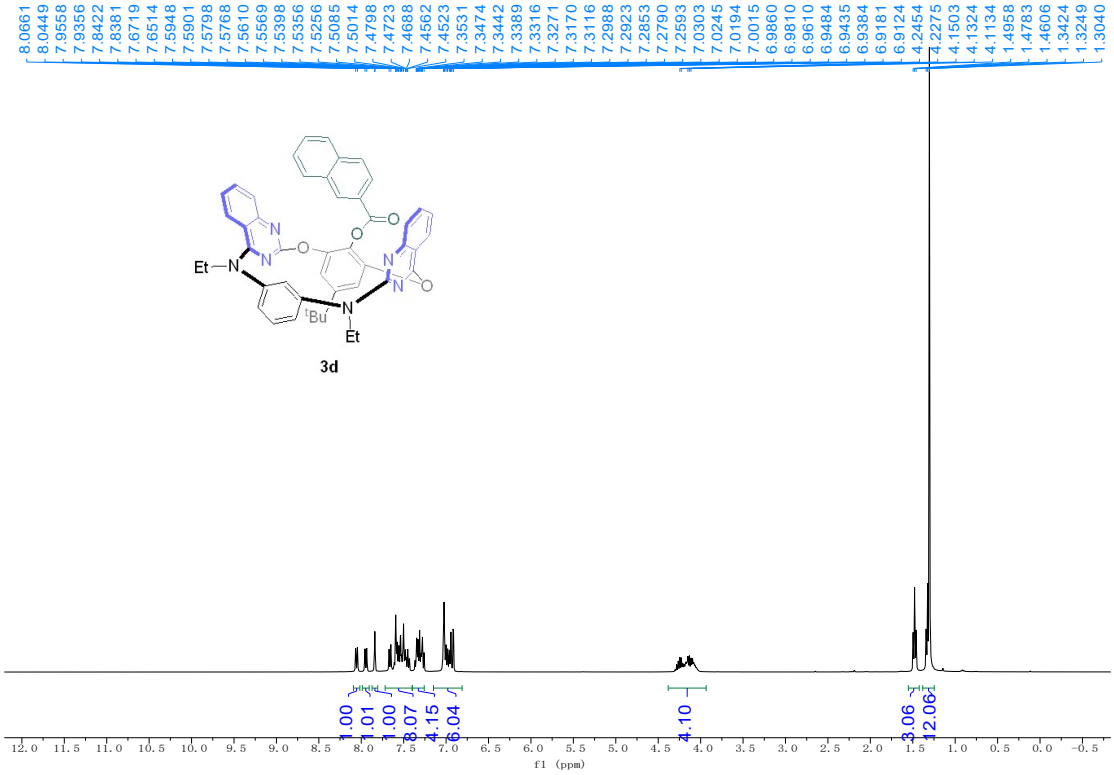
3c

^{13}C NMR (100 MHz, $CDCl_3$) spectra of 3c

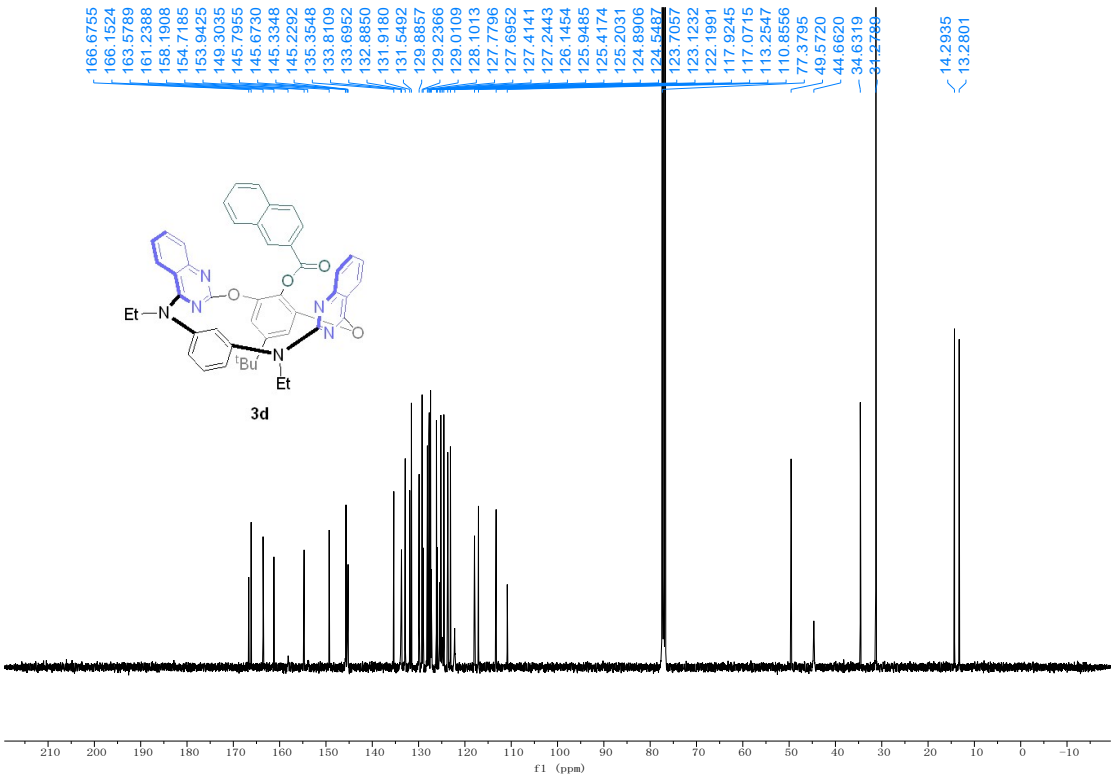


3c

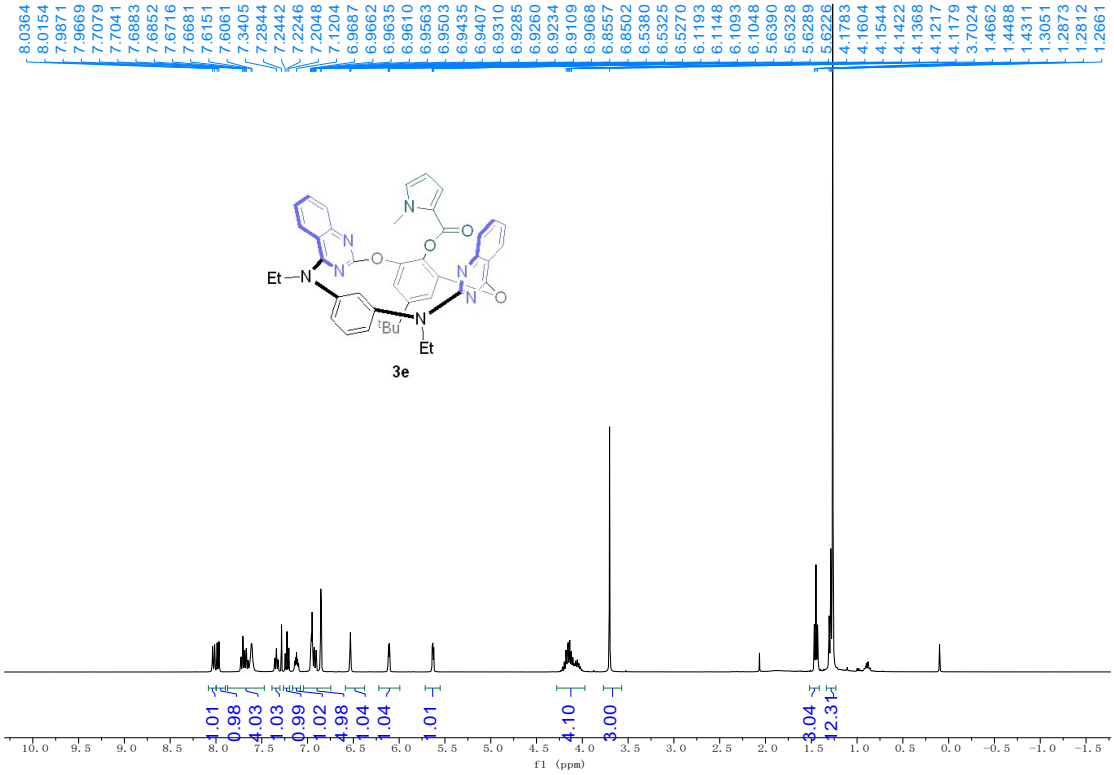
^{1}H NMR (400 MHz, $CDCl_3$) spectra of 3d



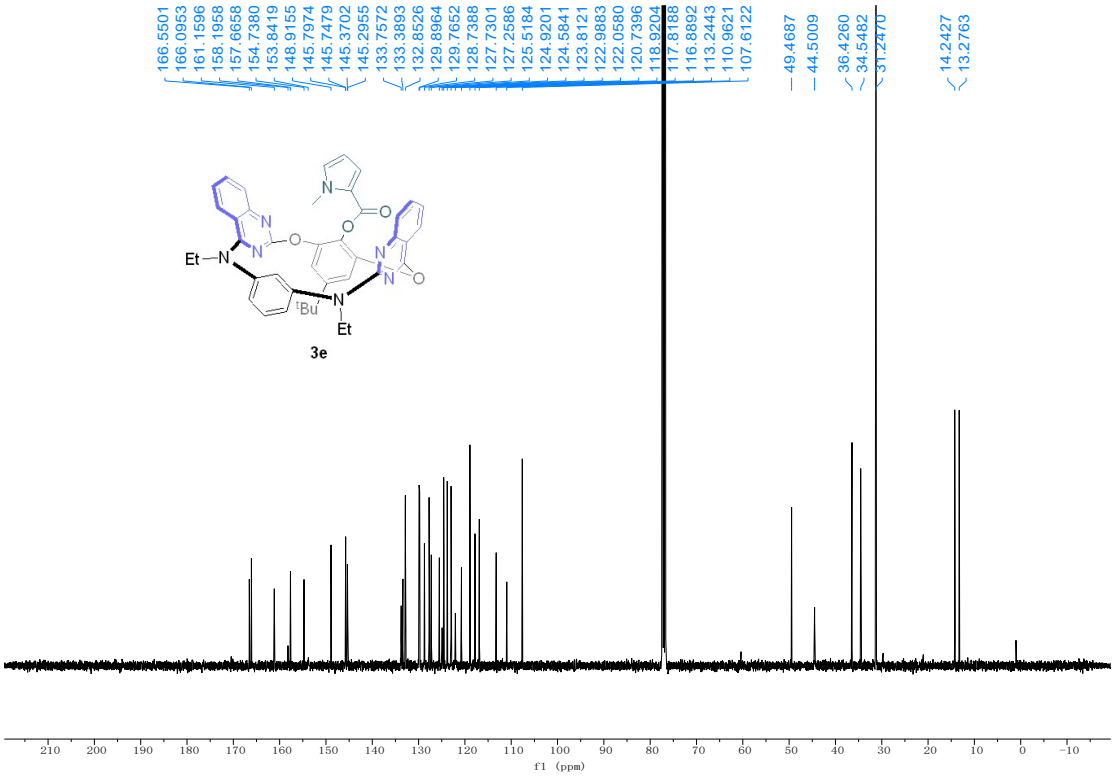
^{13}C NMR (100 MHz, $CDCl_3$) spectra of 3d



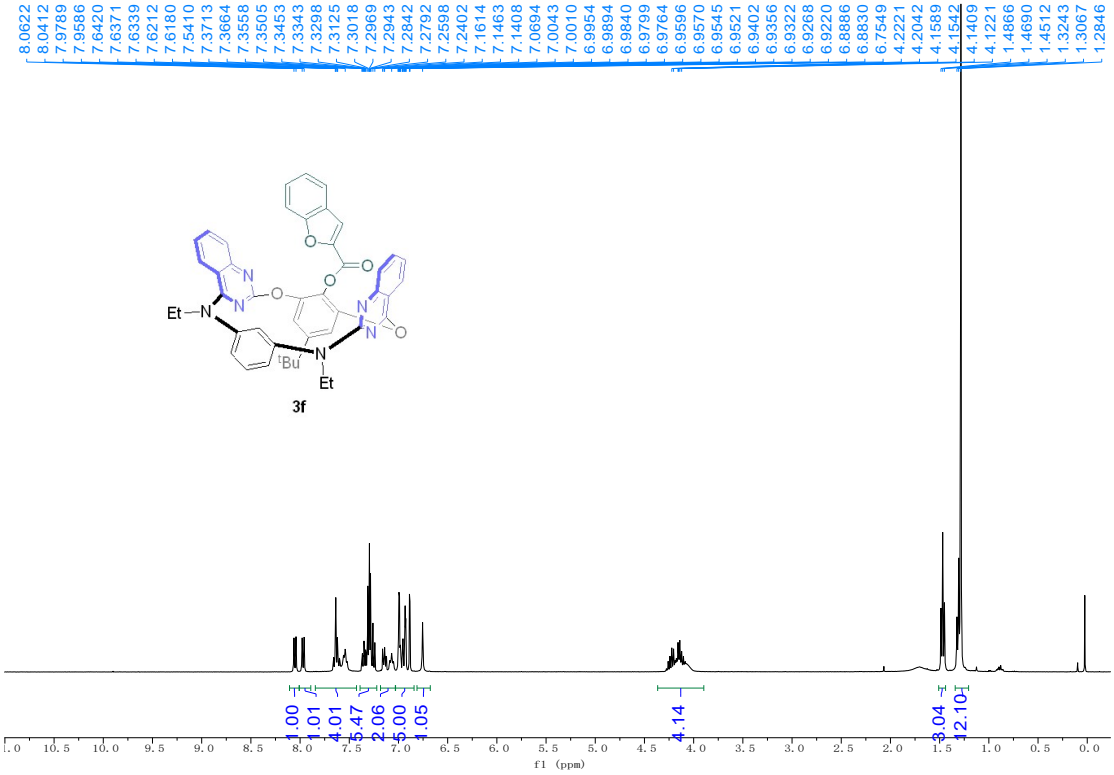
^{1}H NMR (400 MHz, $CDCl_3$) spectra of 3e



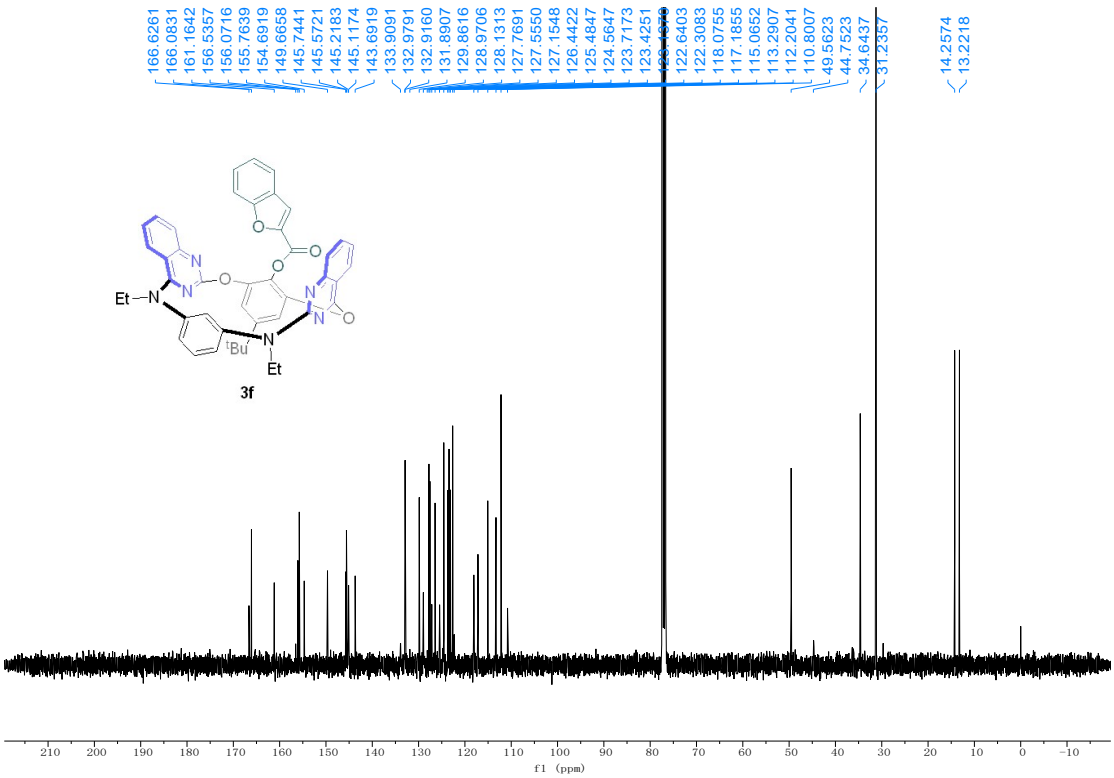
^{13}C NMR (100 MHz, $CDCl_3$) spectra of 3e



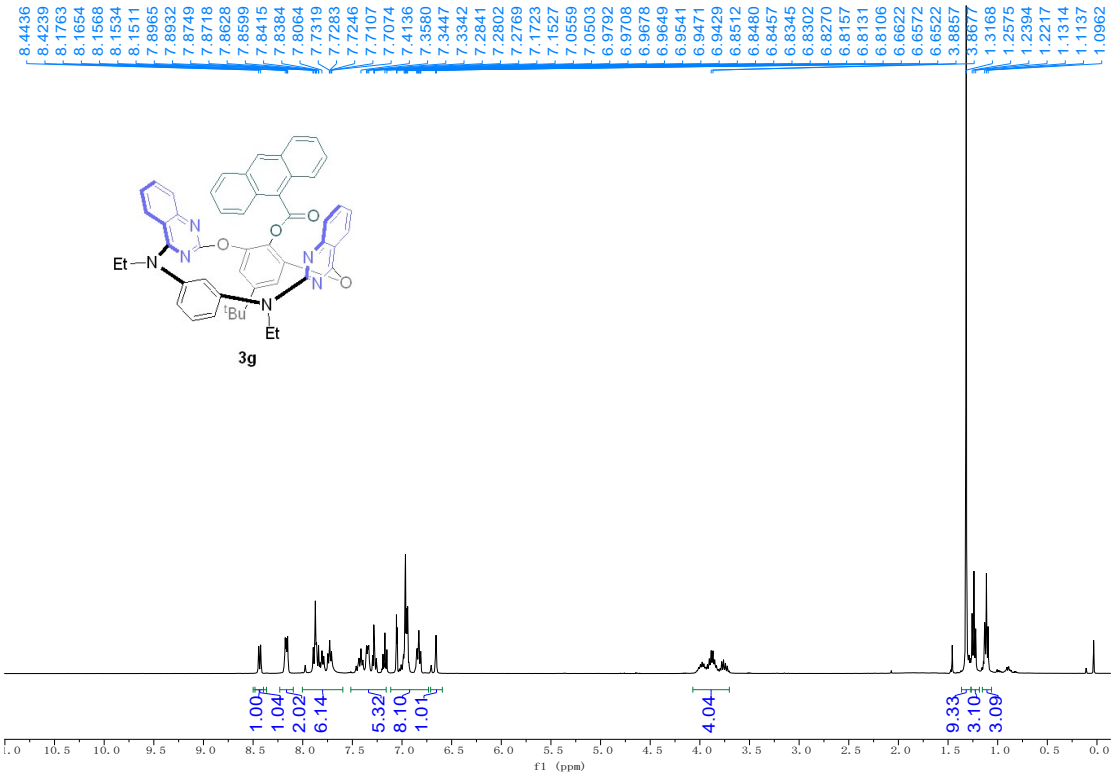
^{1}H NMR (400 MHz, $CDCl_3$) spectra of 3f



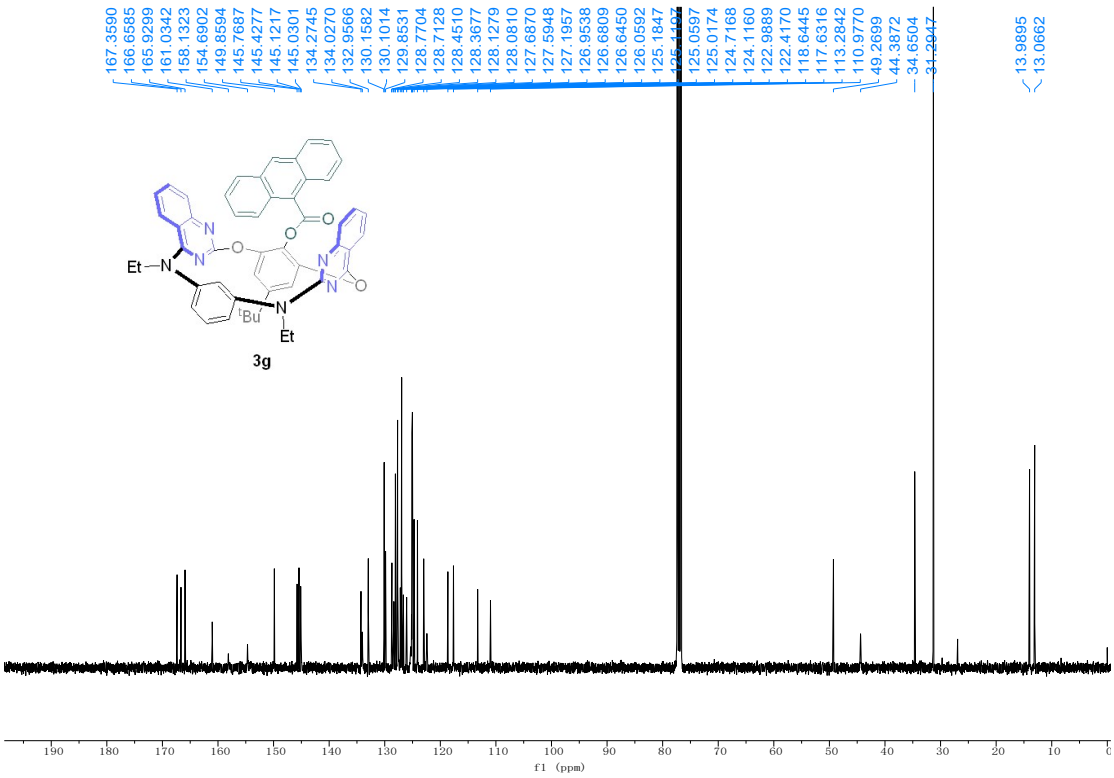
^{13}C NMR (100 MHz, $CDCl_3$) spectra of 3f



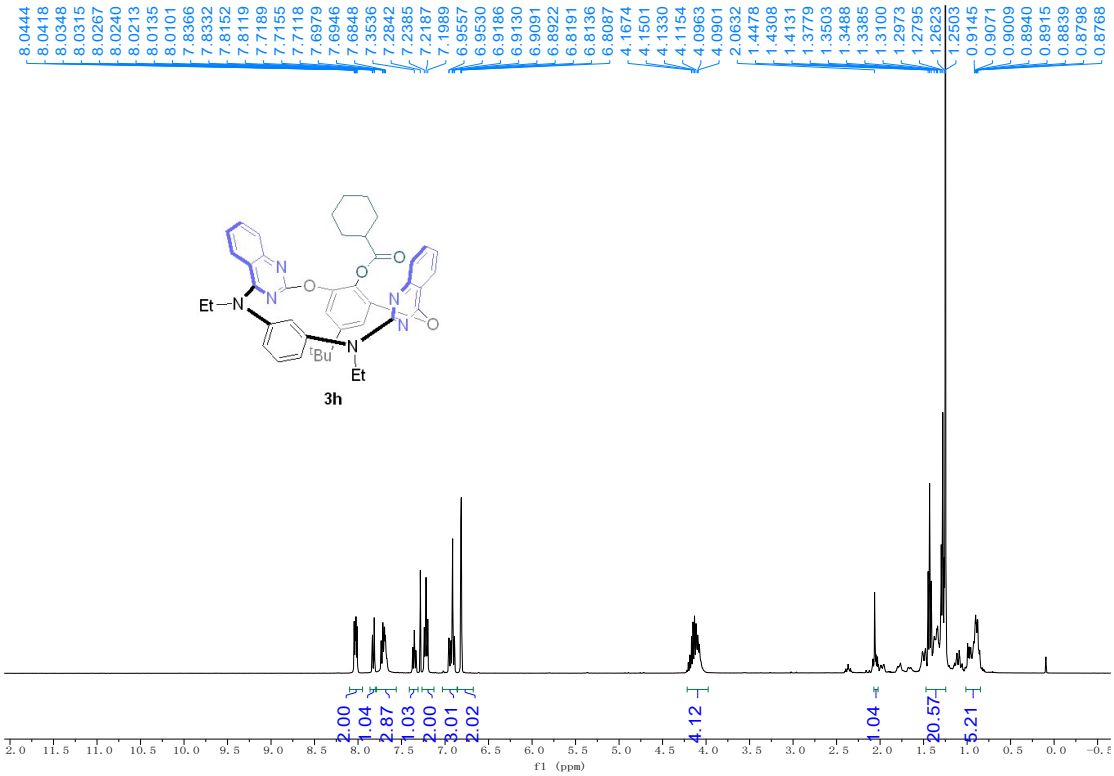
^{1}H NMR (400 MHz, $CDCl_3$) spectra of 3g



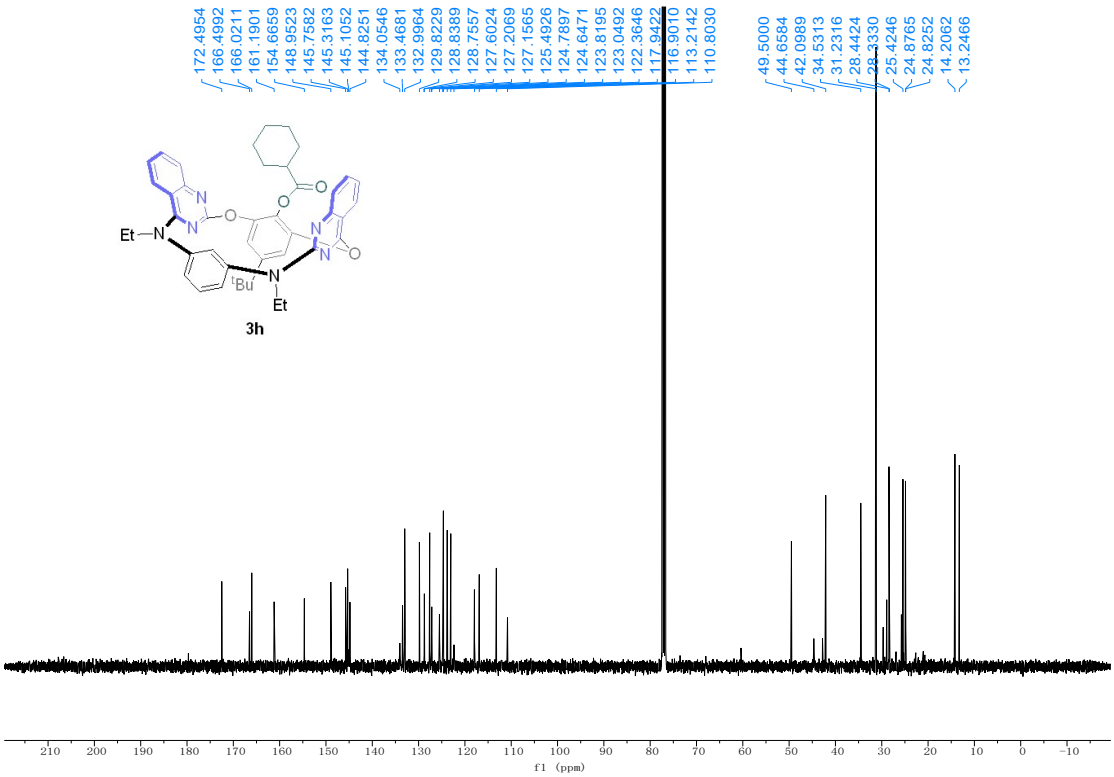
^{13}C NMR (100 MHz, $CDCl_3$) spectra of 3g



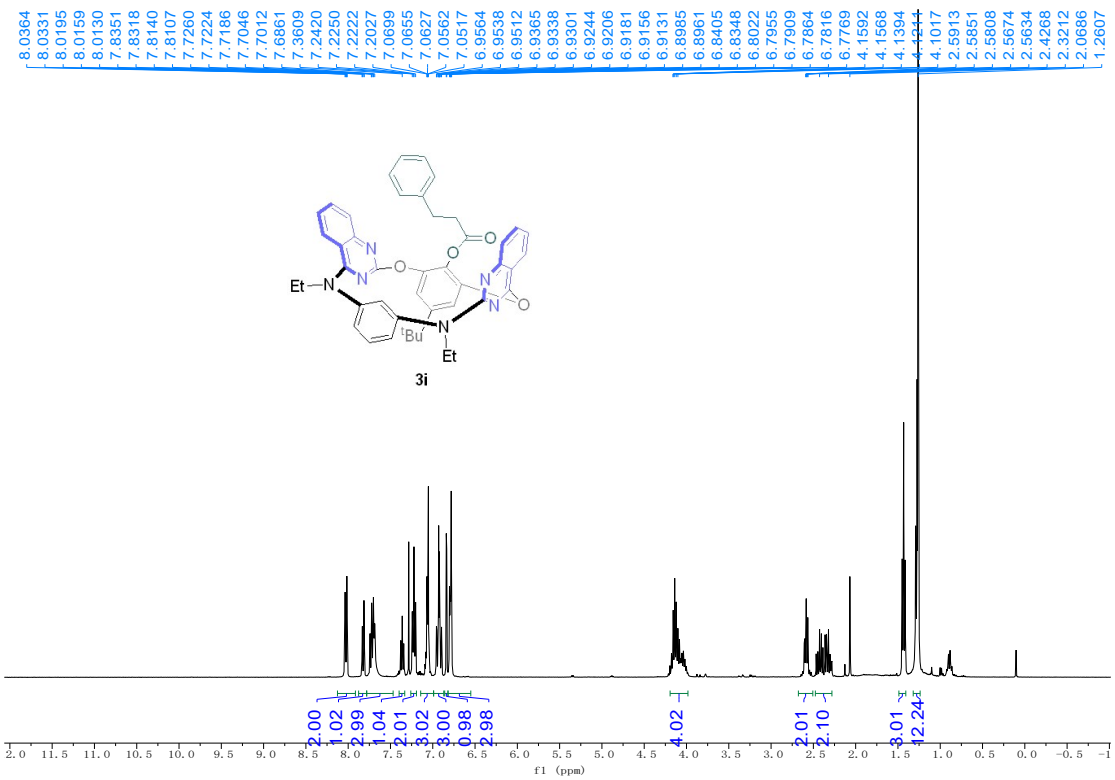
^{1}H NMR (400 MHz, $CDCl_3$) spectra of 3h



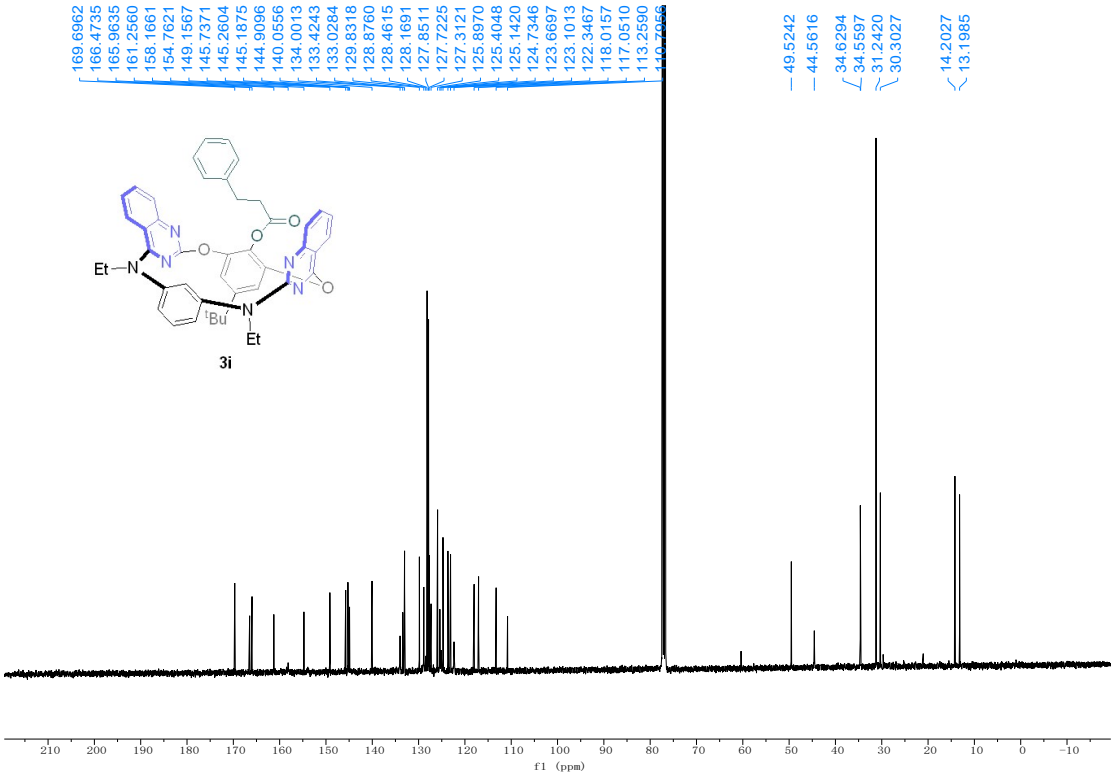
^{13}C NMR (100 MHz, $CDCl_3$) spectra of 3h



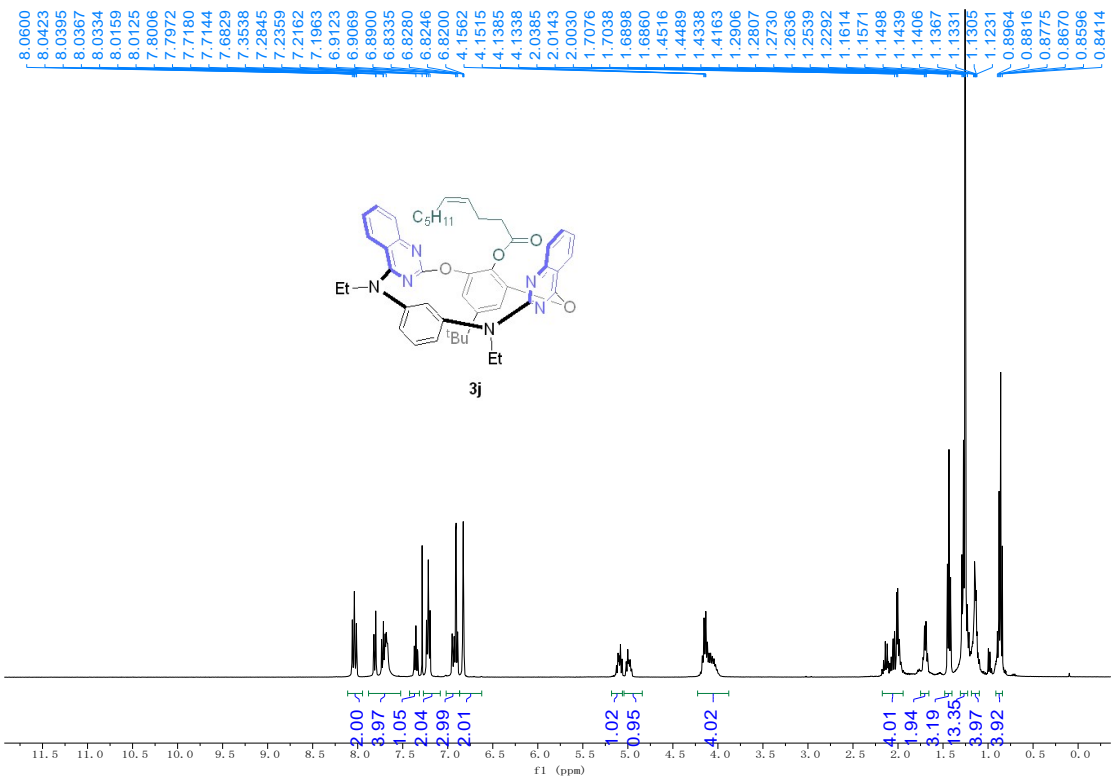
^{1}H NMR (400 MHz, $CDCl_3$) spectra of 3i



^{13}C NMR (100 MHz, $CDCl_3$) spectra of 3i

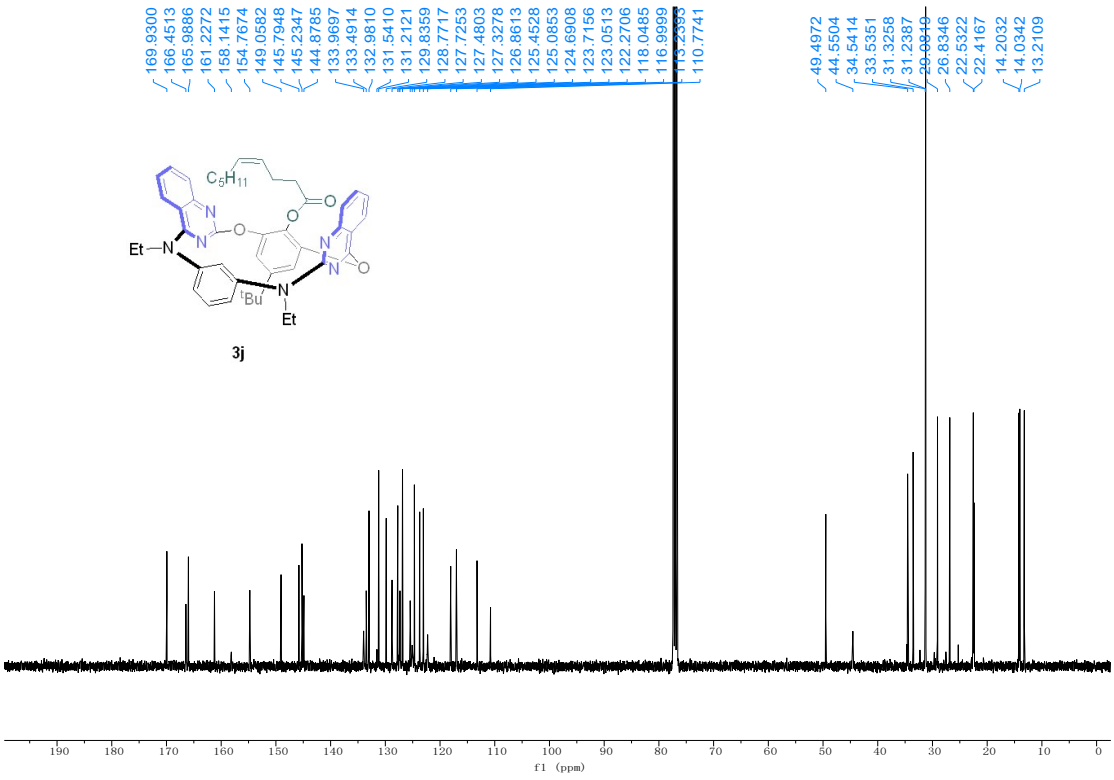


^{1}H NMR (400 MHz, $CDCl_3$) spectra of 3j



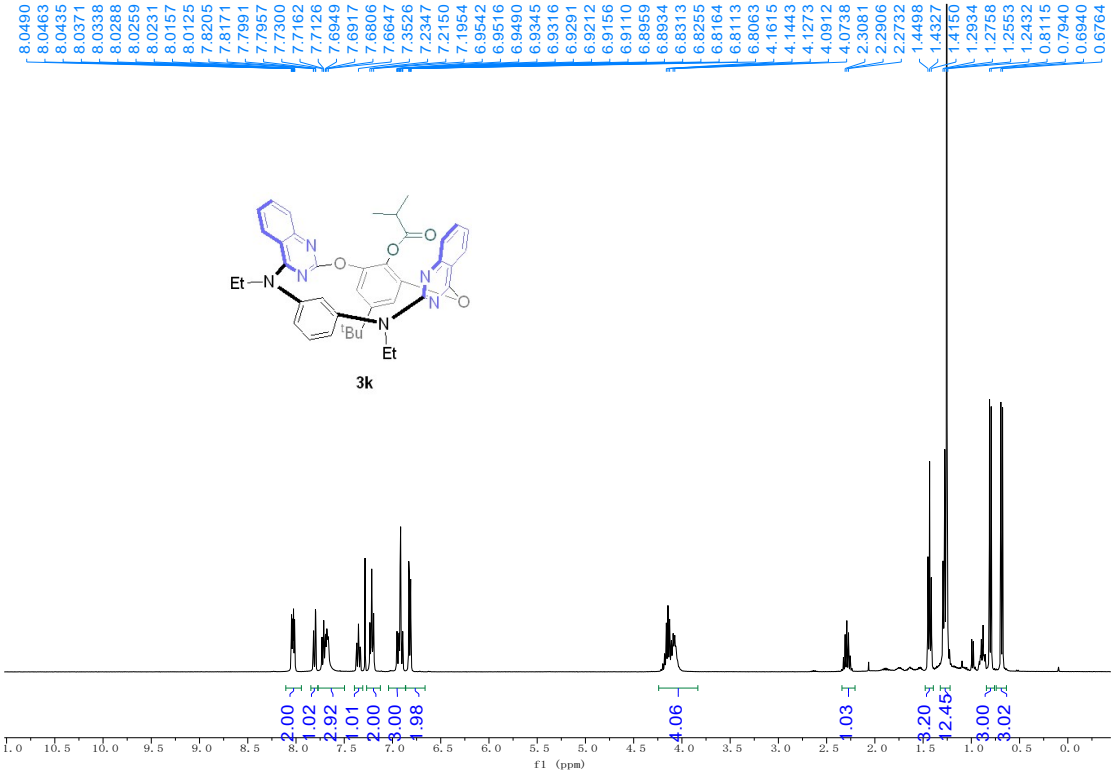
3j

^{13}C NMR (100 MHz, $CDCl_3$) spectra of 3j

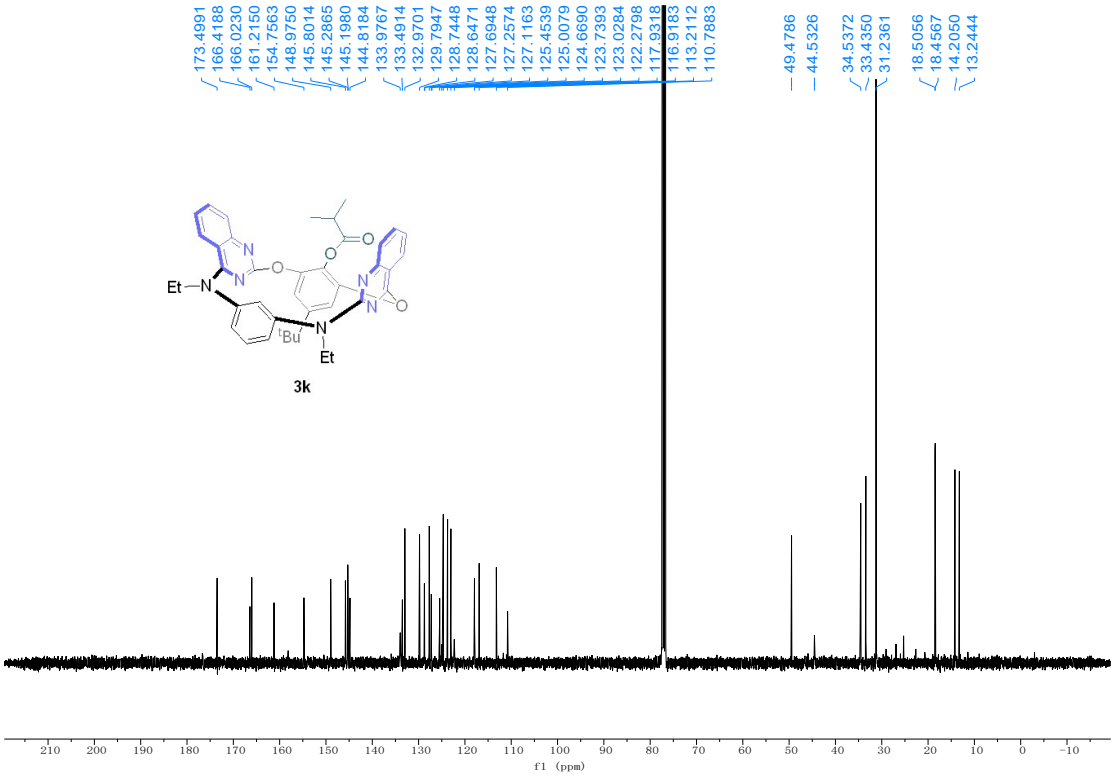


3j

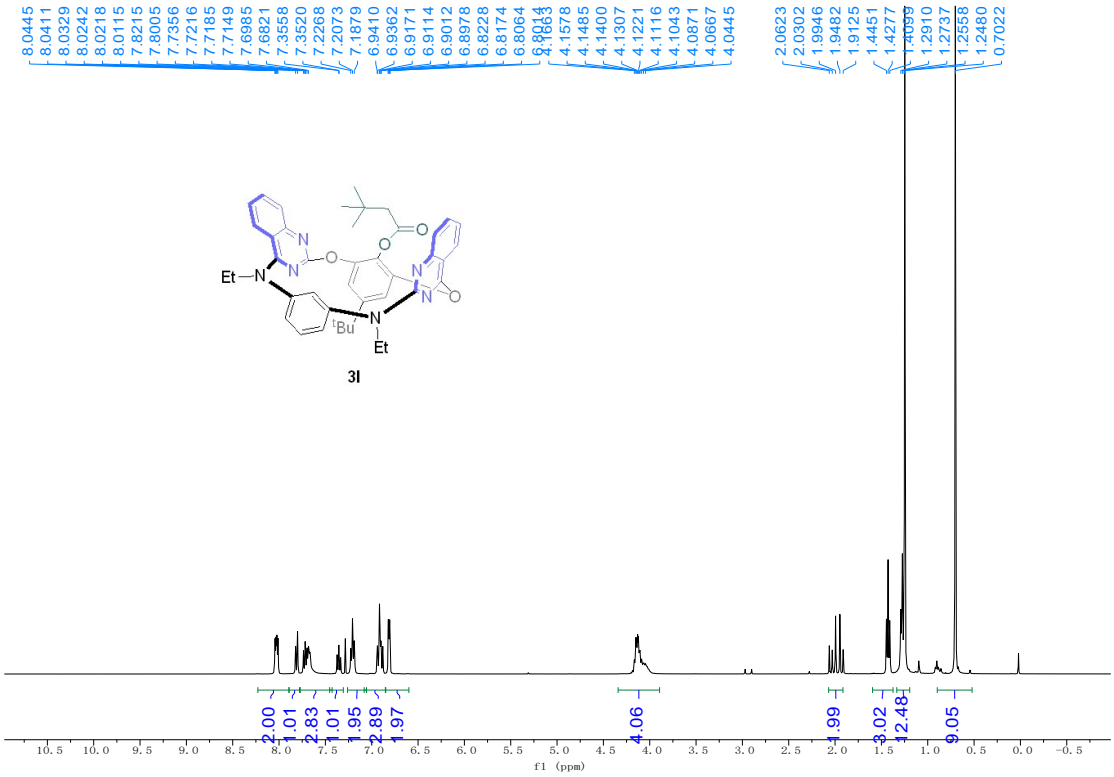
^{1}H NMR (400 MHz, $CDCl_3$) spectra of 3k



^{13}C NMR (100 MHz, $CDCl_3$) spectra of 3k

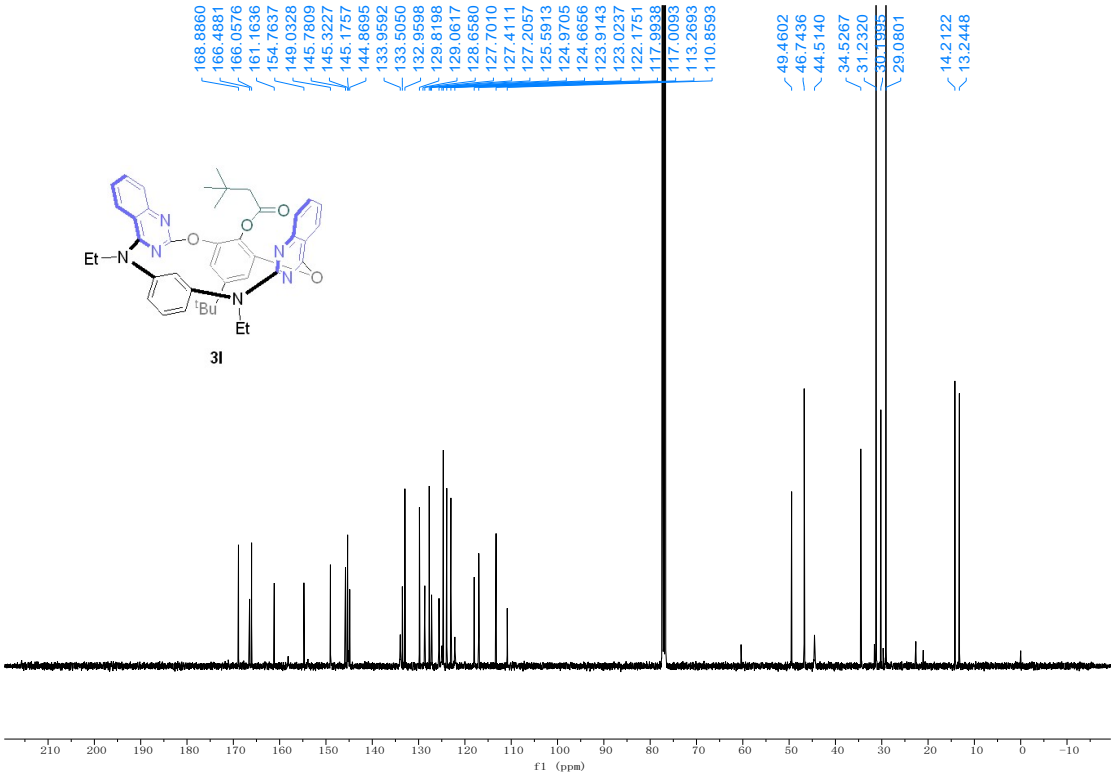


^{1}H NMR (400 MHz, $CDCl_3$) spectra of 3l



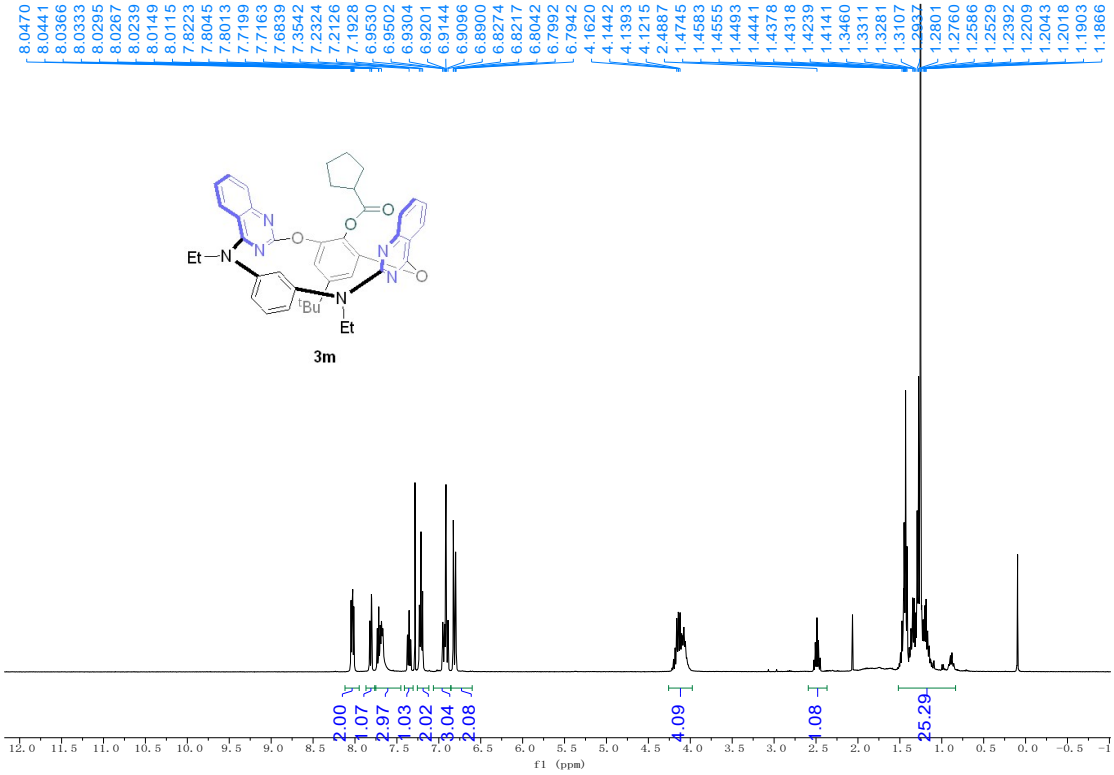
3l

^{13}C NMR (100 MHz, $CDCl_3$) spectra of 3l

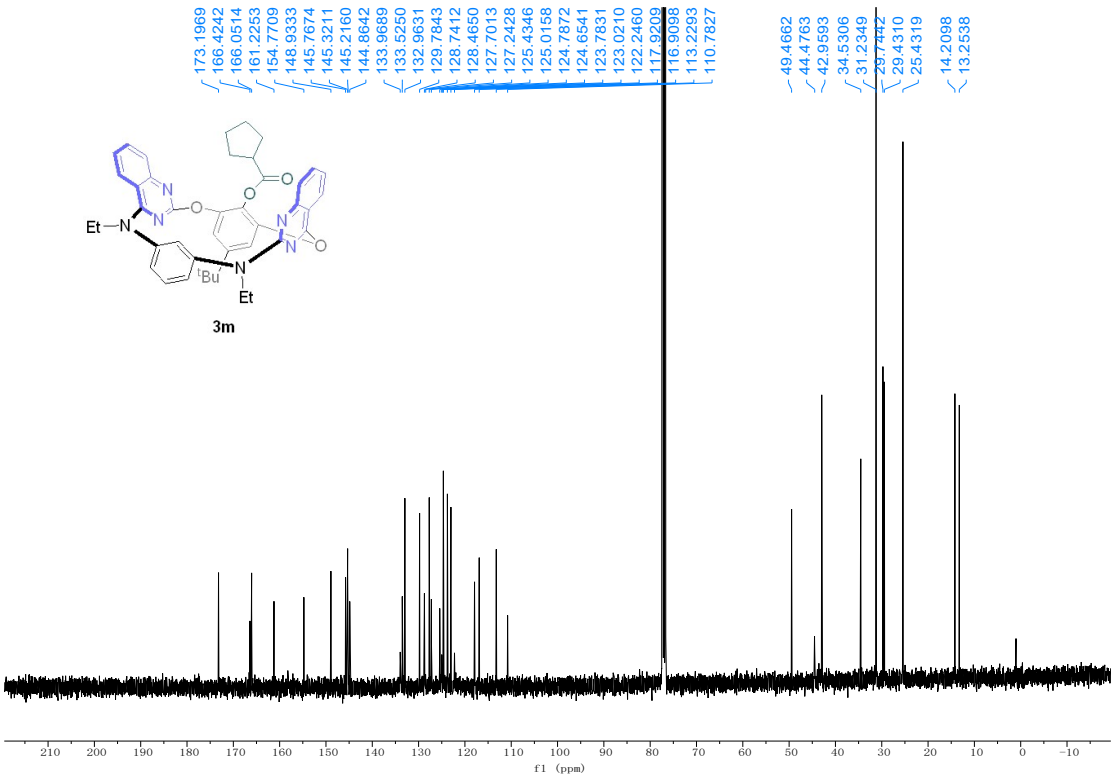


3l

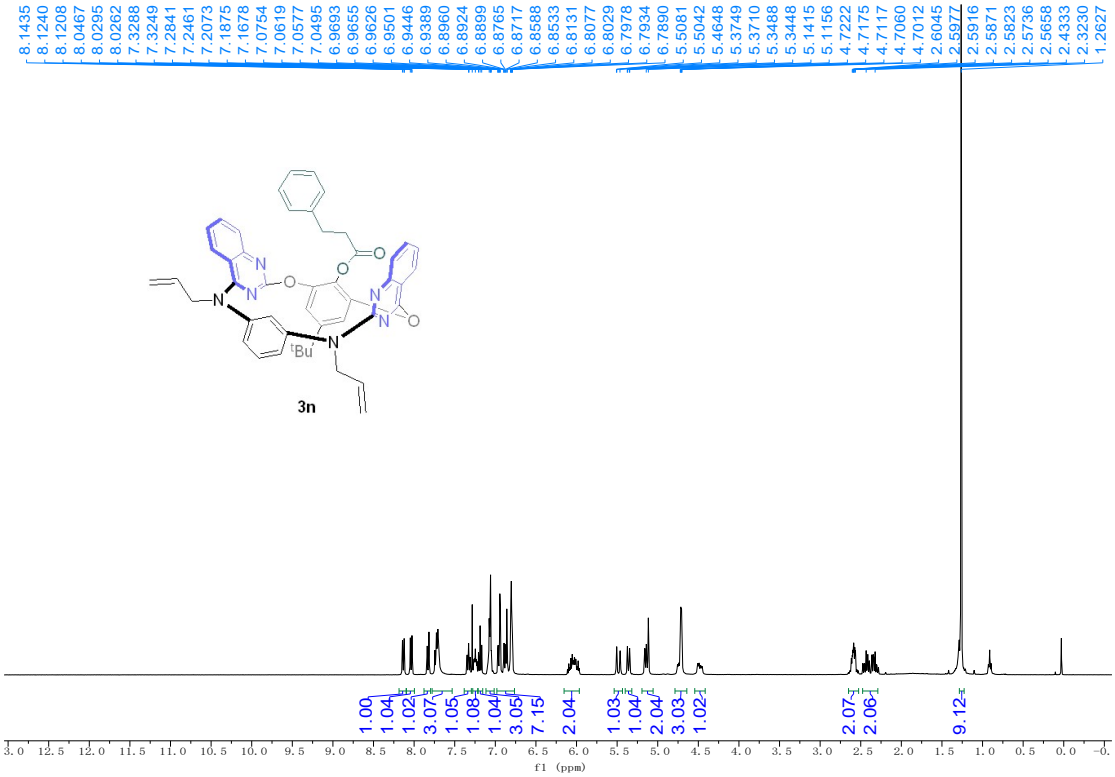
^{1}H NMR (400 MHz, $CDCl_3$) spectra of 3m



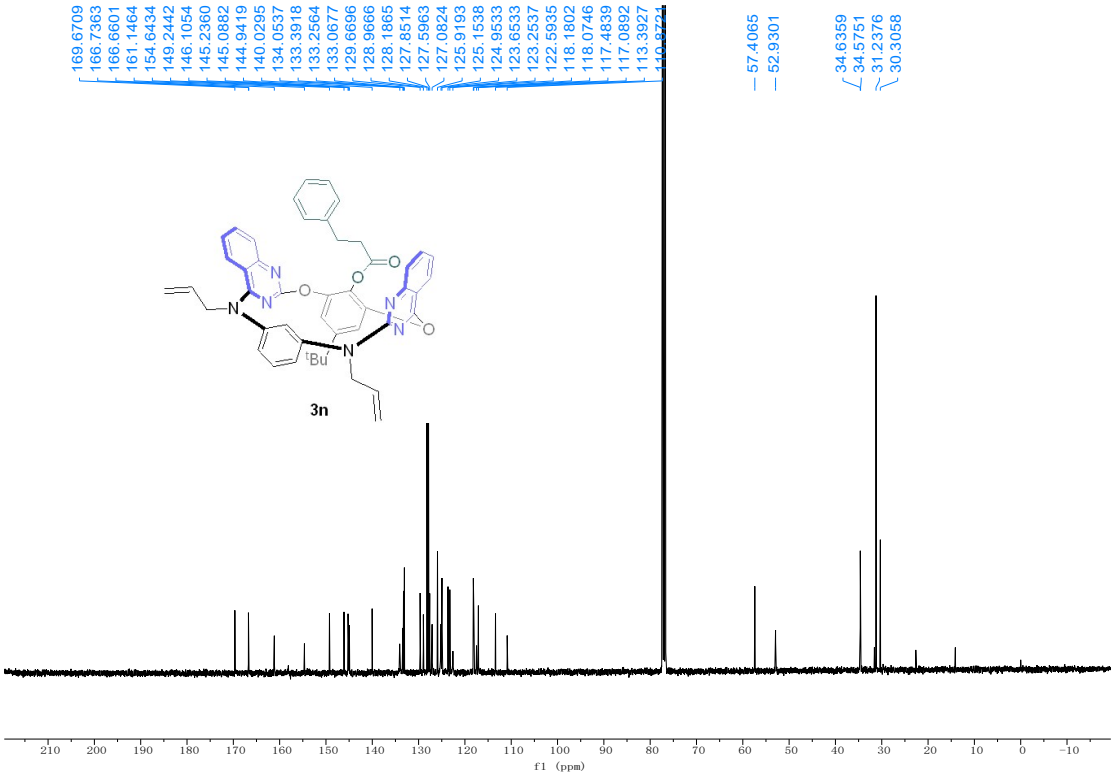
^{13}C NMR (100 MHz, $CDCl_3$) spectra of 3m



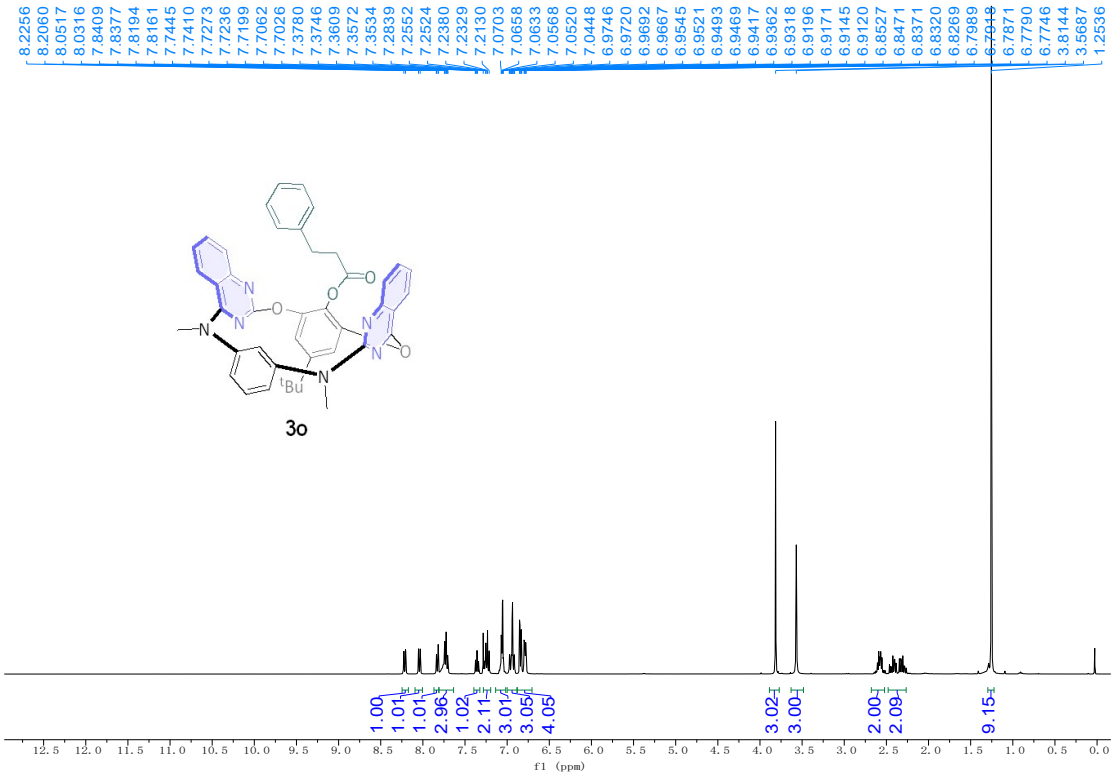
^{1}H NMR (400 MHz, $CDCl_3$) spectra of 3n



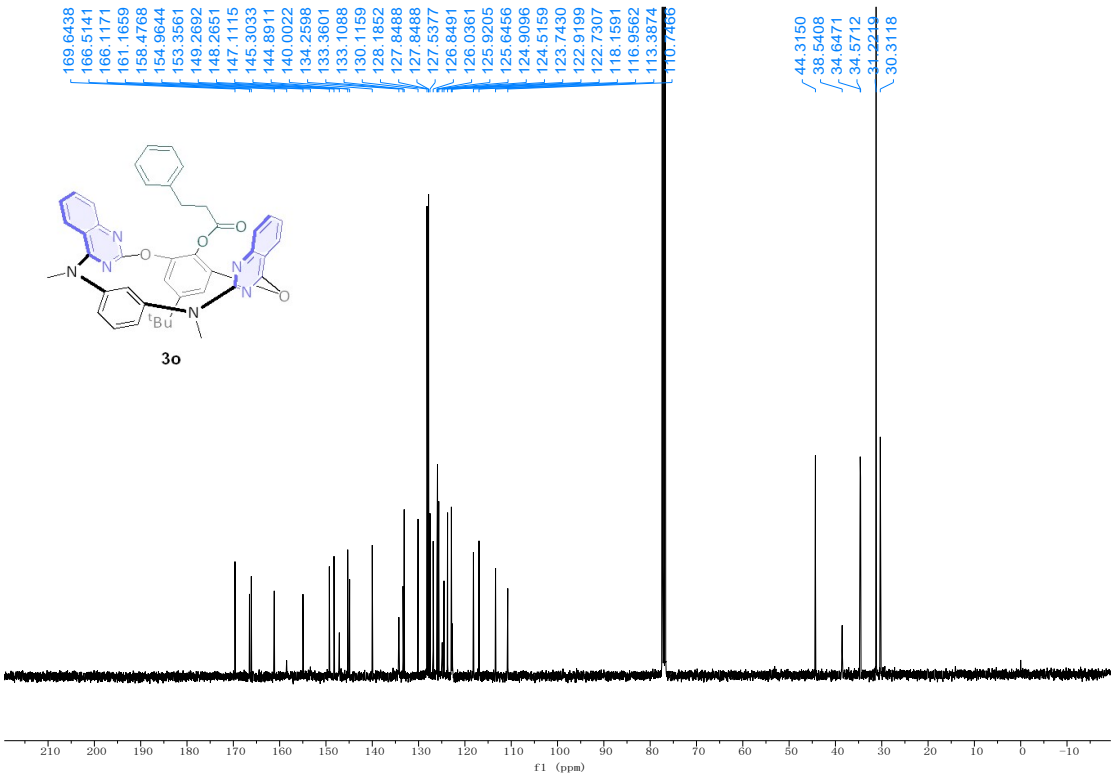
^{13}C NMR (100 MHz, $CDCl_3$) spectra of 3n



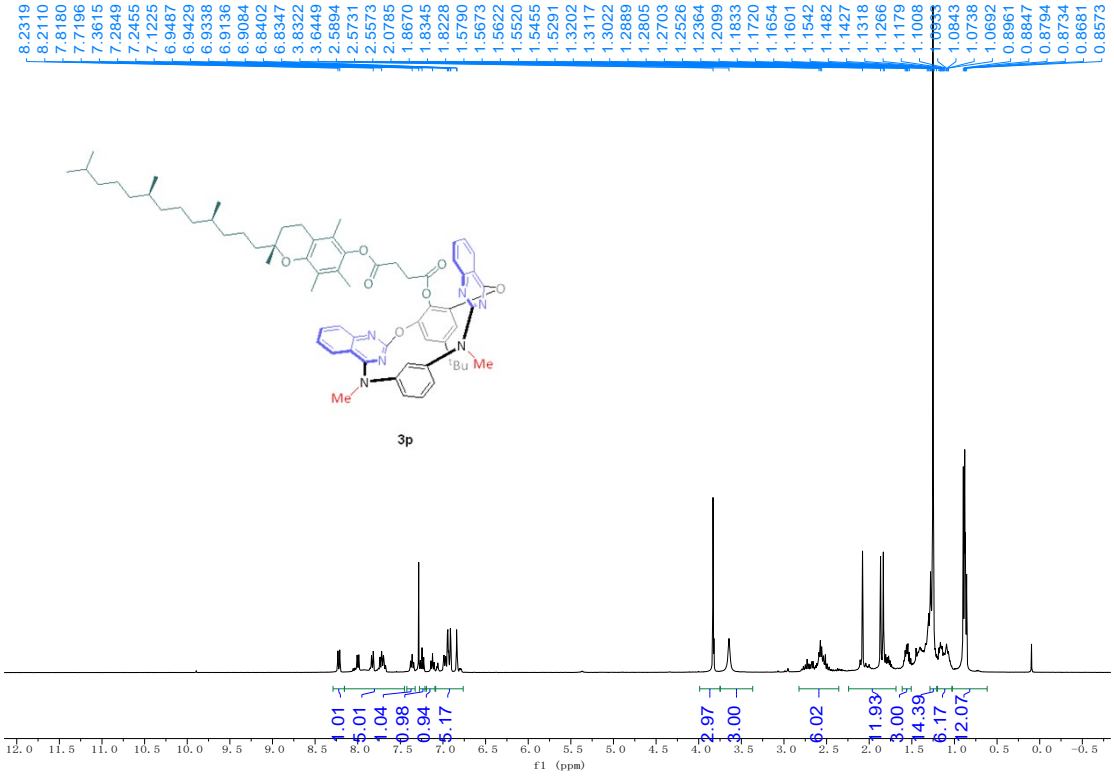
^{1}H NMR (400 MHz, $CDCl_3$) spectra of 3o



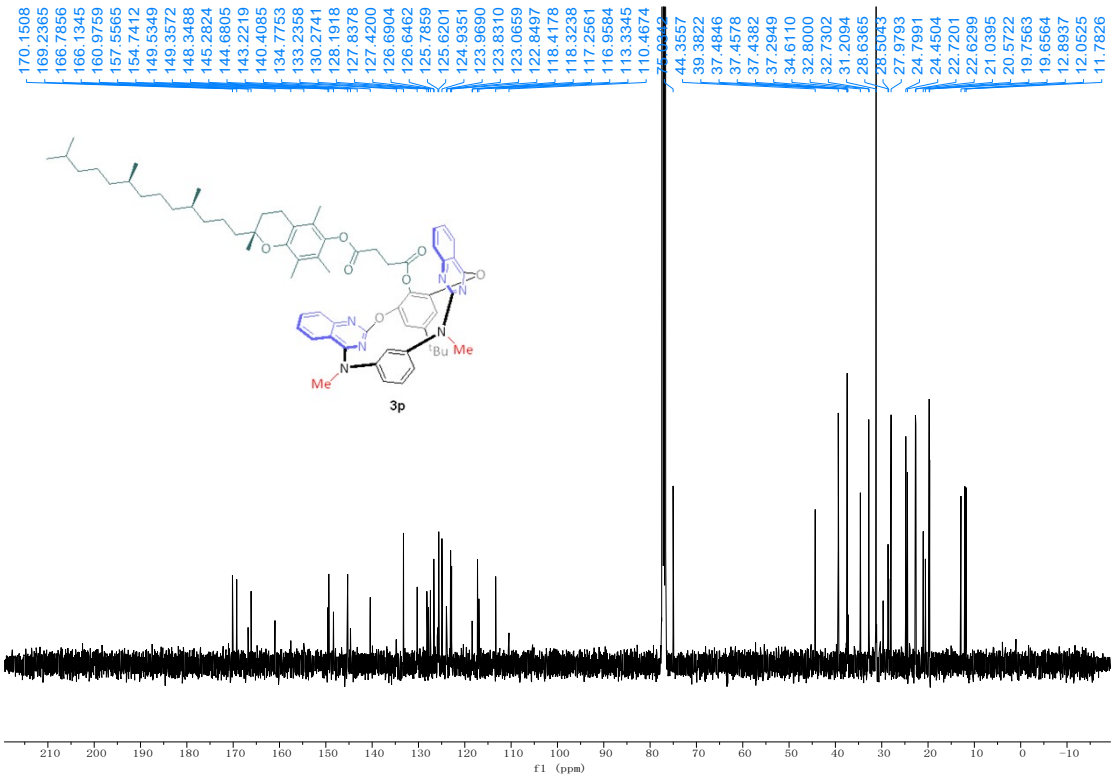
^{13}C NMR (100 MHz, $CDCl_3$) spectra of 3o



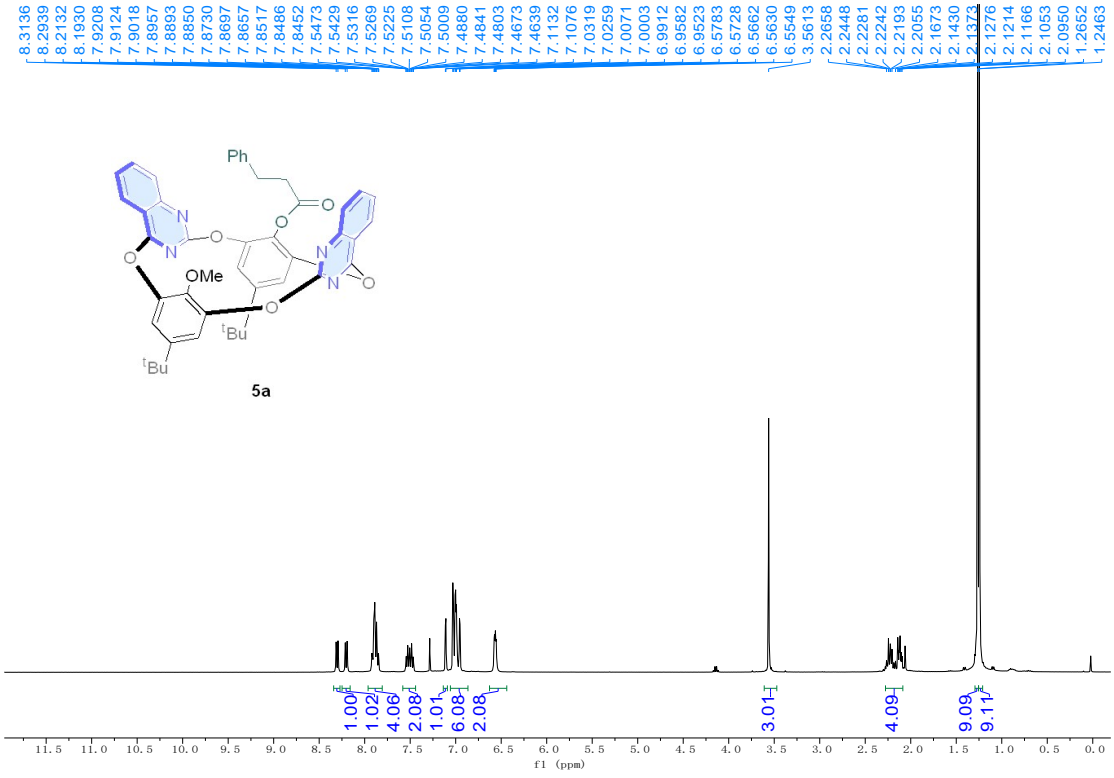
^{1}H NMR (400 MHz, $CDCl_3$) spectra of 3p



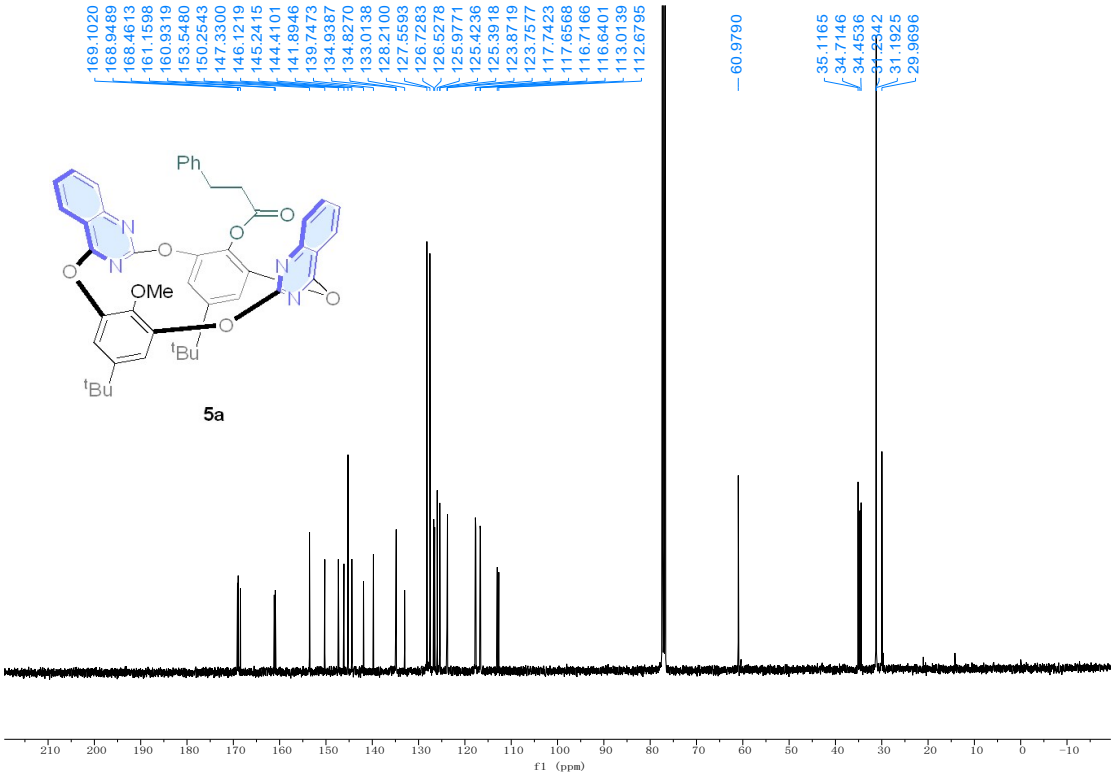
^{13}C NMR (100 MHz, $CDCl_3$) spectra of 3p



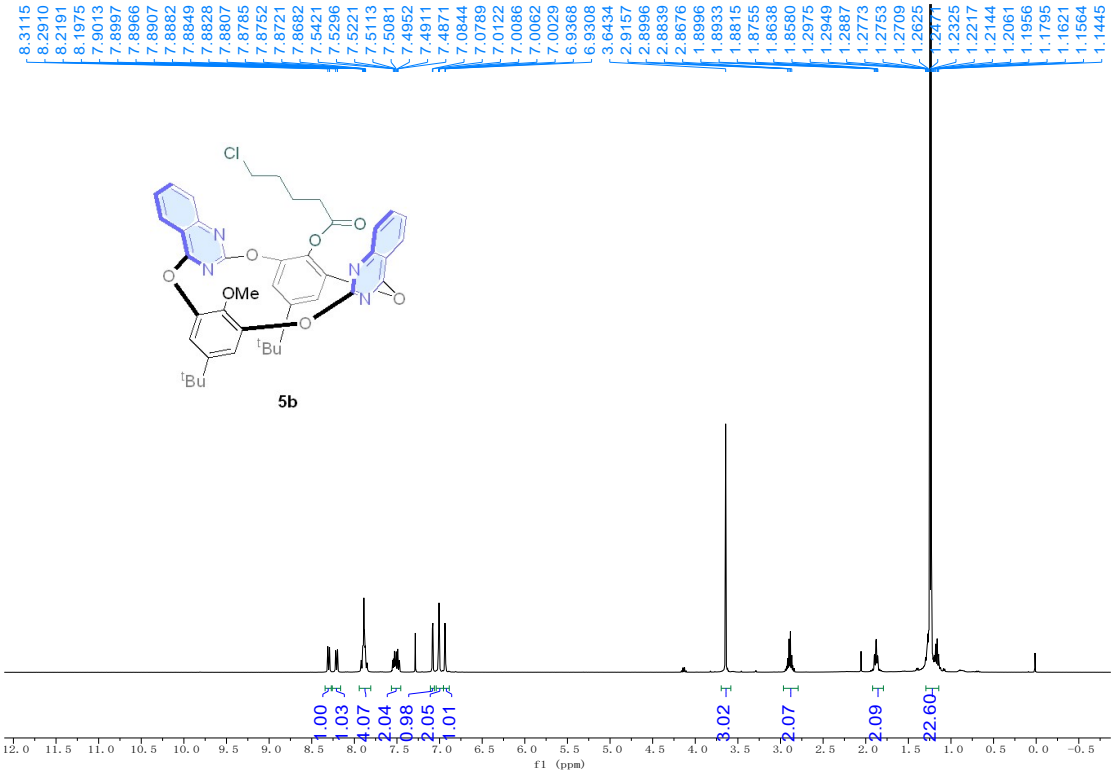
^{1}H NMR (400 MHz, $CDCl_3$) spectra of 5a



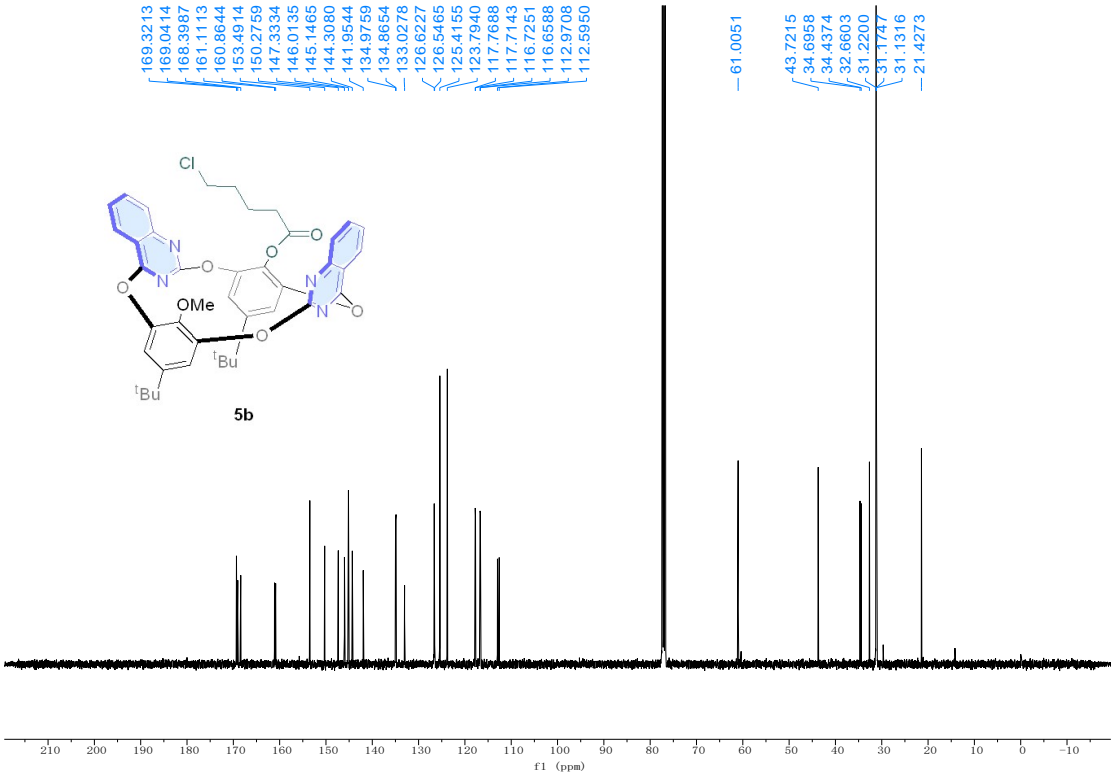
^{13}C NMR (100 MHz, $CDCl_3$) spectra of 5a



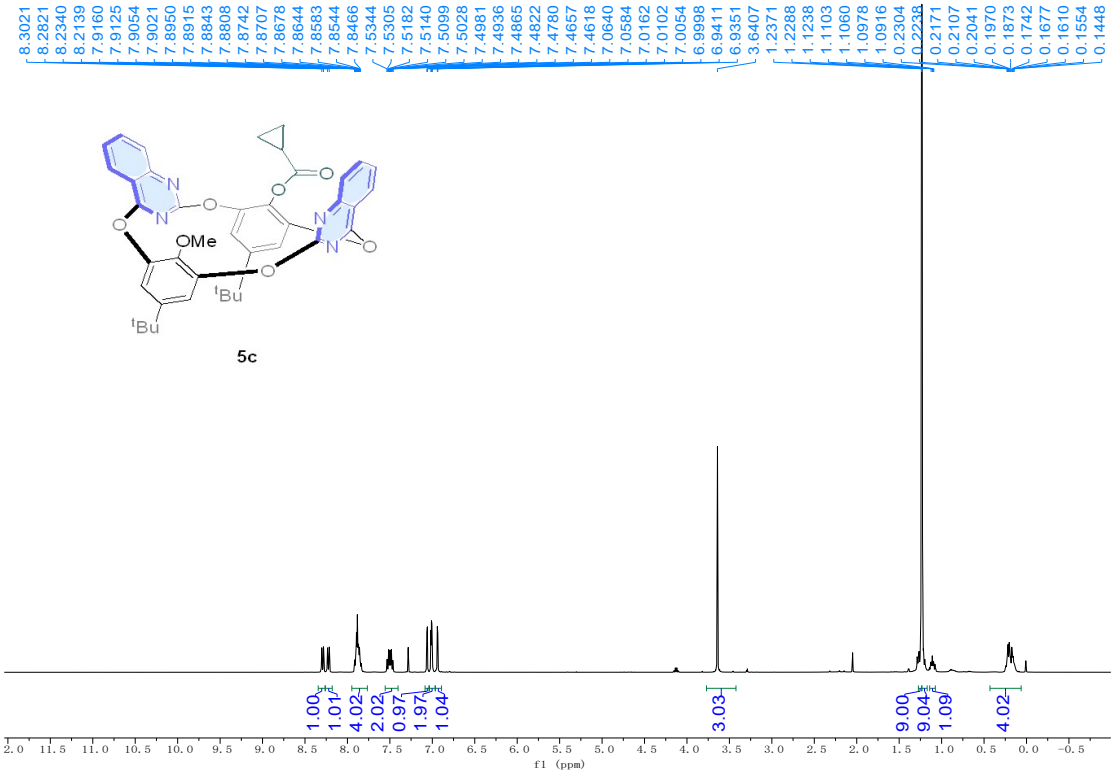
^{1}H NMR (400 MHz, $CDCl_3$) spectra of 5b



^{13}C NMR (100 MHz, $CDCl_3$) spectra of 5b

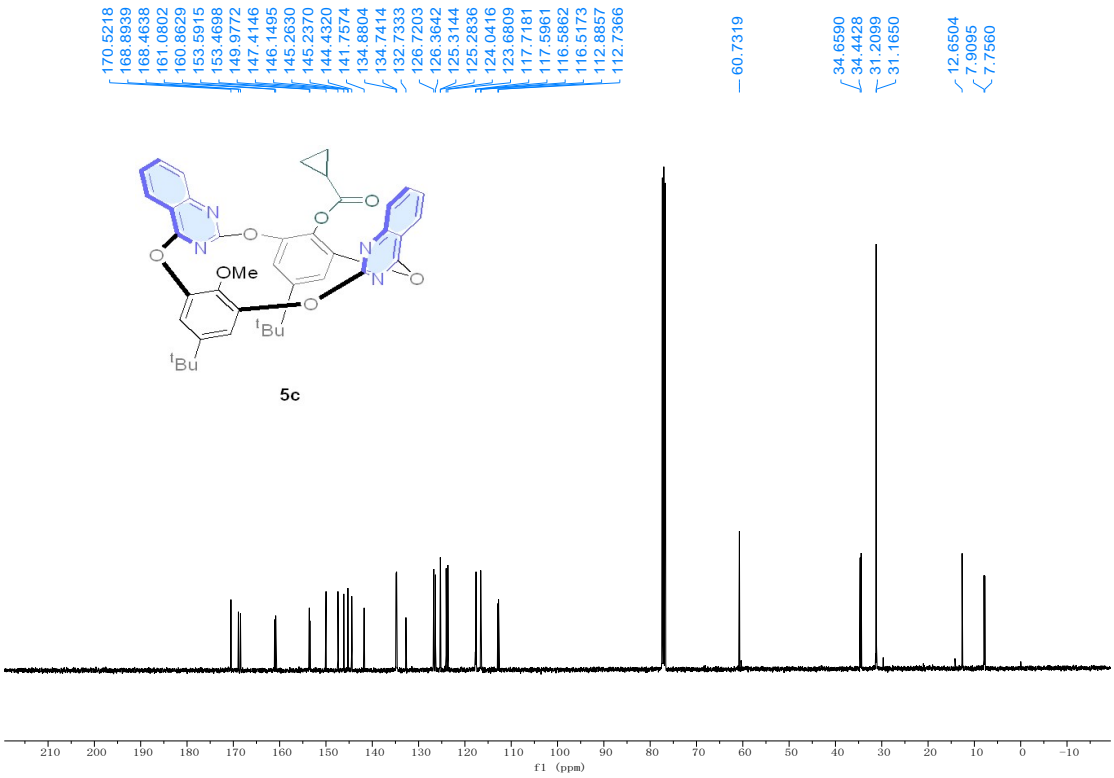


^{1}H NMR (400 MHz, $CDCl_3$) spectra of 5c



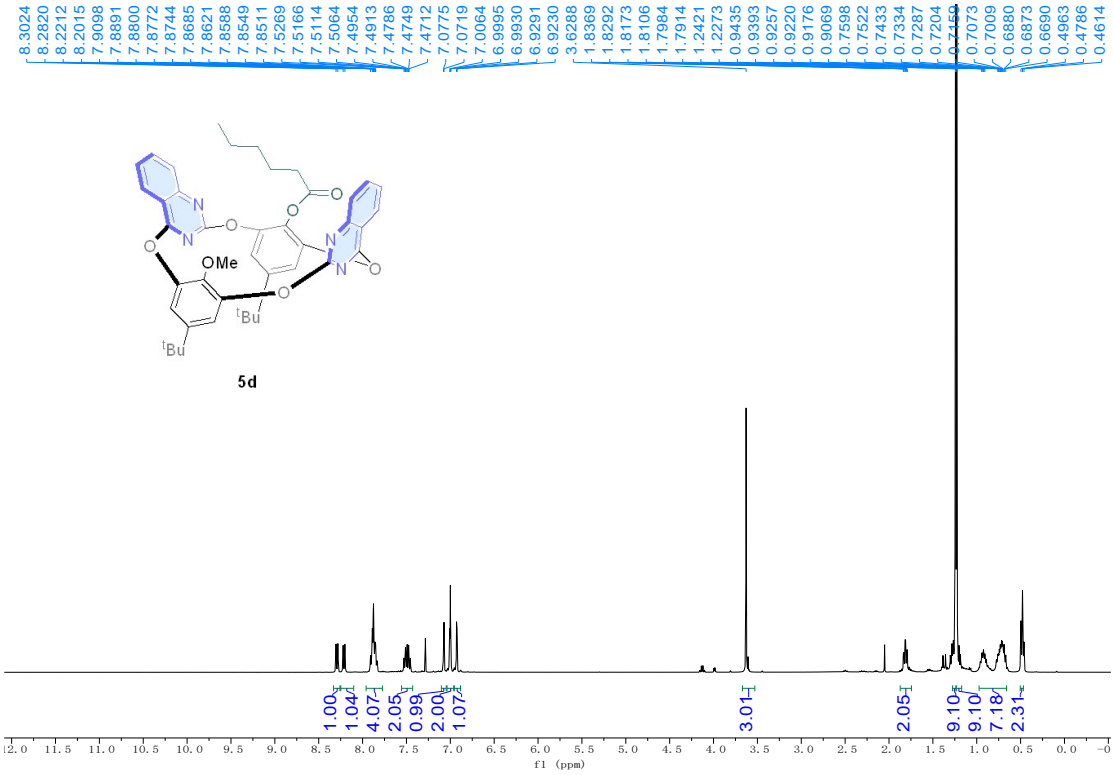
5c

^{13}C NMR (100 MHz, $CDCl_3$) spectra of 5c

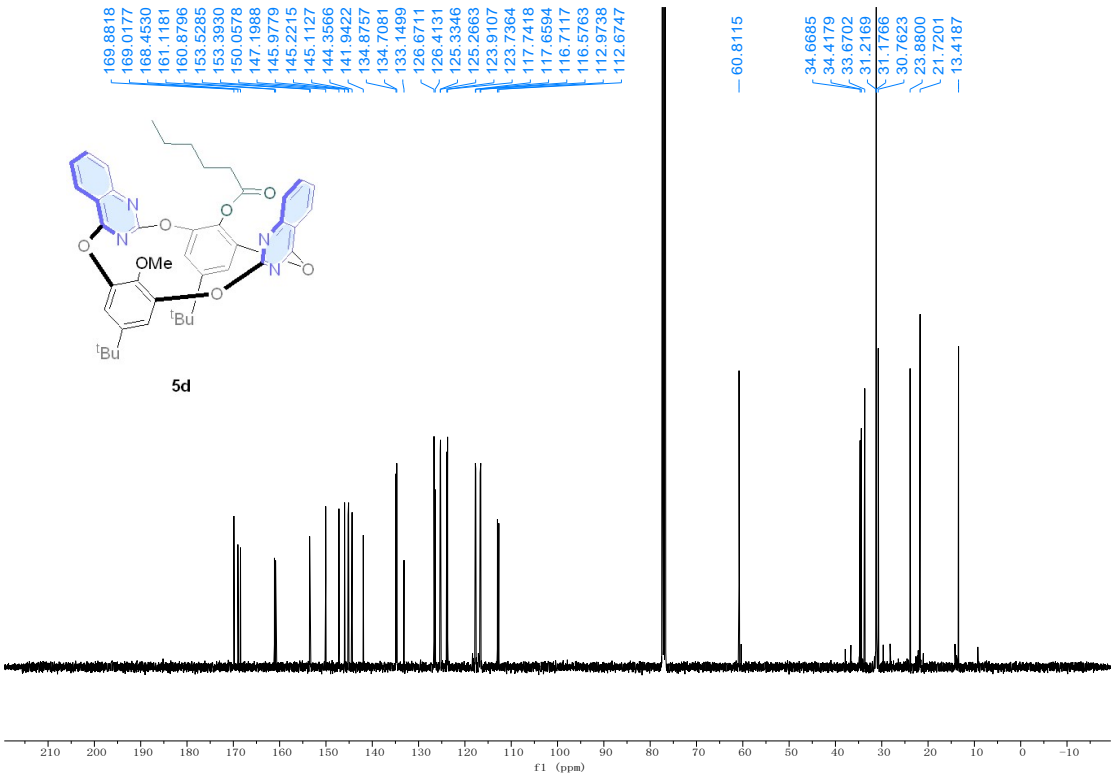


5c

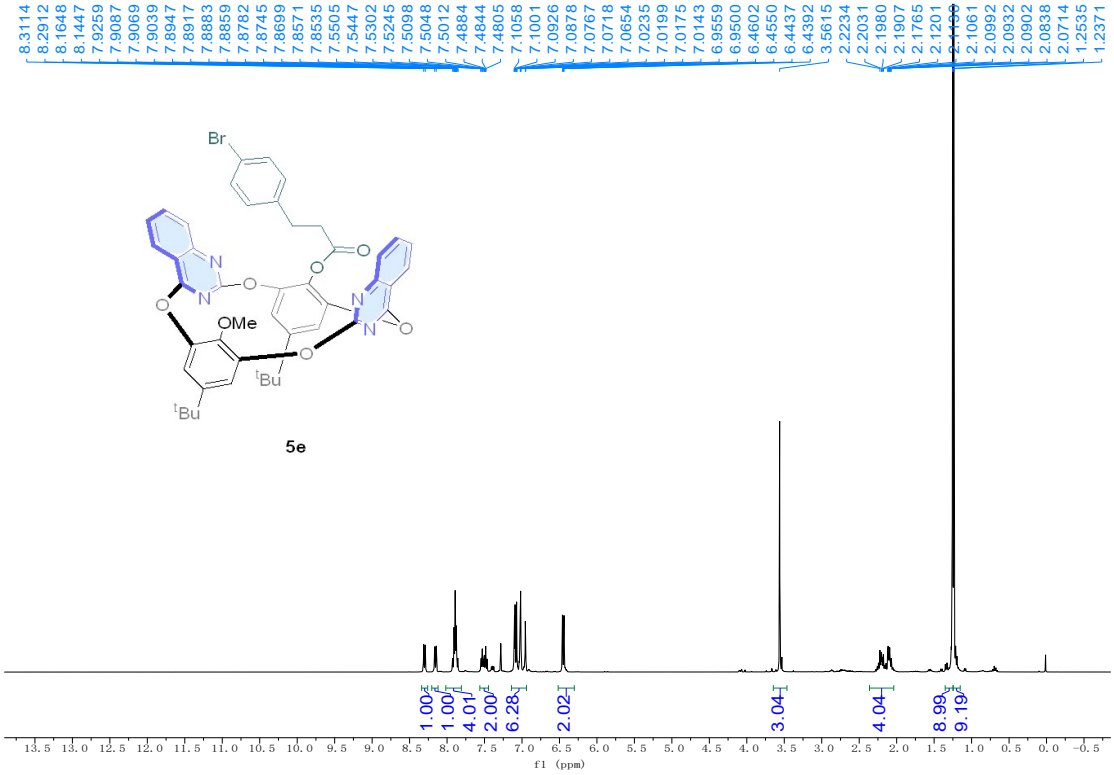
^{1}H NMR (400 MHz, $CDCl_3$) spectra of 5d



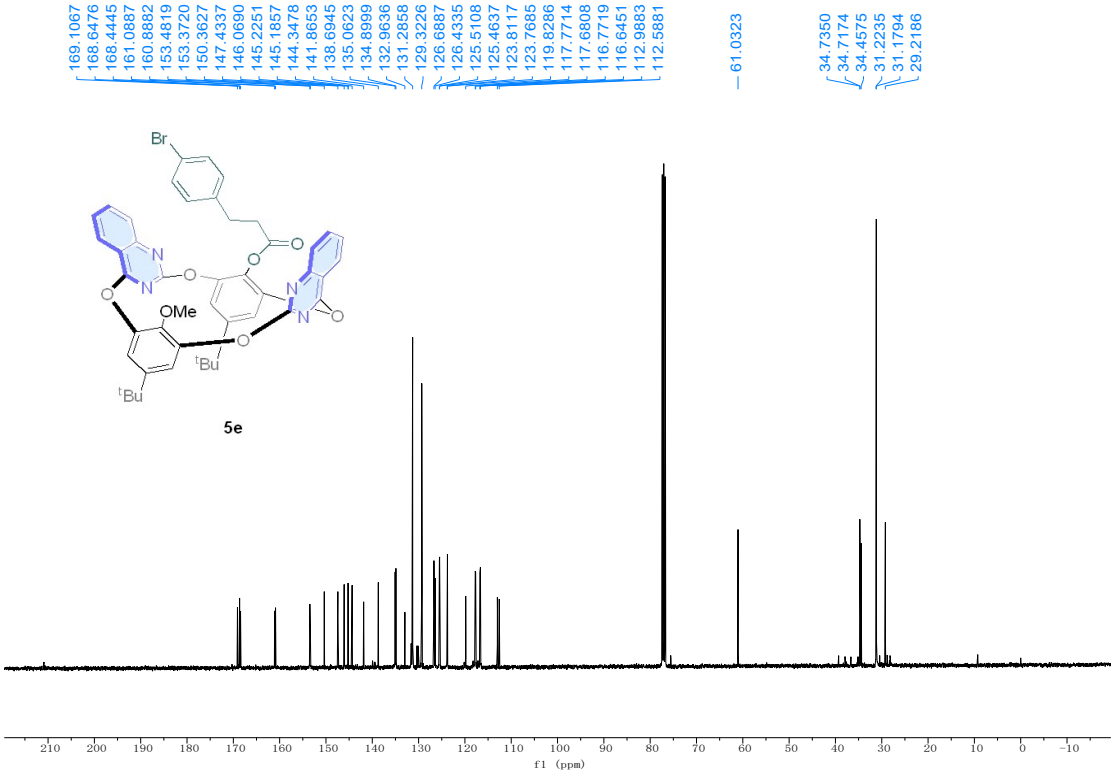
^{13}C NMR (100 MHz, $CDCl_3$) spectra of 5d



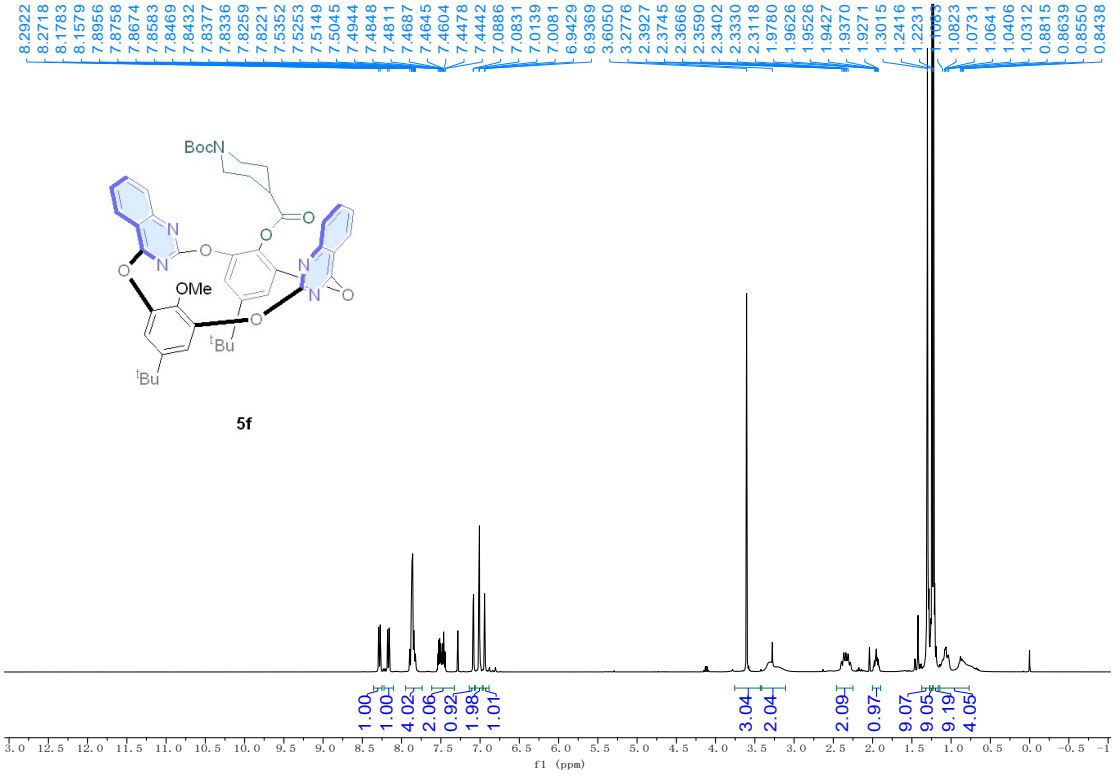
^{1}H NMR (400 MHz, $CDCl_3$) spectra of 5e



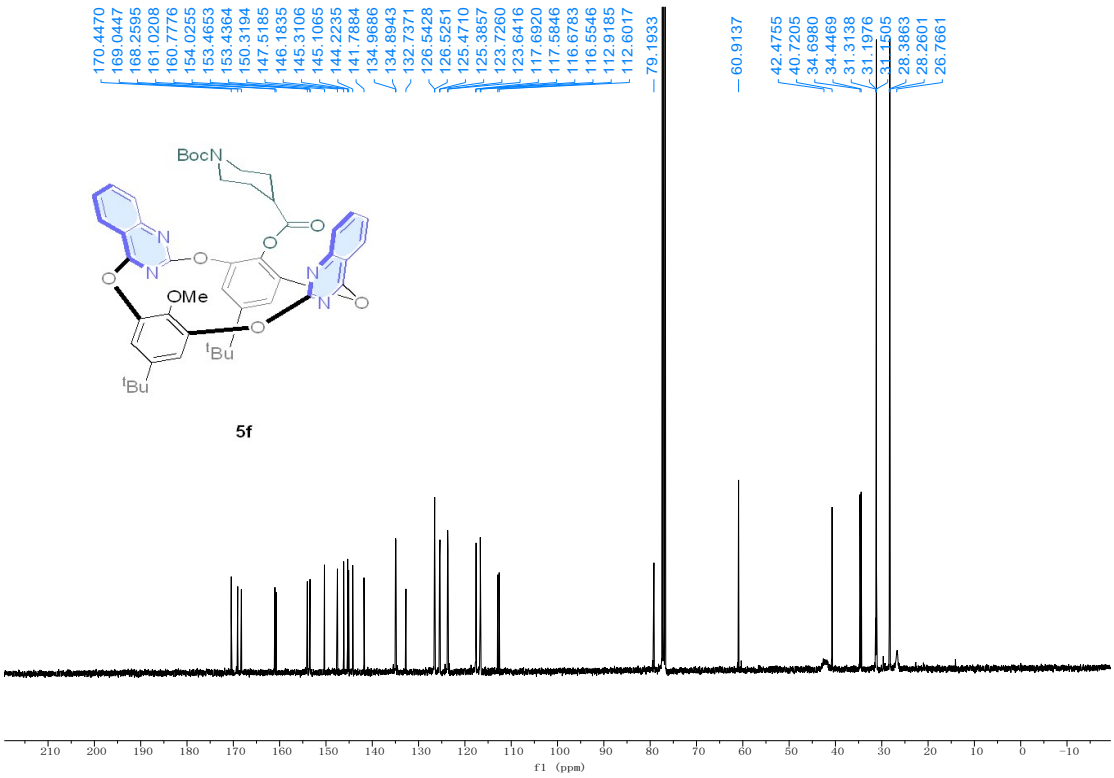
^{13}C NMR (100 MHz, $CDCl_3$) spectra of 5e



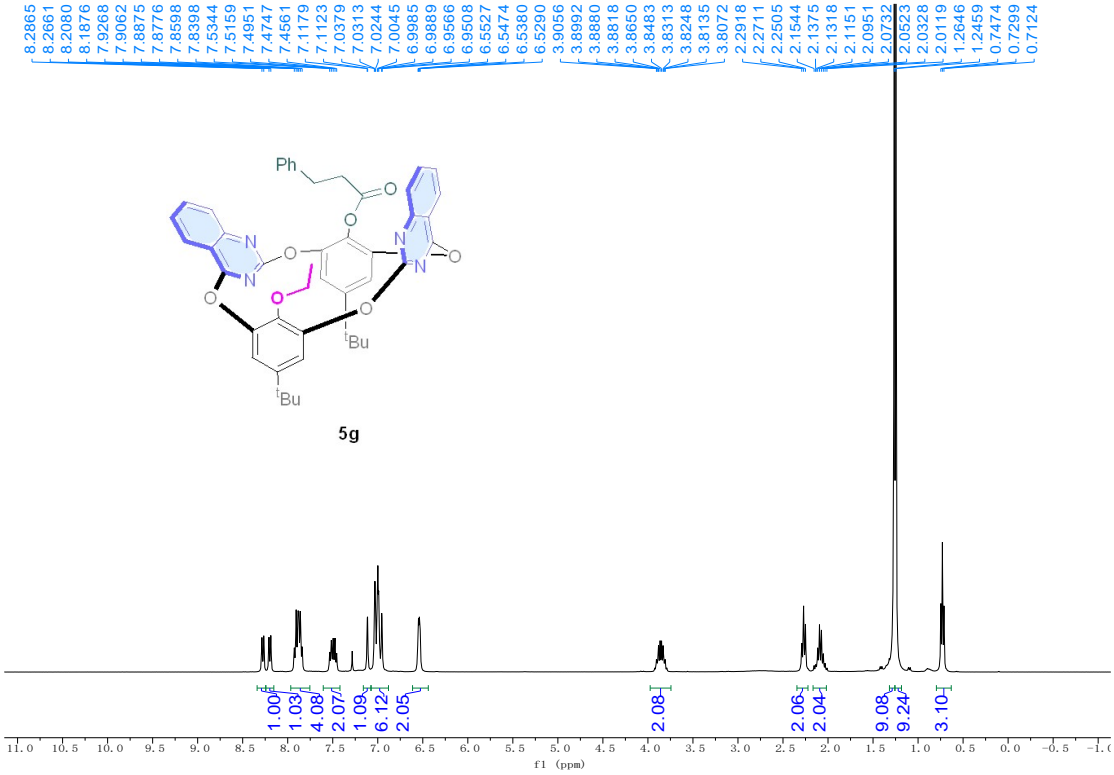
^{1}H NMR (400 MHz, $CDCl_3$) spectra of 5f



^{13}C NMR (100 MHz, $CDCl_3$) spectra of 5f

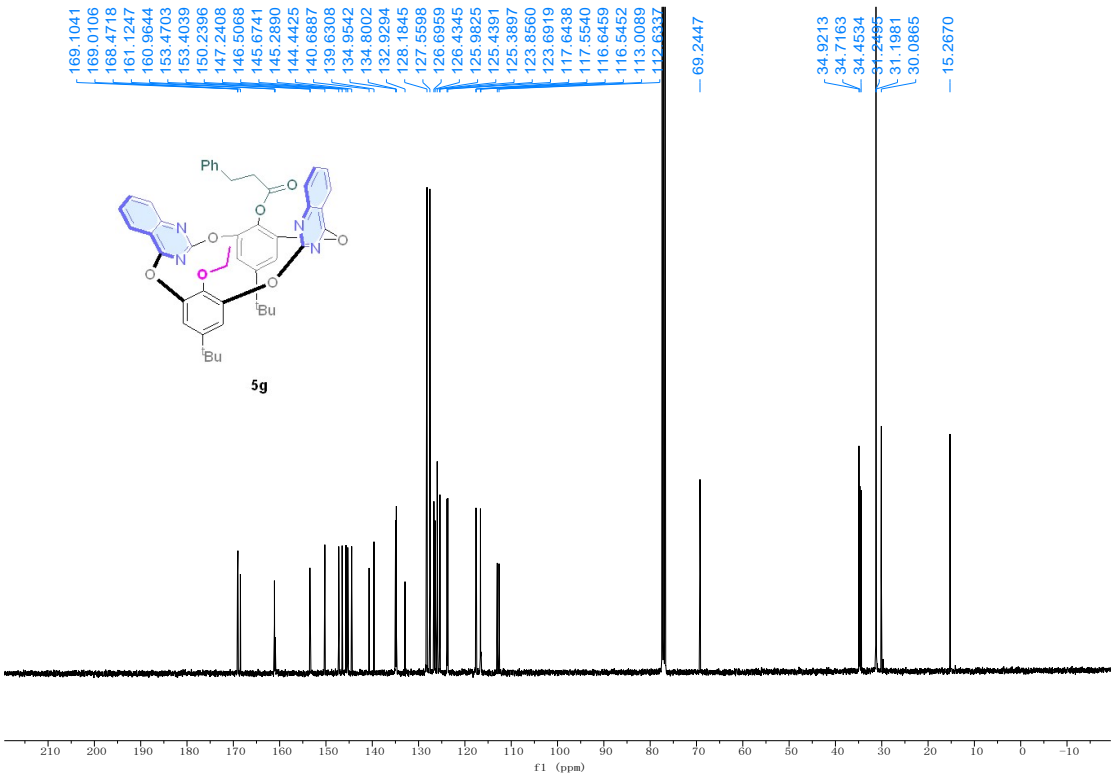


^{1}H NMR (400 MHz, $CDCl_3$) spectra of 5g



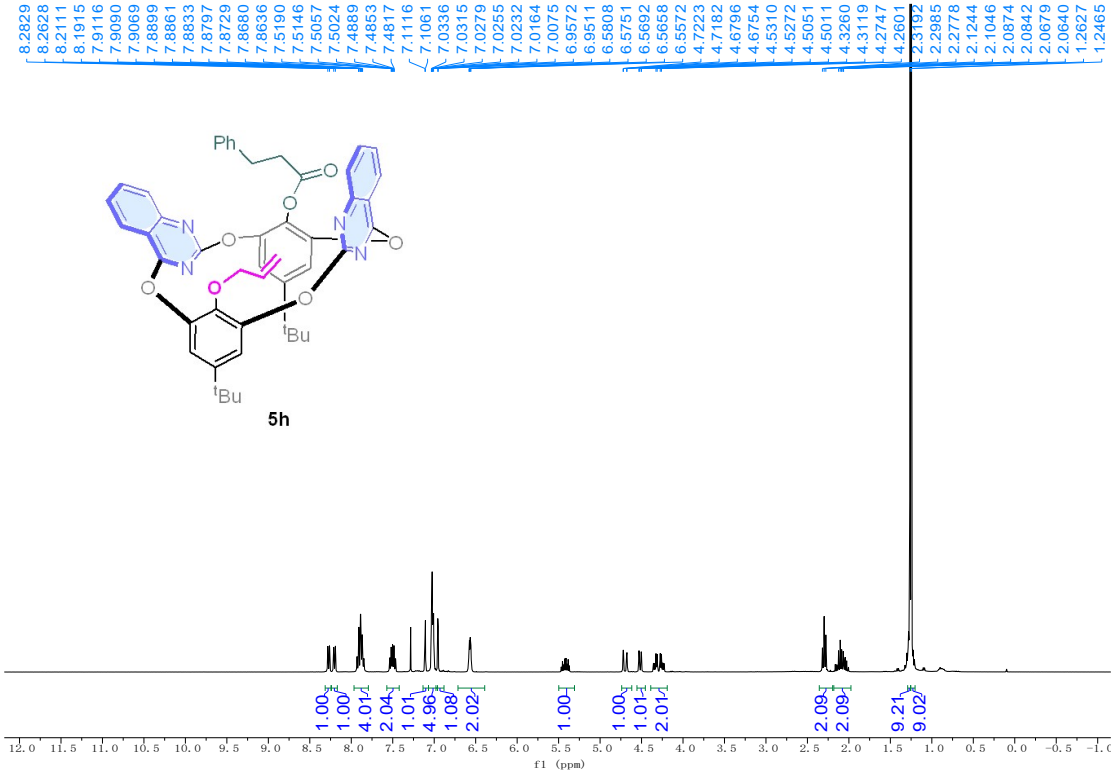
5g

^{13}C NMR (100 MHz, $CDCl_3$) spectra of 5g

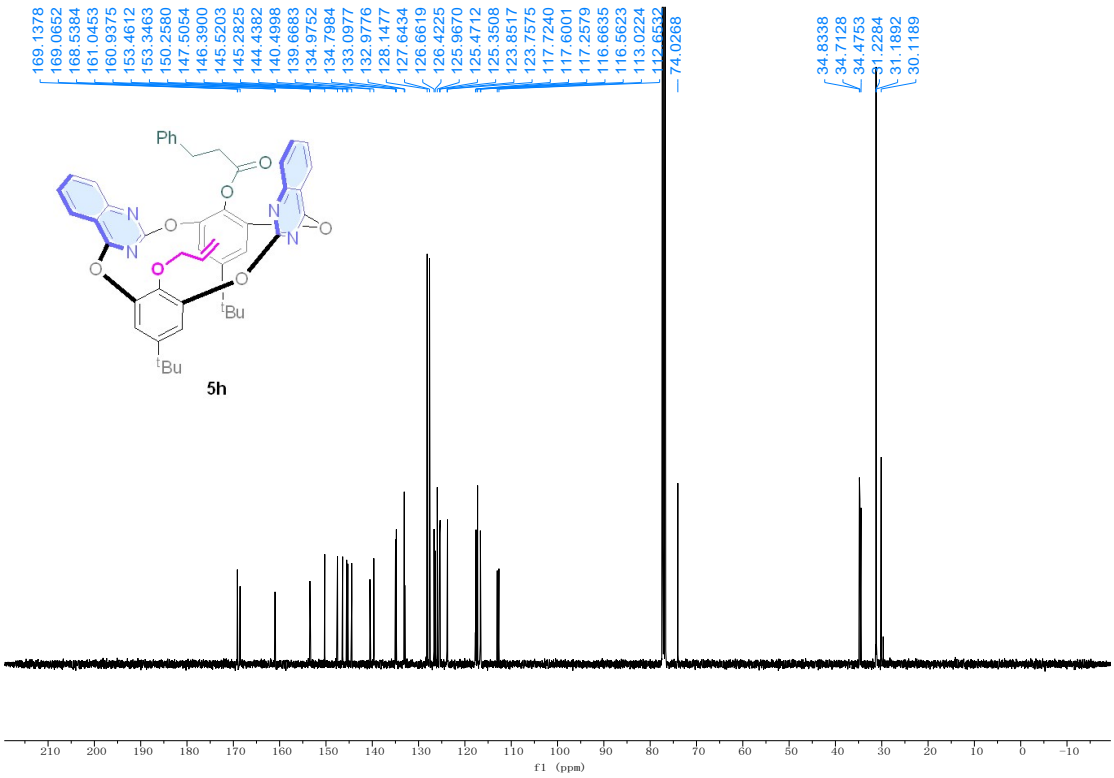


5g

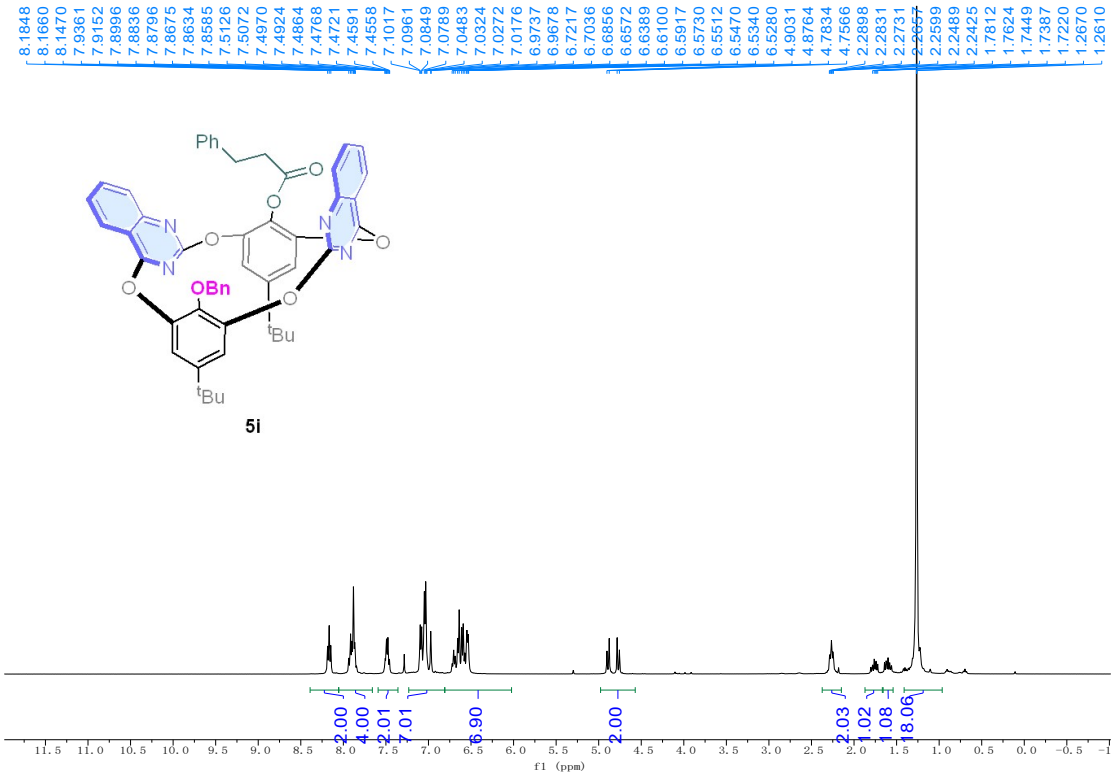
^{1}H NMR (400 MHz, $CDCl_3$) spectra of 5h



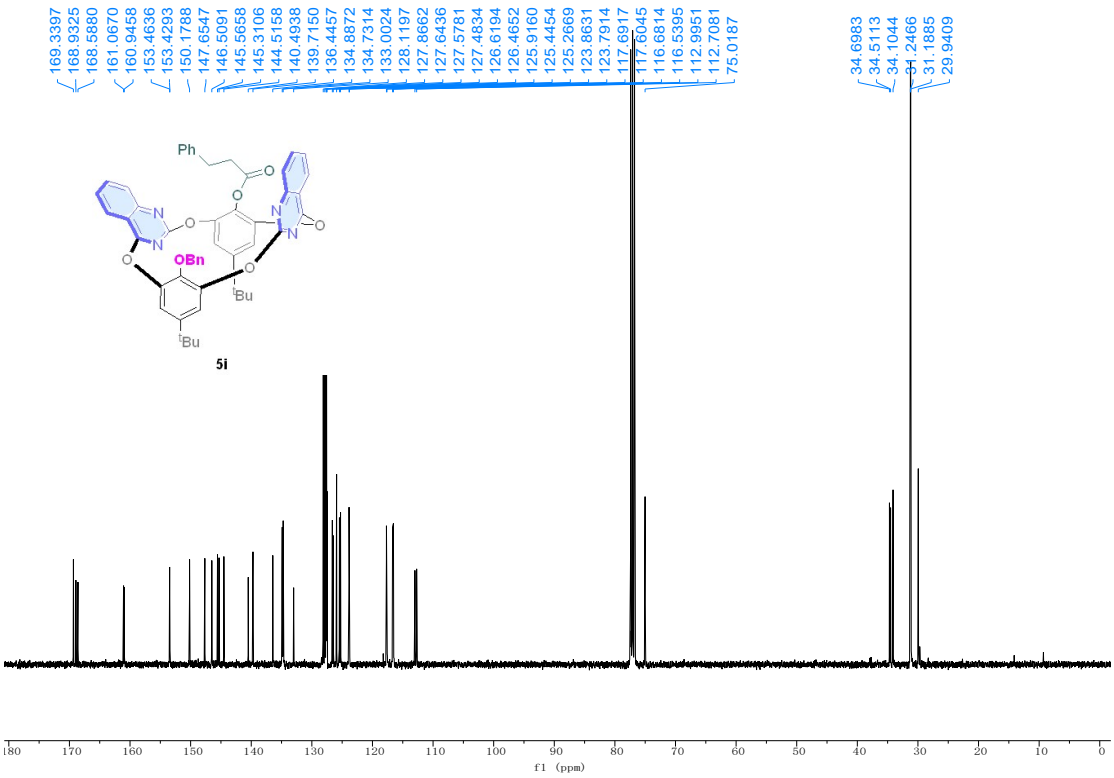
^{13}C NMR (100 MHz, $CDCl_3$) spectra of 5h



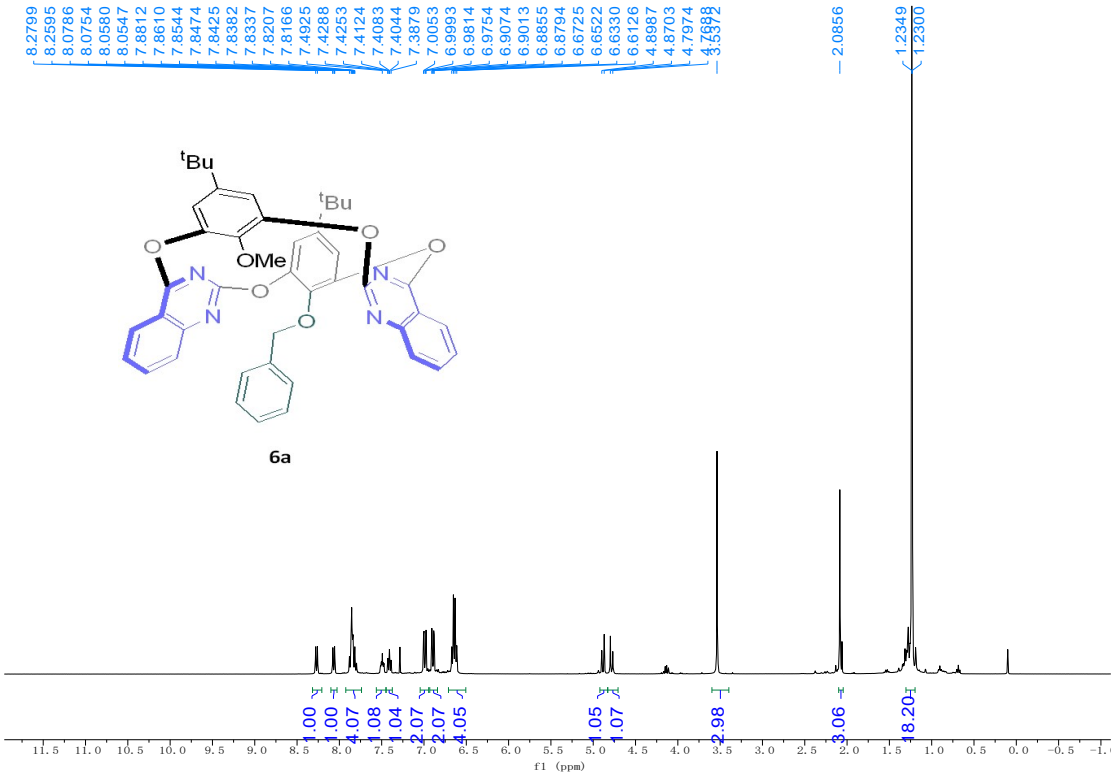
^{1}H NMR (400 MHz, $CDCl_3$) spectra of 5i



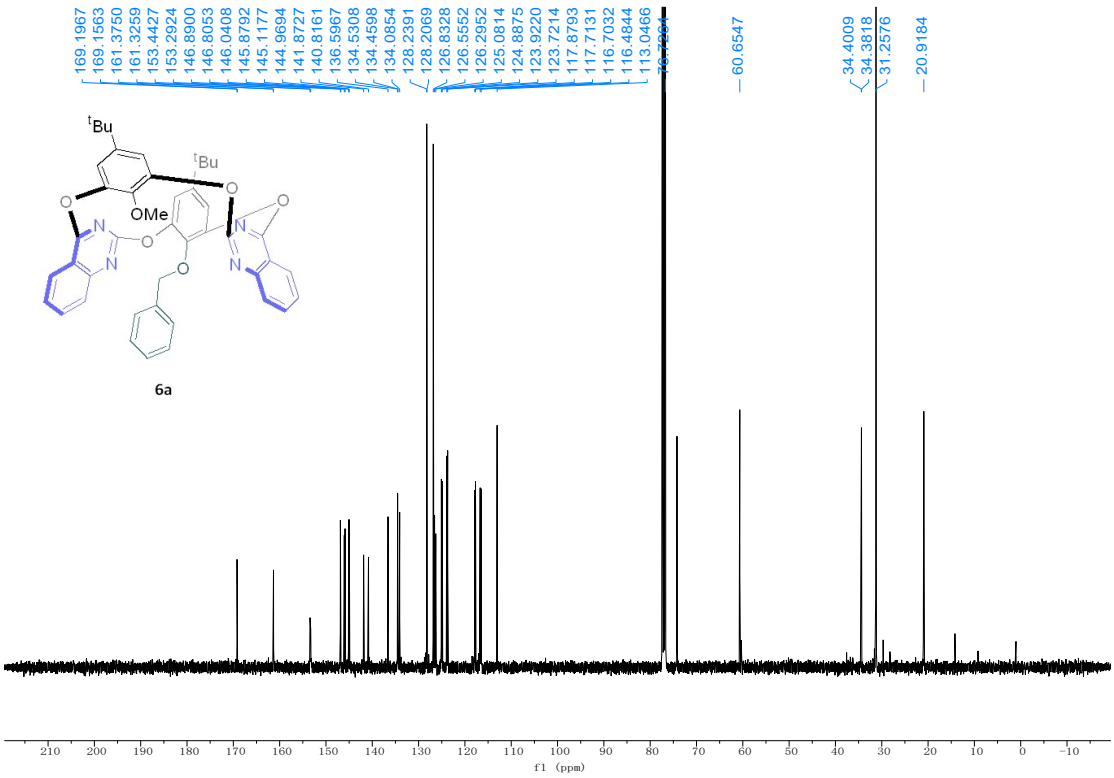
^{13}C NMR (100 MHz, $CDCl_3$) spectra of 5i



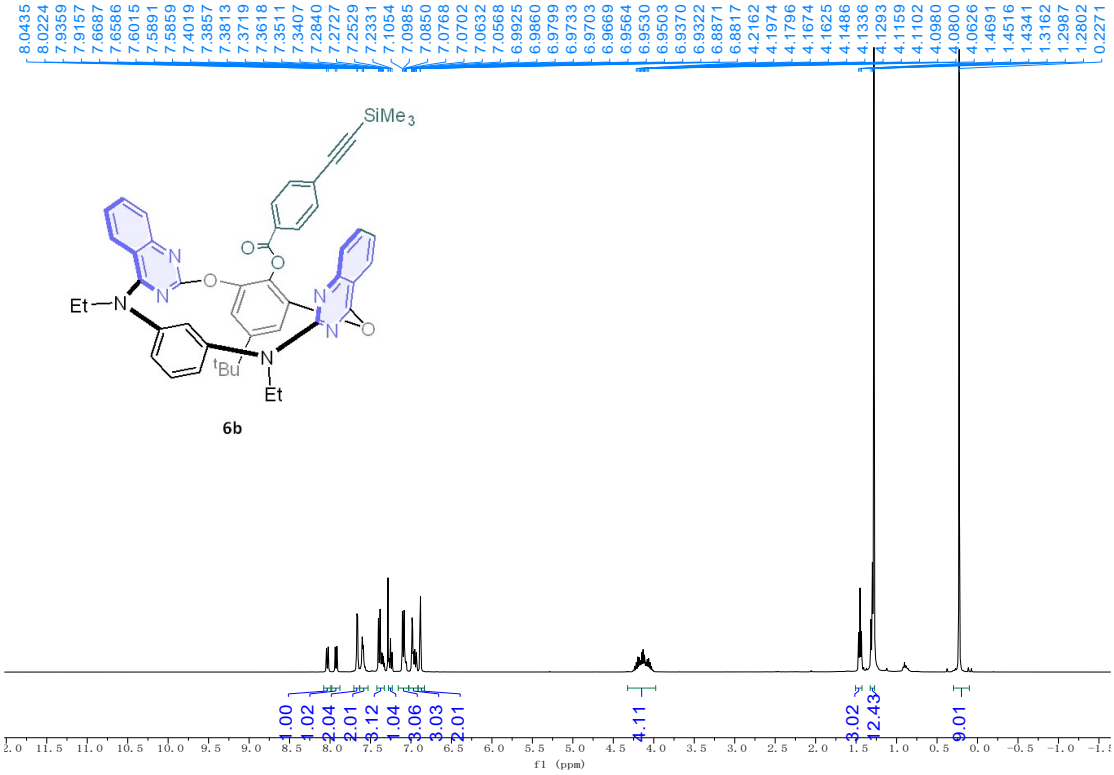
^{1}H NMR (400 MHz, $CDCl_3$) spectra of 6a



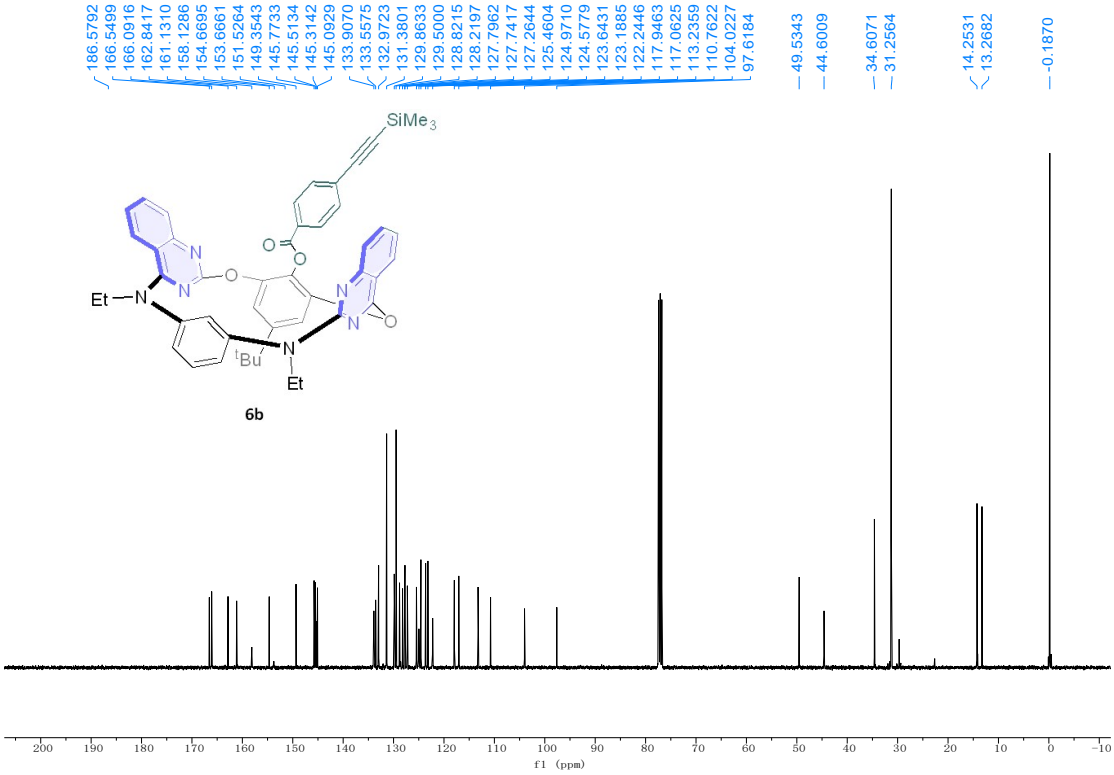
^{13}C NMR (100 MHz, $CDCl_3$) spectra of 6a



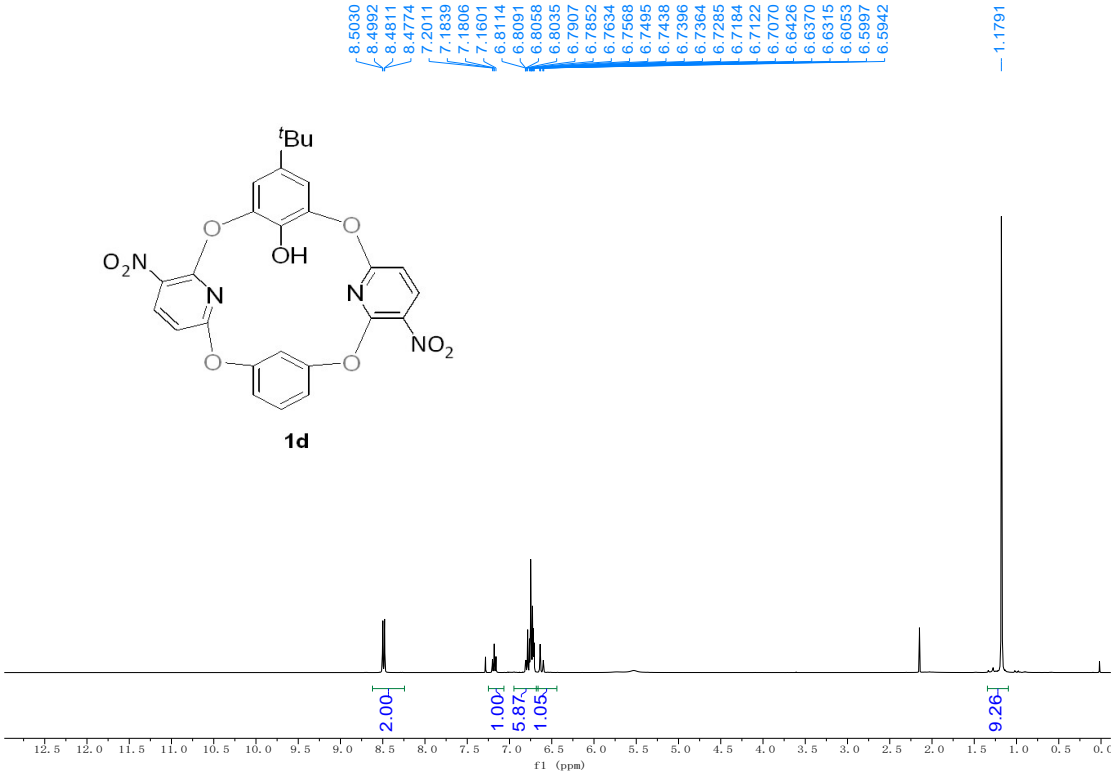
^{1}H NMR (400 MHz, $CDCl_3$) spectra of 6b



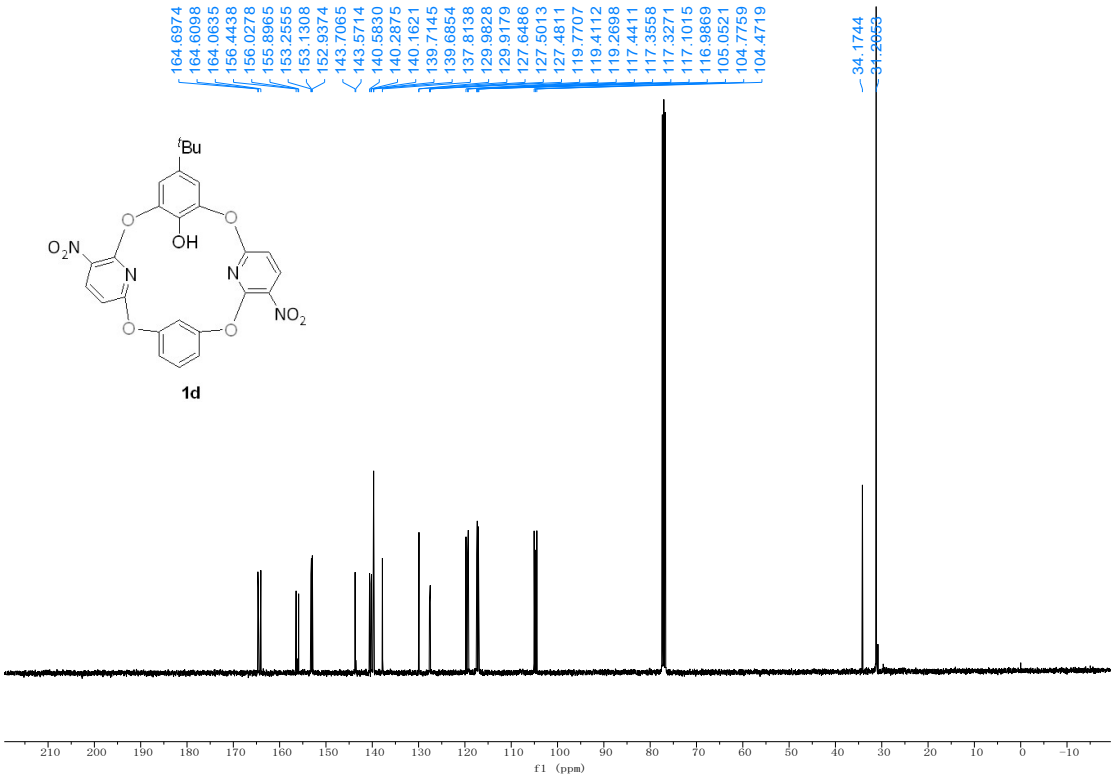
^{13}C NMR (100 MHz, $CDCl_3$) spectra of 6b



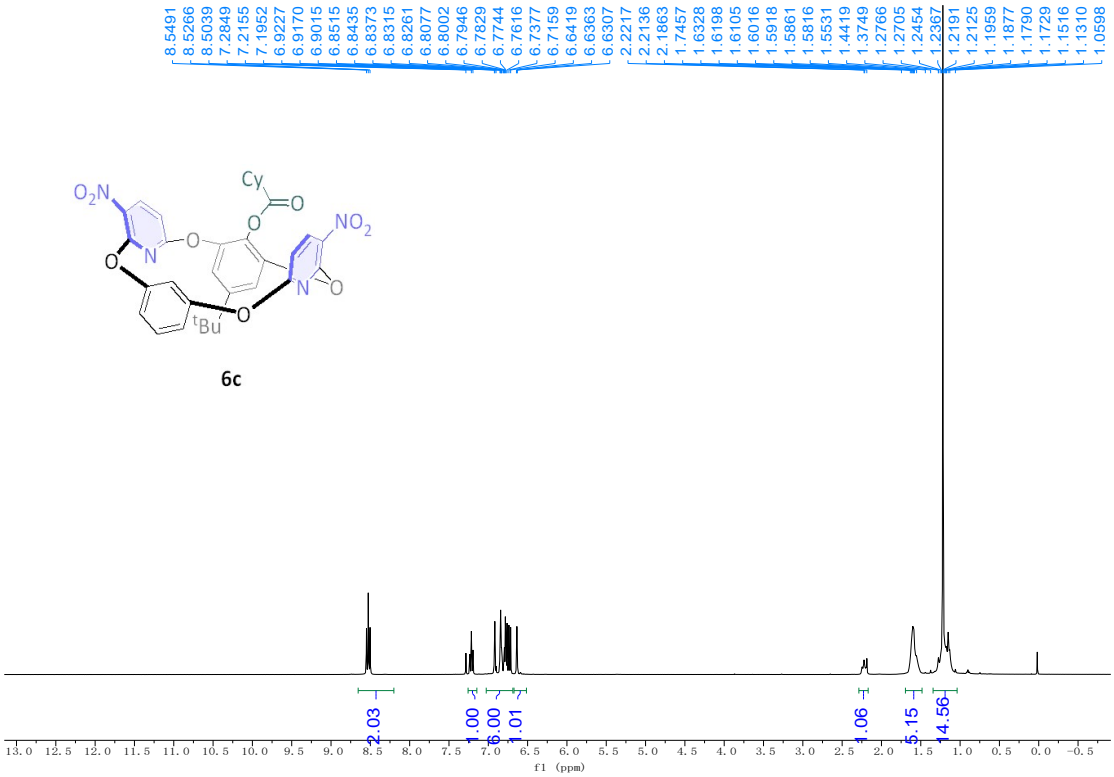
^{1}H NMR (400 MHz, $CDCl_3$) spectra of 1d



^{13}C NMR (100 MHz, $CDCl_3$) spectra of 1d

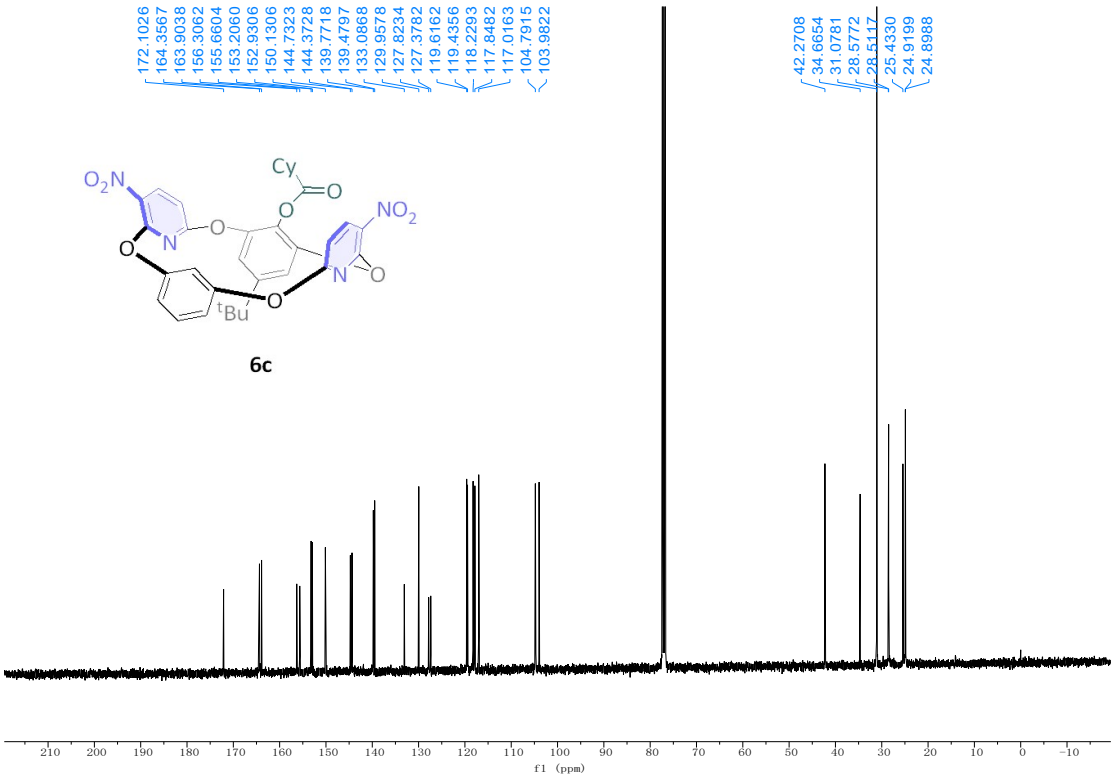


^{1}H NMR (400 MHz, $CDCl_3$) spectra of 6c



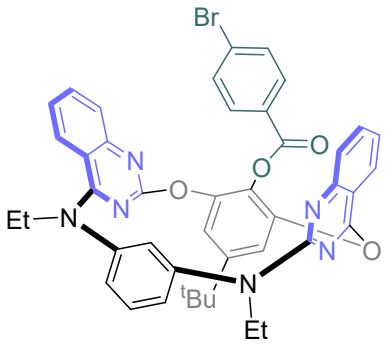
6c

^{13}C NMR (100 MHz, $CDCl_3$) spectra of 6c



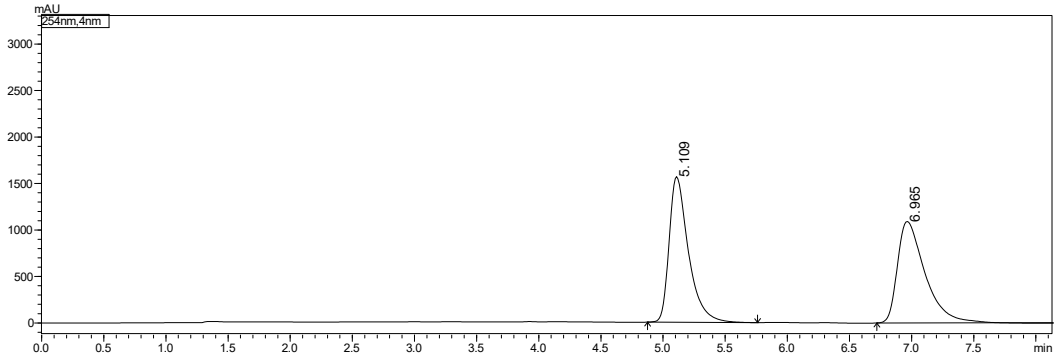
6c

HPLC Spectra



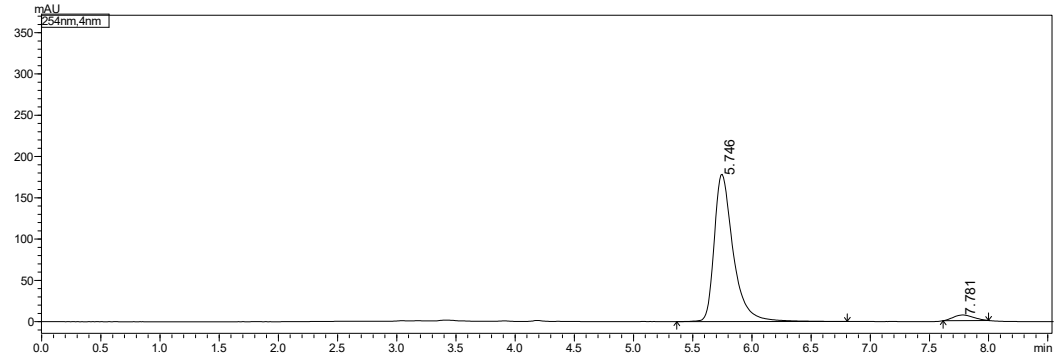
3a

Chiral HPLC spectrum of racemic **3a**

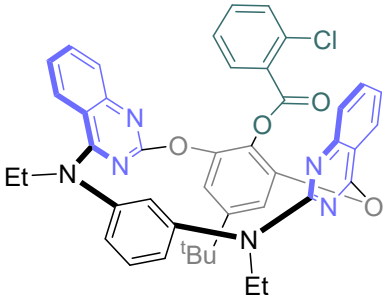


Peak	RT	Area	Height	Area%	Height%
1	5.109	16949988	1566097	50.387	58.928
2	6.965	16689517	1091553	49.613	41.072
Total		33639505	2657650	100.000	100.000

Chiral HPLC spectrum of **3a**

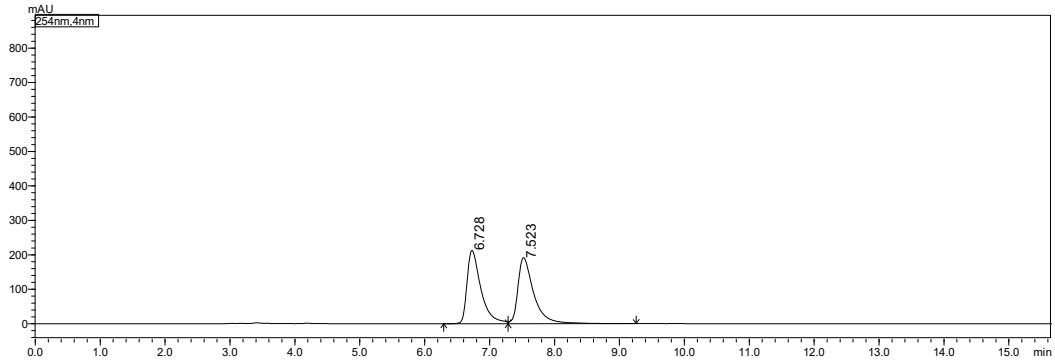


Peak	RT	Area	Height	Area%	Height%
1	5.746	1989703	178272	96.073	96.317
2	7.781	81323	6816	3.927	3.683
Total		2071027	185088	100.000	100.000



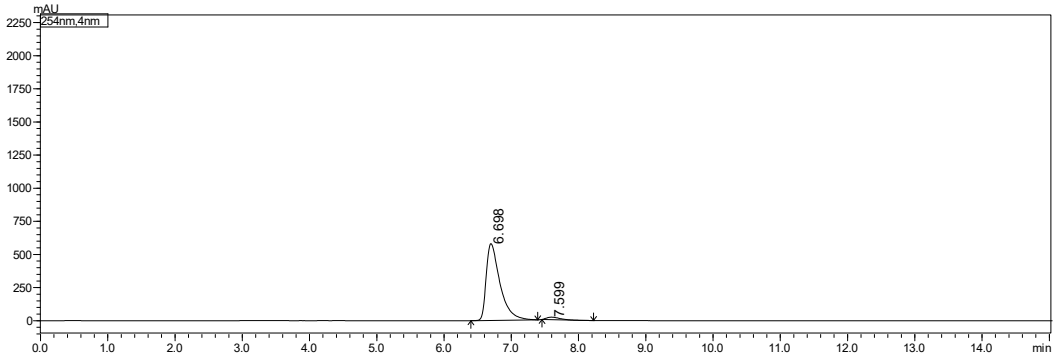
3b

Chiral HPLC spectrum of racemic **3b**

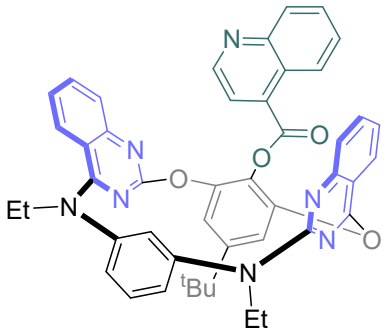


Peak	RT	Area	Height	Area%	Height%
1	6.728	3181441	213012	49.401	52.613
2	7.523	3258607	191851	50.599	47.387
Total		6440048	404863	100.000	100.000

Chiral HPLC spectrum of **3a**

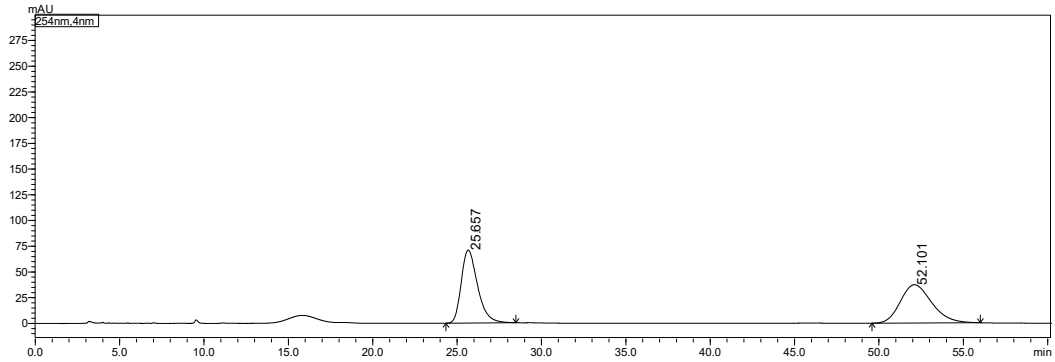


Peak	RT	Area	Height	Area%	Height%
1	6.698	8261232	580256	97.256	96.896
2	7.599	233103	18585	2.744	3.104
Total		8494336	598841	100.000	100.000



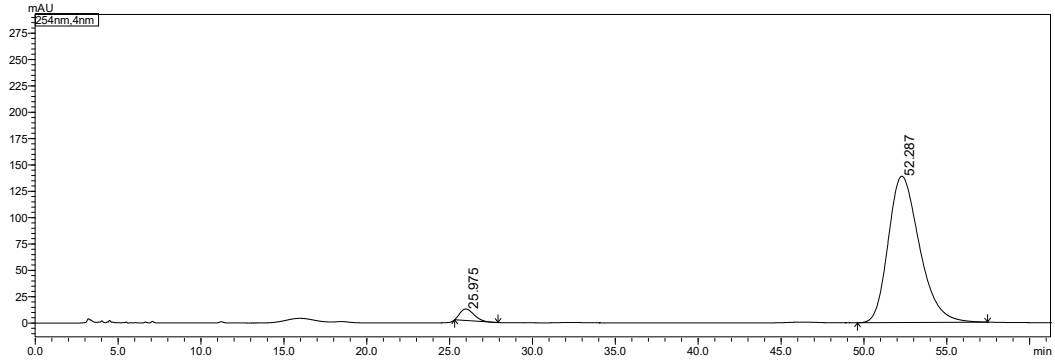
3c

Chiral HPLC spectrum of racemic **3c**

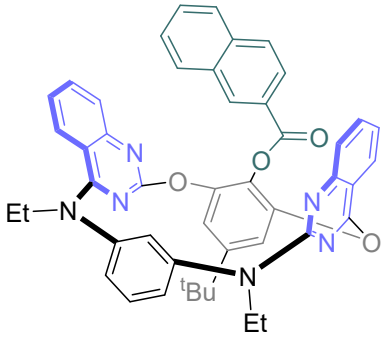


Peak	RT	Area	Height	Area%	Height%
1	25.657	4786006	70937	49.794	65.577
2	52.101	4825608	37237	50.206	34.423
Total		9611614	108174	100.000	100.000

Chiral HPLC spectrum of **3c**

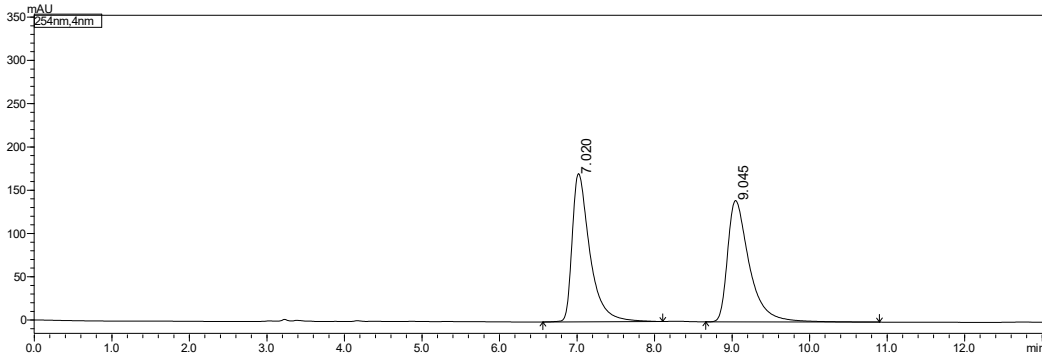


Peak	RT	Area	Height	Area%	Height%
1	25.975	630372	10916	3.350	7.290
2	52.287	18189027	138833	96.650	92.710
Total		18819399	149749	100.000	100.000



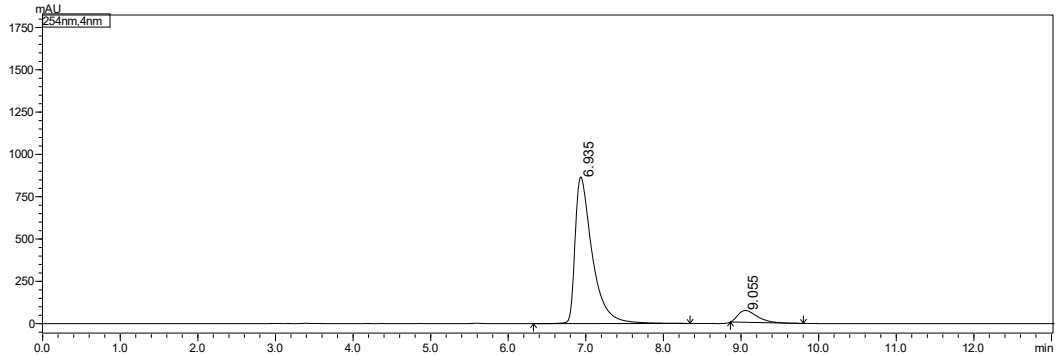
3d

Chiral HPLC spectrum of racemic **3d**

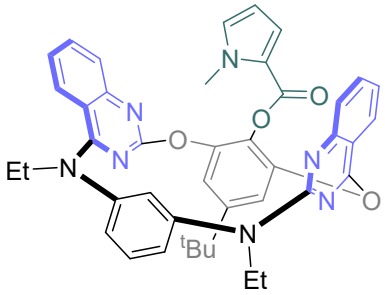


Peak	RT	Area	Height	Area%	Height%
1	7.020	2720473	171249	49.803	54.956
2	9.045	2741995	140365	50.197	45.044
Total		5462468	311613	100.000	100.000

Chiral HPLC spectrum of **3d**

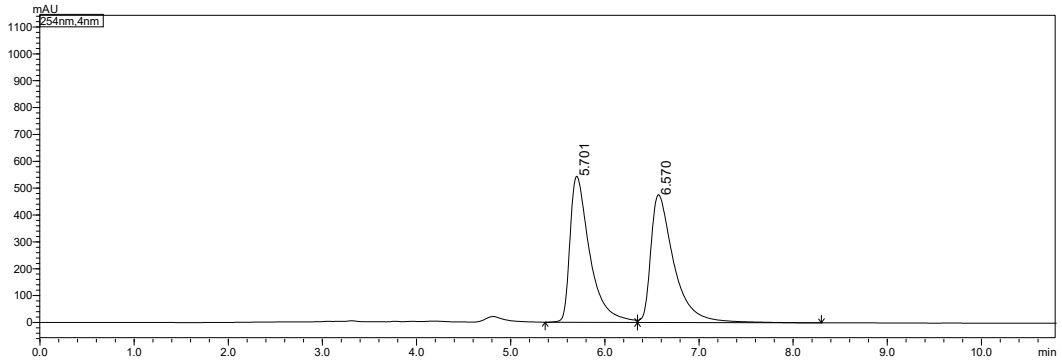


Peak	RT	Area	Height	Area%	Height%
1	6.935	13294431	866948	91.704	92.507
2	9.055	1202631	70227	8.296	7.493
Total		14497063	937175	100.000	100.000



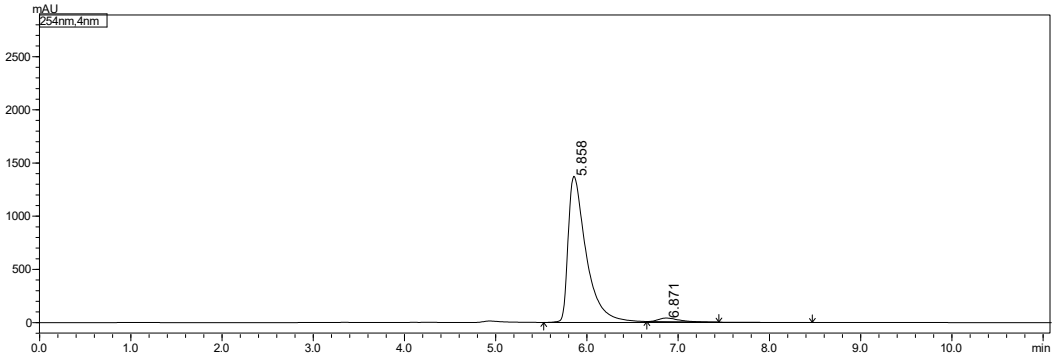
3e

Chiral HPLC spectrum of racemic **3e**

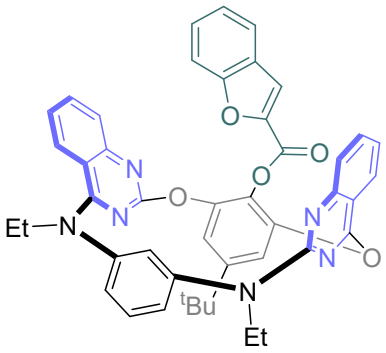


Peak	RT	Area	Height	Area%	Height%
1	5.701	7971122	543518	49.538	53.316
2	6.570	8119813	475917	50.462	46.684
Total		16090935	1019435	100.000	100.000

Chiral HPLC spectrum of **3e**

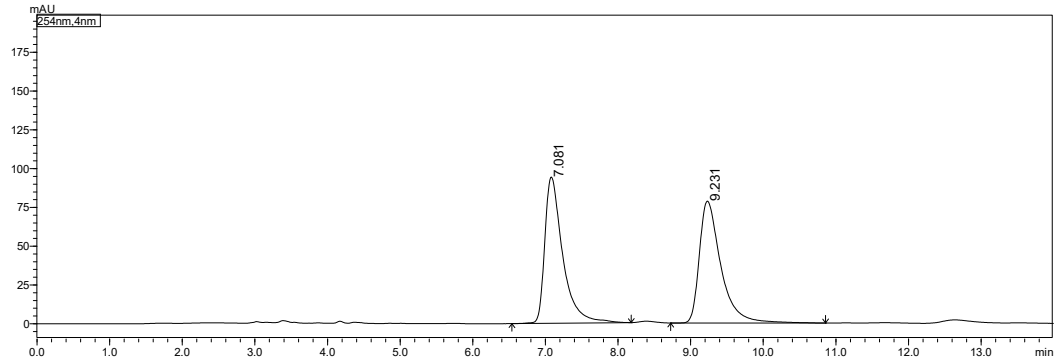


Peak	RT	Area	Height	Area%	Height%
1	5.858	19340518	1374845	97.369	97.583
2	6.871	522658	34053	2.631	2.417
Total		19863175	1408898	100.000	100.000



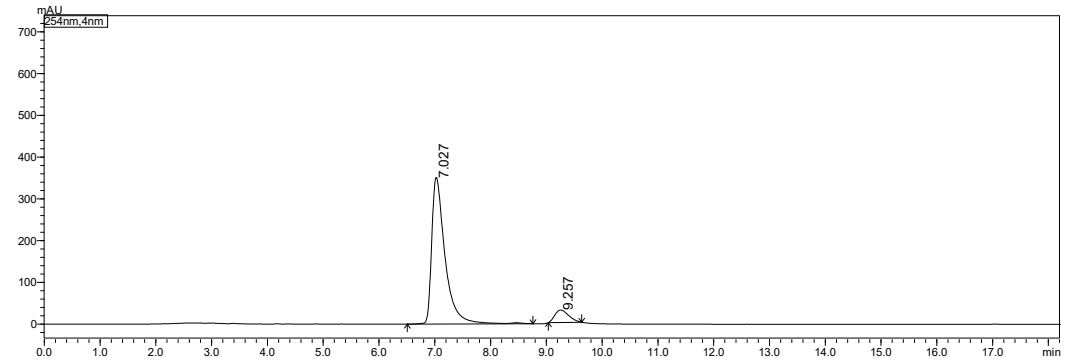
3f

Chiral HPLC spectrum of racemic **3f**

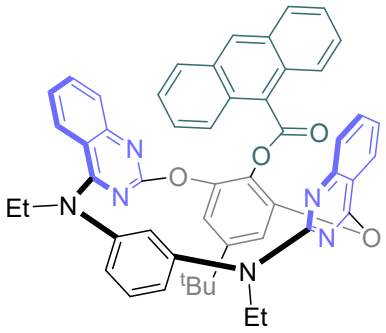


Peak	RT	Area	Height	Area%	Height%
1	7.081	1623435	94371	50.009	54.562
2	9.231	1622880	78590	49.991	45.438
Total		3246315	172961	100.000	100.000

Chiral HPLC spectrum of **3f**

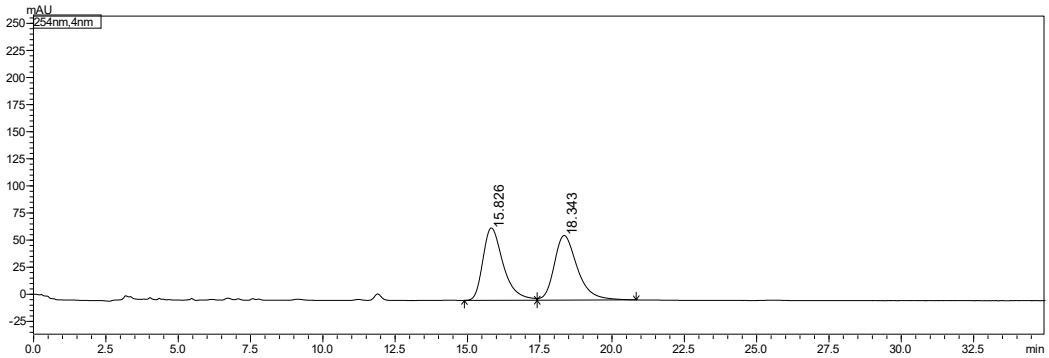


Peak	RT	Area	Height	Area%	Height%
1	7.027	5850186	351222	91.914	92.161
2	9.257	514655	29874	8.086	7.839
Total		6364841	381097	100.000	100.000



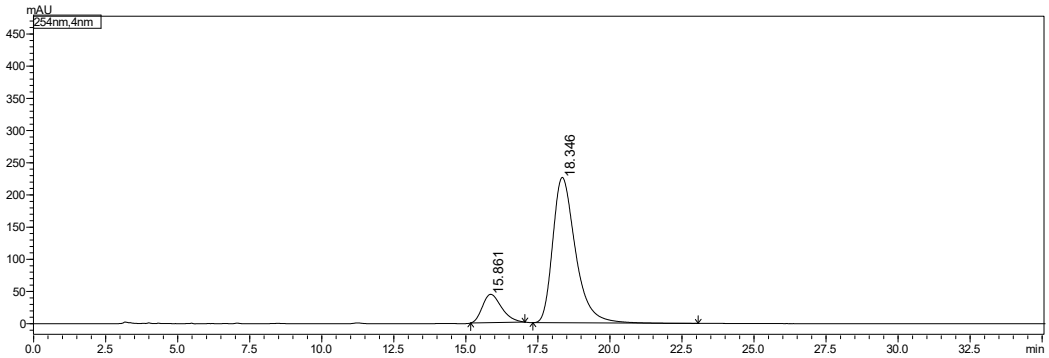
3g

Chiral HPLC spectrum of racemic **3g**

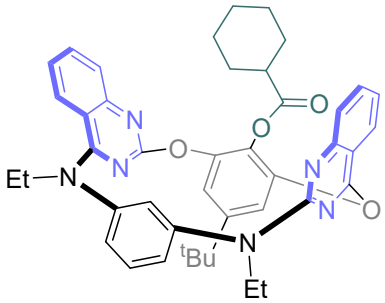


Peak	RT	Area	Height	Area%	Height%
1	15.826	3270969	66752	49.661	52.825
2	18.343	3315669	59612	50.339	47.175
Total		6586638	126364	100.000	100.000

Chiral HPLC spectrum of racemic **3g**

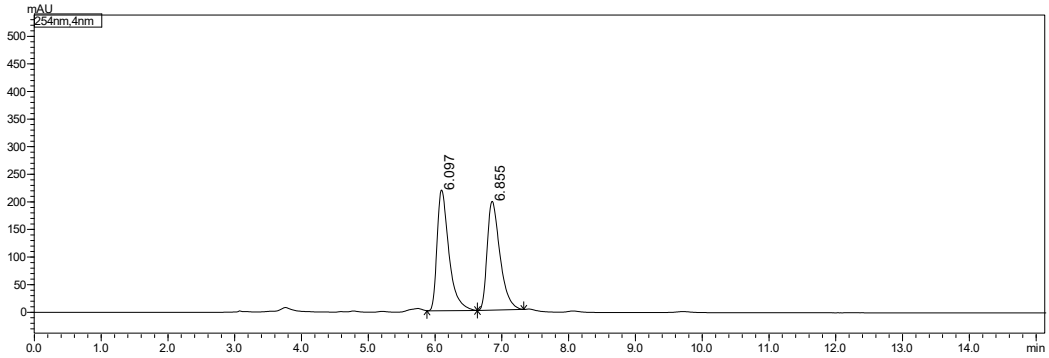


Peak	RT	Area	Height	Area%	Height%
1	15.861	2036557	44050	14.107	16.320
2	18.346	12400335	225868	85.893	83.680
Total		14436892	269918	100.000	100.000



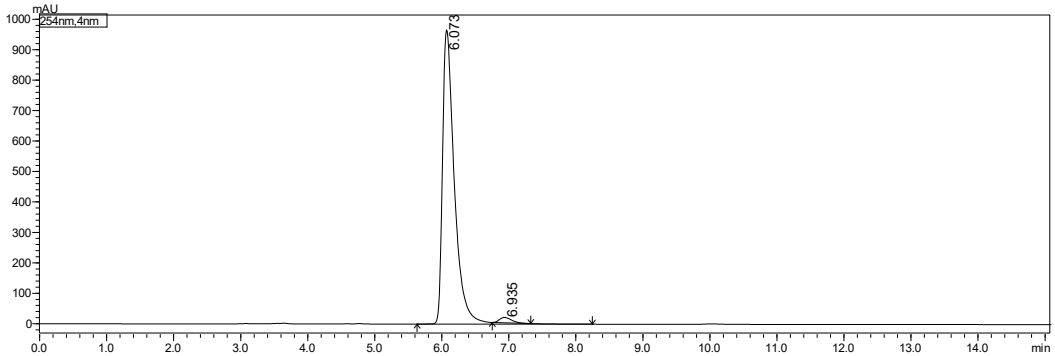
3h

Chiral HPLC spectrum of racemic **3h**

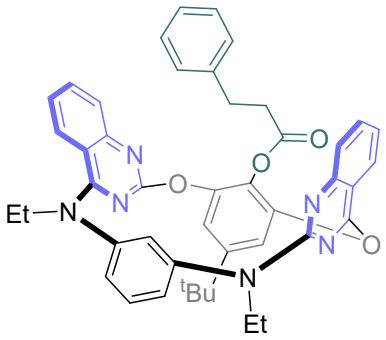


Peak	RT	Area	Height	Area%	Height%
1	6.097	2694736	218749	50.667	52.611
2	6.855	2623758	197038	49.333	47.389
Total		5318494	415787	100.000	100.000

Chiral HPLC spectrum of **3h**

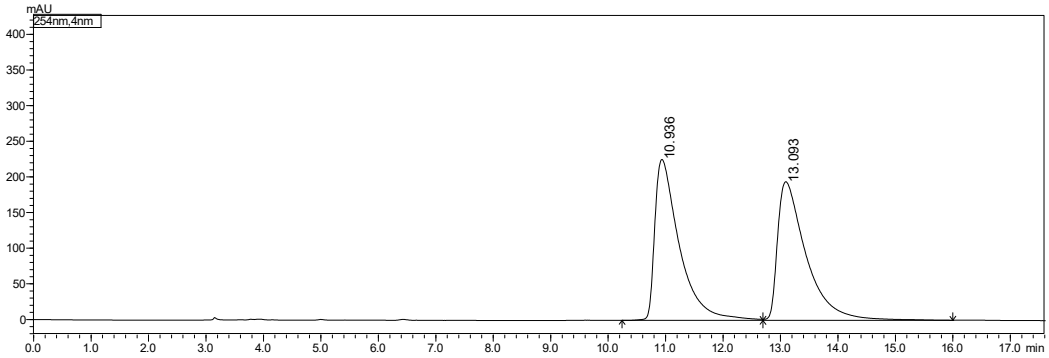


Peak	RT	Area	Height	Area%	Height%
1	6.073	11978273	966298	98.170	98.200
2	6.935	223281	17715	1.830	1.800
Total		12201554	984013	100.000	100.000



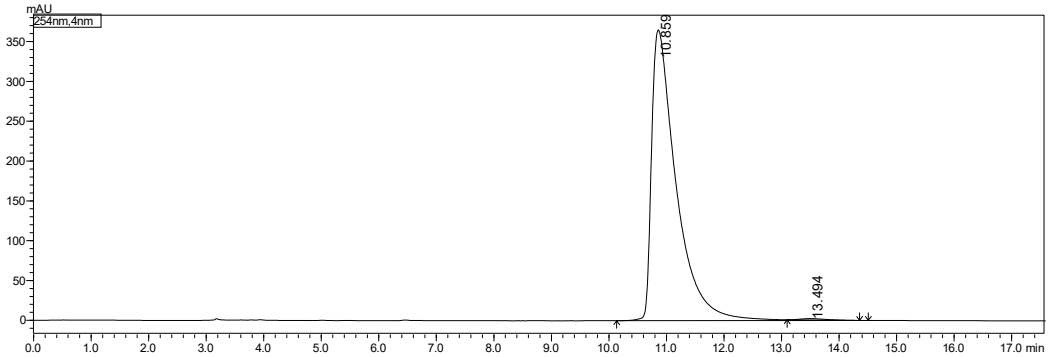
3i

Chiral HPLC spectrum of racemic **3i**

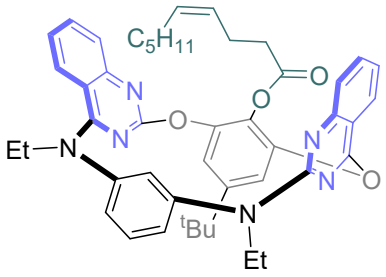


Peak	RT	Area	Height	Area%	Height%
1	10.936	6719675	225832	49.953	53.739
2	13.093	6732190	194409	50.047	46.261
Total		13451865	420241	100.000	100.000

Chiral HPLC spectrum of **3i**

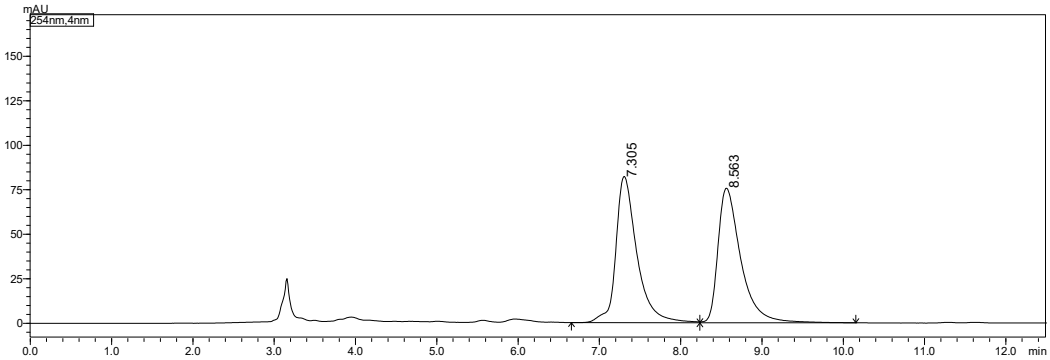


Peak	RT	Area	Height	Area%	Height%
1	10.859	10869444	365034	99.507	99.519
2	13.494	53886	1763	0.493	0.481
Total		10923331	366797	100.000	100.000



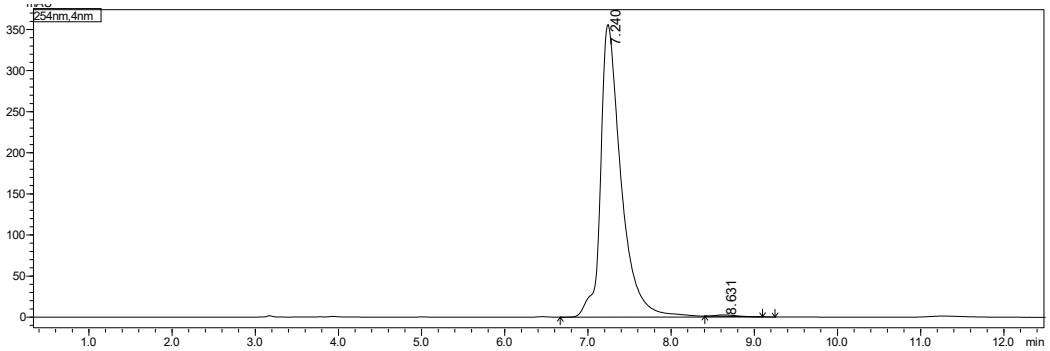
3j

Chiral HPLC spectrum of racemic **3j**

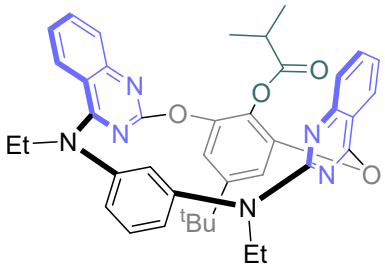


Peak	RT	Area	Height	Area%	Height%
1	7.305	1482924	82132	50.168	52.074
2	8.563	1472990	75591	49.832	47.926
Total		2955914	157724	100.000	100.000

Chiral HPLC spectrum of **3j**

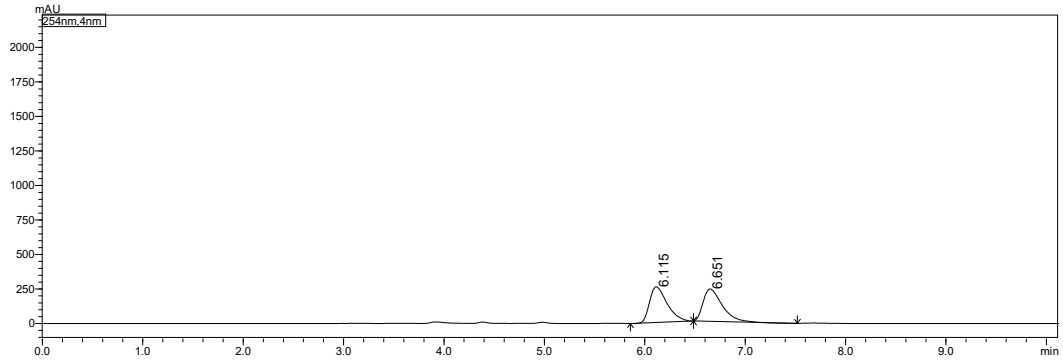


Peak	RT	Area	Height	Area%	Height%
1	7.240	6124325	356034	99.522	99.490
2	8.631	29396	1824	0.478	0.510
Total		6153721	357858	100.000	100.000



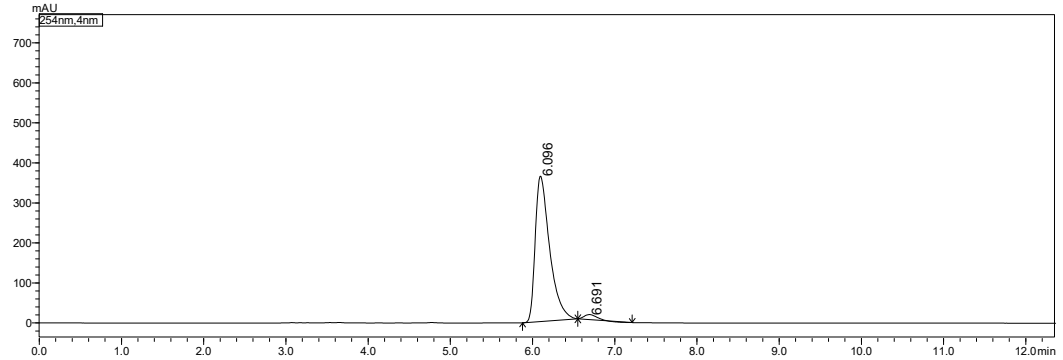
3k

Chiral HPLC spectrum of racemic **3k**

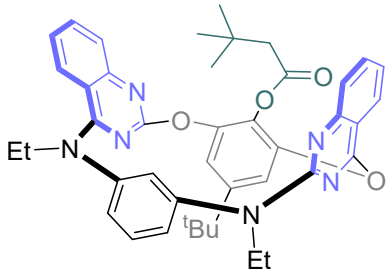


Peak	RT	Area	Height	Area%	Height%
1	6.115	3131362	257636	50.523	52.450
2	6.651	3066567	233564	49.477	47.550
Total		6197928	491200	100.000	100.000

Chiral HPLC spectrum of **3k**

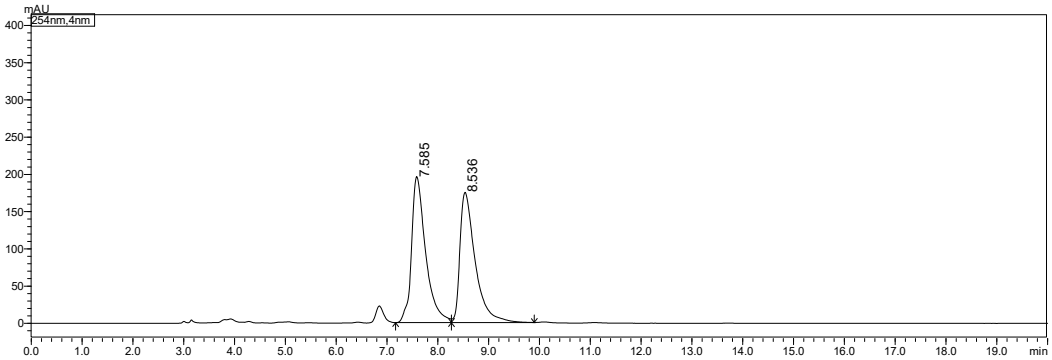


Peak	RT	Area	Height	Area%	Height%
1	6.096	4435930	363046	97.445	96.685
2	6.691	116301	12448	2.555	3.315
Total		4552230	375494	100.000	100.000



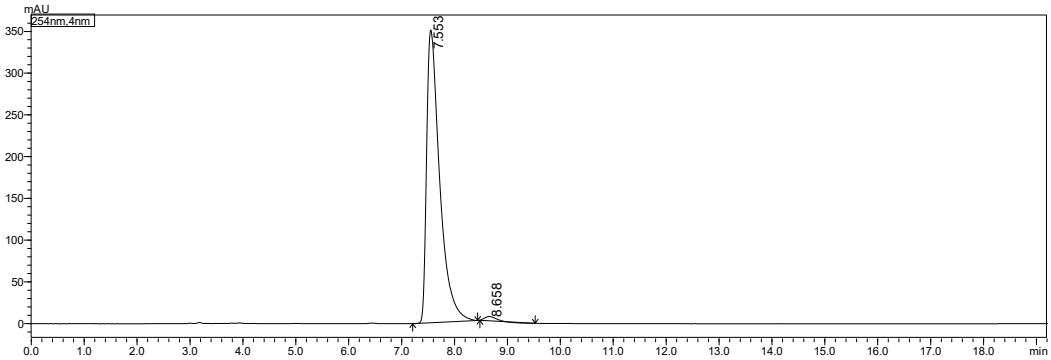
3l

Chiral HPLC spectrum of racemic **3l**

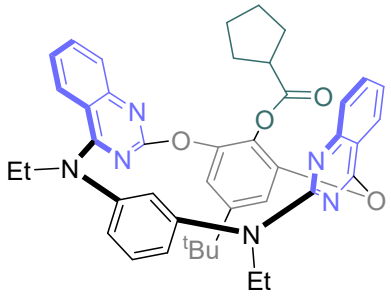


Peak	RT	Area	Height	Area%	Height%
1	7.585	3803620	196266	51.005	52.882
2	8.536	3653669	174872	48.995	47.118
Total		7457289	371139	100.000	100.000

Chiral HPLC spectrum of **3l**

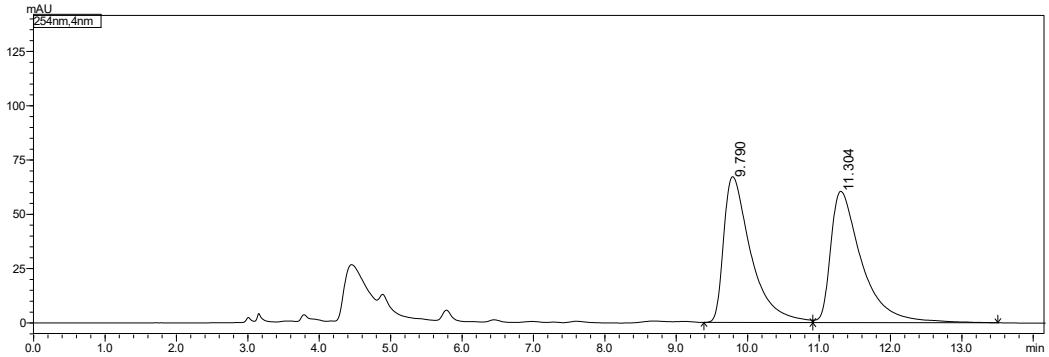


Peak	RT	Area	Height	Area%	Height%
1	7.553	6010989	350745	99.007	98.587
2	8.658	60276	5027	0.993	1.413
Total		6071264	355772	100.000	100.000



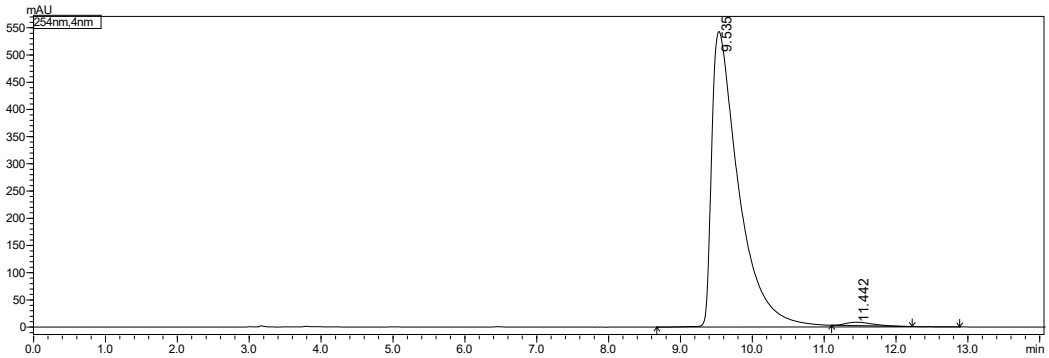
3m

Chiral HPLC spectrum of racemic **3m**

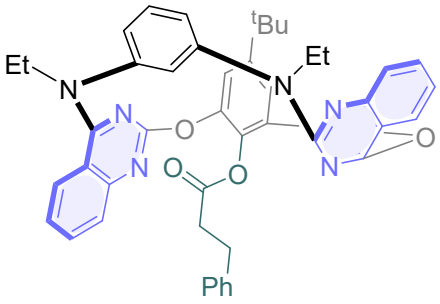


Peak	RT	Area	Height	Area%	Height%
1	9.790	1779414	67134	49.701	52.674
2	11.304	1800847	60318	50.299	47.326
Total		3580260	127453	100.000	100.000

Chiral HPLC spectrum of **3m**

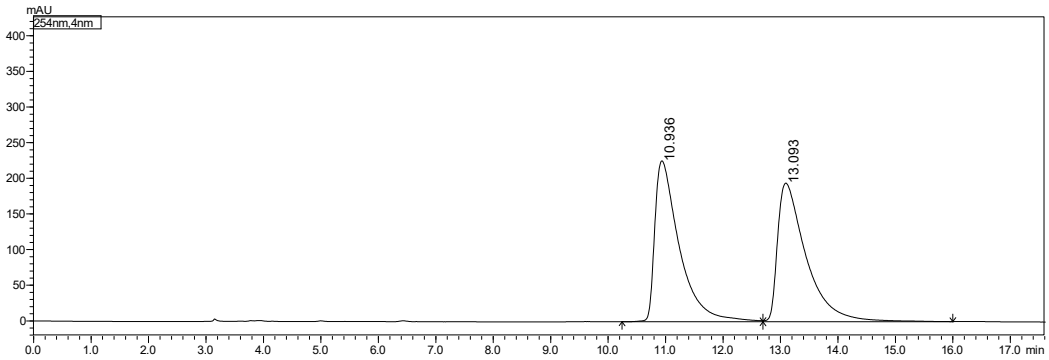


Peak	RT	Area	Height	Area%	Height%
1	9.535	14339414	543306	98.845	98.831
2	11.442	167585	6426	1.155	1.169
Total		14506999	549732	100.000	100.000



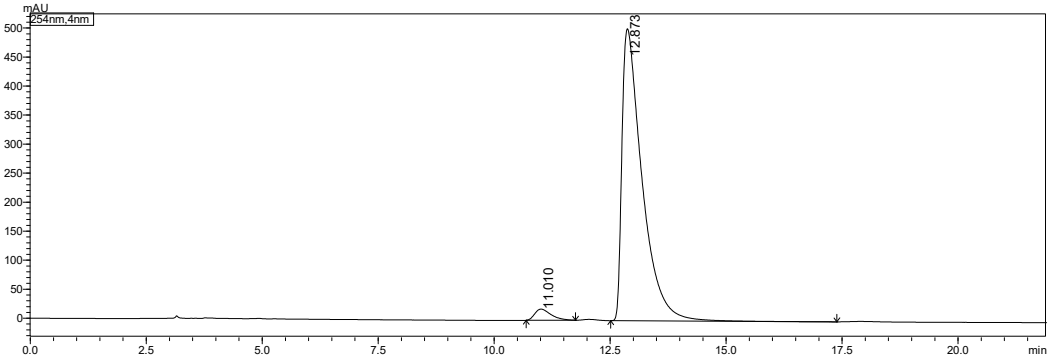
ent-**3i**

Chiral HPLC spectrum of racemic **3i**

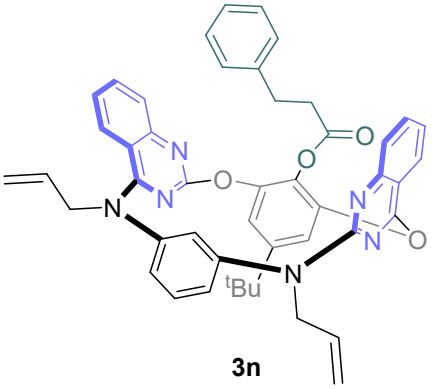


Peak	RT	Area	Height	Area%	Height%
1	10.936	6719675	225832	49.953	53.739
2	13.093	6732190	194409	50.047	46.261
Total		13451865	420241	100.000	100.000

Chiral HPLC spectrum of *ent*-**3i**

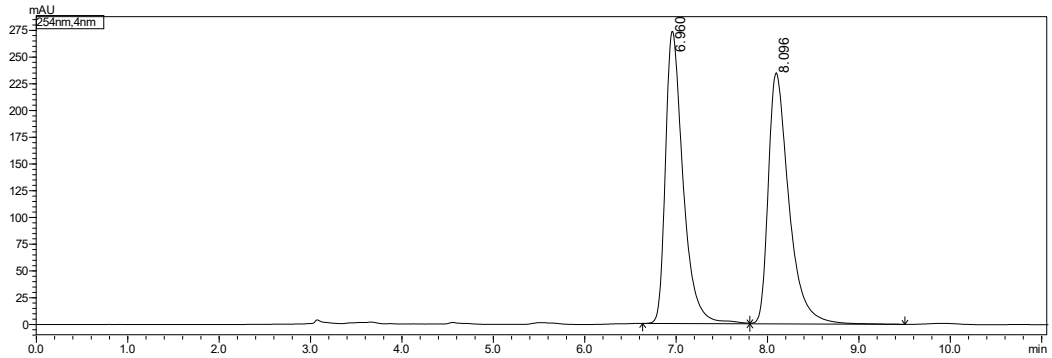


Peak	RT	Area	Height	Area%	Height%
1	11.010	466738	19270	2.980	3.688
2	12.873	15196199	503156	97.020	96.312
Total		15662937	522425	100.000	100.000



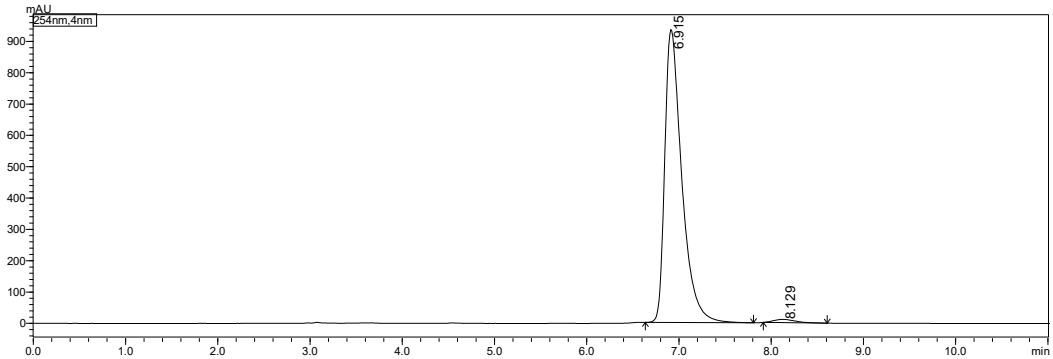
3n

Chiral HPLC spectrum of racemic **3n**

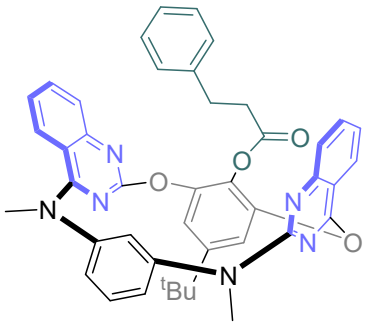


Peak	RT	Area	Height	Area%	Height%
1	6.960	3664591	273037	49.887	53.765
2	8.096	3681155	234793	50.113	46.235
Total		7345746	507830	100.000	100.000

Chiral HPLC spectrum of **3n**

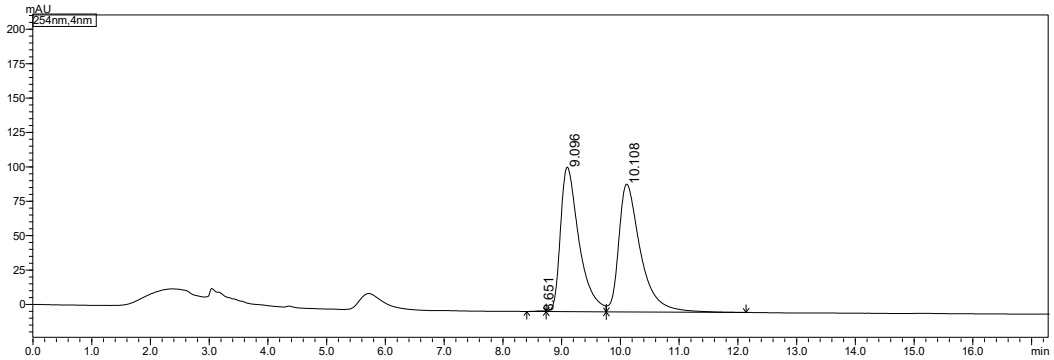


Peak	RT	Area	Height	Area%	Height%
1	6.915	12002068	935042	98.626	98.905
2	8.129	167191	10356	1.374	1.095
Total		12169259	945398	100.000	100.000



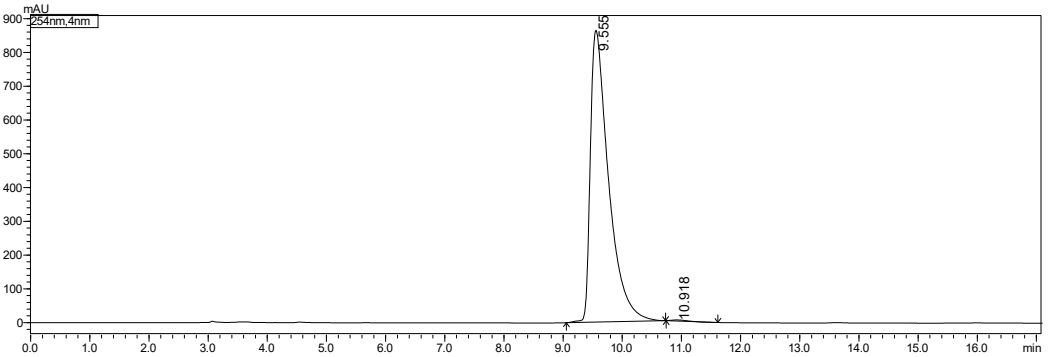
3o

Chiral HPLC spectrum of racemic **3o**

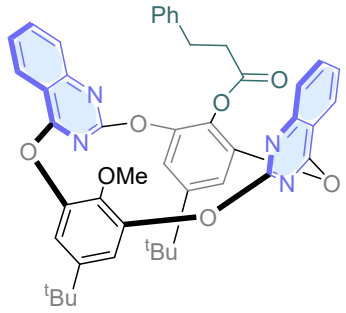


Peak	RT	Area	Height	Area%	Height%
1	8.651	5423	450	0.115	0.227
2	9.096	2311471	105030	49.001	52.956
3	10.108	2400329	92854	50.884	46.817
Total		4717222	198334	100.000	100.000

Chiral HPLC spectrum of **3o**

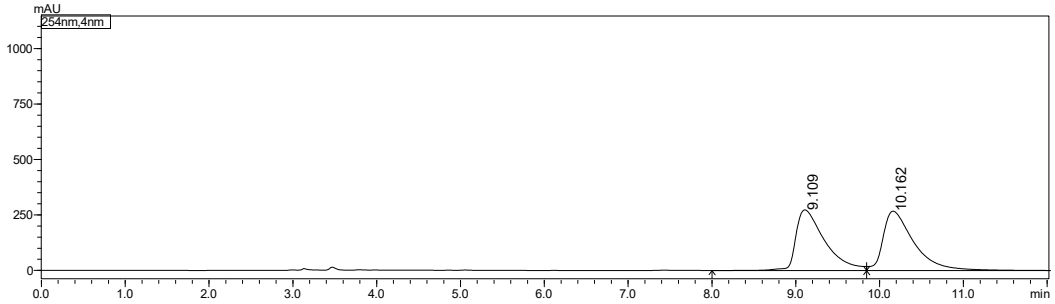


Peak	RT	Area	Height	Area%	Height%
1	9.555	18462846	863603	99.731	99.639
2	10.918	49710	3131	0.269	0.361
Total		18512555	866733	100.000	100.000



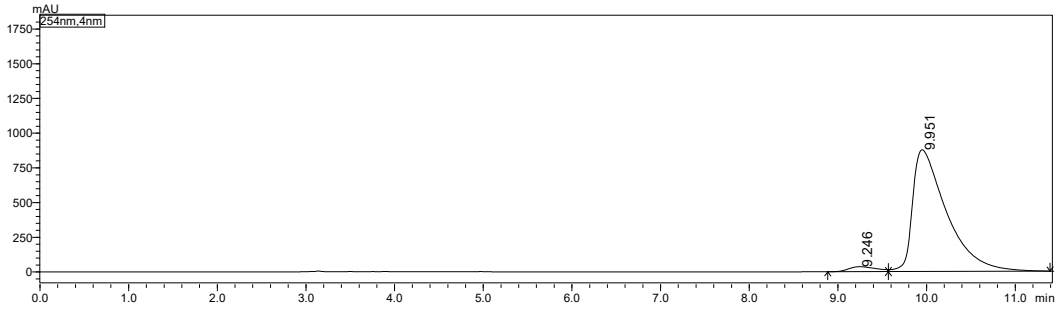
5a

Chiral HPLC spectrum of racemic **5a**



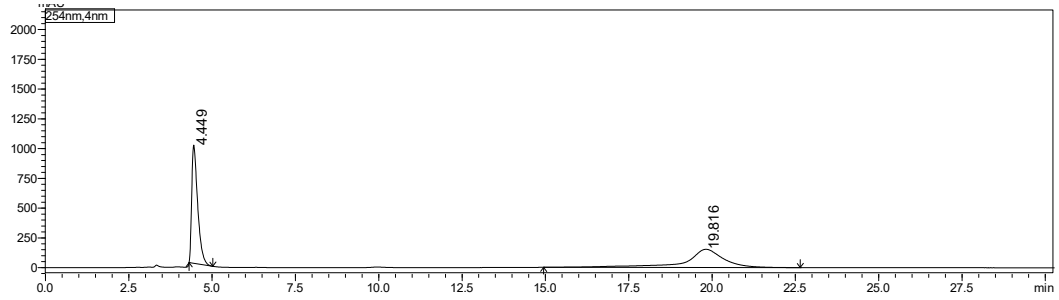
Peak	RT	Area	Height	Area%	Height%
1	9.109	6581988	273419	48.996	50.560
2	10.162	6851773	267363	51.004	49.440
Total		13433761	540782	100.000	100.000

Chiral HPLC spectrum of **5a**



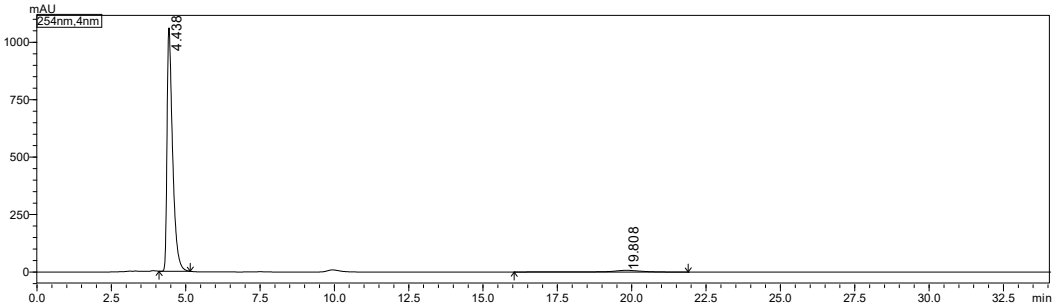
Peak	RT	Area	Height	Area%	Height%
1	9.246	779396	35641	3.213	3.906
2	9.951	23477884	876744	96.787	96.094
Total		24257281	912385	100.000	100.000

Chiral HPLC spectrum of racemic **4a**

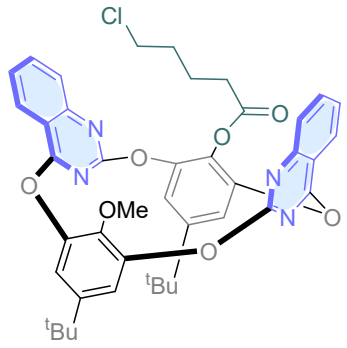


Peak	RT	Area	Height	Area%	Height%
1	4.449	12342802	993913	50.041	86.638
2	19.816	12322691	153289	49.959	13.362
Total		24665494	1147203	100.000	100.000

Chiral HPLC spectrum of *R*-**4a**

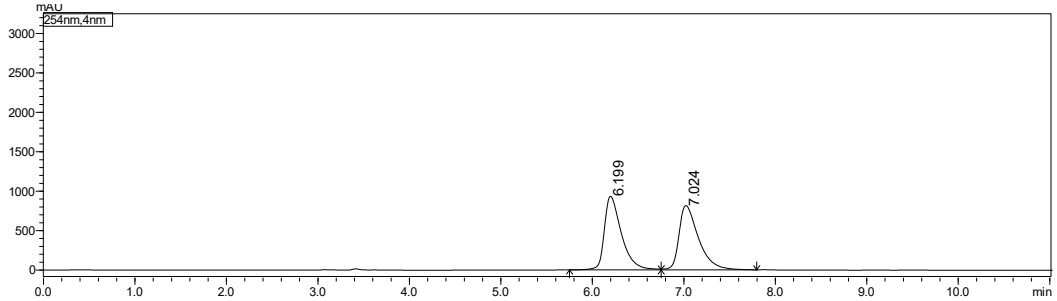


Peak	RT	Area	Height	Area%	Height%
1	4.438	13790174	1059977	96.043	99.300
2	19.808	568165	7477	3.957	0.700
Total		14358340	1067453	100.000	100.000



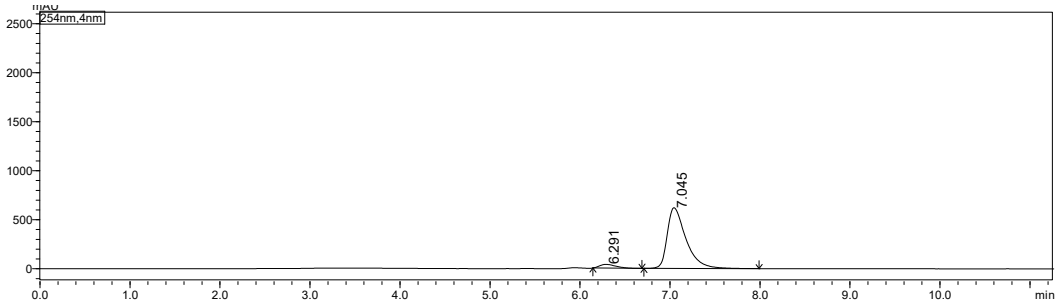
5b

Chiral HPLC spectrum of racemic **5b**



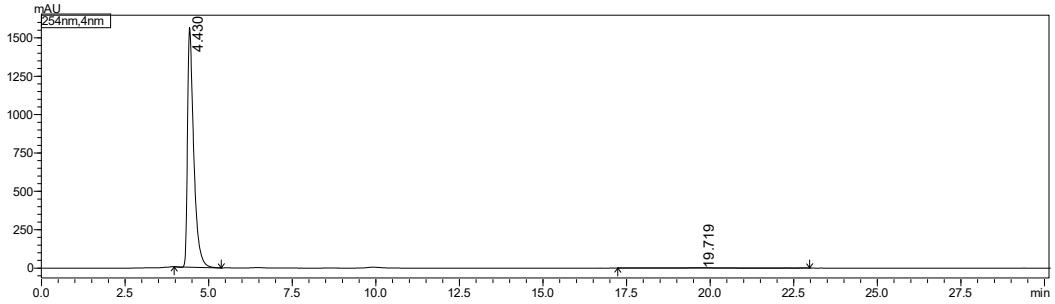
Peak	RT	Area	Height	Area%	Height%
1	6.199	12183653	933687	50.135	53.382
2	7.024	12118216	815381	49.865	46.618
Total		24301869	1749068	100.000	100.000

Chiral HPLC spectrum of **5b**

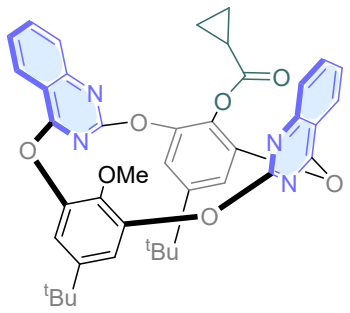


Peak	RT	Area	Height	Area%	Height%
1	6.291	470767	37810	4.988	5.753
2	7.045	8966927	619411	95.012	94.247
Total		9437694	657220	100.000	100.000

Chiral HPLC spectrum of *R*-**4a**

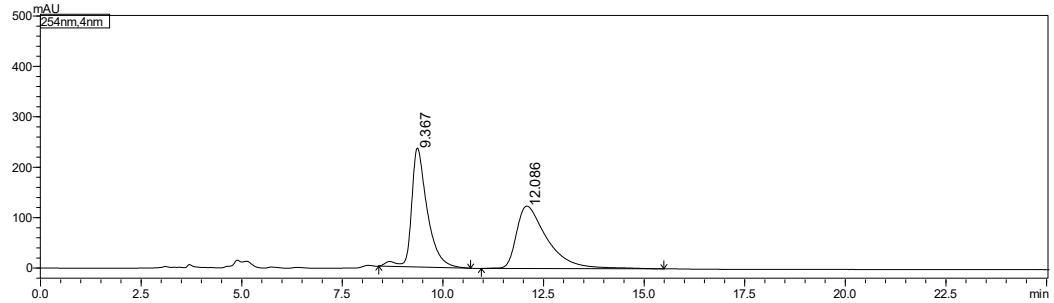


Peak	RT	Area	Height	Area%	Height%
1	4.430	20130641	1561564	99.437	99.856
2	19.719	113989	2253	0.563	0.144
Total		20244630	1563817	100.000	100.000



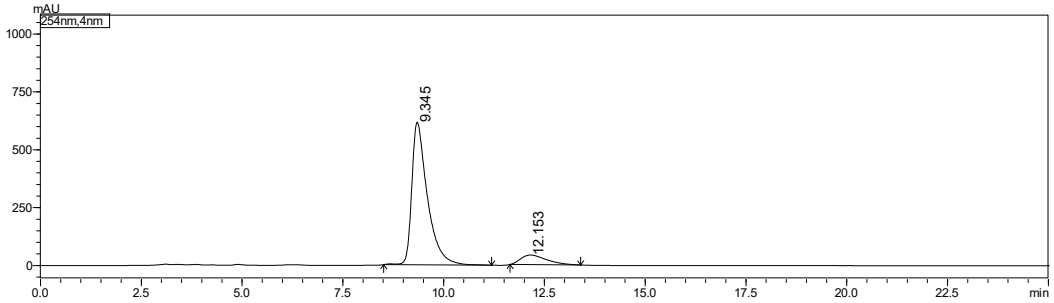
5c

Chiral HPLC spectrum of racemic **5c**



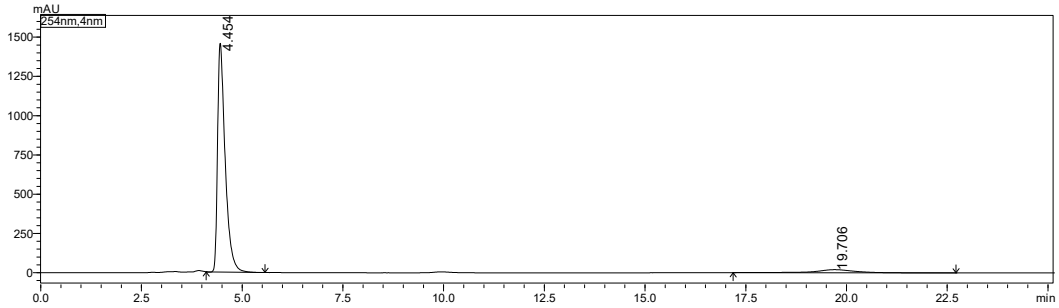
Peak	RT	Area	Height	Area%	Height%
1	9.367	6453345	236124	49.406	65.573
2	12.086	6608561	123970	50.594	34.427
Total		13061906	360094	100.000	100.000

Chiral HPLC spectrum of **5c**

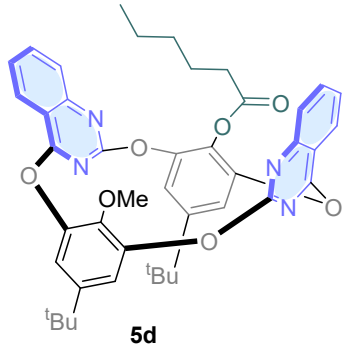


Peak	RT	Area	Height	Area%	Height%
1	9.345	16614564	616363	89.955	93.698
2	12.153	1855248	41455	10.045	6.302
Total		18469812	657818	100.000	100.000

Chiral HPLC spectrum of *R*-**4a**

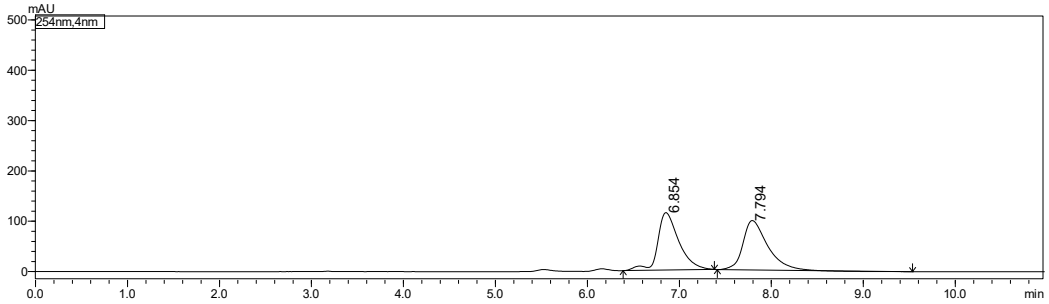


Peak	RT	Area	Height	Area%	Height%
1	4.454	19173564	1456228	93.625	98.671
2	19.706	1305620	19612	6.375	1.329
Total		20479184	1475840	100.000	100.000



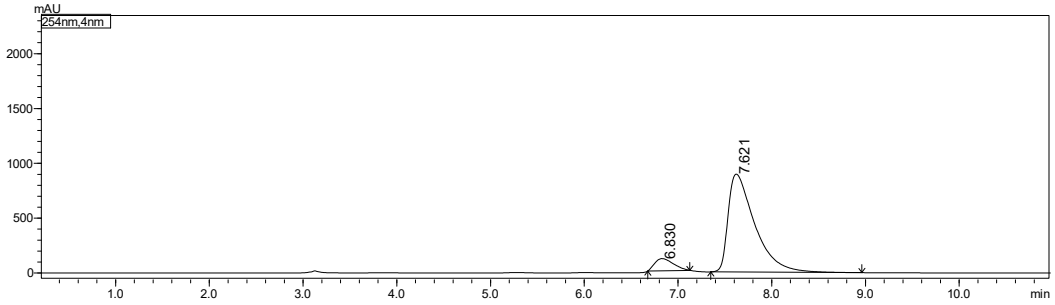
5d

Chiral HPLC spectrum of racemic **5d**



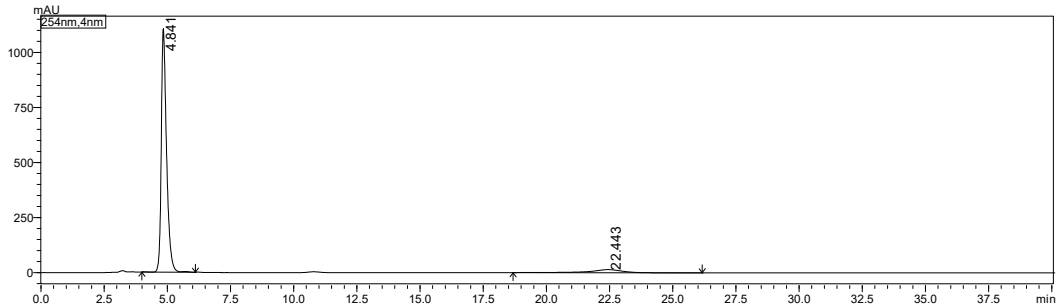
Peak	RT	Area	Height	Area%	Height%
1	6.854	1827621	114131	50.126	53.749
2	7.794	1818425	98211	49.874	46.251
Total		3646046	212341	100.000	100.000

Chiral HPLC spectrum of **5d**

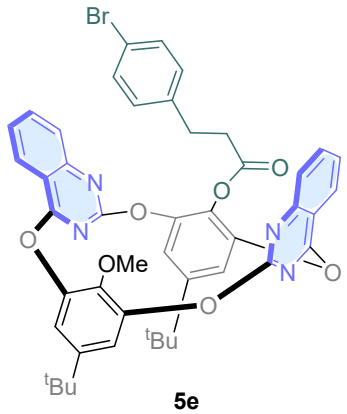


Peak	RT	Area	Height	Area%	Height%
1	6.830	1529171	110495	7.964	11.018
2	7.621	17672008	892366	92.036	88.982
Total		19201179	1002860	100.000	100.000

Chiral HPLC spectrum of *R*-**4a**

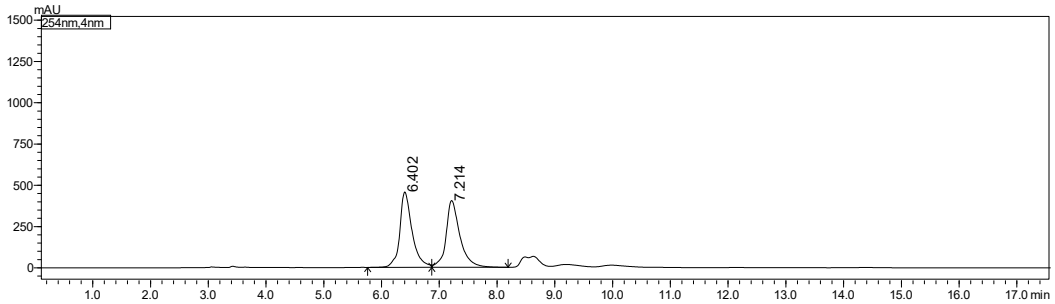


Peak	RT	Area	Height	Area%	Height%
1	4.841	16065510	1105930	92.774	98.736
2	22.443	1251221	14162	7.226	1.264
Total		17316731	1120092	100.000	100.000



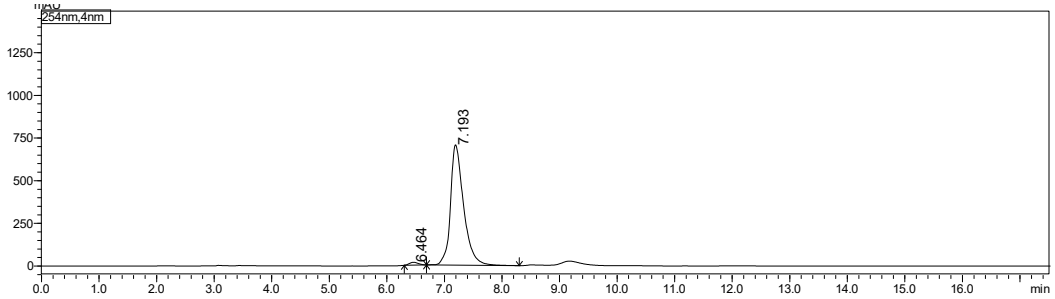
5e

Chiral HPLC spectrum of racemic **5e**



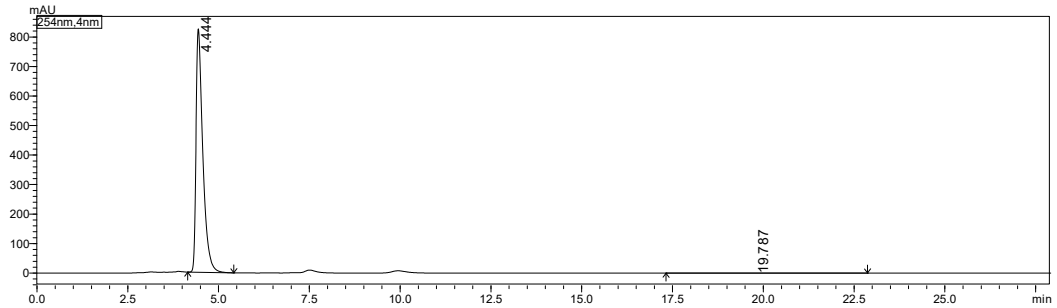
Peak	RT	Area	Height	Area%	Height%
1	6.402	6789301	456531	50.080	53.031
2	7.214	6767671	404341	49.920	46.969
Total		13556972	860871	100.000	100.000

Chiral HPLC spectrum of **5e**

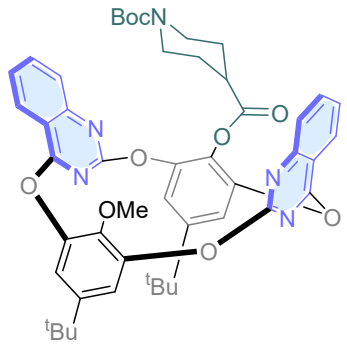


Peak	RT	Area	Height	Area%	Height%
1	6.464	178117	16449	1.564	2.279
2	7.193	11207244	705242	98.436	97.721
Total		11385361	721691	100.000	100.000

Chiral HPLC spectrum of *R*-**4a**

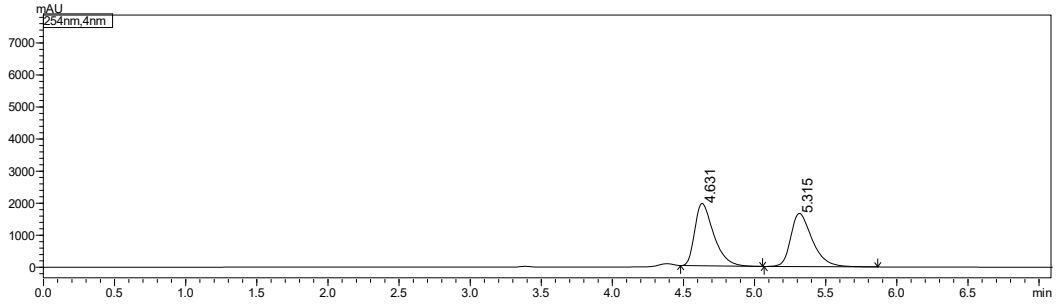


Peak	RT	Area	Height	Area%	Height%
1	4.444	10773003	825174	99.848	99.960
2	19.787	16425	334	0.152	0.040
Total		10789429	825509	100.000	100.000



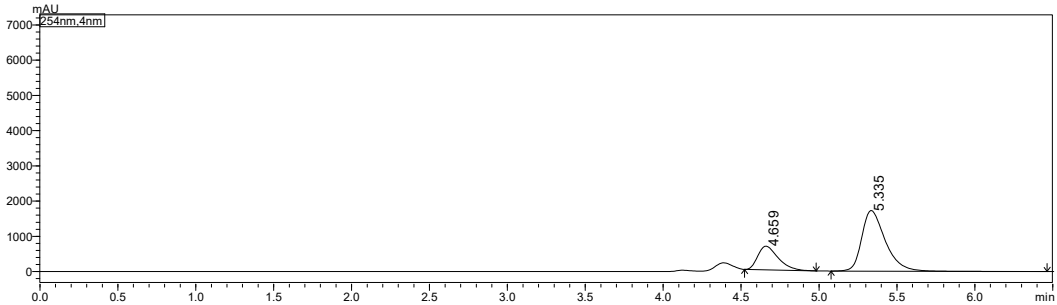
5f

Chiral HPLC spectrum of racemic **5f**



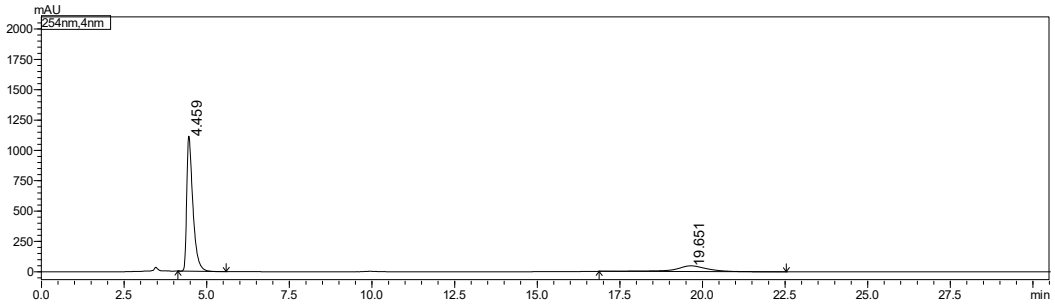
Peak	RT	Area	Height	Area%	Height%
1	4.631	17995089	1950829	50.711	53.985
2	5.315	17490270	1662843	49.289	46.015
Total		35485359	3613672	100.000	100.000

Chiral HPLC spectrum of **5f**

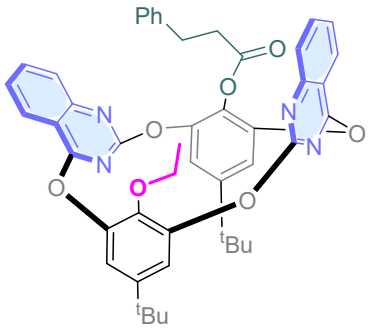


Peak	RT	Area	Height	Area%	Height%
1	4.659	6108664	673117	25.317	28.104
2	5.335	18019997	1722014	74.683	71.896
Total		24128660	2395131	100.000	100.000

Chiral HPLC spectrum of *R*-**4a**

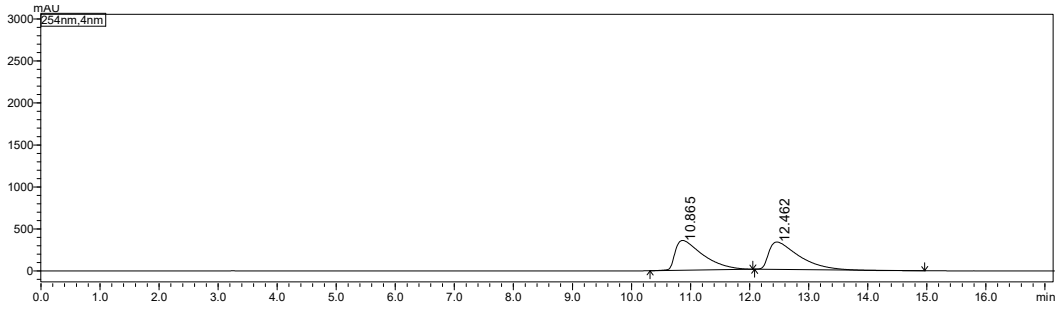


Peak	RT	Area	Height	Area%	Height%
1	4.459	14416193	1112836	81.908	95.921
2	19.651	3184288	47324	18.092	4.079
Total		17600480	1160160	100.000	100.000



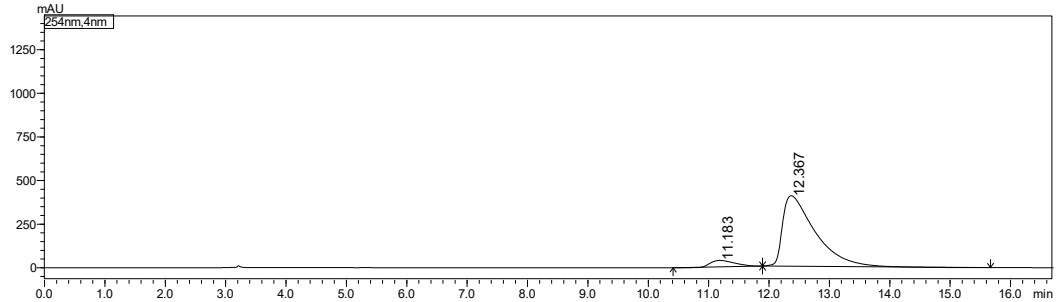
5g

Chiral HPLC spectrum of racemic **5g**



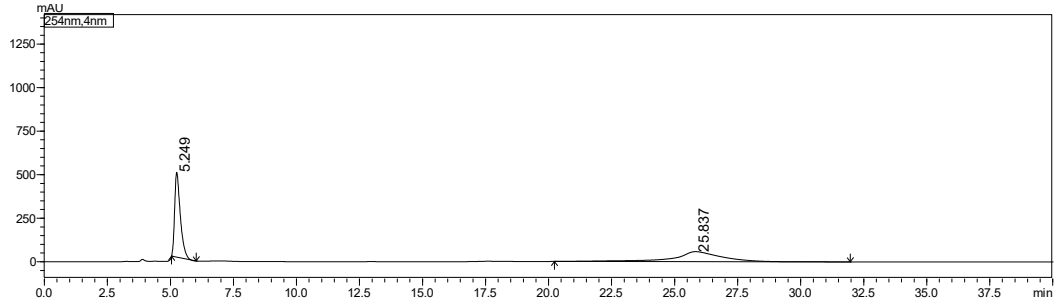
Peak	RT	Area	Height	Area%	Height%
1	10.865	11578088	354402	50.311	52.170
2	12.462	11434761	324914	49.689	47.830
Total		23012849	679316	100.000	100.000

Chiral HPLC spectrum of **5g**



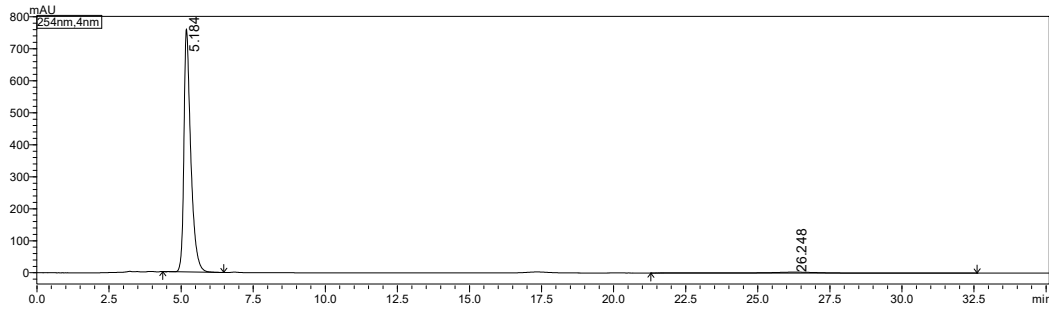
Peak	RT	Area	Height	Area%	Height%
1	11.183	978862	36690	6.103	8.322
2	12.367	15059384	404199	93.897	91.678
Total		16038246	440889	100.000	100.000

Chiral HPLC spectrum of racemic **4b**

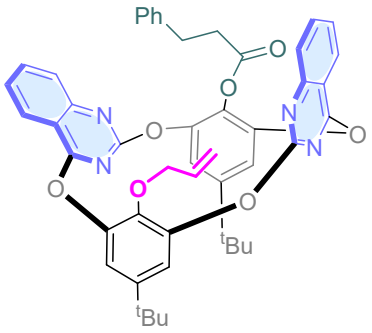


Peak	RT	Area	Height	Area%	Height%
1	5.249	7571283	486541	50.367	89.459
2	25.837	7460906	57330	49.633	10.541
Total		15032188	543871	100.000	100.000

Chiral HPLC spectrum of *R*-**4b**

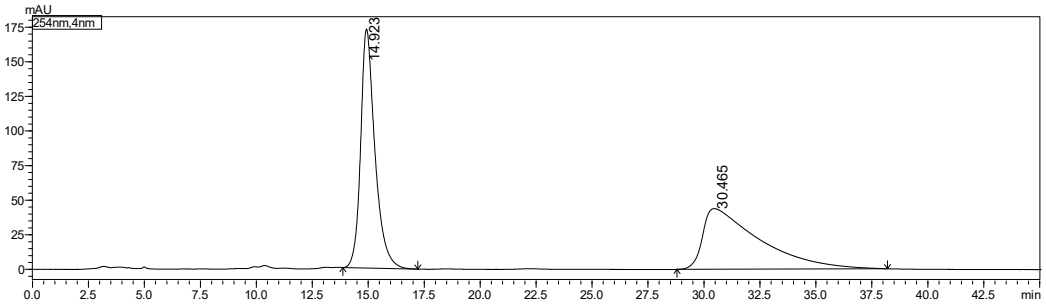


Peak	RT	Area	Height	Area%	Height%
1	5.184	12525244	759741	97.428	99.626
2	26.248	330690	2854	2.572	0.374
Total		12855934	762595	100.000	100.000



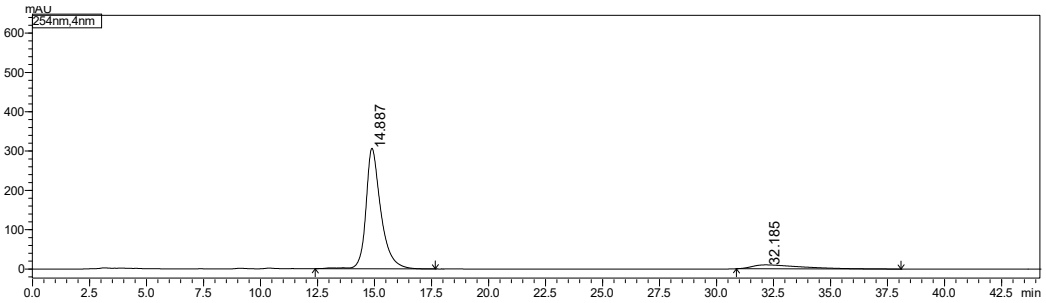
5h

Chiral HPLC spectrum of racemic **5h**



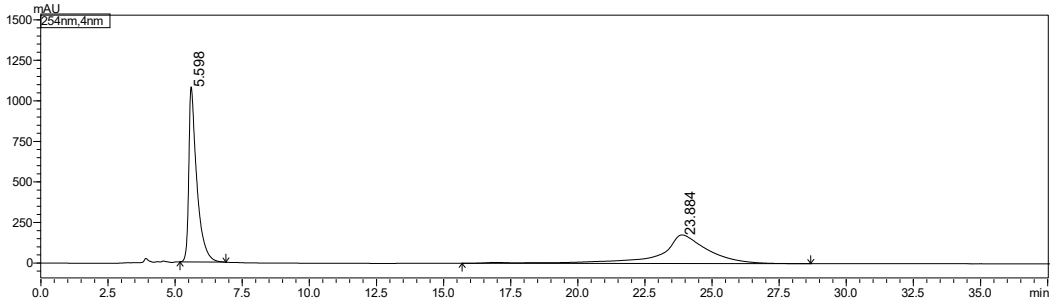
Peak	RT	Area	Height	Area%	Height%
1	14.923	7676098	172725	49.947	79.768
2	30.465	7692512	43809	50.053	20.232
Total		15368610	216534	100.000	100.000

Chiral HPLC spectrum of **5h**



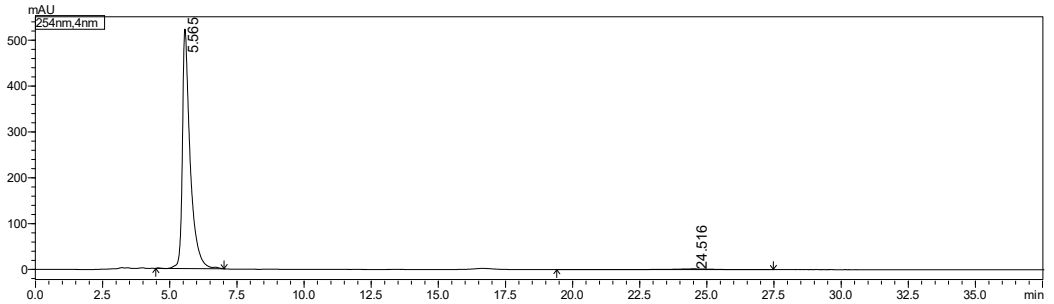
Peak	RT	Area	Height	Area%	Height%
1	14.887	13969124	306456	90.353	96.857
2	32.185	1491446	9944	9.647	3.143
Total		15460569	316400	100.000	100.000

Chiral HPLC spectrum of racemic **4c**

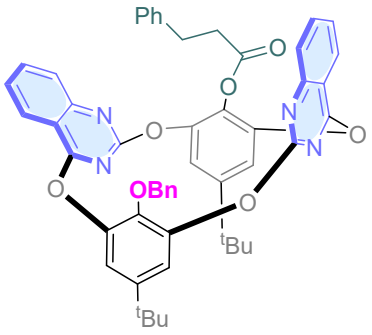


Peak	RT	Area	Height	Area%	Height%
1	5.598	22405928	1079629	50.494	85.948
2	23.884	21967118	176508	49.506	14.052
Total		44373046	1256138	100.000	100.000

Chiral HPLC spectrum of *R*-**4c**

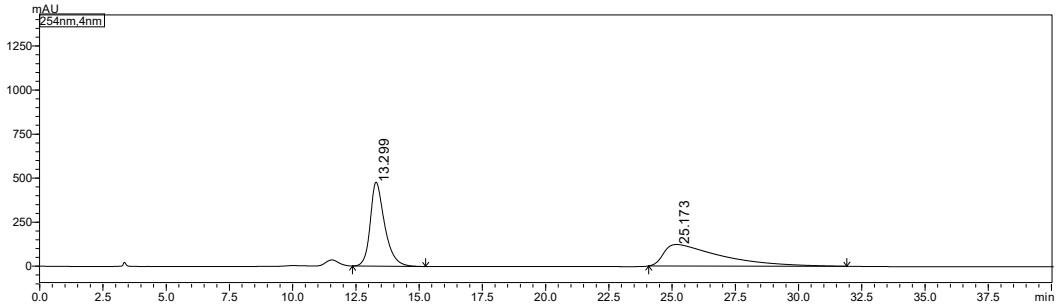


Peak	RT	Area	Height	Area%	Height%
1	5.565	10565976	522643	98.297	99.690
2	24.516	183025	1628	1.703	0.310
Total		10749001	524270	100.000	100.000



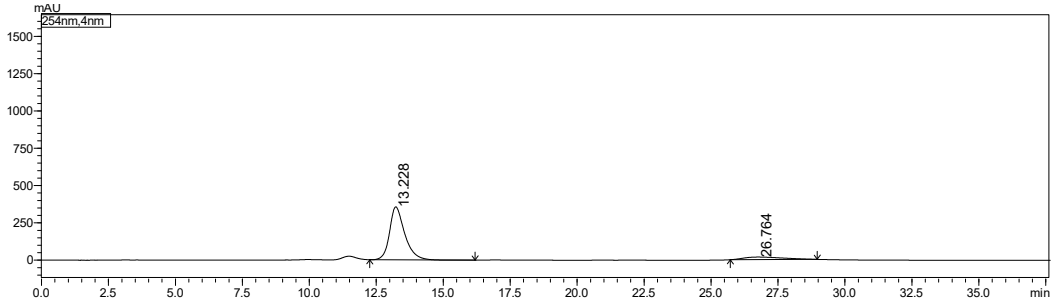
5i

Chiral HPLC spectrum of racemic **5i**



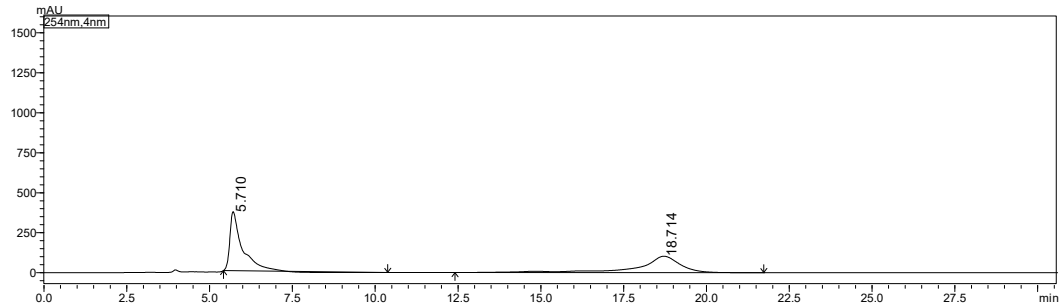
Peak	RT	Area	Height	Area%	Height%
1	13.299	18913213	476989	50.028	79.646
2	25.173	18892105	121895	49.972	20.354
Total		37805318	598884	100.000	100.000

Chiral HPLC spectrum of **5i**



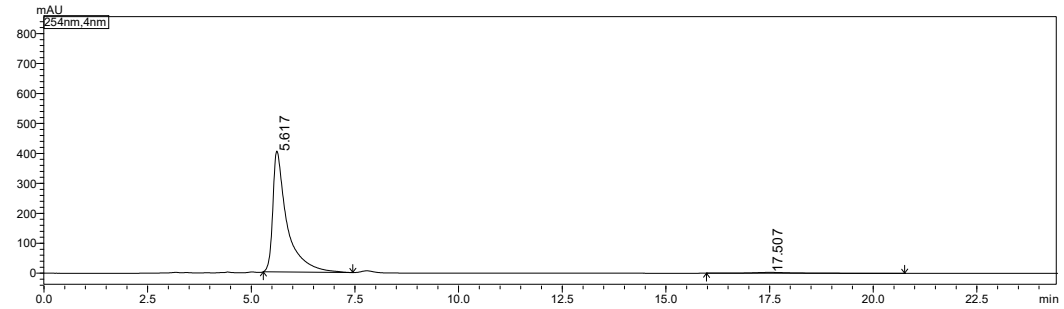
Peak	RT	Area	Height	Area%	Height%
1	13.228	13977479	355359	88.869	95.416
2	26.764	1750668	17072	11.131	4.584
Total		15728147	372430	100.000	100.000

Chiral HPLC spectrum of racemic **4d**

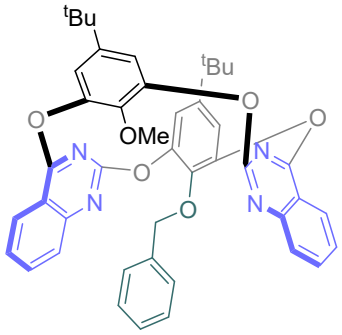


Peak	RT	Area	Height	Area%	Height%
1	5.710	9268012	369220	50.677	78.288
2	18.714	9020259	102398	49.323	21.712
Total		18288271	471618	100.000	100.000

Chiral HPLC spectrum of *R*-**4d**

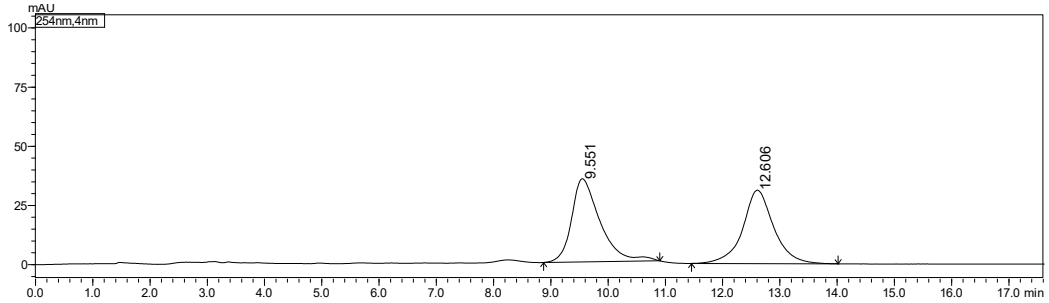


Peak	RT	Area	Height	Area%	Height%
1	5.617	9615244	403018	98.046	99.313
2	17.507	191676	2788	1.954	0.687
Total		9806920	405806	100.000	100.000



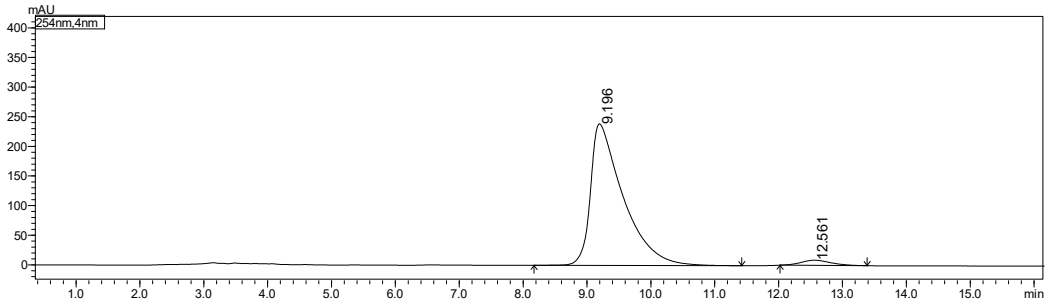
6a

Chiral HPLC spectrum of racemic **6a**

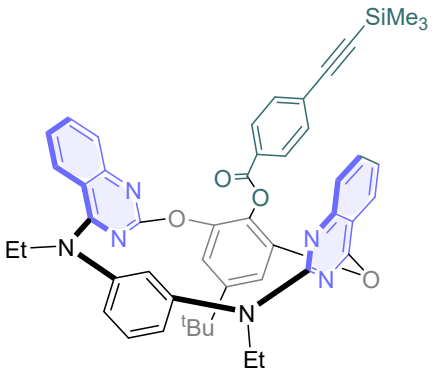


Peak	RT	Area	Height	Area%	Height%
1	9.551	1212841	35098	50.898	53.091
2	12.606	1170054	31012	49.102	46.909
Total		2382895	66111	100.000	100.000

Chiral HPLC spectrum of **6a**

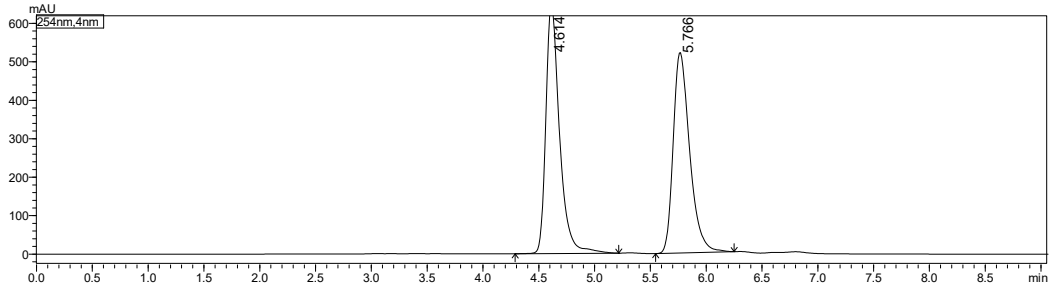


Peak	RT	Area	Height	Area%	Height%
1	9.196	8505744	238976	96.760	96.479
2	12.561	284818	8722	3.240	3.521
Total		8790563	247698	100.000	100.000



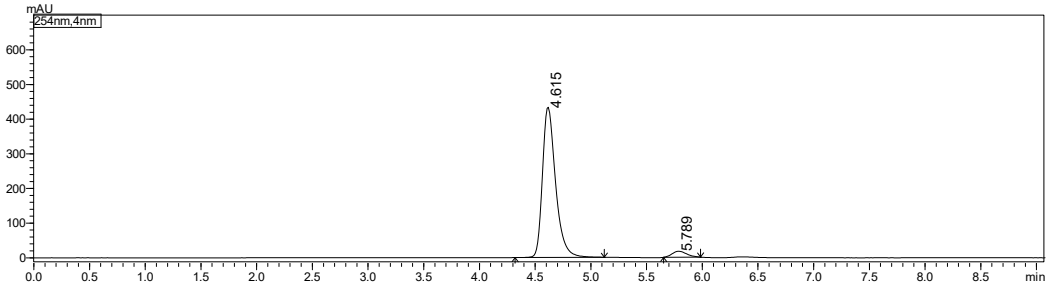
6b

Chiral HPLC spectrum of racemic **6b**

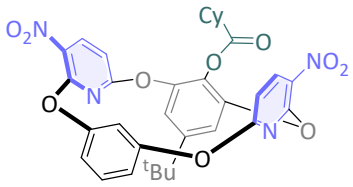


Peak	RT	Area	Height	Area%	Height%
1	4.614	5565042	651205	50.975	55.557
2	5.766	5352259	520929	49.025	44.443
Total		10917302	1172135	100.000	100.000

Chiral HPLC spectrum of **6b**

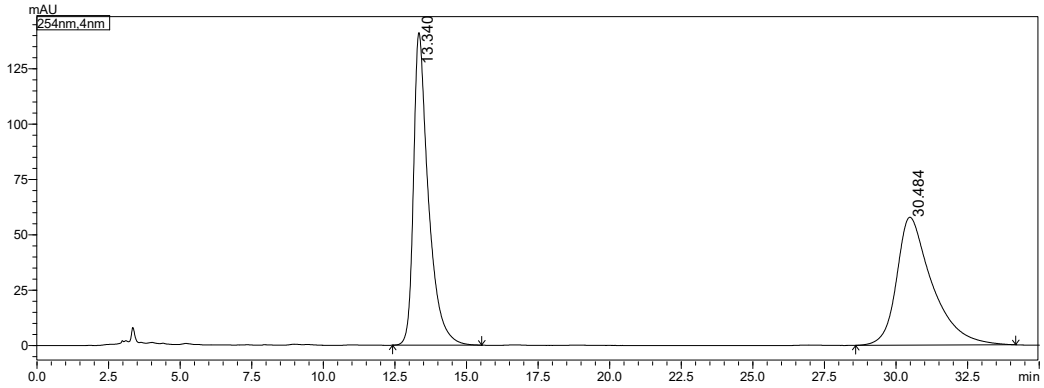


Peak	RT	Area	Height	Area%	Height%
1	4.615	3535956	433246	95.711	96.162
2	5.789	158464	17291	4.289	3.838
Total		3694419	450536	100.000	100.000



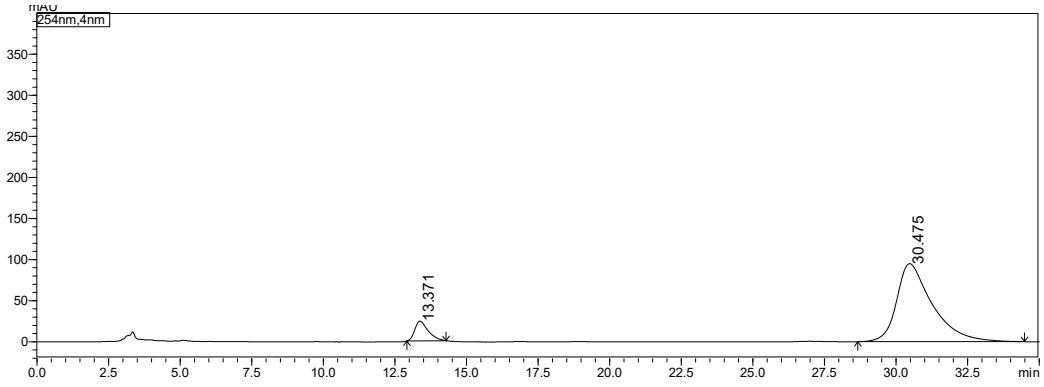
6c

Chiral HPLC spectrum of racemic **6c**



Peak	RT	Area	Height	Area%	Height%
1	13.340	5091383	141289	50.574	70.973
2	30.484	4975828	57785	49.426	29.027
Total		10067211	199073	100.000	100.000

Chiral HPLC spectrum of **6c**



Peak	RT	Area	Height	Area%	Height%
1	13.371	777829	24027	8.648	20.186
2	30.475	8216441	94999	91.352	79.814
Total		8994270	119026	100.000	100.000