

Supporting Information

Carbene-Catalyzed [2 + 2] Cycloaddition of Chloroaldehydes and Isatin-Derived Ketimines for Enantioselective Synthesis of Spirocyclic β -Lactams

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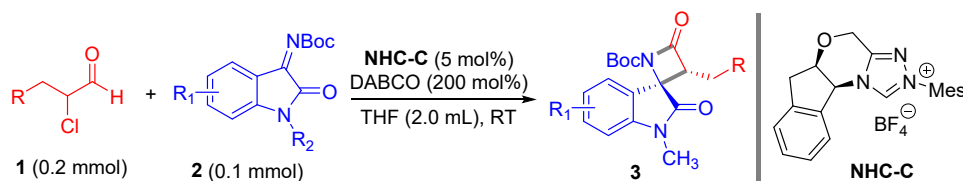
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I. General Information

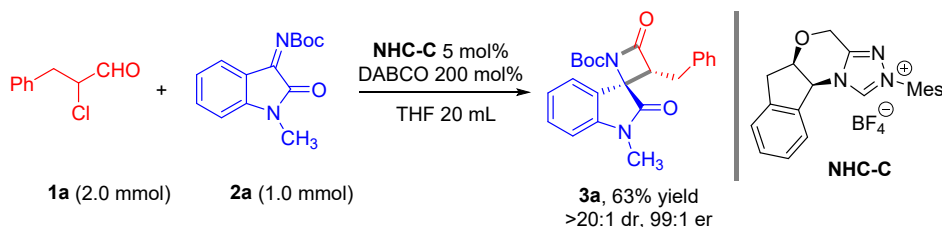
Commercially available materials and extra dry solvents (e.g., THF, dioxane, MTBE, EtOAc) purchased from *Bidepharm* and *Energy Chemical* were used without additional purification. Proton nuclear magnetic resonance (^1H NMR) spectra were recorded on a Bruker ASCEND (400 MHz and 600 MHz) spectrometer. Chemical shifts were recorded in parts per million (ppm, δ) relative to tetramethylsilane (δ 0.00) and chloroform (δ = 7.26 ppm). ^1H NMR splitting patterns are designated as singlet (s), doublet (d), triplet (t), quartet (q), dd (doublet of doublets); m (multiplets), and etc. All first-order splitting patterns were assigned on the basis of the appearance of the multiplet. Splitting patterns that could not be easily interpreted are designated as multiplet (m) or broad (br). Carbon nuclear magnetic resonance (^{13}C NMR) spectra were recorded on a Bruker ASCEND (101 MHz) spectrometer. Chemical shifts were recorded in parts per million (ppm, δ) relative to tetramethylsilane (δ 0.00) and chloroform (δ = 77.16 ppm). High resolution mass spectral analysis (HRMS) was performed on a Waters G2-XSQTof mass spectrometer. The determination of enantiomeric excess was performed via chiral HPLC analysis using Shimadzu LC-20AD and Agilent 1260 workstation. Chiralcel brand chiral columns from Daicel Chemical Industries were used with models IA and IG in 4.6 x 250 mm size. Optical rotations were measured on an Insmark IP-digi Polarimeter in a 1 dm cuvette. The concentration (c) is given in g/100 mL. Analytical thin-layer chromatography (TLC) was carried out on pre-coated silica gel plate (0.2 mm thickness). Visualization was performed using a UV lamp.

II. General procedure for the catalytic synthesis of products.



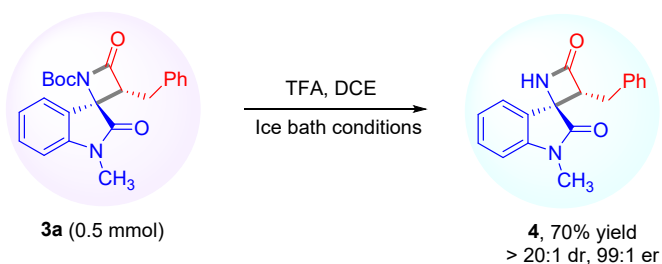
To a 10 mL flame-dry Schlenk reaction tube equipped with a magnetic stir bar, was added isatin-derived ketimines **2** (0.1 mmol, 1.0 equiv.), NHC-C (0.005 mmol, 0.05 equiv.) and DABCO (0.2 mmol). The Schlenk tube was sealed with a septum, evacuated and refilled with N₂ (5 cycles). α -chloro aldehydes **1** (0.2 mmol, 2.0 equiv.) and THF (2.0 mL) was then added via syringe and the reaction mixture was allowed to stir for 12 hours at room temperature (25-30 °C). After completion of the reaction, monitored by TLC plate, the reaction mixture was concentrated under reduced pressure and the residue was subjected to column chromatography directly using PE/EtOAc (most use 6/1) as eluent to afford the desired product **3**.

III. Scale-up Synthesis of 3a.



To a 100 mL flame-dry Schlenk reaction tube equipped with a magnetic stir bar, was added isatin-derived ketimine **2b** (1.0 mmol, 1.0 equiv.), NHC-C (0.05 mmol, 0.05 equiv.) and DABCO (2.0 mmol, 2.0 equiv.). The Schlenk tube was sealed with a septum, evacuated and refilled with N₂ (5 cycles). α -chloro aldehyde **1a** (2.0 mmol, 2.0 equiv.) and THF (20.0 mL) was then added via syringe and the reaction mixture was allowed to stir for 24 hours at room temperature. After completion of the reaction, monitored by TLC plate, the reaction mixture was concentrated under reduced pressure and the residue was subjected to column chromatography directly using PE/EA as eluent to afford the desired product **3a**.

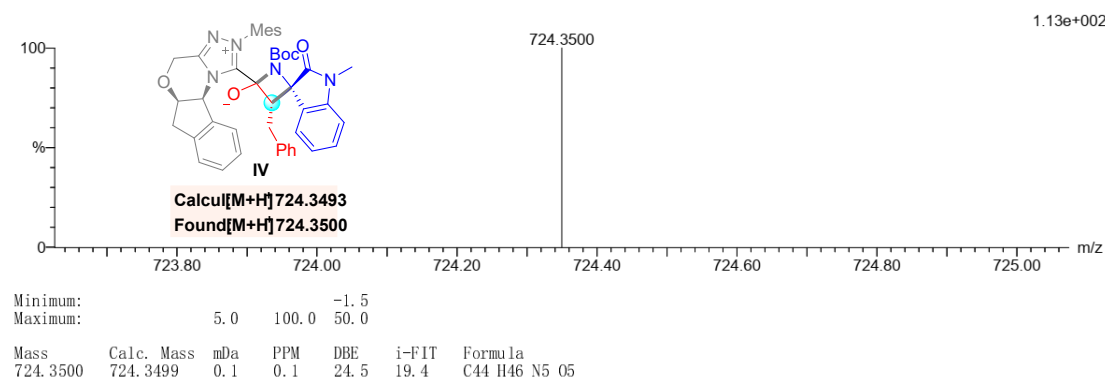
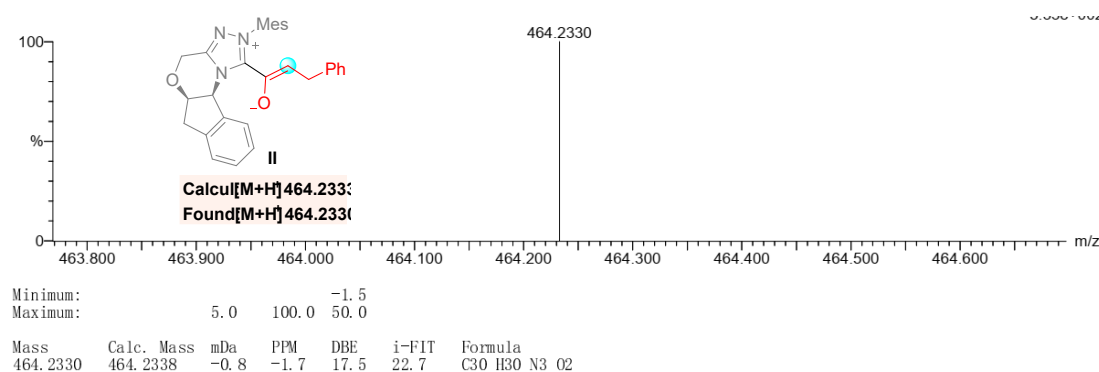
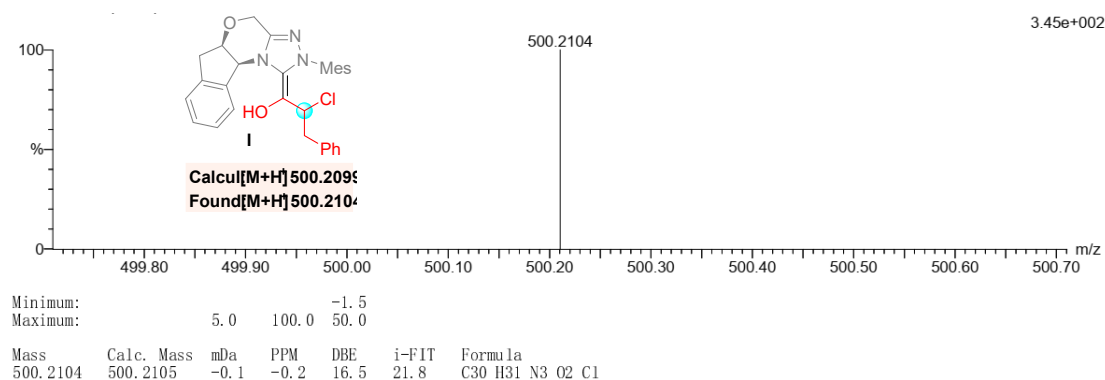
IV. Transformation of **3a**



To a stirred solution of **3a** (196 mg, 0.5 mmol, 99:1 er) in DCE (15 mL) was carefully added TFA (2.5 mL) an ice-water bath and the reaction mixture was stirred at ice-water bath condition, and the reaction was stirred to completion under the same conditions (monitored by TLC). The reaction mixture was quenched by saturated NaHCO_3 aq. (20 mL). The aqueous phase was extracted with DCM, and the combined organic phase, dried over Na_2SO_4 . Filtration and removal of solvent under reduced pressure gave a residue, which was purified by column chromatography using hexane/EtOAc = 2/1 as eluent to afford the desired product **4** (137.4 mg, 70% yield, >20:1 dr, 99:1 er).

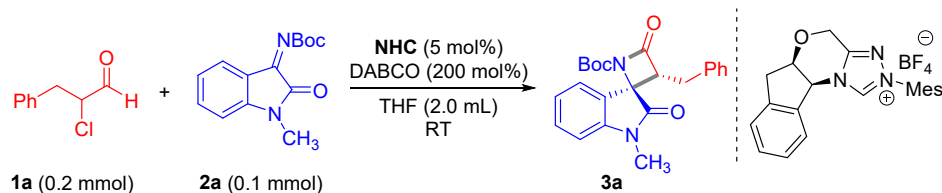
V. General procedure for the HRMS detection of intermediates

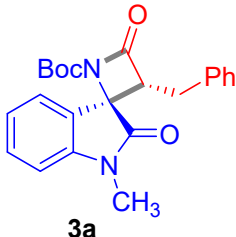
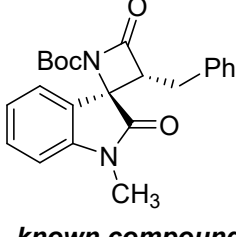
To a 10 mL flame-dry Schlenk reaction tube equipped with a magnetic stir bar, was added isatin-derived ketimines **2** (0.1 mmol, 1.0 equiv.), NHC-C (0.005 mmol, 0.05 equiv.) and DABCO (0.2 mmol). The Schlenk tube was sealed with a septum, evacuated and refilled with N₂ (5 cycles). α -Chloro aldehydes **1** (0.2 mmol, 2.0 equiv.) and THF (2.0 mL) were then added via syringe and the reaction mixture was allowed to stir at room temperature (25-30 °C) for a specified time. After the reaction proceeded for 2 hours, the crude reaction mixture was dissolved in solvent to prepare a test solution of suitable concentration. The test solution was then analyzed by HRMS.



VI. Determination of the absolute configuration of the products 3

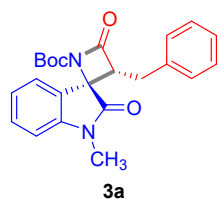
The absolute configuration of the **3a** was determined by correlation with a known compound.^[1]



 3a ¹H NMR (400 MHz, CDCl₃) δ 7.44 – 7.36 (m, 2H), 7.17 (t, <i>J</i> = 7.6 Hz, 1H), 7.09 – 7.03 (m, 3H), 6.77 (d, <i>J</i> = 7.8 Hz, 1H), 6.73 – 6.68 (m, 2H), 3.94 (dd, <i>J</i> = 10.1, 6.3 Hz, 1H), 3.23 (dd, <i>J</i> = 14.8, 6.2 Hz, 1H), 3.10 (s, 3H), 2.81 (dd, <i>J</i> = 14.8, 10.1 Hz, 1H), 1.28 (s, 9H). ¹³C NMR (101 MHz, CDCl₃) δ 173.3, 165.5, 145.9, 144.6, 136.6, 130.6, 128.4, 128.1, 126.5, 124.4, 123.0, 122.8, 108.7, 83.9, 62.7, 60.0, 30.6, 27.7, 26.5. $[\alpha]_D^{25} = -18.7$ (<i>c</i> = 0.5 in CHCl₃).	 known compound ¹H NMR (400 MHz, CDCl₃) δ 7.42-7.37 (m, 2H), 7.16 (t, <i>J</i> = 8.0 Hz, 1H), 7.07-7.05 (m, 3H), 6.76 (d, <i>J</i> = 7.6 Hz, 1H), 6.72-6.70 (m, 2H), 3.94 (dd, <i>J</i> = 10.0 Hz, <i>J</i> = 6.0 Hz, 1H), 3.27-3.21 (m, 1H), 3.10 (s, 3H), 2.81 (dd, <i>J</i> = 14.8 Hz, <i>J</i> = 10.0 Hz, 1H), 1.28 (s, 9H); ¹³C NMR (100 MHz, CDCl₃) δ 173.3, 165.4, 146.0, 144.6, 136.6, 130.5, 128.3, 128.1, 126.5, 124.4, 123.1, 122.7, 108.6, 83.9, 62.7, 60.0, 30.6, 27.7, 26.4; $[\alpha]_D^{20} = -40.8$ (<i>c</i> = 0.25 in CHCl₃).
According to the optical rotations of our product and the known compound, the absolute configuration of product could be confirmed.	

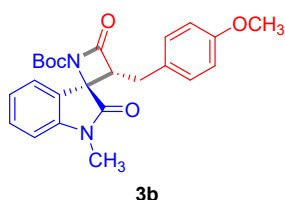
(1) Xu, J.; Yuan, S.; Peng, J.; Miao, M.; Cheng, Z.; Ren, H. Enantioselective [2+2] Annulation of Simple Aldehydes with Isatin Derived Ketimines via Oxidative N-Heterocyclic Carbene Catalysis. *Chem. Commun.* **2017**, 53, 3430-3433.

VII. Characterization of products



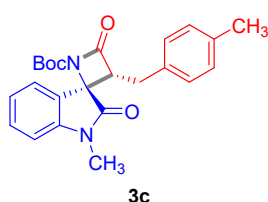
tert-butyl (2R,3R)-3-benzyl-1'-methyl-2',4-dioxospiro [azetidine-2,3'-indoline]-1-carboxylate (3a):

Colorless paste, yield: 29.1 mg (74%); >20:1 dr; $[\alpha]^{25}_D = -18.7$ ($c = 0.5$ in CHCl_3); **¹H NMR** (400 MHz, CDCl_3) δ 7.45-7.35 (m, 2H), 7.16 (td, $J = 7.6, 1.0$ Hz, 1H), 7.08-7.03 (m, 3H), 6.76 (d, $J = 7.9$ Hz, 1H), 6.73 – 6.68 (m, 2H), 3.94 (dd, $J = 10.1, 6.3$ Hz, 1H), 3.23 (dd, $J = 14.8, 6.2$ Hz, 1H), 3.10 (s, 3H), 2.81 (dd, $J = 14.8, 10.1$ Hz, 1H), 1.28 (s, 9H). **¹³C NMR** (101 MHz, CDCl_3) δ 173.3, 165.5, 145.9, 144.6, 136.6, 130.6, 128.4, 128.1, 126.5, 124.4, 123.0, 122.8, 108.7, 83.9, 62.7, 60.0, 30.6, 27.7, 26.5. **HRMS** (ESI-TOF) m/z : $[\text{M}+\text{Na}]^+$ calcd. for $\text{C}_{23}\text{H}_{24}\text{N}_2\text{NaO}_4^+$ 415.1628, found 415.1636; **HPLC** analysis: 99:1 er, (CHIRALPAK IA column, 254 nm, 80:20 hexanes/*i*PrOH, 0.8 mL/min), R_t (minor) = 24.9 min, R_t (major) = 33.9 min.



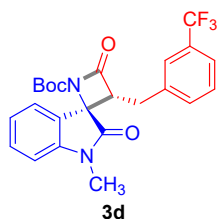
tert-butyl (2R,3R)-3-(4-methoxybenzyl)-1'-methyl-2',4-dioxospiro[azetidine-2,3'-indoline]-1-carboxylate (3b):

Colorless paste, yield: 33.2 mg (79%); >20:1 dr; $[\alpha]^{25}_D = -7.9$ ($c = 0.3$ in CHCl_3); **¹H NMR** (400 MHz, CDCl_3) δ 7.44 – 7.36 (m, 2H), 7.17 (t, $J = 7.6$ Hz, 1H), 6.79 (d, $J = 7.8$ Hz, 1H), 6.67 – 6.57 (m, 4H), 3.88 (dd, $J = 9.9, 6.4$ Hz, 1H), 3.71 (s, 3H), 3.16 (dd, $J = 14.8, 6.4$ Hz, 1H), 3.12 (s, 3H), 2.75 (dd, $J = 14.8, 9.9$ Hz, 1H), 1.27 (s, 9H). **¹³C NMR** (101 MHz, CDCl_3) δ 173.4, 165.6, 158.1, 145.9, 144.6, 130.6, 129.2, 128.6, 124.4, 123.1, 122.8, 113.8, 108.7, 83.9, 62.7, 60.3, 55.2, 29.9, 27.7, 26.5. **HRMS** (ESI-TOF) m/z : $[\text{M}+\text{Na}]^+$ calcd. for $\text{C}_{24}\text{H}_{26}\text{N}_2\text{NaO}_5^+$ 445.1734, found 445.1739; **HPLC** analysis: 98:2 er, (CHIRALPAK IA column, 254 nm, 80:20 hexanes/*i*PrOH, 0.6 mL/min), R_t (minor) = 25.6 min, R_t (major) = 30.7 min.



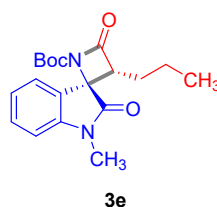
tert-butyl (2R,3R)-1'-methyl-3-(4-methylbenzyl)-2',4-dioxospiro[azetidine-2,3'-indoline]-1-carboxylate (3c):

Colorless paste, yield: 28.9 mg (71%); >20:1 dr; $[\alpha]^{25}_D = -17.4$ ($c = 0.2$ in CHCl_3); **¹H NMR** (400 MHz, CDCl_3) δ 7.43 – 7.36 (m, 2H), 7.17 (t, $J = 7.6$ Hz, 1H), 6.88 (d, $J = 7.8$ Hz, 2H), 6.79 (d, $J = 7.7$ Hz, 1H), 6.61 (d, $J = 7.9$ Hz, 2H), 3.90 (dd, $J = 9.8, 6.4$ Hz, 1H), 3.18 (dd, $J = 14.8, 6.4$ Hz, 1H), 3.12 (s, 3H), 2.77 (dd, $J = 14.8, 9.8$ Hz, 1H), 2.21 (s, 3H), 1.28 (s, 9H). **¹³C NMR** (101 MHz, CDCl_3) δ 173.4, 165.6, 146.0, 144.6, 136.0, 133.6, 130.6, 129.1, 128.0, 124.5, 123.1, 122.8, 108.7, 83.9, 62.8, 60.1, 30.3, 27.7, 26.5, 20.9. **HRMS** (ESI-TOF) m/z : $[\text{M}+\text{Na}]^+$ calcd. for $\text{C}_{24}\text{H}_{26}\text{N}_2\text{NaO}_4^+$ 429.1785, found 429.1780; **HPLC** analysis: 99:1 er, (CHIRALPAK IA column, 254 nm, 80:20 hexanes/*i*PrOH, 0.6 mL/min), R_t (minor) = 18.5 min, R_t (major) = 23.2 min.



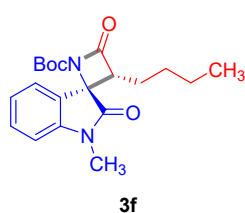
tert-butyl (2R,3R)-1'-methyl-2',4-dioxo-3-(3-(trifluoromethyl)benzyl)spiro[azetidine-2,3'-indoline]-1-carboxylate (3d):

Colorless paste, yield: 26.8 mg (58%); >20:1 dr; $[\alpha]^{25}_D = -32.7$ ($c = 0.5$ in CHCl_3); **¹H NMR** (400 MHz, CDCl_3) δ 7.45 – 7.37 (m, 2H), 7.33 (d, $J = 7.9$ Hz, 1H), 7.25 (t, $J = 7.8$ Hz, 1H), 7.18 (td, $J = 7.6$, 1.0 Hz, 1H), 7.09 (d, $J = 7.7$ Hz, 1H), 6.79 (d, $J = 7.7$ Hz, 1H), 6.72 (s, 1H), 3.92 (dd, $J = 10.6$, 5.8 Hz, 1H), 3.29 (dd, $J = 15.0$, 5.8 Hz, 1H), 3.11 (s, 3H), 2.93 (dd, $J = 15.0$, 10.6 Hz, 1H), 1.28 (s, 9H). **¹³C NMR** (101 MHz, CDCl_3) δ 173.1, 164.9, 145.8, 144.5, 137.7, 131.7, 131.0, 130.6 (q, $J = 32.3$ Hz), 129.0, 124.7 (q, $J = 3.9$ Hz), 124.3, 123.8 (q, $J = 272.4$ Hz), 123.5 (q, $J = 3.8$ Hz), 122.9, 122.7, 108.9, 84.2, 62.6, 59.5, 30.3, 27.7, 26.4. **HRMS** (ESI-TOF) m/z : $[\text{M}+\text{Na}]^+$ calcd. for $\text{C}_{24}\text{H}_{23}\text{F}_3\text{N}_2\text{NaO}_4^+$ 483.1502, found 483.1509; **HPLC** analysis: 99:1 er, (CHIRALPAK IA column, 254 nm, 80:20 hexanes/*i*PrOH, 0.6 mL/min), R_t (minor) = 12.7 min, R_t (major) = 18.1 min.



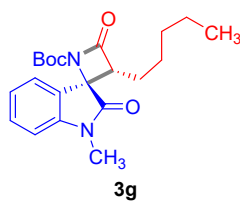
tert-butyl (2R,3R)-1'-methyl-2',4-dioxo-3-propylspiro[azetidine-2,3'-indoline]-1-carboxylate (3e):

Colorless paste, yield: 31.5 mg (92%); >20:1 dr; $[\alpha]^{25}_D = -69.2$ ($c = 0.5$ in CHCl_3); **¹H NMR** (400 MHz, CDCl_3) δ 7.41 (td, $J = 7.8$, 1.3 Hz, 1H), 7.33 (d, $J = 6.8$ Hz, 1H), 7.13 (t, $J = 7.5$ Hz, 1H), 6.90 (d, $J = 7.8$ Hz, 1H), 3.56 (t, $J = 8.2$ Hz, 1H), 3.27 (s, 3H), 1.90 – 1.78 (m, 1H), 1.54 – 1.41 (m, 1H), 1.32 – 1.19 (m, 10H), 1.07 – 0.94 (m, 1H), 0.74 (t, $J = 7.3$ Hz, 3H). **¹³C NMR** (101 MHz, CDCl_3) δ 173.9, 166.4, 146.0, 144.6, 130.4, 124.5, 123.1, 122.8, 108.7, 83.7, 62.6, 58.7, 27.7, 27.4, 26.6, 20.4, 13.5. **HRMS** (ESI-TOF) m/z : $[\text{M}+\text{Na}]^+$ calcd. for $\text{C}_{19}\text{H}_{24}\text{N}_2\text{NaO}_4^+$ 367.1628, found 367.1626; **HPLC** analysis: 94:6 er, (CHIRALPAK IG column, 254 nm, 98:2 hexanes/*i*PrOH, 1.0 mL/min), R_t (minor) = 16.1 min, R_t (major) = 17.1 min.



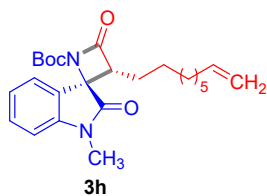
tert-butyl (2R,3R)-3-butyl-1'-methyl-2',4-dioxospiro[azetidine-2,3'-indoline]-1-carboxylate (3f):

Colorless paste, yield: 34.2 mg (96%); >20:1 dr; $[\alpha]^{25}_D = -49.6$ ($c = 0.5$ in CHCl_3); **¹H NMR** (400 MHz, CDCl_3) δ 7.41 (td, $J = 7.8$, 1.3 Hz, 1H), 7.33 (d, $J = 7.5$ Hz, 1H), 7.13 (t, $J = 7.6$ Hz, 1H), 6.91 (d, $J = 7.8$ Hz, 1H), 3.54 (dd, $J = 8.9$, 7.6 Hz, 1H), 3.27 (s, 3H), 1.92 – 1.81 (m, 1H), 1.55 – 1.45 (m, 1H), 1.32 – 1.20 (m, 10H), 1.18 – 1.08 (m, 2H), 0.96 – 0.84 (m, 1H), 0.73 (t, $J = 7.3$ Hz, 3H). **¹³C NMR** (101 MHz, CDCl_3) δ 173.9, 166.5, 146.0, 144.5, 130.5, 124.5, 123.1, 122.8, 108.7, 83.7, 62.6, 58.9, 29.1, 27.7, 26.7, 25.0, 22.1, 13.6. **HRMS** (ESI-TOF) m/z : $[\text{M}+\text{Na}]^+$ calcd. for $\text{C}_{20}\text{H}_{26}\text{N}_2\text{NaO}_4^+$ 381.1785, found 381.1779; **HPLC** analysis: 94:6 er, (CHIRALPAK IA column, 254 nm, 80:20 hexanes/*i*PrOH, 0.6 mL/min), R_t (minor) = 12.3 min, R_t (major) = 13.7 min.



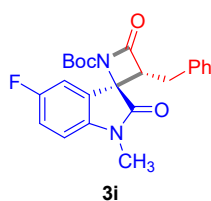
tert-butyl (2R,3R)-1'-methyl-2',4-dioxo-3-pentylspiro [azetidine-2,3'-indoline]-1-carboxylate (3g):

Colorless paste, yield: 33.1 mg (89%); >20:1 dr; $[\alpha]_D^{25} = -57.0$ ($c = 1.0$ in CHCl_3); **¹H NMR** (400 MHz, CDCl_3) δ 7.41 (td, $J = 7.8$, 1.3 Hz, 1H), 7.32 (d, $J = 7.4$ Hz, 1H), 7.13 (t, $J = 7.6$ Hz, 1H), 6.91 (d, $J = 7.8$ Hz, 1H), 3.55 (dd, $J = 9.0$, 7.4 Hz, 1H), 3.27 (s, 3H), 1.92 – 1.80 (m, 1H), 1.56 – 1.42 (m, 1H), 1.32 – 1.20 (m, 10H), 1.15 – 1.02 (m, 4H), 0.97 – 0.87 (m, 1H), 0.74 (t, $J = 6.9$ Hz, 3H). **¹³C NMR** (101 MHz, CDCl_3) δ 173.9, 166.5, 146.0, 144.5, 130.5, 124.5, 123.1, 122.8, 108.7, 83.7, 62.6, 59.0, 31.1, 27.7, 26.7, 26.6, 25.2, 22.1, 13.8. **HRMS** (ESI-TOF) m/z : $[\text{M}+\text{Na}]^+$ calcd. for $\text{C}_{21}\text{H}_{28}\text{N}_2\text{NaO}_4^+$ 395.1941, found 395.1946; **HPLC** analysis: 95:5 er, (CHIRALPAK IG column, 254 nm, 98:2 hexanes/*i*PrOH, 1.0 mL/min), R_t (minor) = 14.8 min, R_t (major) = 13.4 min.



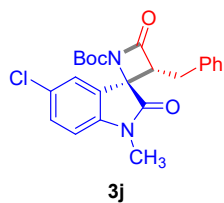
tert-butyl (2R,3R)-1'-methyl-3-(non-8-en-1-yl)-2',4-dioxospiro [azetidine-2,3'-indoline]-1-carboxylate (3h):

Colorless paste, yield: 27.6 mg (74%); >20:1 dr; $[\alpha]_D^{25} = -66.9$ ($c = 0.5$ in CHCl_3); **¹H NMR** (400 MHz, CDCl_3) δ 7.41 (td, $J = 7.7$, 1.3 Hz, 1H), 7.32 (dd, $J = 7.5$, 1.2 Hz, 1H), 7.13 (td, $J = 7.6$, 1.0 Hz, 1H), 6.90 (d, $J = 7.8$ Hz, 1H), 5.83 – 5.71 (m, 1H), 5.00 – 4.88 (m, 2H), 3.54 (dd, $J = 9.0$, 7.4 Hz, 1H), 3.27 (s, 3H), 2.02 – 1.93 (m, 2H), 1.90 – 1.80 (m, 1H), 1.54 – 1.43 (m, 1H), 1.33 – 1.19 (m, 12H), 1.17 – 1.03 (m, 6H), 0.97 – 0.84 (m, 1H). **¹³C NMR** (101 MHz, CDCl_3) δ 173.9, 166.4, 146.0, 144.6, 139.1, 130.4, 124.5, 123.1, 122.8, 114.2, 108.6, 83.7, 62.6, 59.0, 33.7, 28.9, 28.8, 28.8, 28.7, 27.7, 27.0, 26.6, 25.2. **HRMS** (ESI-TOF) m/z : $[\text{M}+\text{Na}]^+$ calcd. for $\text{C}_{25}\text{H}_{34}\text{N}_2\text{NaO}_4^+$ 449.2411, found 449.2409; **HPLC** analysis: 96:4 er, (CHIRALPAK IA column, 254 nm, 98:2 hexanes/*i*PrOH, 1.0 mL/min), R_t (minor) = 13.1 min, R_t (major) = 11.8 min.



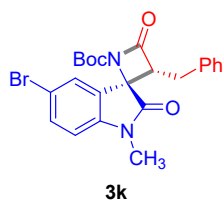
tert-butyl (2R,3R)-3-benzyl-5'-fluoro-1'-methyl-2',4-dioxospiro [azetidine-2,3'-indoline]-1-carboxylate (3i):

Colorless paste, yield: 26.4 mg (64%); >20:1 dr; $[\alpha]_D^{25} = -24.3$ ($c = 0.5$ in CHCl_3); **¹H NMR** (400 MHz, CDCl_3) δ 7.17 (dd, $J = 7.5$, 2.6 Hz, 1H), 7.13 – 7.03 (m, 4H), 6.80 – 6.71 (m, 2H), 6.67 (dd, $J = 8.6$, 4.0 Hz, 1H), 3.98 (dd, $J = 10.3$, 6.4 Hz, 1H), 3.26 (dd, $J = 15.0$, 6.4 Hz, 1H), 3.09 (s, 3H), 2.80 (dd, $J = 15.0$, 10.3 Hz, 1H), 1.32 (s, 9H). **¹³C NMR** (101 MHz, CDCl_3) δ 173.1, 164.9, 159.1 (d, $J = 242.5$ Hz), 145.9, 140.5 (d, $J = 2.1$ Hz), 136.2, 128.4, 128.0, 126.6, 124.6 (d, $J = 7.9$ Hz), 116.8 (d, $J = 23.5$ Hz), 112.6 (d, $J = 25.3$ Hz), 109.3 (d, $J = 8.0$ Hz), 84.3, 62.7, 60.0, 30.6, 27.8, 26.6. **HRMS** (ESI-TOF) m/z : $[\text{M}+\text{Na}]^+$ calcd. for $\text{C}_{23}\text{H}_{23}\text{FN}_2\text{NaO}_4^+$ 433.1534, found 433.1544; **HPLC** analysis: 99.7:0.3 er, (CHIRALPAK IA column, 254 nm, 80:20 hexanes/*i*PrOH, 0.6 mL/min), R_t (minor) = 17.3 min, R_t (major) = 34.5 min.



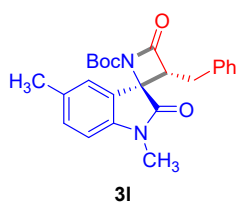
tert-butyl (2R,3R)-3-benzyl-5'-chloro-1'-methyl-2',4-dioxospiro[azetidine-2,3'-indoline]-1-carboxylate (3j):

Colorless paste, yield: 29.1 mg (68%); >20:1 dr; $[\alpha]^{25}_D = +13.8$ ($c = 0.8$ in CHCl_3); **¹H NMR** (400 MHz, CDCl_3) δ 7.39 (d, $J = 2.1$ Hz, 1H), 7.34 (dd, $J = 8.3, 2.1$ Hz, 1H), 7.13 – 7.04 (m, 3H), 6.79 – 6.72 (m, 2H), 6.66 (d, $J = 8.3$ Hz, 1H), 3.97 (dd, $J = 10.3, 6.4$ Hz, 1H), 3.26 (dd, $J = 14.9, 6.4$ Hz, 1H), 3.08 (s, 3H), 2.80 (dd, $J = 14.9, 10.3$ Hz, 1H), 1.33 (s, 9H). **¹³C NMR** (101 MHz, CDCl_3) δ 173.0, 164.8, 145.9, 143.0, 136.2, 130.4, 128.4, 128.3, 128.1, 126.6, 124.8, 124.7, 109.6, 84.4, 62.4, 60.0, 30.6, 27.8, 26.6. **HRMS** (ESI-TOF) m/z : $[\text{M}+\text{Na}]^+$ calcd. for $\text{C}_{23}\text{H}_{23}\text{ClN}_2\text{NaO}_4^+$ 449.1239, found 449.1241; **HPLC** analysis: 99.6:0.4 er, (CHIRALPAK IA column, 254 nm, 80:20 hexanes/*i*PrOH, 0.6 mL/min), R_t (minor) = 17.6 min, R_t (major) = 35.7 min.



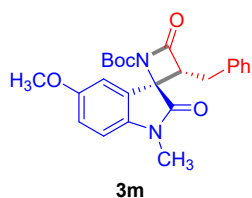
tert-butyl (2R,3R)-3-benzyl-5'-bromo-1'-methyl-2',4-dioxospiro[azetidine-2,3'-indoline]-1-carboxylate (3k):

Colorless paste, yield: 29.7 mg (63%); >20:1 dr; $[\alpha]^{15}_D = +16.8$ ($c = 1.0$ in CHCl_3); **¹H NMR** (400 MHz, CDCl_3) δ 7.52 (d, $J = 1.9$ Hz, 1H), 7.49 (dd, $J = 8.3, 2.0$ Hz, 1H), 7.12 – 7.03 (m, 3H), 6.79 – 6.72 (m, 2H), 6.61 (d, $J = 8.3$ Hz, 1H), 3.97 (dd, $J = 10.4, 6.4$ Hz, 1H), 3.26 (dd, $J = 14.9, 6.4$ Hz, 1H), 3.08 (s, 3H), 2.80 (dd, $J = 14.9, 10.3$ Hz, 1H), 1.33 (s, 9H). **¹³C NMR** (101 MHz, CDCl_3) δ 172.8, 164.8, 146.0, 143.5, 136.1, 133.3, 128.4, 128.1, 127.5, 126.6, 125.2, 115.4, 110.1, 84.4, 62.3, 60.1, 30.6, 27.8, 26.6. **HRMS** (ESI-TOF) m/z : $[\text{M}+\text{Na}]^+$ calcd. for $\text{C}_{23}\text{H}_{23}\text{BrN}_2\text{NaO}_4^+$ 493.0733, found 493.0738; **HPLC** analysis: 98:2 er, (CHIRALPAK IA column, 254 nm, 80:20 hexanes/*i*PrOH, 0.6 mL/min), R_t (minor) = 17.0 min, R_t (major) = 40.0 min.



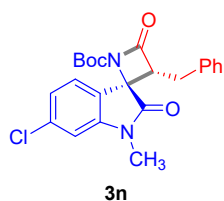
tert-butyl (2R,3R)-3-benzyl-1',5'-dimethyl-2',4-dioxospiro[azetidine-2,3'-indoline]-1-carboxylate (3l):

Colorless paste, yield: 35.9 mg (88%); >20:1 dr; $[\alpha]^{25}_D = -11.6$ ($c = 1.0$ in CHCl_3); **¹H NMR** (400 MHz, CDCl_3) δ 7.22 (s, 1H), 7.18 (dd, $J = 7.9, 1.8$ Hz, 1H), 7.09 – 7.04 (m, 3H), 6.76 – 6.69 (m, 2H), 6.67 (d, $J = 7.9$ Hz, 1H), 3.91 (dd, $J = 9.8, 6.4$ Hz, 1H), 3.22 (dd, $J = 14.8, 6.4$ Hz, 1H), 3.09 (s, 3H), 2.81 (dd, $J = 14.8, 9.9$ Hz, 1H), 2.40 (s, 3H), 1.29 (s, 9H). **¹³C NMR** (101 MHz, CDCl_3) δ 173.3, 165.6, 146.0, 142.2, 136.7, 132.4, 130.8, 128.4, 128.2, 126.5, 125.2, 123.0, 108.5, 83.9, 62.9, 59.9, 30.7, 27.7, 26.5, 21.2. **HRMS** (ESI-TOF) m/z : $[\text{M}+\text{Na}]^+$ calcd. for $\text{C}_{24}\text{H}_{26}\text{N}_2\text{NaO}_4^+$ 429.1785, found 429.1792; **HPLC** analysis: 99:1 er, (CHIRALPAK IA column, 254 nm, 80:20 hexanes/*i*PrOH, 0.6 mL/min), R_t (minor) = 17.1 min, R_t (major) = 24.5 min.



tert-butyl (2R,3R)-3-benzyl-5'-methoxy-1'-methyl-2',4-dioxospiro[azetidine-2,3'-indoline]-1-carboxylate (3m):

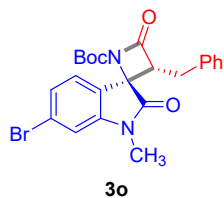
Colorless paste, yield: 36.7 mg (87%); >20:1 dr; $[\alpha]^{25}_D = -15.5$ ($c = 1.0$ in CHCl_3); **¹H NMR** (400 MHz, CDCl_3) δ 7.12 – 7.04 (m, 3H), 7.01 (d, $J = 2.5$ Hz, 1H), 6.90 (dd, $J = 8.5, 2.6$ Hz, 1H), 6.79 – 6.72 (m, 2H), 6.68 (d, $J = 8.5$ Hz, 1H), 3.94 (dd, $J = 9.9, 6.4$ Hz, 1H), 3.84 (s, 3H), 3.23 (dd, $J = 14.9, 6.4$ Hz, 1H), 3.09 (s, 3H), 2.82 (dd, $J = 14.8, 9.9$ Hz, 1H), 1.30 (s, 9H). **¹³C NMR** (101 MHz, CDCl_3) δ 173.0, 165.5, 156.1, 146.0, 138.0, 136.6, 128.4, 128.1, 126.5, 124.2, 114.8, 111.8, 109.1, 84.0, 63.0, 59.9, 56.0, 30.7, 27.7, 26.6. **HRMS** (ESI-TOF) m/z : $[\text{M}+\text{Na}]^+$ calcd. for $\text{C}_{24}\text{H}_{26}\text{N}_2\text{NaO}_5^+$ 445.1734, found 445.1730; **HPLC** analysis: 99:1 er, (CHIRALPAK IA column, 254 nm, 80:20 hexanes/*i*PrOH, 0.6 mL/min), R_t (minor) = 25.6 min, R_t (major) = 41.3 min.



3n

tert-butyl (2*R*,3*R*)-3-benzyl-6'-chloro-1'-methyl-2',4-dioxospiro [azetidine-2,3'-indoline]-1-carboxylate (**3n**):

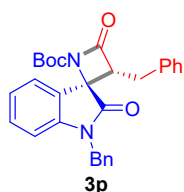
Colorless paste, yield: 30.1 mg (70%); >20:1 dr; $[\alpha]^{25}_D = -44.4$ ($c = 0.3$ in CHCl_3); **¹H NMR** (400 MHz, CDCl_3) δ 7.33 (d, $J = 7.9$ Hz, 1H), 7.15 (dd, $J = 7.9, 1.8$ Hz, 1H), 7.11 – 7.07 (m, 3H), 6.78 – 6.72 (m, 3H), 3.95 (dd, $J = 10.2, 6.4$ Hz, 1H), 3.24 (dd, $J = 14.9, 6.4$ Hz, 1H), 3.08 (s, 3H), 2.76 (dd, $J = 14.9, 10.2$ Hz, 1H), 1.32 (s, 9H). **¹³C NMR** (101 MHz, CDCl_3) δ 173.3, 165.0, 145.9, 145.7, 136.5, 136.2, 128.5, 128.1, 126.7, 125.2, 122.7, 121.4, 109.5, 84.3, 62.3, 60.0, 30.6, 27.8, 26.6. **HRMS** (ESI-TOF) m/z : $[\text{M}+\text{Na}]^+$ calcd. for $\text{C}_{23}\text{H}_{23}\text{ClN}_2\text{NaO}_4^+$ 449.1239, found 449.1241; **HPLC** analysis: 99.7:0.3 er, (CHIRALPAK IA column, 254 nm, 80:20 hexanes/*i*PrOH, 0.6 mL/min), R_t (minor) = 22.6 min, R_t (major) = 29.3 min.



3o

tert-butyl (2*R*,3*R*)-3-benzyl-6'-bromo-1'-methyl-2',4-dioxospiro [azetidine-2,3'-indoline]-1-carboxylate (**3o**):

Colorless paste, yield: 35.6 mg (76%); >20:1 dr; $[\alpha]^{25}_D = -7.0$ ($c = 0.4$ in CHCl_3); **¹H NMR** (400 MHz, CDCl_3) δ 7.31 (dd, $J = 7.9, 1.6$ Hz, 1H), 7.26 (d, $J = 3.4$ Hz, 1H), 7.12 – 7.06 (m, 3H), 6.90 (d, $J = 1.6$ Hz, 1H), 6.75 (dd, $J = 6.7, 2.9$ Hz, 2H), 3.95 (dd, $J = 10.1, 6.5$ Hz, 1H), 3.23 (dd, $J = 14.9, 6.4$ Hz, 1H), 3.08 (s, 3H), 2.75 (dd, $J = 14.9, 10.1$ Hz, 1H), 1.32 (s, 9H). **¹³C NMR** (101 MHz, CDCl_3) δ 173.2, 164.9, 145.7, 136.2, 128.5, 128.1, 126.7, 125.6, 125.5, 124.4, 122.0, 112.3, 84.4, 62.3, 60.0, 30.6, 27.8, 26.6. **HRMS** (ESI-TOF) m/z : $[\text{M}+\text{Na}]^+$ calcd. for $\text{C}_{23}\text{H}_{23}\text{BrN}_2\text{NaO}_4^+$ 493.0733, found 493.0738; **HPLC** analysis: 99.6:0.4 er, (CHIRALPAK IA column, 254 nm, 80:20 hexanes/*i*PrOH, 0.6 mL/min), R_t (minor) = 23.2 min, R_t (major) = 28.6 min.

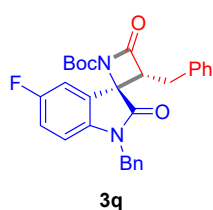


3p

tert-butyl (2*R*,3*R*)-1',3-dibenzyl-2',4-dioxospiro [azetidine-2,3'-indoline]-1-carboxylate (**3p**):

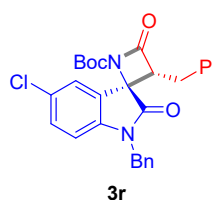
Colorless paste, yield: 36.6 mg (78%); 8:1 dr; $[\alpha]^{15}_D = -5.4$ ($c = 0.52$ in CHCl_3); **¹H NMR** (600 MHz, CDCl_3) δ 7.46 (dd, $J = 7.5, 1.2$ Hz, 1H), 7.28-7.21 (m, 4H), 7.15 (td, $J = 7.6, 1.0$ Hz, 1H), 7.11-7.06 (m, 1H),

7.01 (t, $J = 7.6$ Hz, 2H), 6.96-6.93 (m, 2H), 6.65-6.59 (m, 3H), 5.03 (d, $J = 15.9$ Hz, 1H), 4.57 (d, $J = 16.0$ Hz, 1H), 4.02 (dd, $J = 11.5, 4.7$ Hz, 1H), 3.28 (dd, $J = 14.8, 4.8$ Hz, 1H), 2.92 (dd, $J = 14.9, 11.4$ Hz, 1H), 1.29 (s, 9H). **^{13}C NMR** (101 MHz, CDCl_3) δ 173.6, 165.5, 146.0, 143.9, 136.6, 134.9, 130.6, 128.9, 128.5, 128.2, 127.6, 126.8, 126.6, 124.5, 123.1, 122.8, 109.9, 84.1, 62.8, 60.6, 44.1, 30.4, 27.7. **HRMS** (ESI-TOF) m/z : $[\text{M}+\text{Na}]^+$ calcd. for $\text{C}_{29}\text{H}_{28}\text{N}_2\text{NaO}_4^+$ 491.1941, found 491.1945; **HPLC** analysis: 99:1 er, (CHIRALPAK IA column, 254 nm, 90:10 hexanes/*i*PrOH, 1.0 mL/min), R_t (minor) = 29.2 min, R_t (major) = 49.3 min.



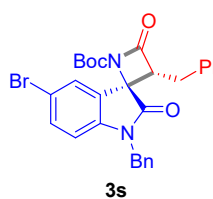
tert-butyl (2*R*,3*R*)-1',3-dibenzyl-5'-fluoro-2',4-dioxospiro [azetidine-2,3'-indoline]-1-carboxylate (**3q**):

Colorless paste, yield: 29.1 mg (60%); > 20:1 dr; $[\alpha]^{15}_{\text{D}} = -2.9$ ($c = 0.56$ in CHCl_3); **^1H NMR** (400 MHz, CDCl_3) δ 7.27-7.18 (m, 4H), 7.13-7.00 (m, 3H), 6.99-6.91 (m, 3H), 6.70 (d, $J = 7.2$ Hz, 2H), 6.50 (dd, $J = 8.6, 4.1$ Hz, 1H), 4.99 (d, $J = 15.9$ Hz, 1H), 4.58 (d, $J = 15.9$ Hz, 1H), 4.05 (dd, $J = 11.5, 5.0$ Hz, 1H), 3.31 (dd, $J = 15.0, 5.0$ Hz, 1H), 2.90 (dd, $J = 15.0, 11.5$ Hz, 1H), 1.33 (s, 9H). **^{13}C NMR** (101 MHz, CDCl_3) δ 173.5, 164.8, 159.1 (d, $J = 242.7$ Hz), 146.0, 139.7 (d, $J = 2.2$ Hz), 136.3, 134.5, 128.9, 128.6, 128.0, 127.7, 126.8, 126.7, 124.8 (d, $J = 8.0$ Hz), 116.8 (d, $J = 23.3$ Hz), 112.6 (d, $J = 25.2$ Hz), 110.5 (d, $J = 8.0$ Hz), 84.5, 62.7, 60.5, 44.3, 30.4, 27.8. **HRMS** (ESI-TOF) m/z : $[\text{M}+\text{Na}]^+$ calcd. for $\text{C}_{29}\text{H}_{27}\text{FN}_2\text{NaO}_4^+$ 509.1847, found 509.1842; **HPLC** analysis: 99:1 er, (CHIRALPAK IA column, 254 nm, 80:20 hexanes/*i*PrOH, 0.8 mL/min), R_t (minor) = 21.0 min, R_t (major) = 30.0 min.



tert-butyl (2*R*,3*R*)-1',3-dibenzyl-5'-chloro-2',4-dioxospiro [azetidine-2,3'-indoline]-1-carboxylate (**3r**):

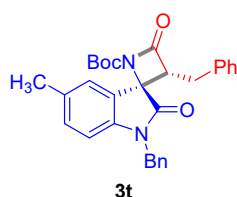
Colorless paste, yield: 31.2 mg (63%); > 20:1 dr; $[\alpha]^{15}_{\text{D}} = +7.9$ ($c = 0.58$ in CHCl_3); **^1H NMR** (400 MHz, CDCl_3) δ 7.43 (d, $J = 2.1$ Hz, 1H), 7.26-7.19 (m, 4H), 7.13-7.00 (m, 3H), 6.97-6.91 (m, 2H), 6.69 (d, $J = 7.1$ Hz, 2H), 6.49 (d, $J = 8.4$ Hz, 1H), 4.97 (d, $J = 15.9$ Hz, 1H), 4.59 (d, $J = 15.9$ Hz, 1H), 4.04 (dd, $J = 11.5, 5.0$ Hz, 1H), 3.31 (dd, $J = 15.0, 5.0$ Hz, 1H), 2.90 (dd, $J = 15.0, 11.5$ Hz, 1H), 1.34 (s, 9H). **^{13}C NMR** (101 MHz, CDCl_3) δ 173.3, 164.7, 146.0, 142.3, 136.2, 134.4, 130.3, 128.9, 128.6, 128.3, 128.1, 127.8, 126.8, 126.7, 124.9, 124.9, 110.8, 84.5, 62.4, 60.5, 44.2, 30.4, 27.8. **HRMS** (ESI-TOF) m/z : $[\text{M}+\text{Na}]^+$ calcd. for $\text{C}_{29}\text{H}_{27}\text{ClN}_2\text{NaO}_4^+$ 525.1552, found 525.1547; **HPLC** analysis: 99:1 er, (CHIRALPAK IA column, 254 nm, 80:20 hexanes/*i*PrOH, 0.8 mL/min), R_t (minor) = 27.1 min, R_t (major) = 35.6 min.



tert-butyl (2*R*,3*R*)-1',3-dibenzyl-5'-bromo-2',4-dioxospiro [azetidine-2,3'-indoline]-1-carboxylate (**3s**):

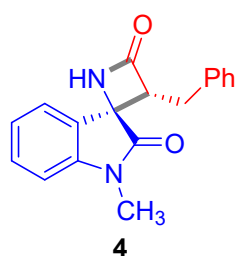
Colorless paste, yield: 36.5 mg (67%); > 20:1 dr; $[\alpha]^{15}_{\text{D}} = +3.2$ ($c = 0.63$ in CHCl_3); **^1H NMR** (400 MHz, CDCl_3) δ 7.57 (d, $J = 2.0$ Hz, 1H), 7.36 (dd, $J = 8.4, 2.0$ Hz, 1H), 7.26-7.20 (m, 3H), 7.12-7.02 (m, 3H), 6.96-6.90 (m, 2H), 6.69 (d, $J = 6.9$ Hz, 2H), 6.44 (d, $J =$

8.4 Hz, 1H), 4.96 (d, $J = 15.9$ Hz, 1H), 4.58 (d, $J = 15.9$ Hz, 1H), 4.04 (dd, $J = 11.5$, 5.0 Hz, 1H), 3.31 (dd, $J = 15.0$, 5.0 Hz, 1H), 2.89 (dd, $J = 14.9$, 11.5 Hz, 1H), 1.34 (s, 9H). **¹³C NMR** (101 MHz, CDCl₃) δ 173.1, 164.7, 146.0, 142.7, 136.2, 134.4, 133.2, 128.9, 128.6, 128.1, 127.8, 127.6, 126.8, 126.7, 125.2, 115.4, 111.2, 84.6, 62.4, 60.5, 44.2, 30.5, 27.8. **HRMS** (ESI-TOF) m/z : $[M+Na]^+$ calcd. for C₂₉H₂₇BrN₂NaO₄⁺ 569.1046, found 569.1054; **HPLC** analysis: 99.8:0.2 er, (CHIRALPAK IA column, 254 nm, 80:20 hexanes/*i*PrOH, 0.8 mL/min), R_t (minor) = 39.8 min, R_t (major) = 53.3 min.



tert-butyl (2*R*,3*R*)-1',3-dibenzyl-5'-methyl-2',4-dioxospiro[azetidine-2,3'-indoline]-1-carboxylate (**3t**):

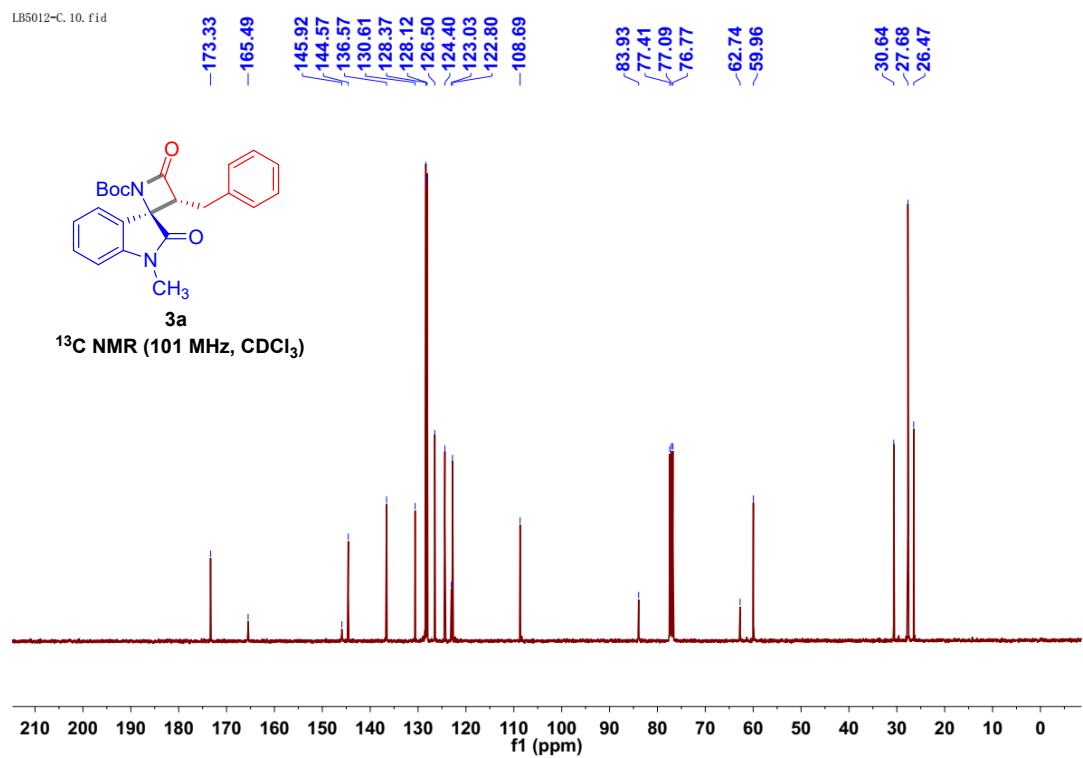
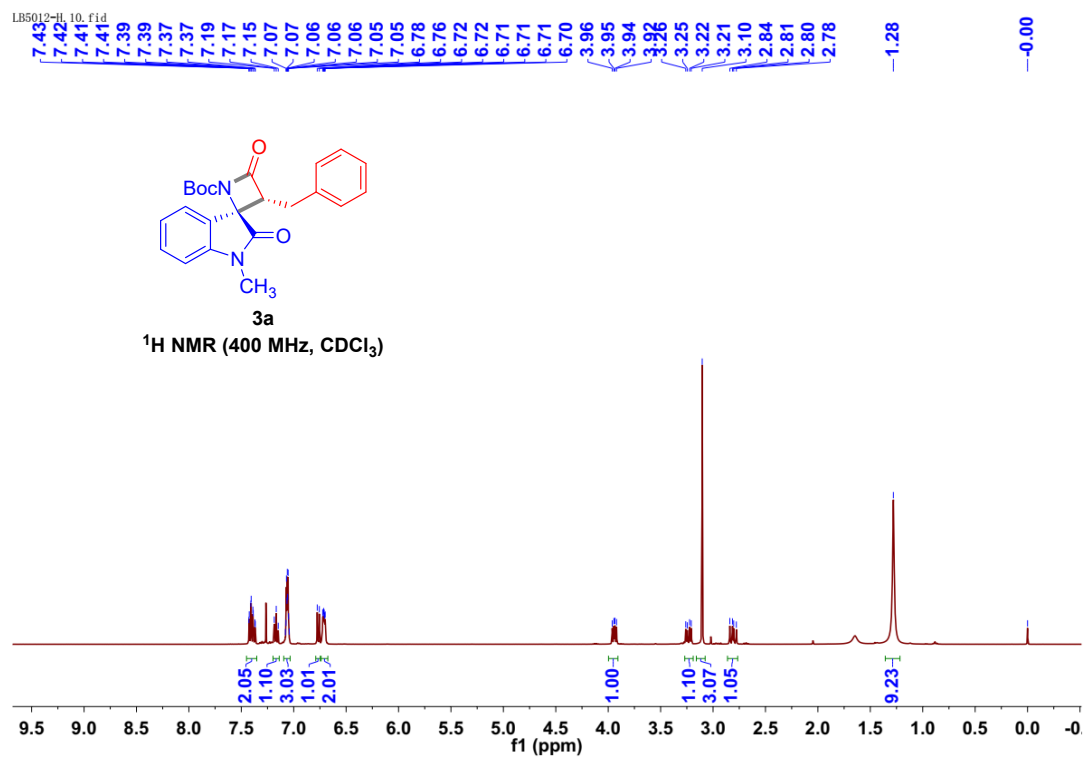
Colorless paste, yield: 40.0 mg (83%); > 20:1 dr; $[\alpha]_D^{15} = +5.2$ ($c = 0.61$ in CHCl₃); **¹H NMR** (400 MHz, CDCl₃) δ 7.28-7.20 (m, 4H), 7.12-7.00 (m, 4H), 6.99-6.93 (m, 2H), 6.64 (d, $J = 7.1$ Hz, 2H), 6.50 (d, $J = 8.0$ Hz, 1H), 5.00 (d, $J = 15.9$ Hz, 1H), 4.56 (d, $J = 15.9$ Hz, 1H), 4.00 (dd, $J = 11.2$, 4.9 Hz, 1H), 3.26 (dd, $J = 14.8$, 4.9 Hz, 1H), 2.93 (dd, $J = 14.8$, 11.2 Hz, 1H), 2.38 (s, 3H), 1.30 (s, 9H). **¹³C NMR** (101 MHz, CDCl₃) δ 173.5, 165.5, 146.1, 141.4, 136.8, 135.0, 132.4, 130.7, 128.8, 128.5, 128.2, 127.5, 126.8, 126.5, 125.3, 123.0, 109.6, 84.0, 62.9, 60.4, 44.1, 30.4, 27.7, 21.2. **HRMS** (ESI-TOF) m/z : $[M+Na]^+$ calcd. for C₃₀H₃₀N₂NaO₄⁺ 505.2098, found 505.2099; **HPLC** analysis: 99.7:0.3 er, (CHIRALPAK IA column, 254 nm, 80:20 hexanes/*i*PrOH, 0.8 mL/min), R_t (minor) = 24.0 min, R_t (major) = 36.8 min.

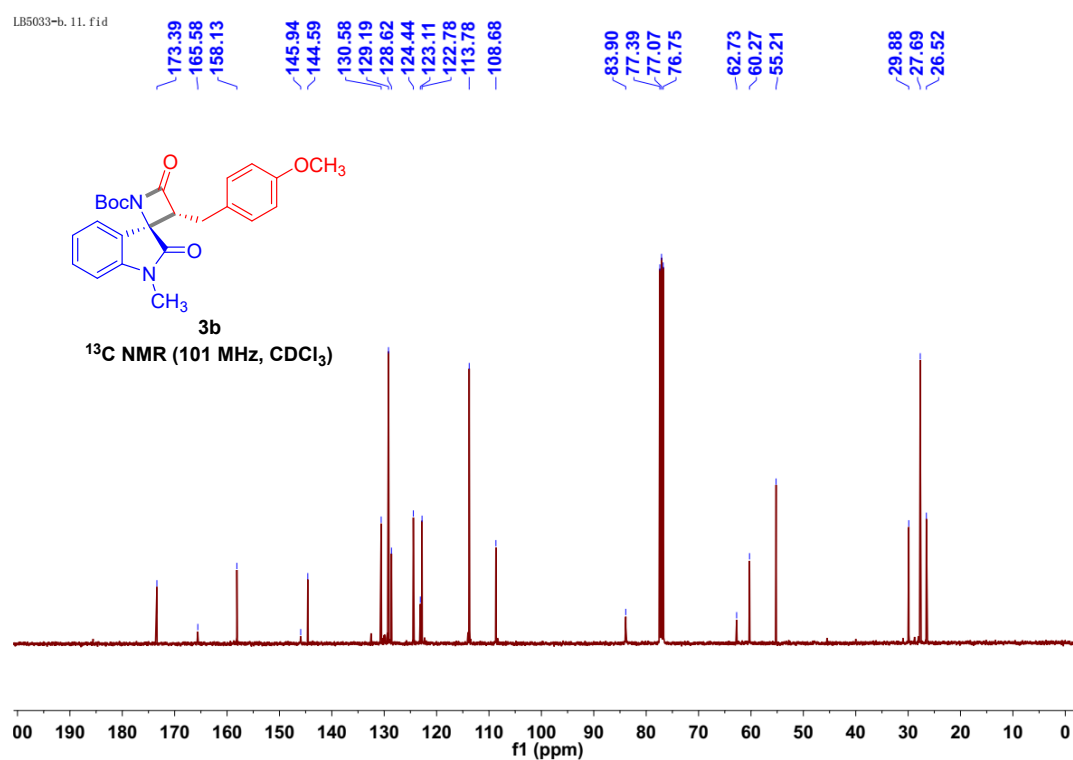
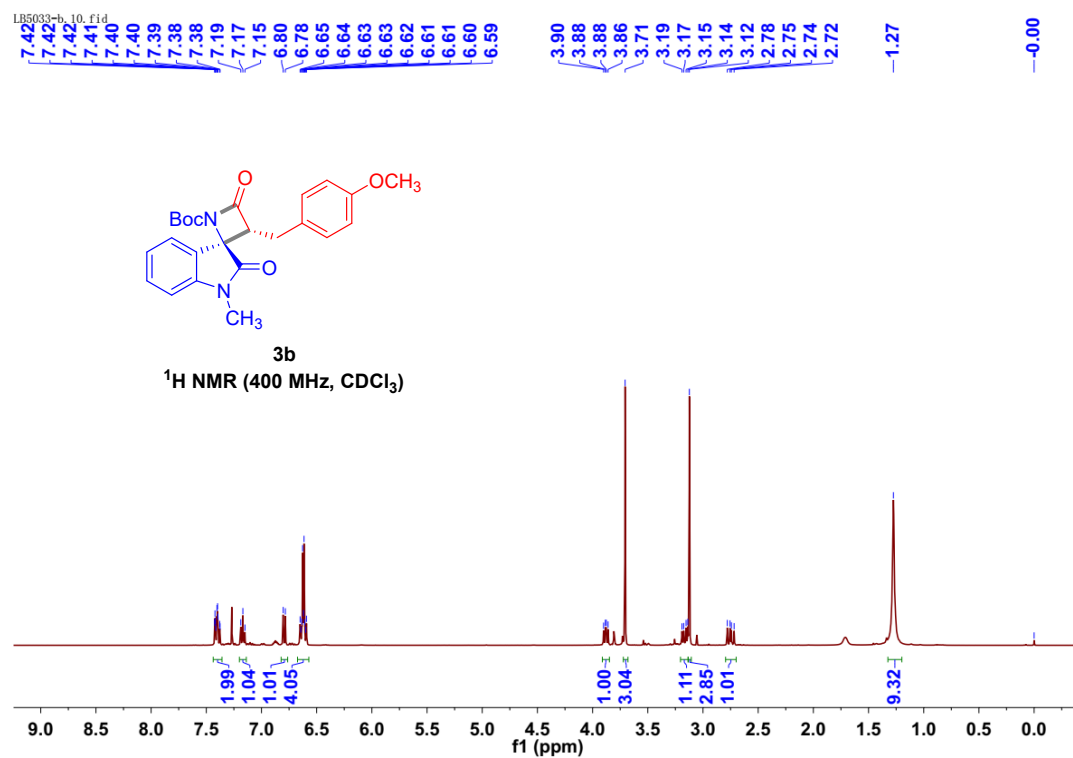


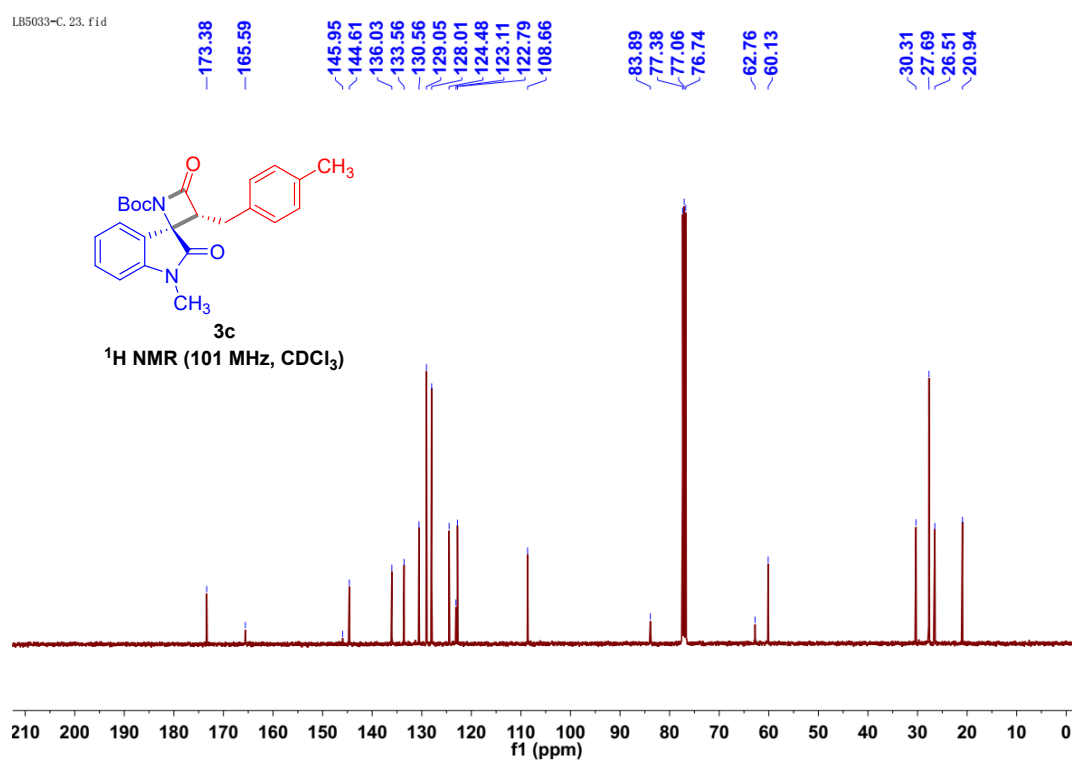
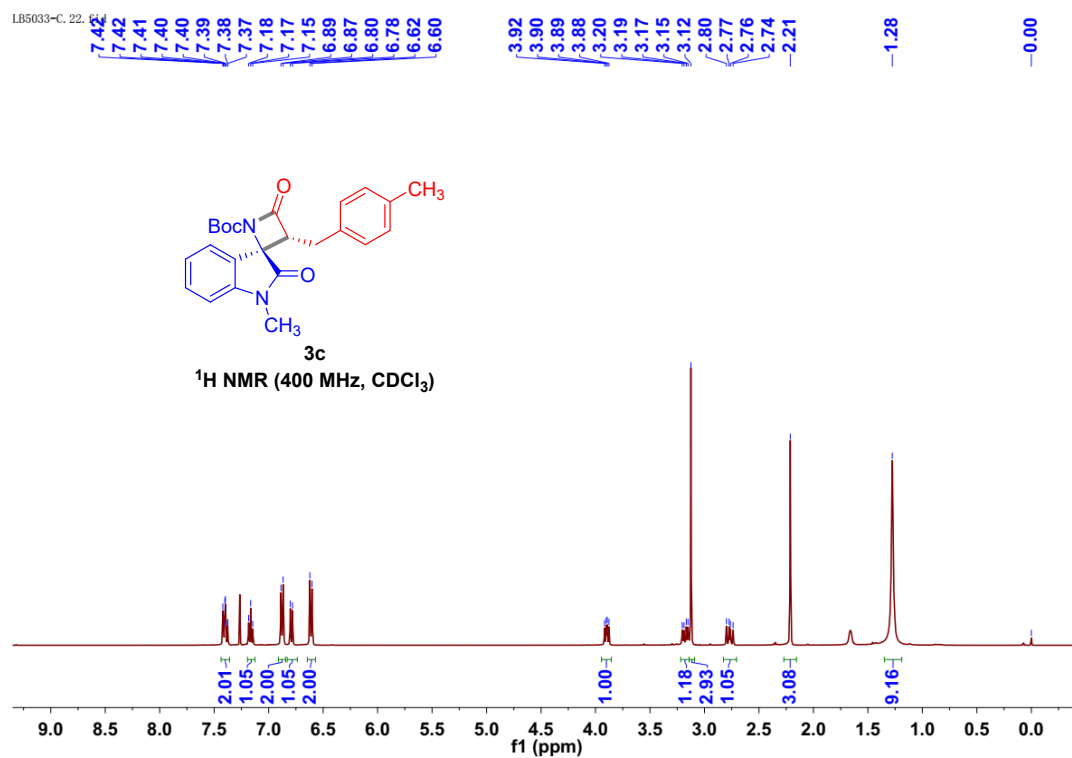
(2*R*,3*R*)-3-benzyl-1'-methylspiro[azetidine-2,3'-indoline]-2',4-dione (**4**):

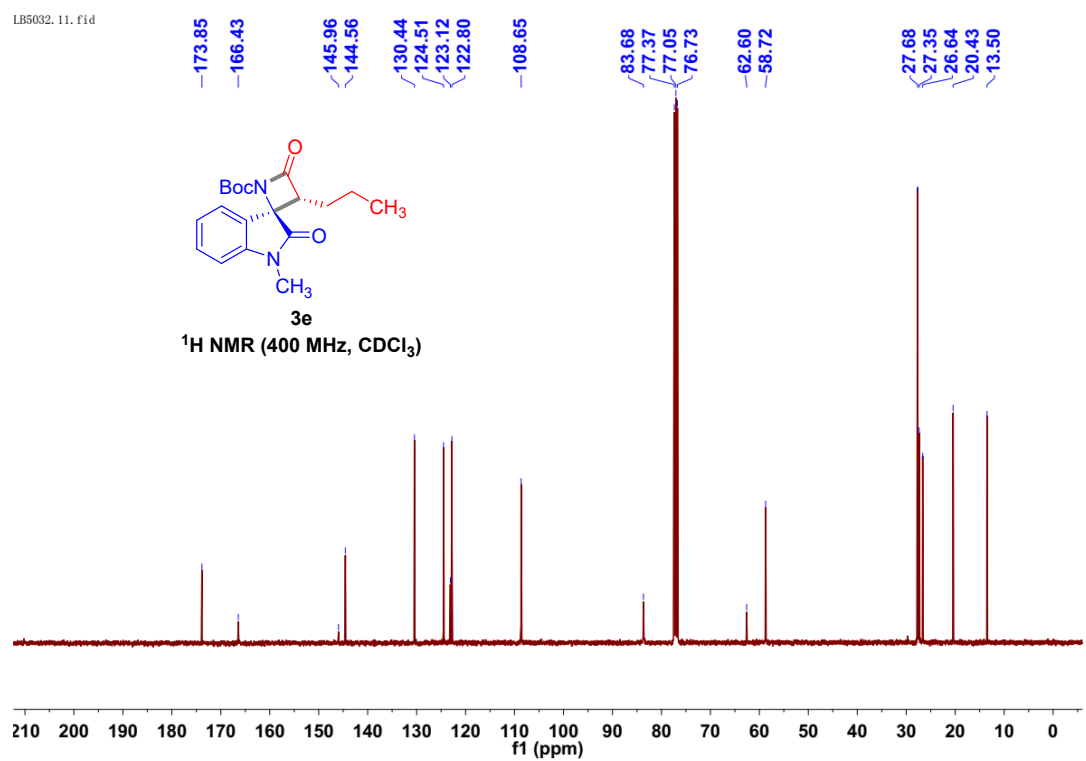
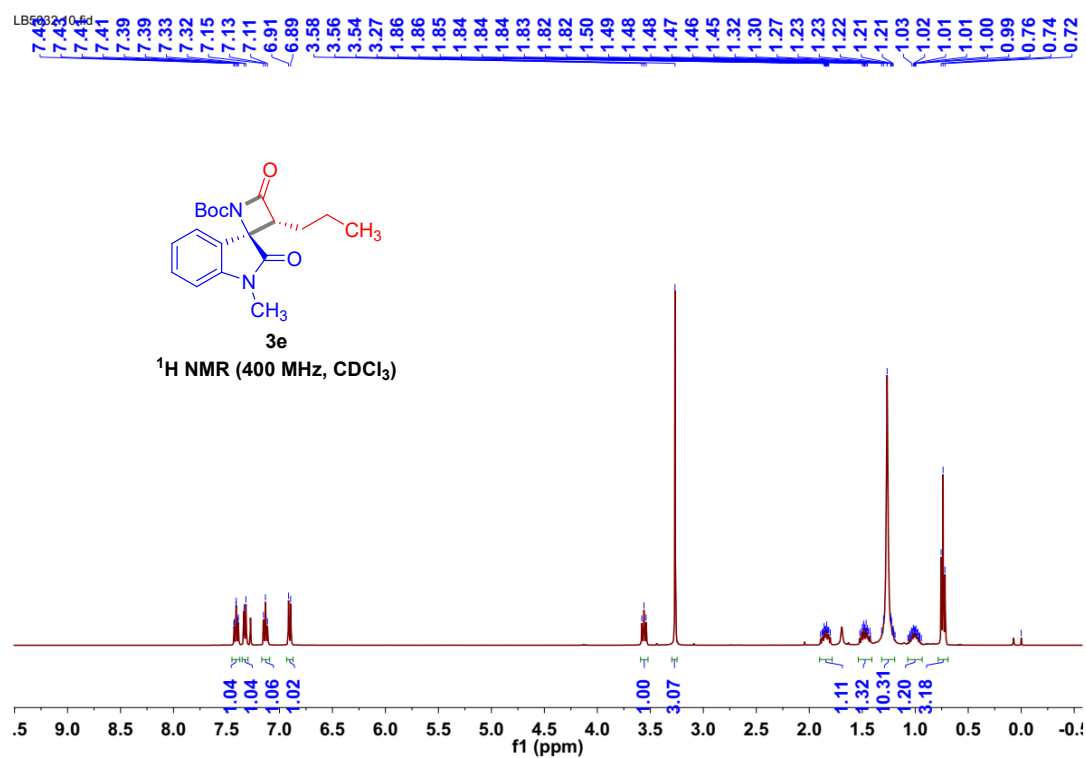
White solid, yield: 137.4 mg (70%); > 20:1 dr; $[\alpha]_D^{15} = +5.2$ ($c = 0.61$ in CHCl₃); **¹H NMR** (400 MHz, CDCl₃) δ 7.48 (d, $J = 7.5$ Hz, 1H), 7.37 (td, $J = 7.8$, 1.3 Hz, 1H), 7.18 (td, $J = 7.6$, 1.0 Hz, 1H), 7.06 – 7.00 (m, 3H), 6.72 (d, $J = 7.8$ Hz, 1H), 6.70 – 6.64 (m, 2H), 6.38 (s, 1H), 3.99 – 3.92 (m, 1H), 3.19 (dd, $J = 14.9$, 6.1 Hz, 1H), 3.04 (s, 3H), 2.74 (dd, $J = 14.8$, 10.3 Hz, 1H). **¹³C NMR** (101 MHz, CDCl₃) δ 175.6, 169.2, 144.0, 137.0, 130.4, 128.2, 128.1, 126.3, 124.9, 124.7, 122.8, 108.7, 63.1, 60.6, 31.4, 26.4. **HRMS** (ESI-TOF) m/z : $[M+H]^+$ calcd. for C₁₈H₁₇N₂O₂⁺ 293.1285, found 293.1287; **HPLC** analysis: 99.7:0.3 er, (CHIRALPAK IB column, 254 nm, 70:30 hexanes/*i*PrOH, 0.7 mL/min), R_t (minor) = 16.6 min, R_t (major) = 26.9 min.

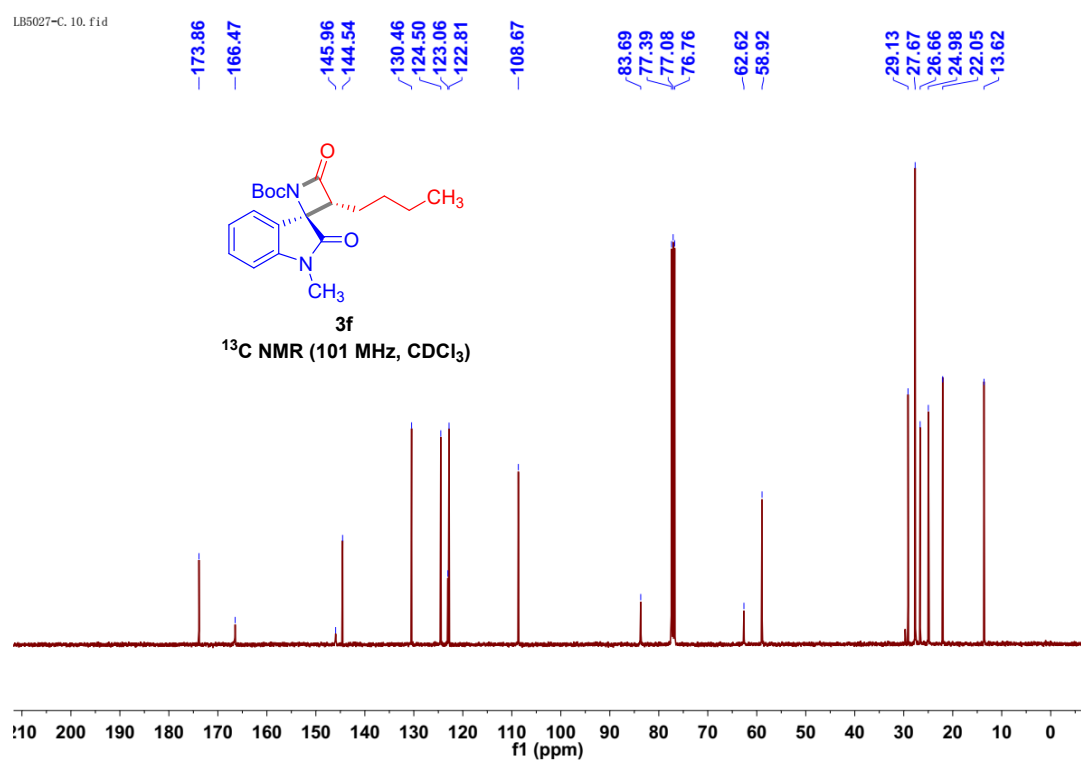
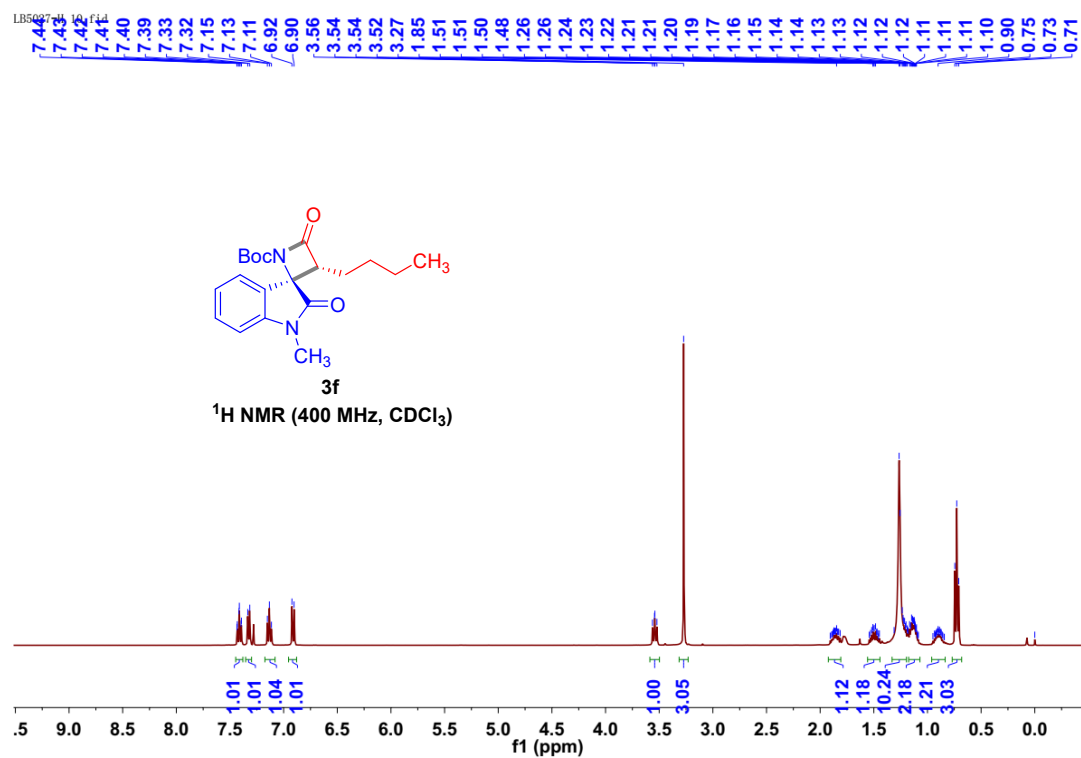
VIII. ^1H , ^{13}C NMR and HPLC spectra

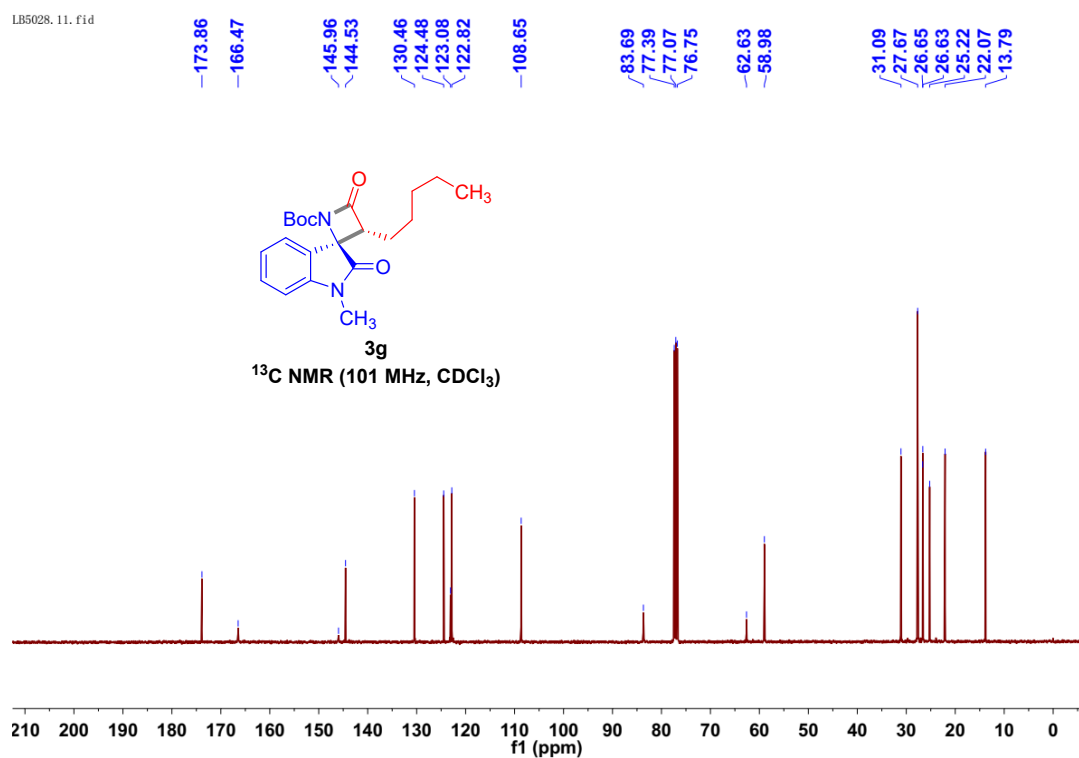
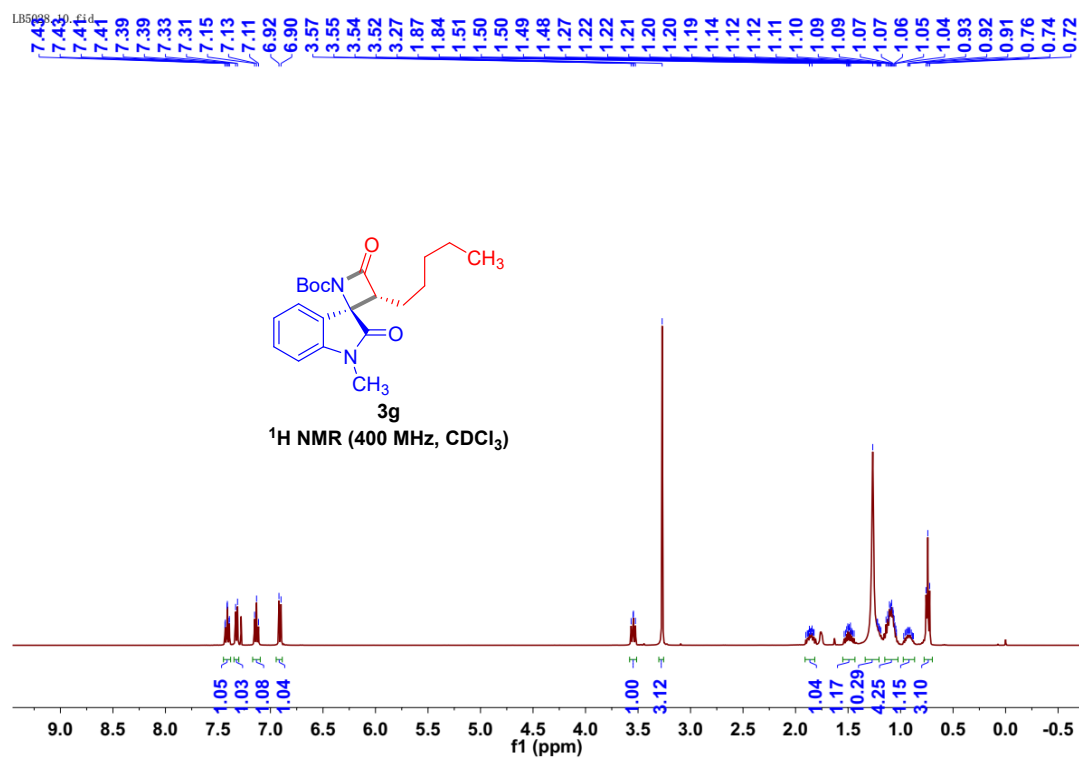


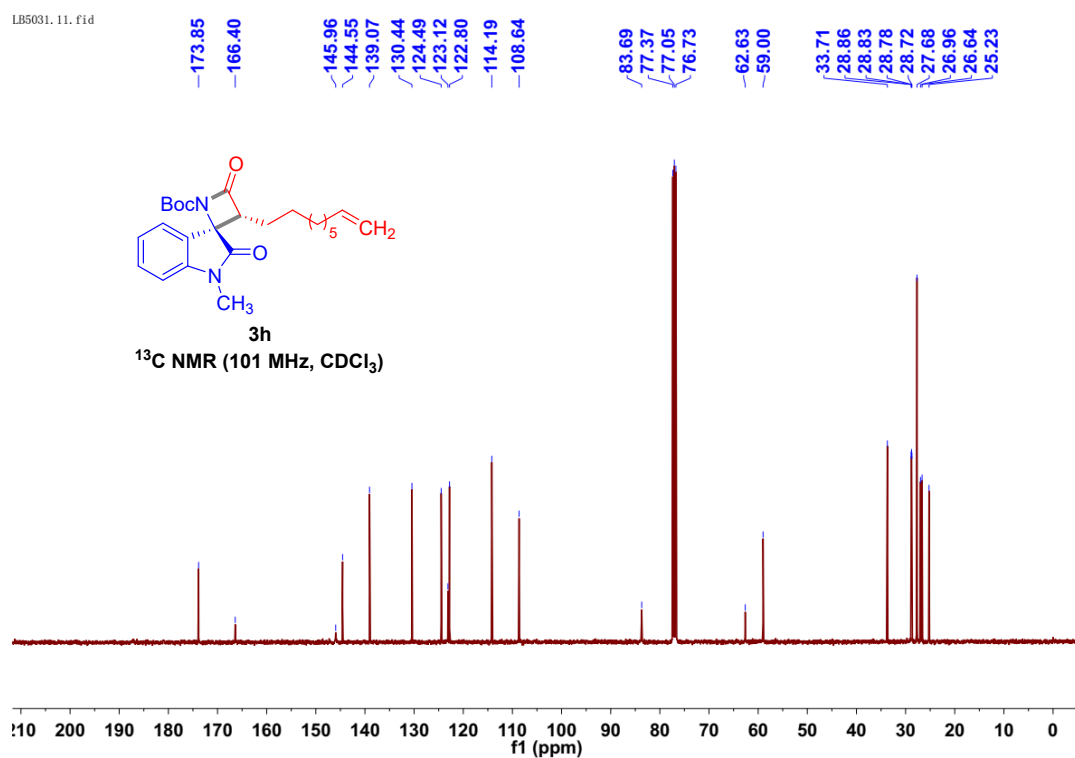
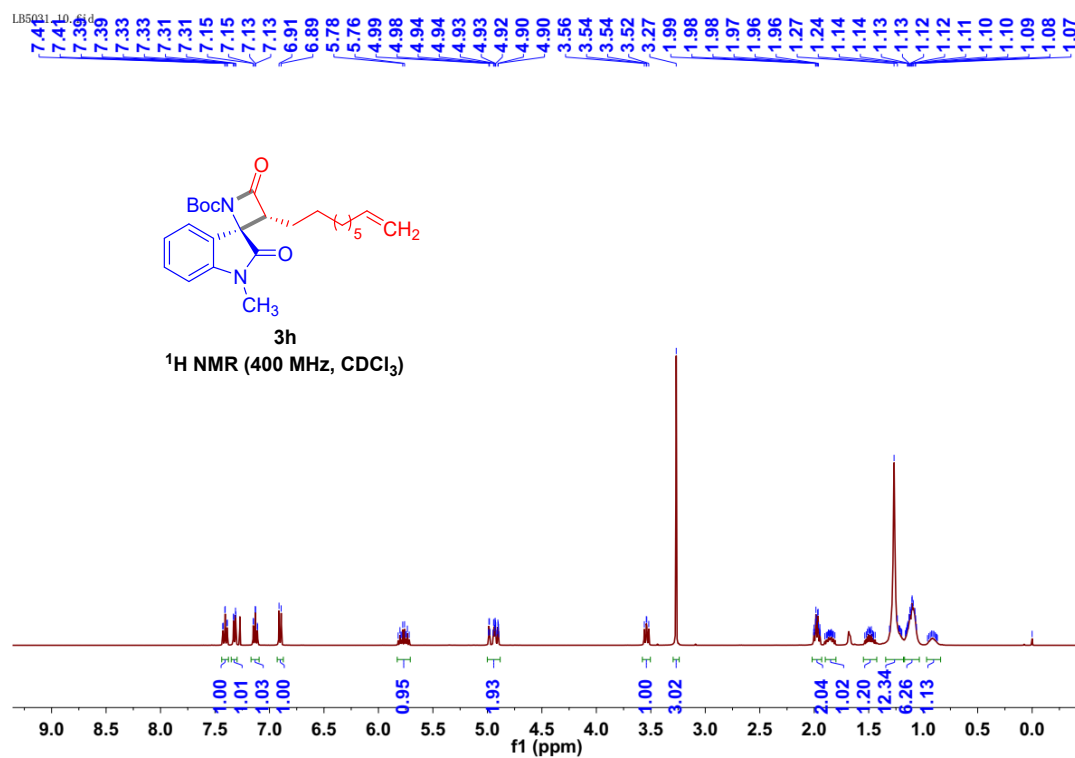


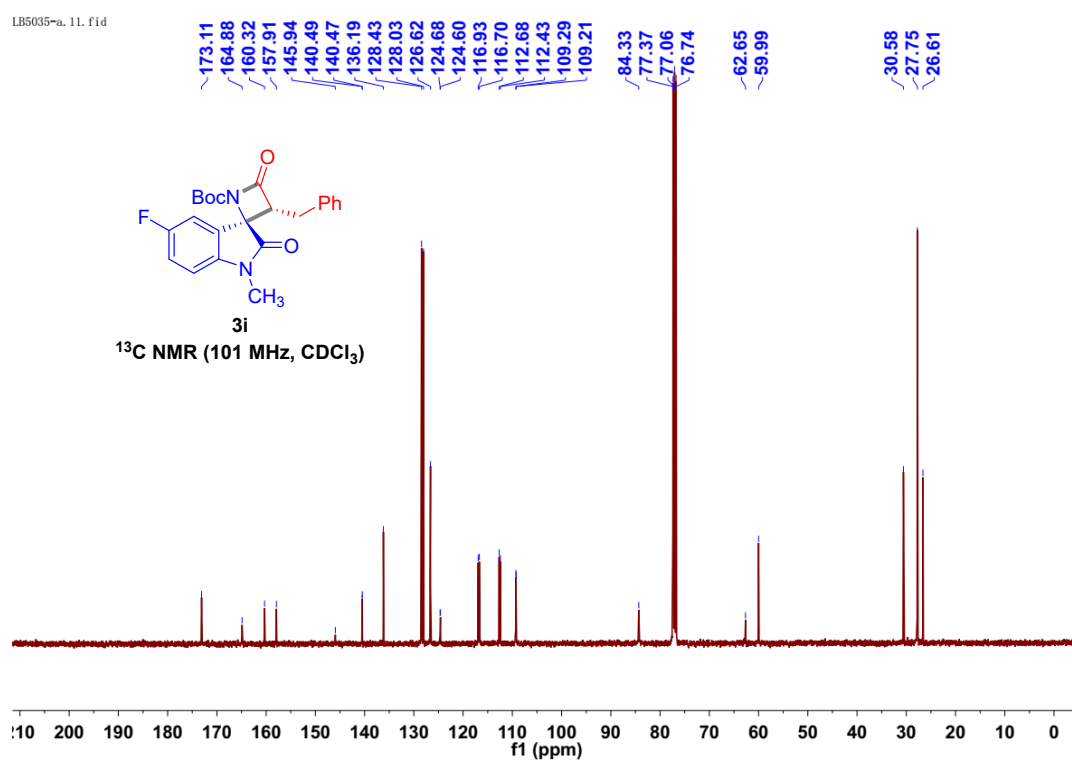
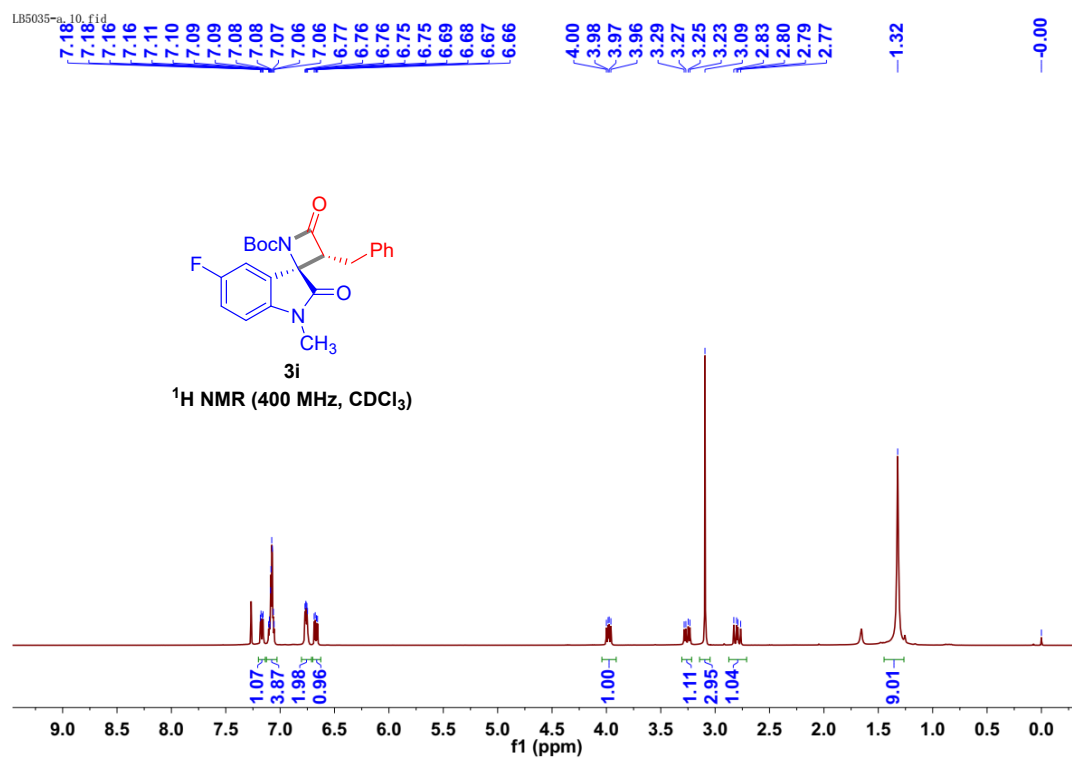


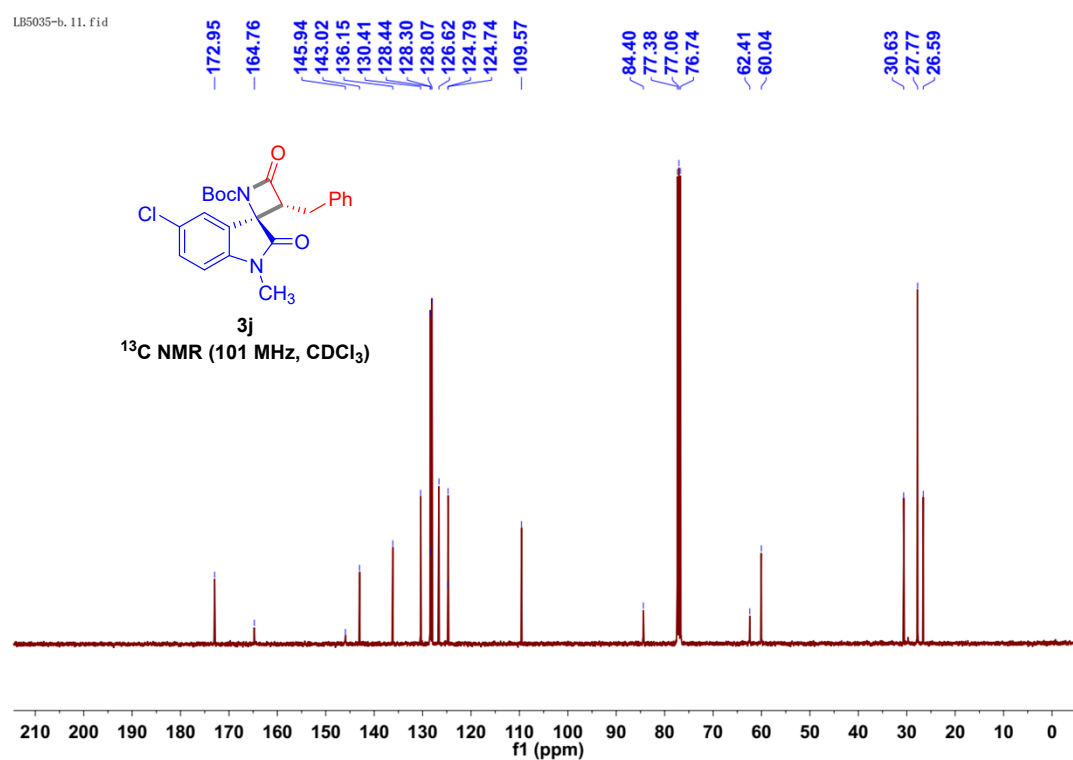
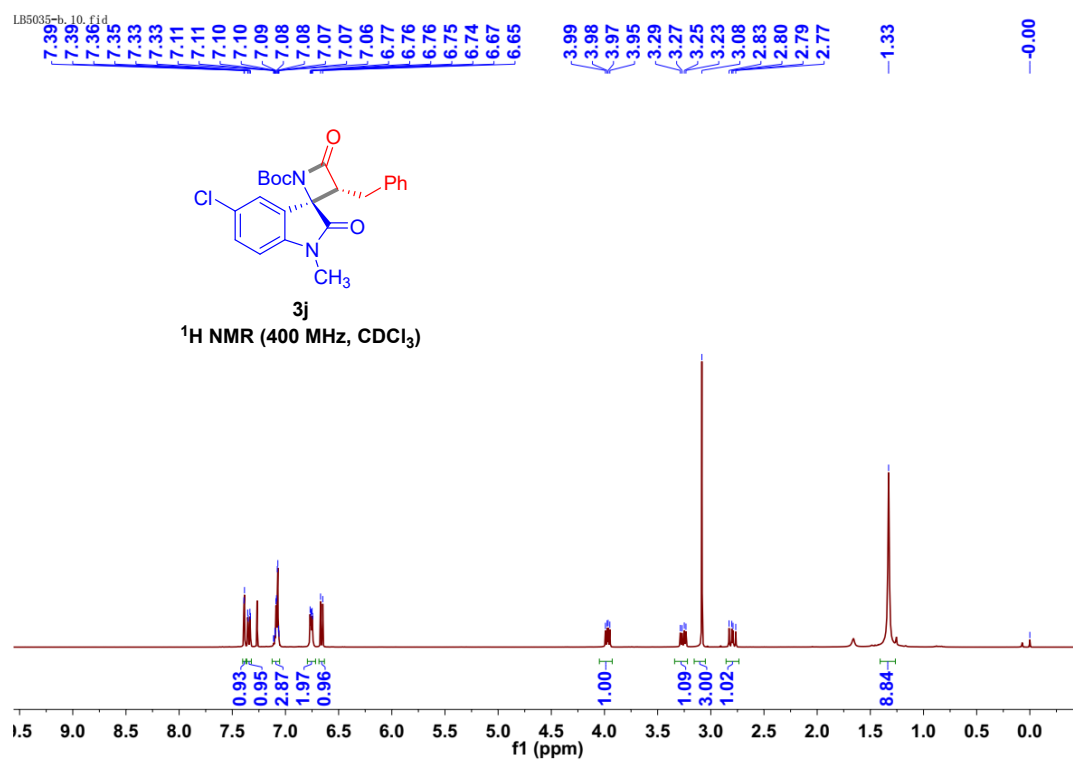


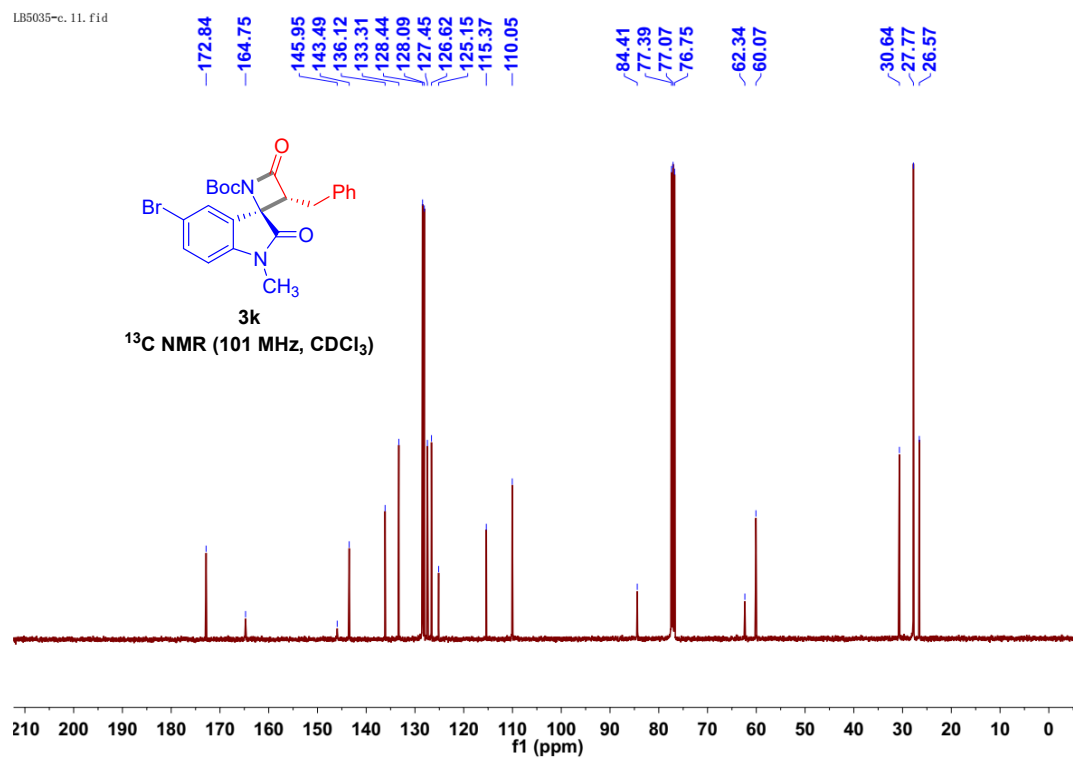
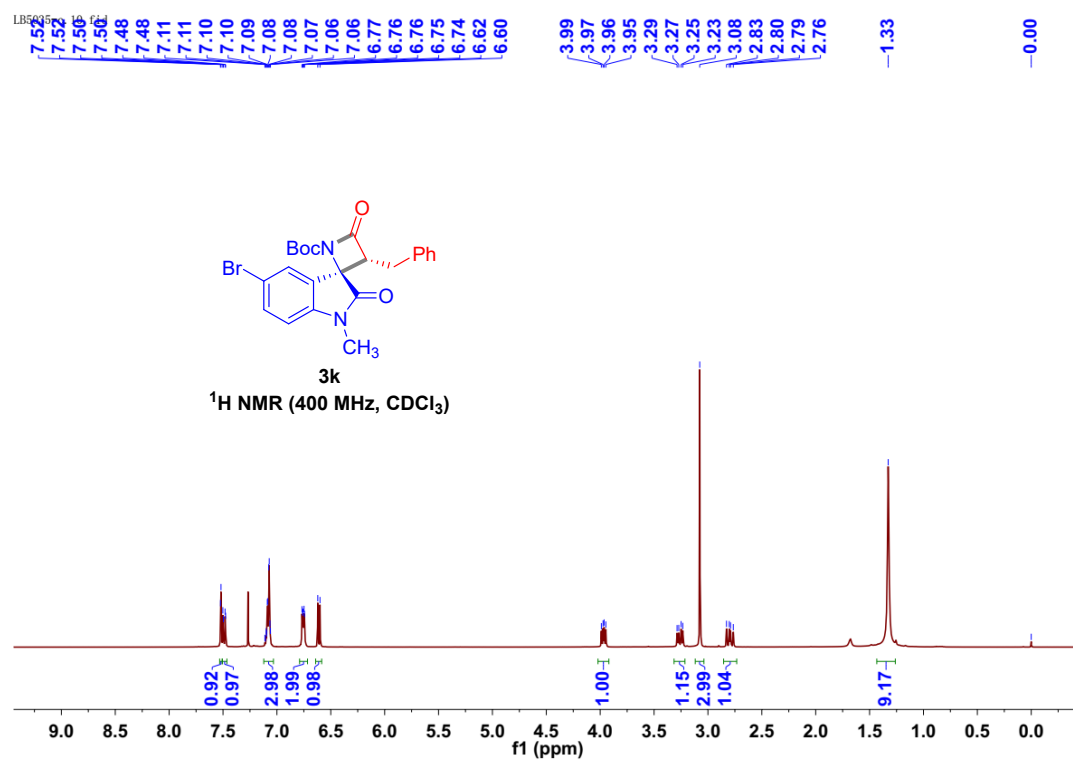


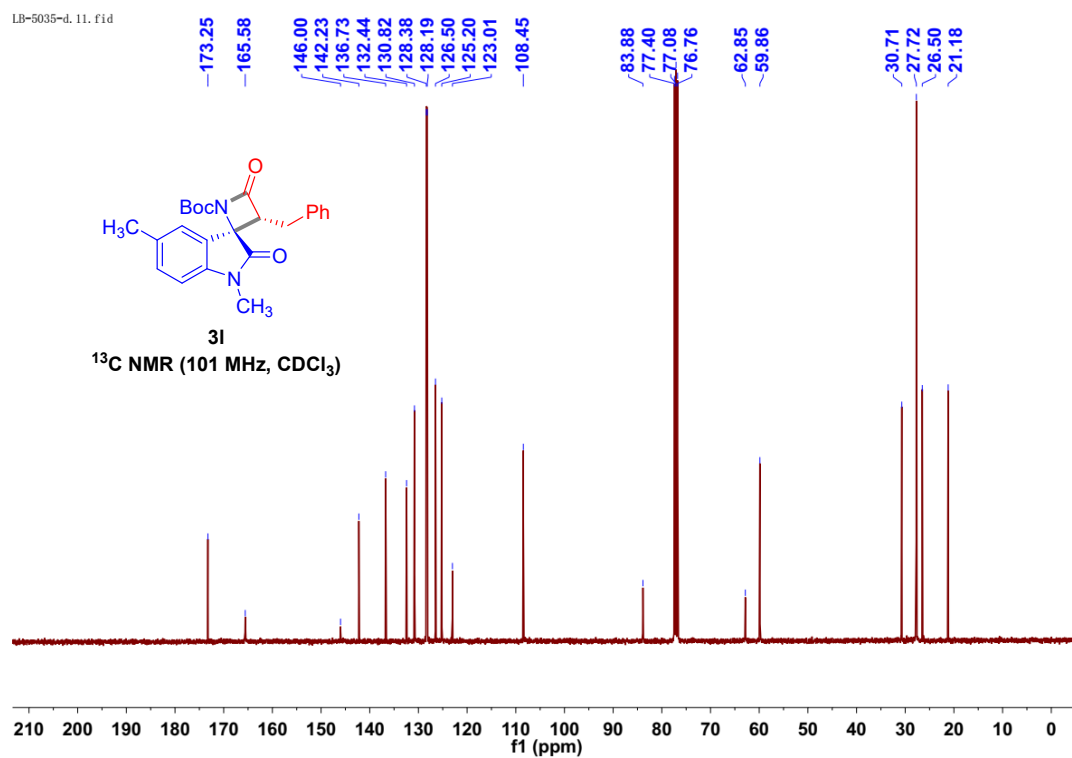
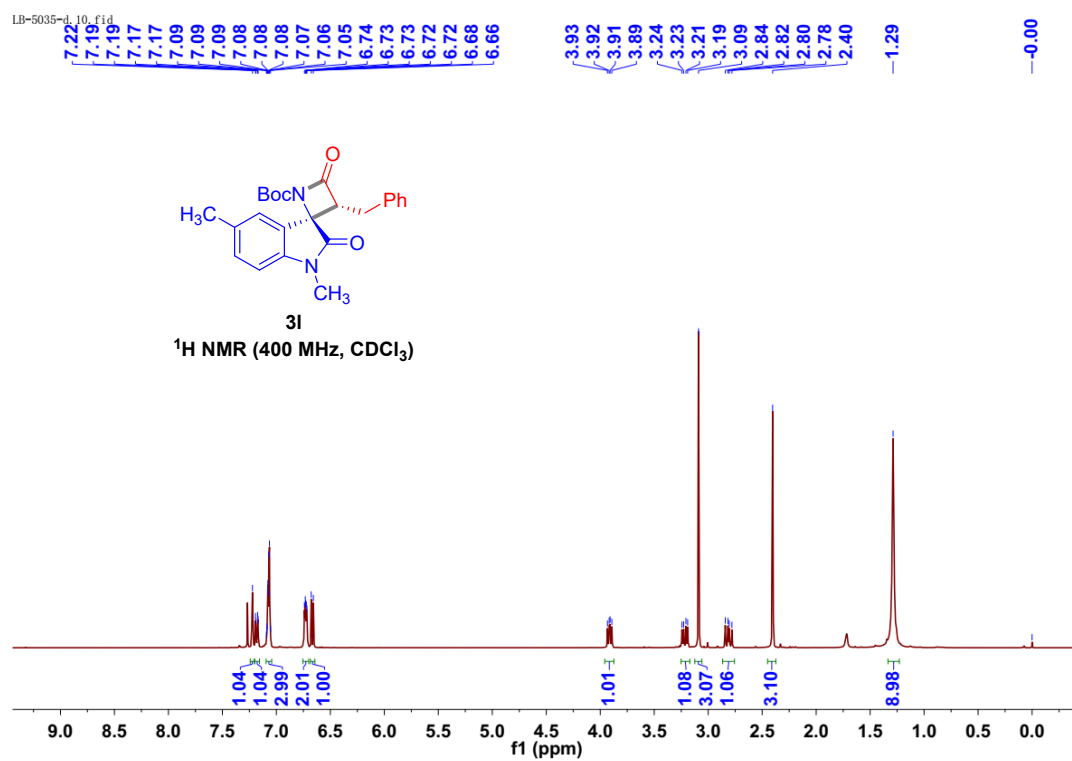


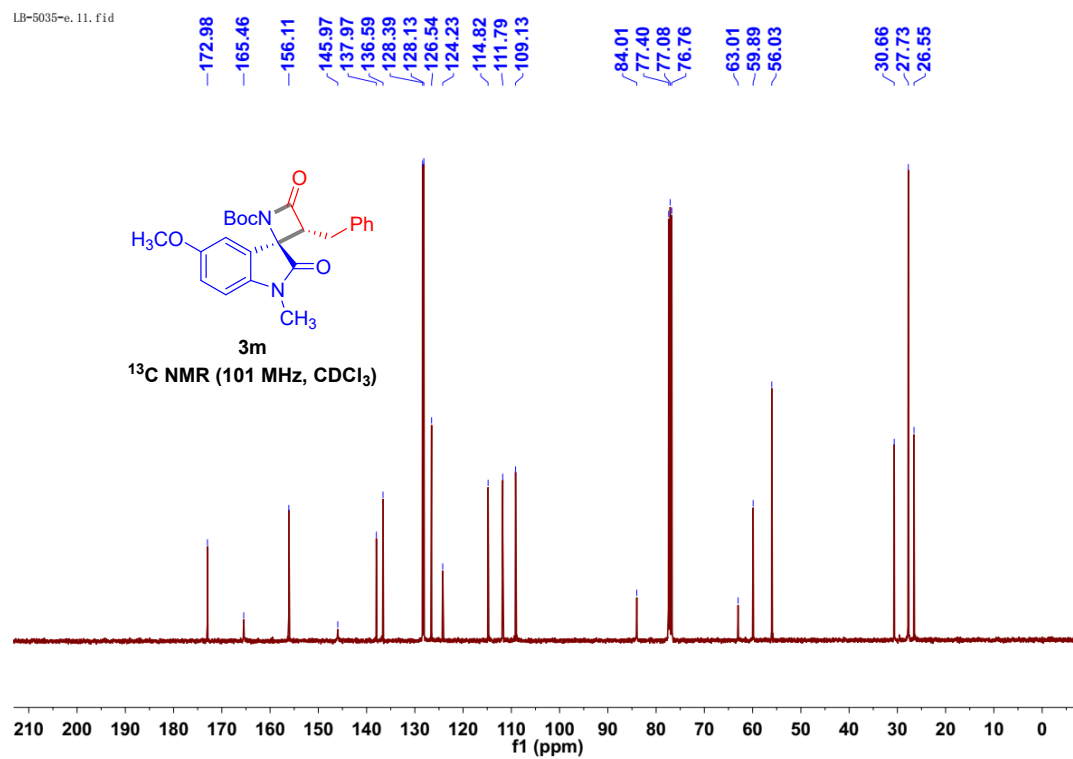
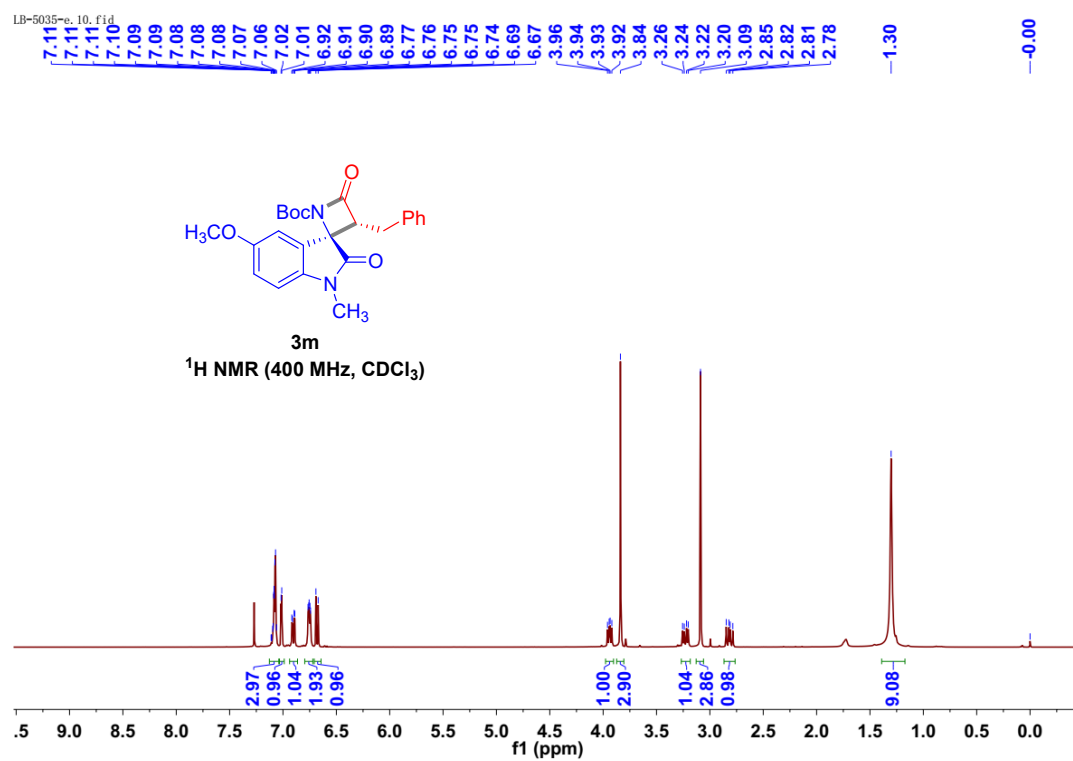


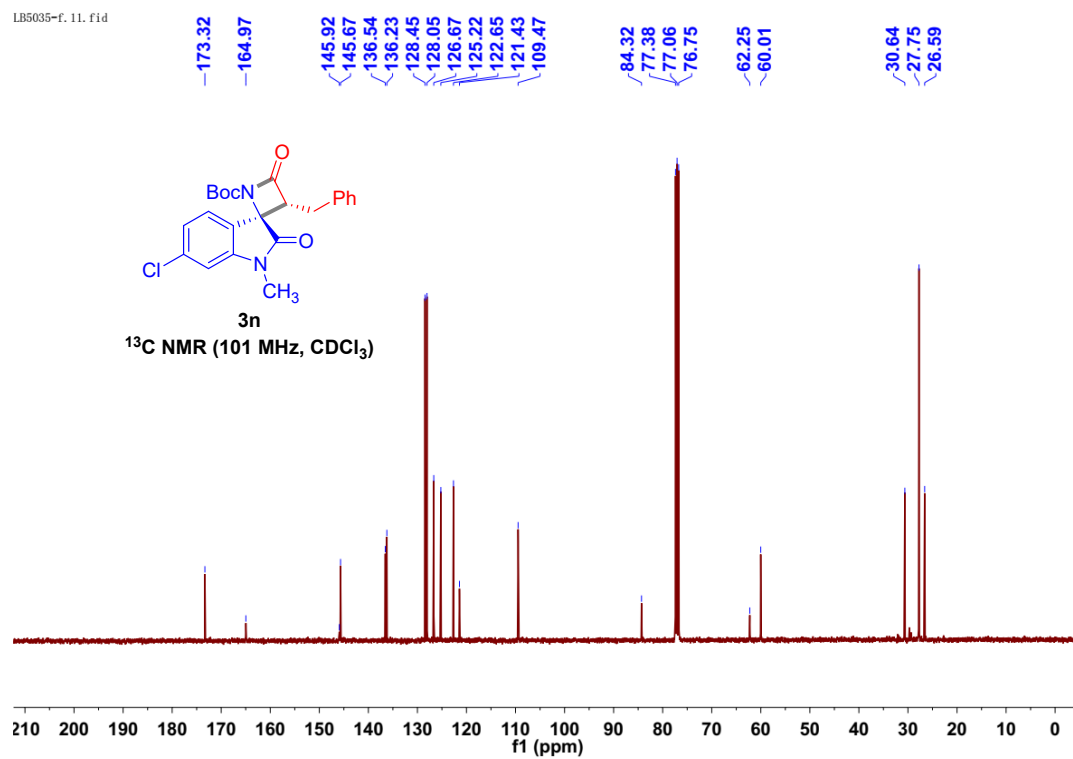
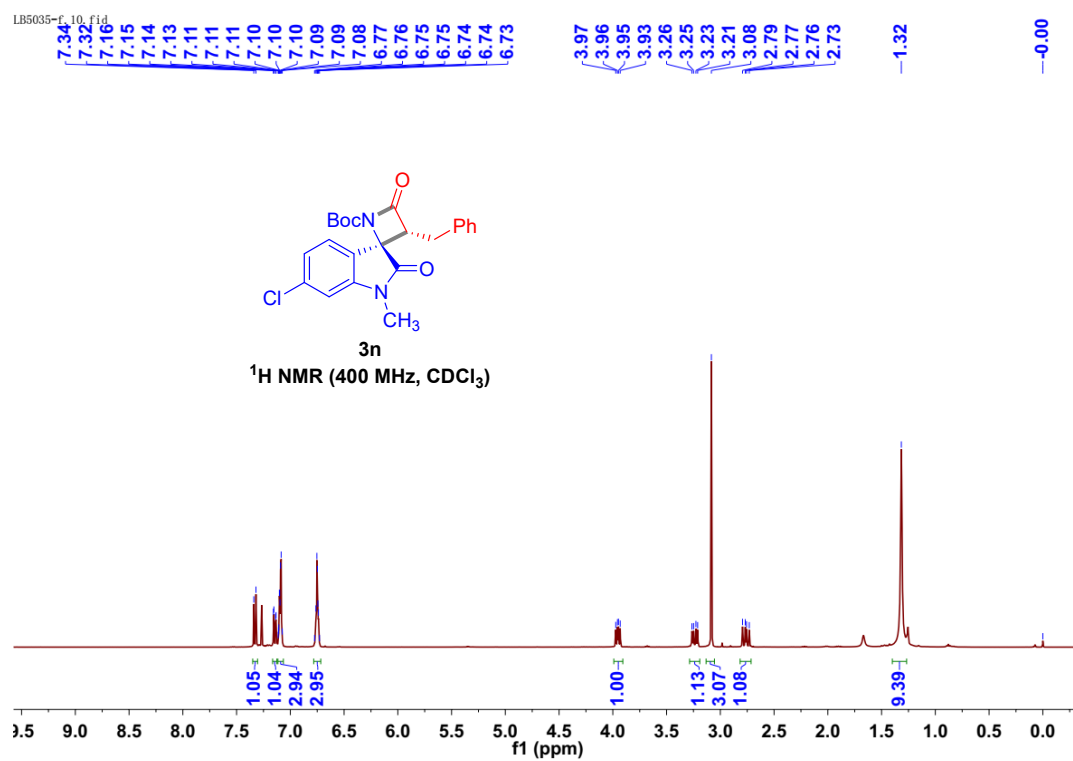


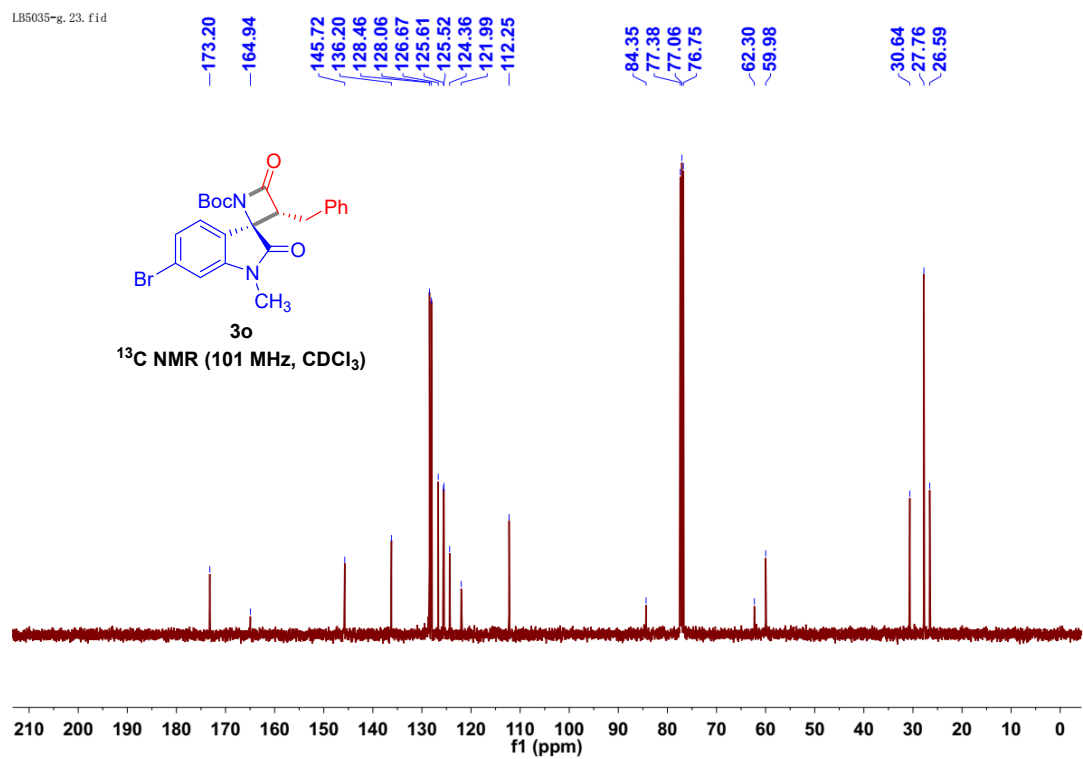
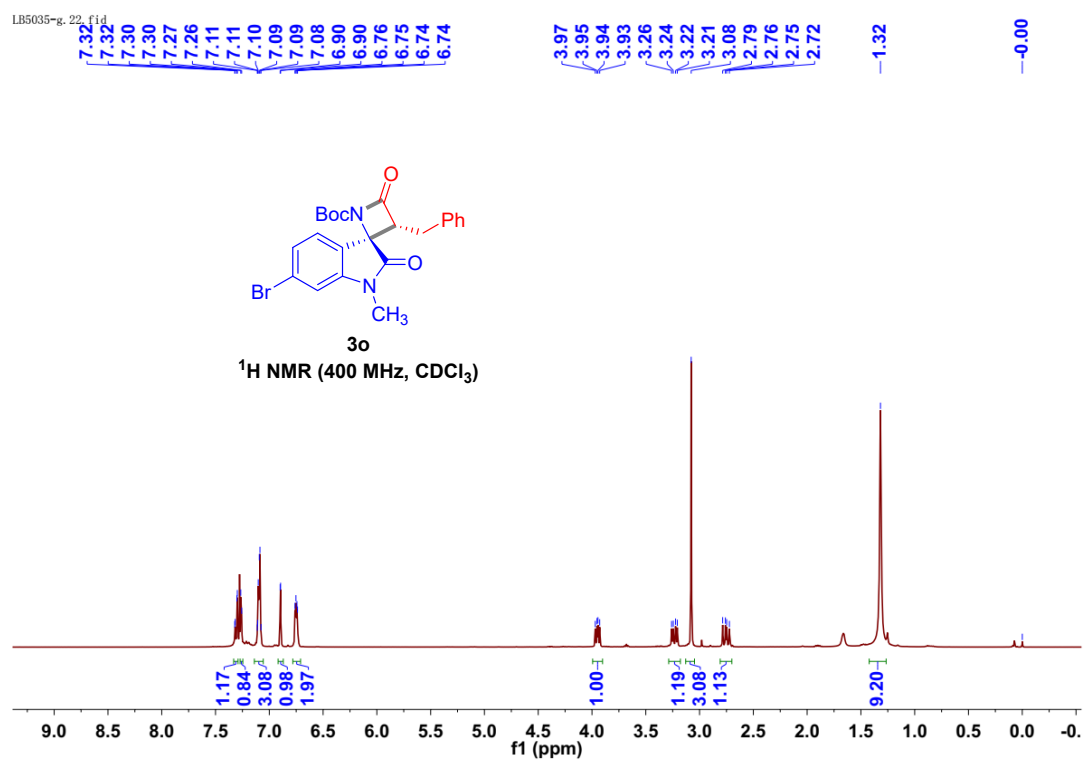


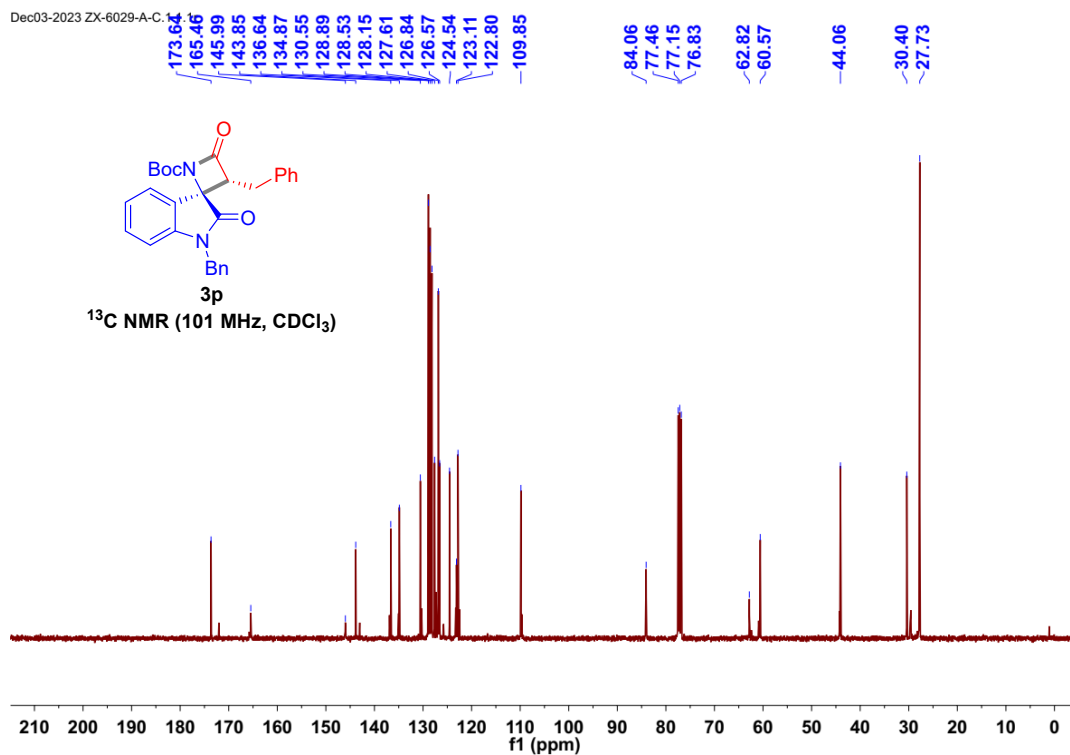
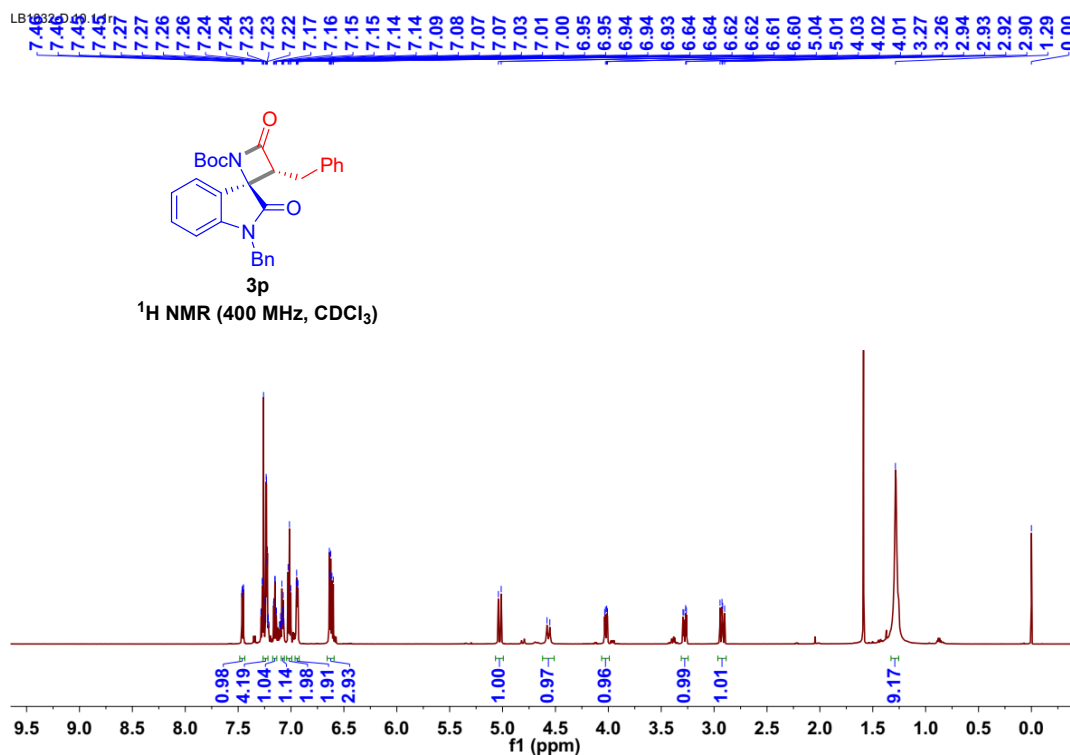


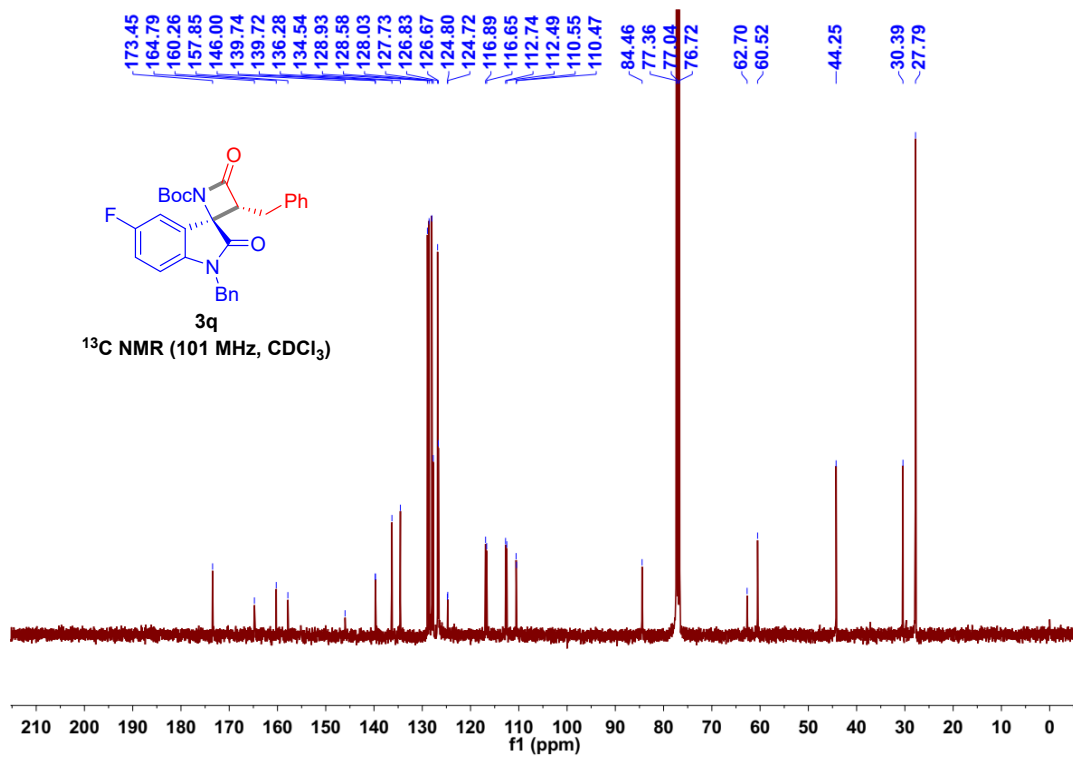
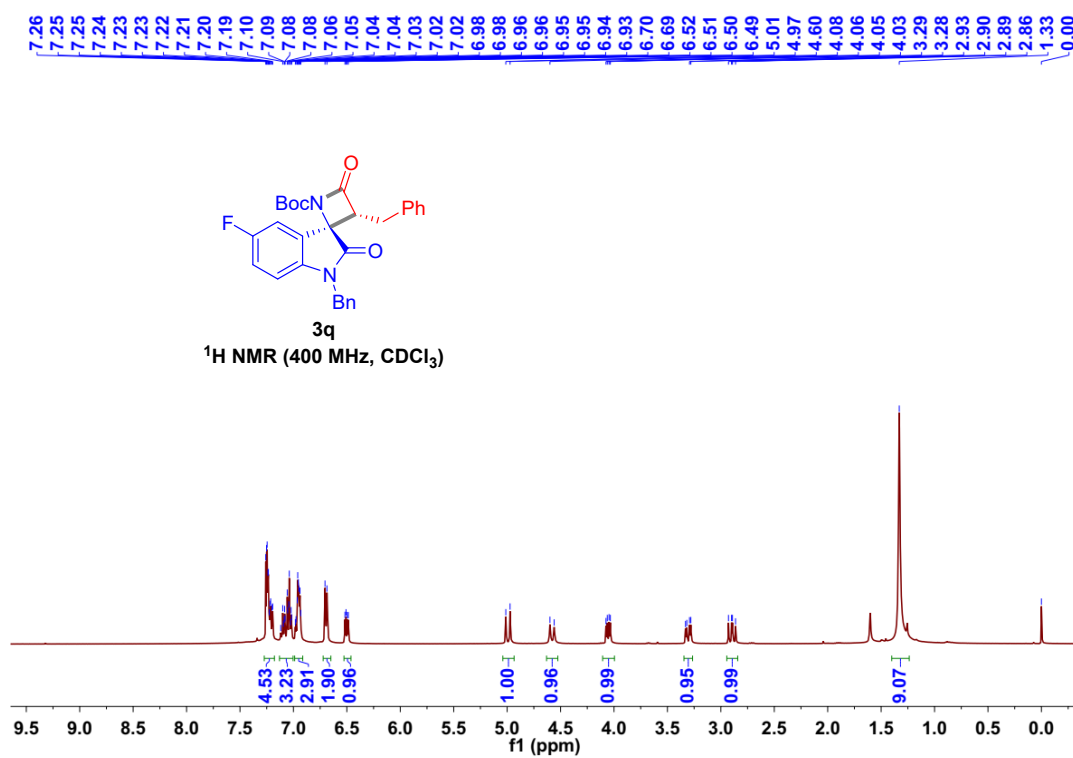




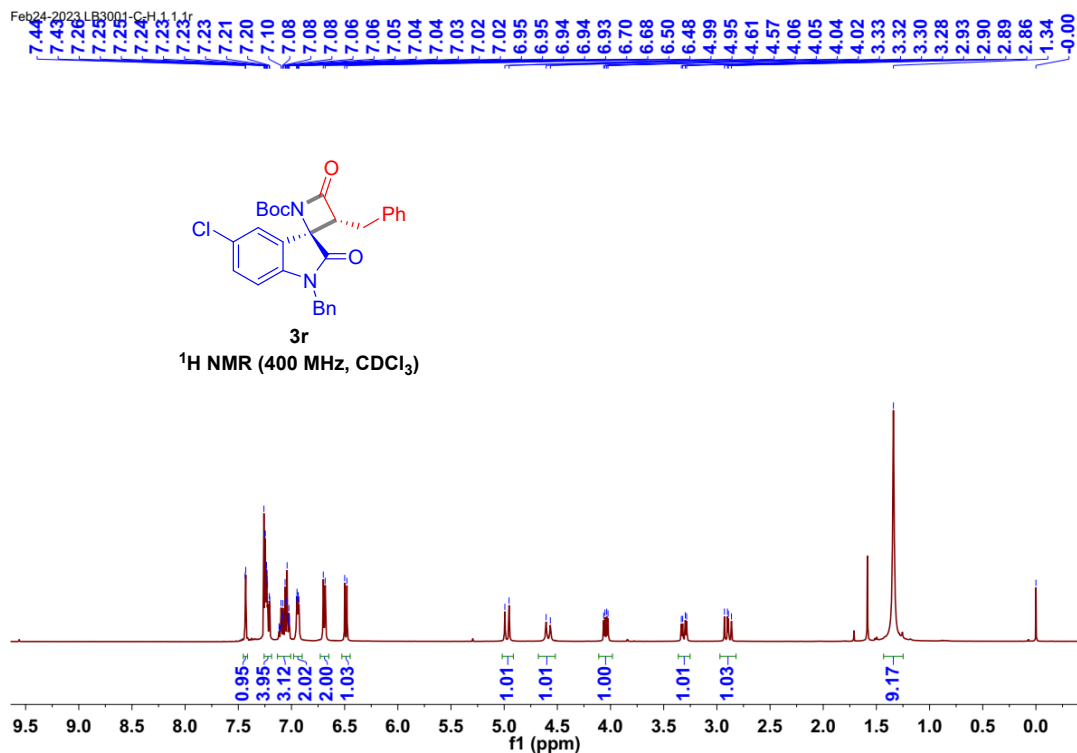




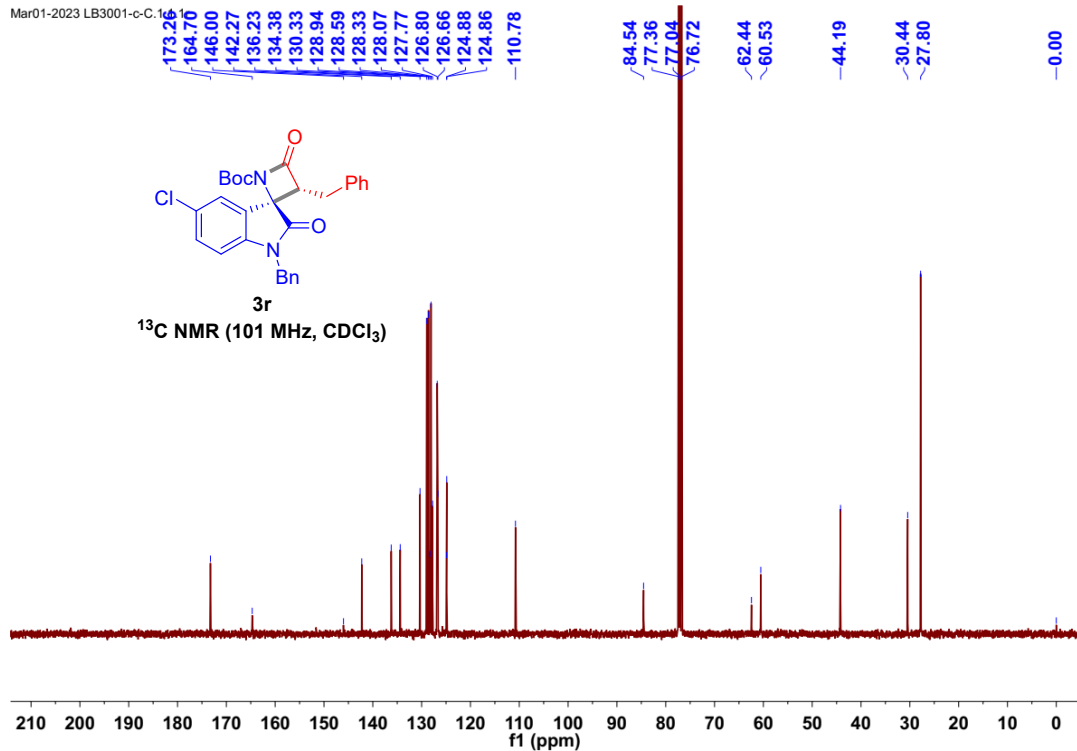


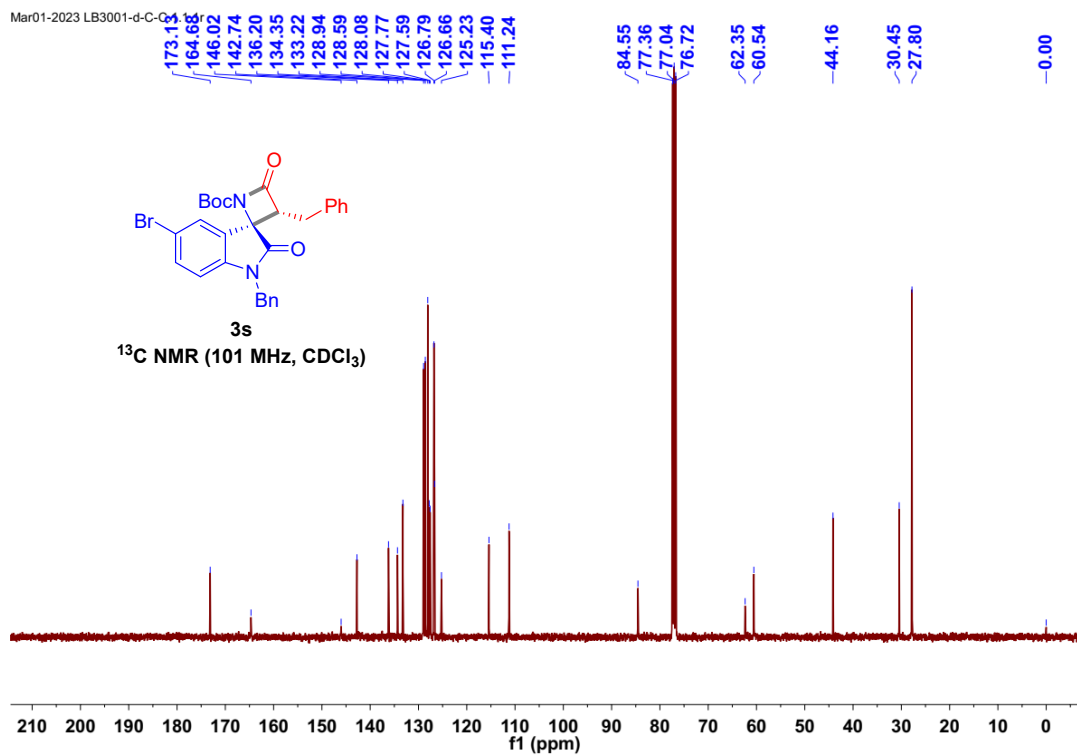
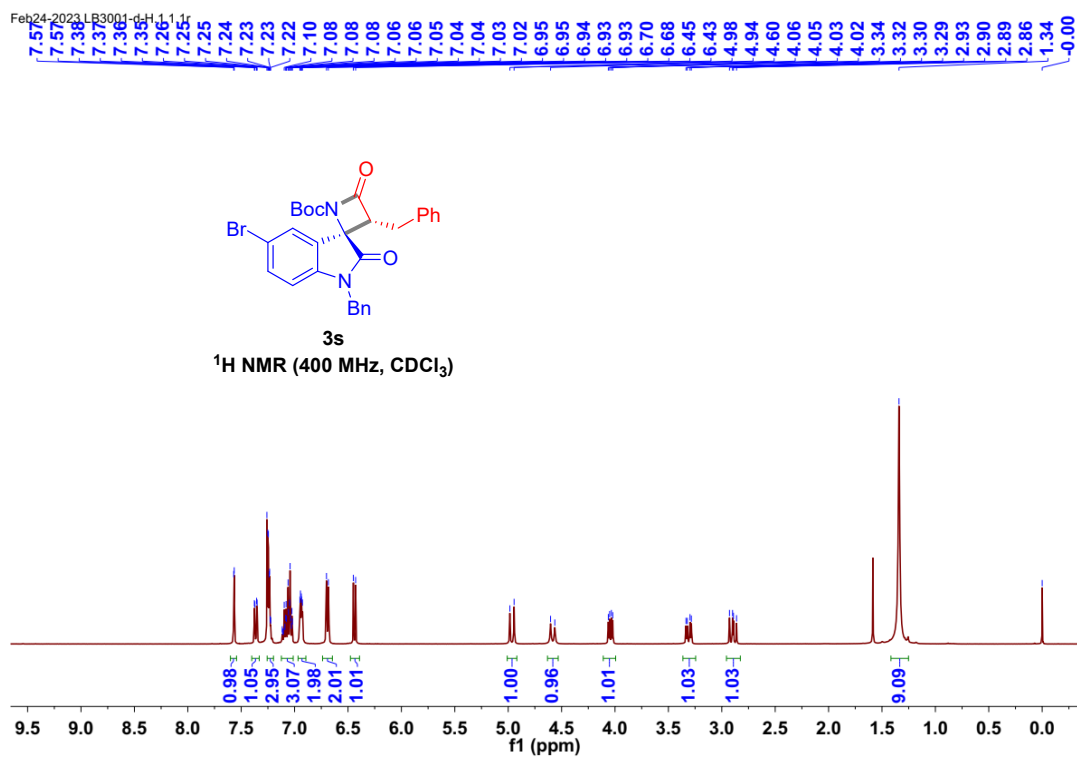


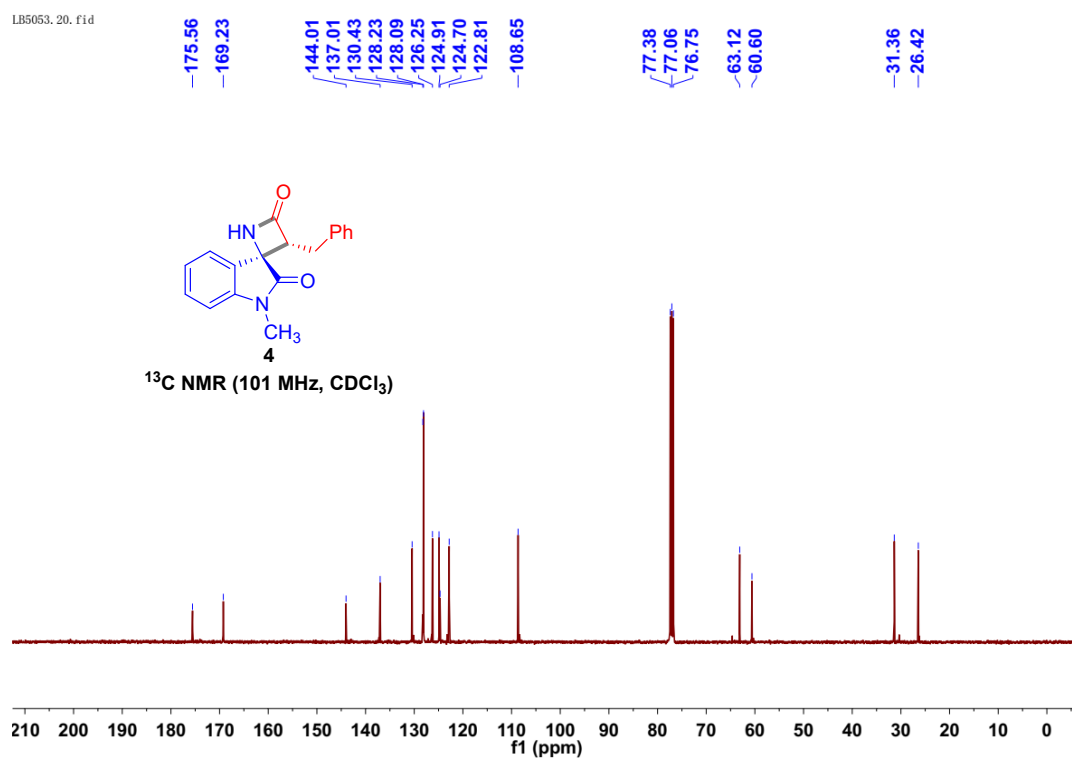
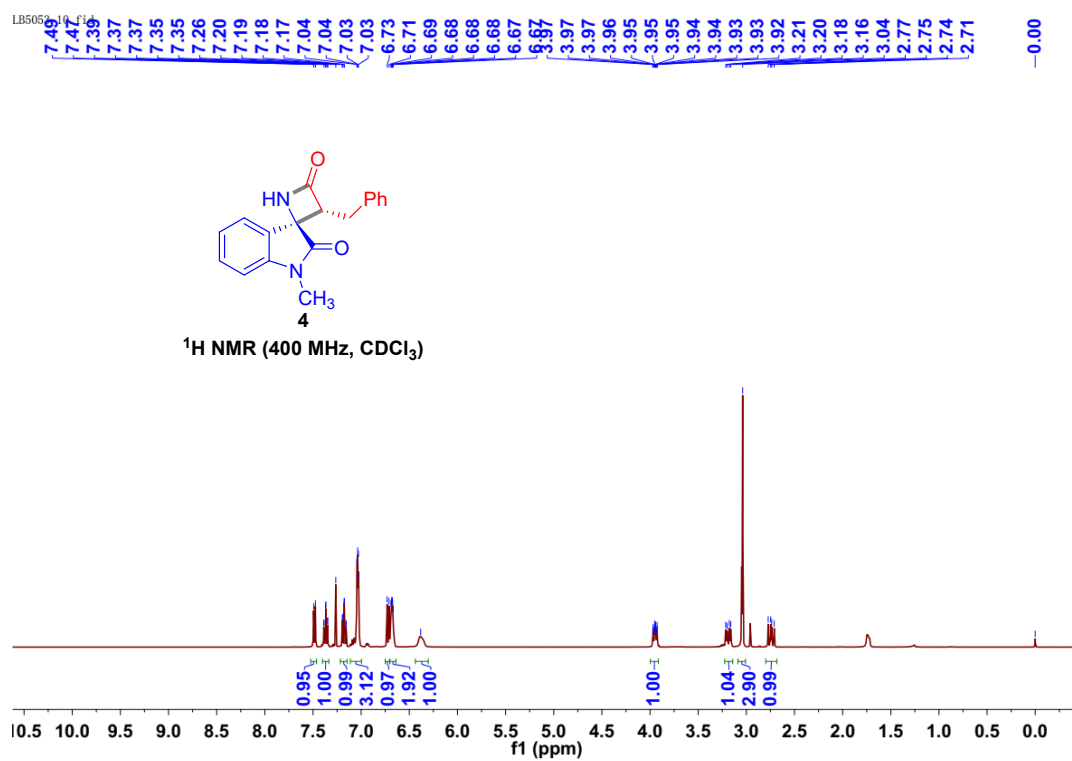
Feb24-2023 LB3001-C-H 1,1-tr

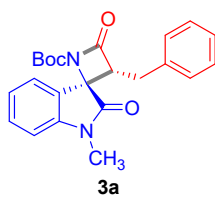


Mar01-2023 LB3001-c-C-16



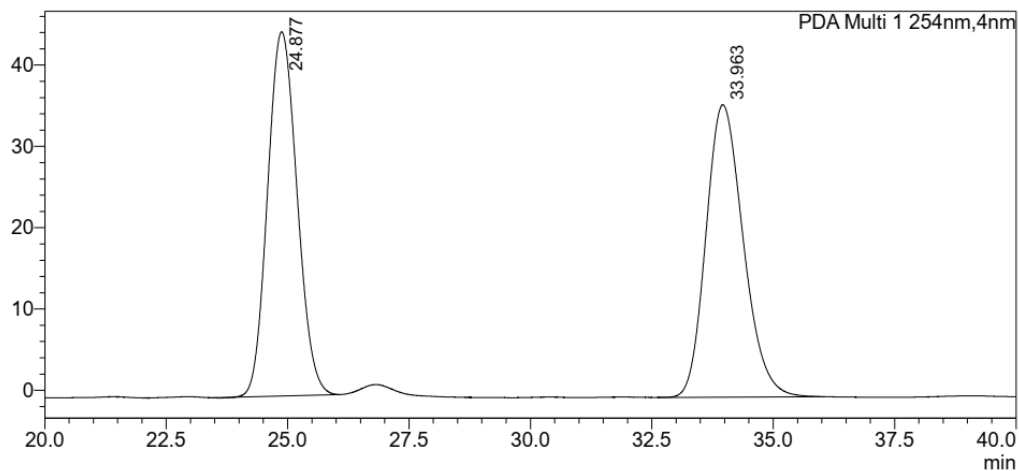






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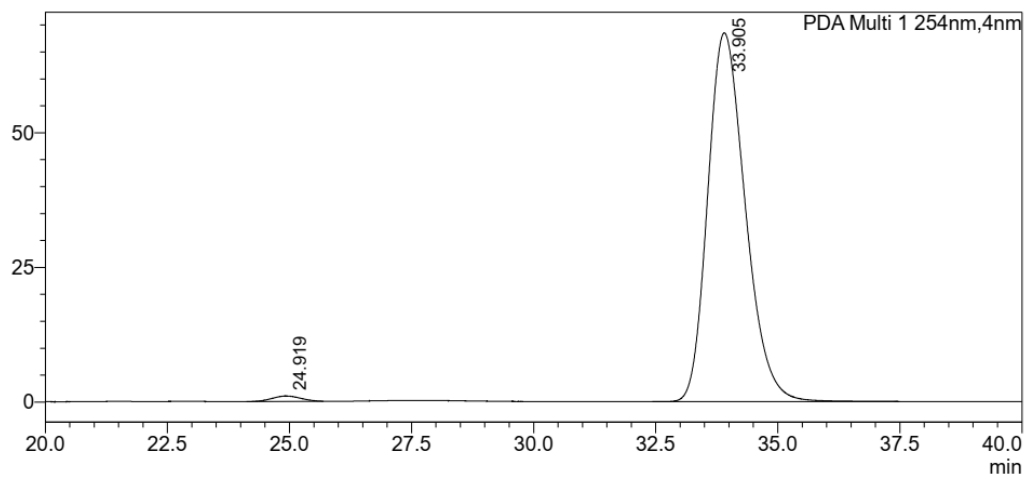
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PDA Ch1 254nm

Ret. Time	Area	Area%
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33.963	1923041	50.423
	3813821	100.000

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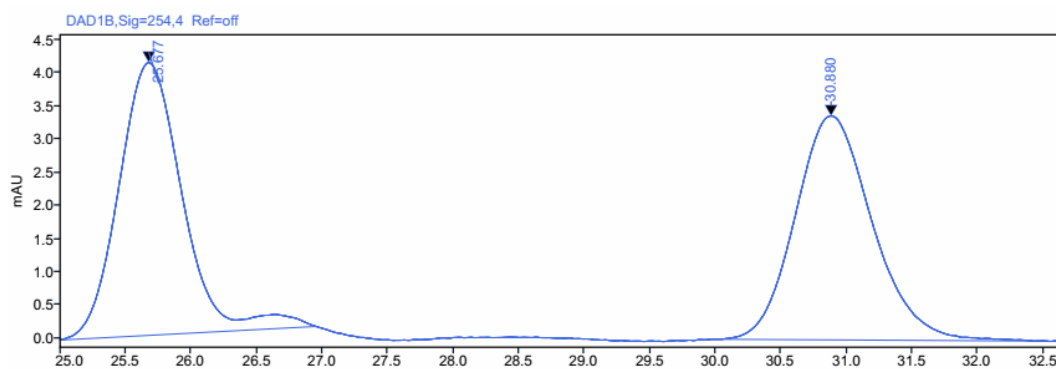
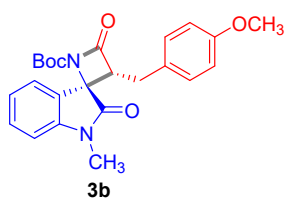
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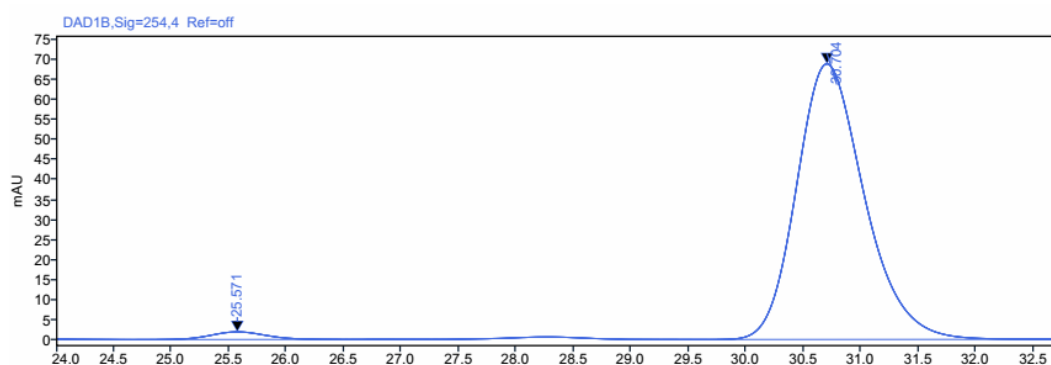
PDA Ch1 254nm

Ret. Time	Area	Area%
24.919	40327	1.089
33.905	3663206	98.911
	3703533	100.000



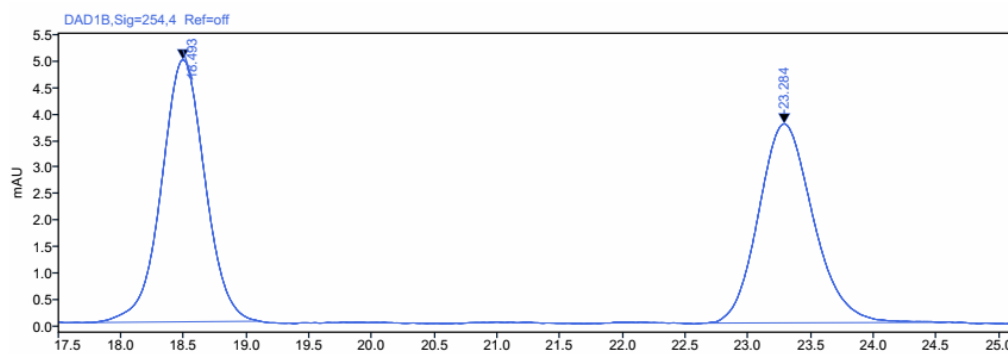
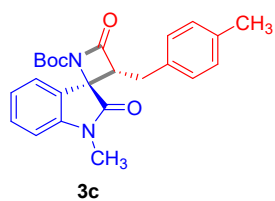
Signal: DAD1B, Sig=254,4 Ref=off

RT [min]	Width [min]	Area	Area%
25.677	1.98	138.77	50.15
30.880	2.39	137.93	49.85
Sum		276.70	



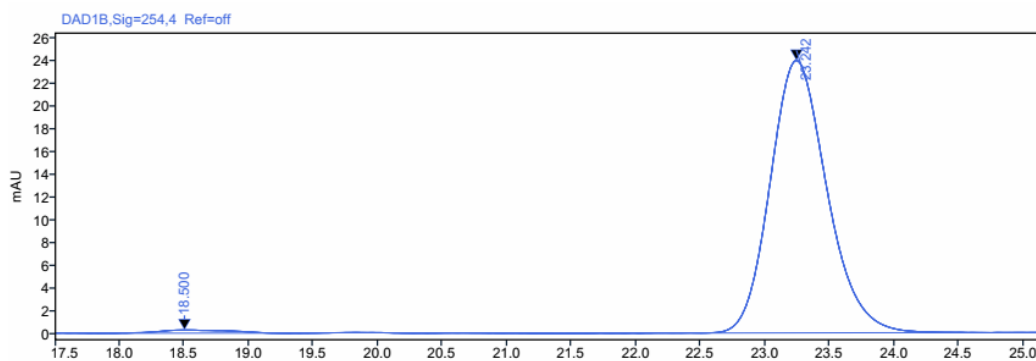
Signal: DAD1B, Sig=254,4 Ref=off

RT [min]	Width [min]	Area	Area%
25.571	1.61	63.54	2.20
30.704	3.43	2831.21	97.80
Sum		2894.75	



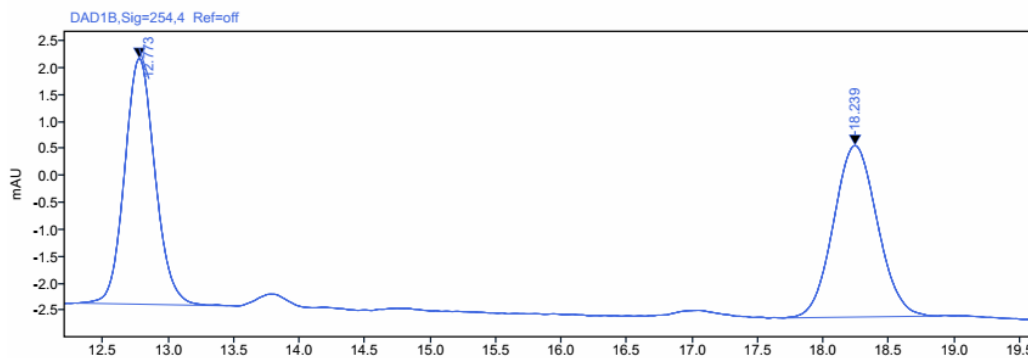
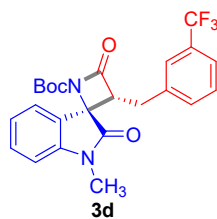
Signal: DAD1B,Sig=254,4 Ref=off

RT [min]	Width [min]	Area	Area%
18.493	1.35	119.73	51.26
23.284	1.88	113.85	48.74
Sum		233.58	



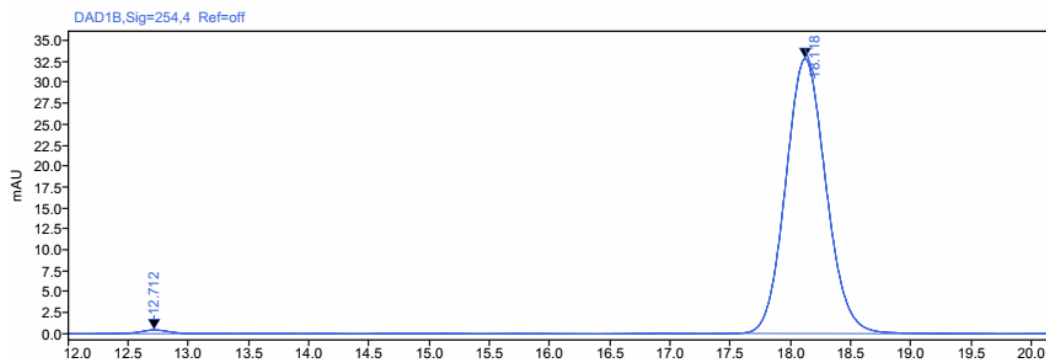
Signal: DAD1B,Sig=254,4 Ref=off

RT [min]	Width [min]	Area	Area%
18.500	1.36	10.78	1.45
23.242	2.07	734.35	98.55
Sum		745.13	



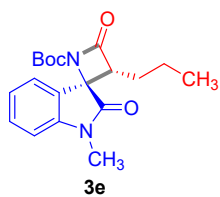
Signal: DAD1B, Sig=254,4 Ref=off

RT [min]	Width [min]	Area	Area%
12.773	1.23	73.72	49.88
18.239	1.19	74.08	50.12
Sum		147.80	

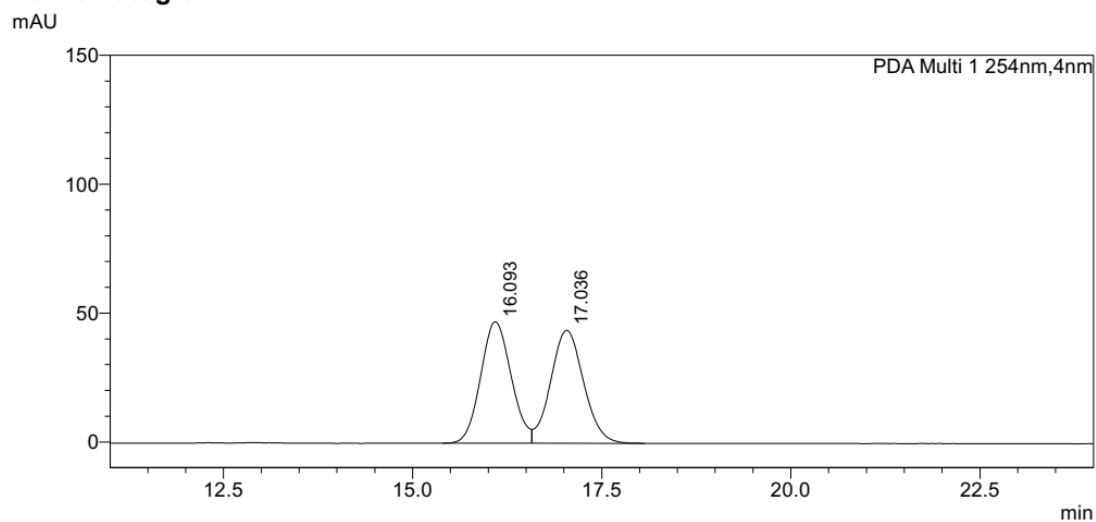


Signal: DAD1B, Sig=254,4 Ref=off

RT [min]	Width [min]	Area	Area%
12.712	1.48	7.19	0.93
18.118	2.17	763.92	99.07
Sum		771.11	



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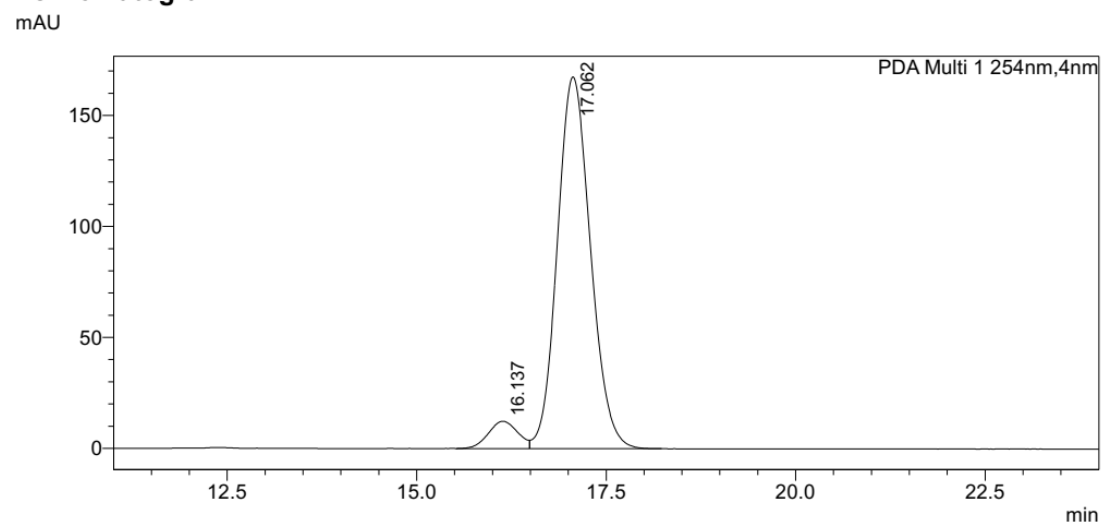


<Peak Table>

PDA Ch1 254nm

Ret. Time	Area	Area%
16.093	1323977	49.917
17.036	1328382	50.083
	2652359	100.000

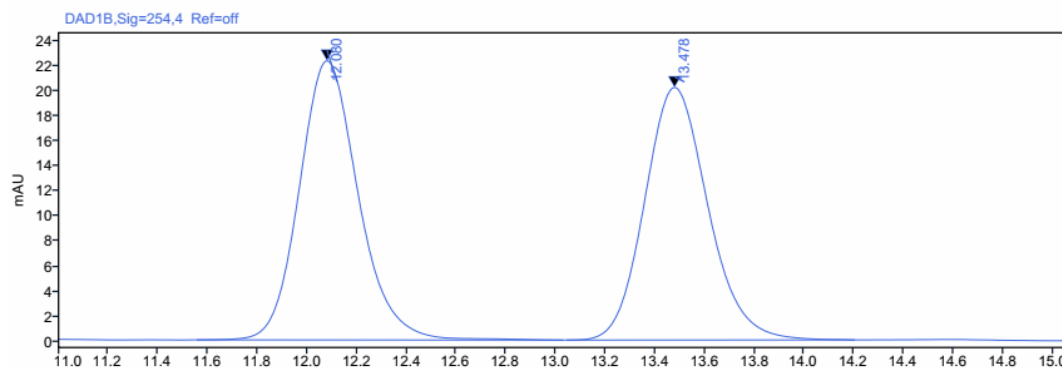
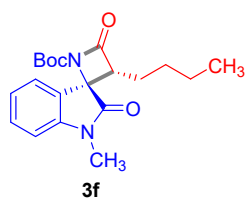
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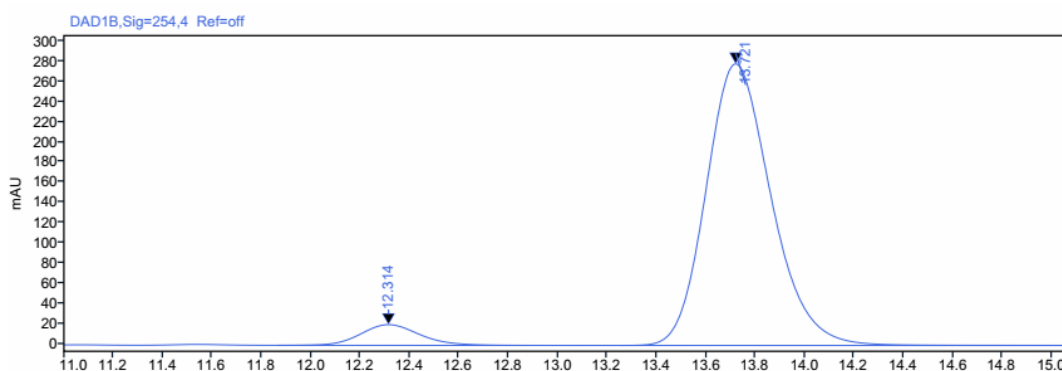
PDA Ch1 254nm

Ret. Time	Area	Area%
16.137	334433	6.158
17.062	5096781	93.842
	5431214	100.000



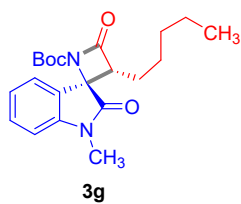
Signal: DAD1B, Sig=254,4 Ref=off

RT [min]	Width [min]	Area	Area%
12.080	1.47	368.53	50.77
13.478	1.16	357.40	49.23
Sum		725.94	



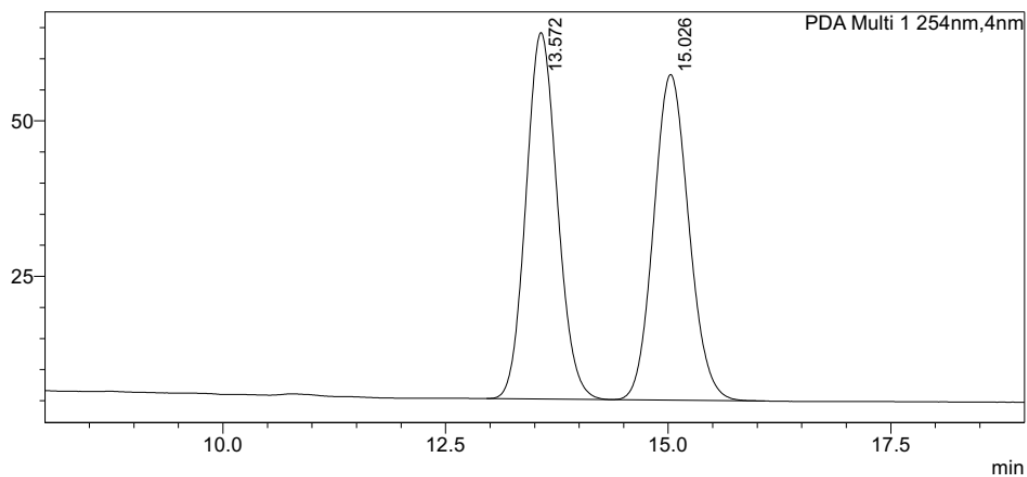
Signal: DAD1B, Sig=254,4 Ref=off

RT [min]	Width [min]	Area	Area%
12.314	1.23	342.40	6.28
13.721	2.21	5110.10	93.72
Sum		5452.50	



<Chromatogram>

mAU



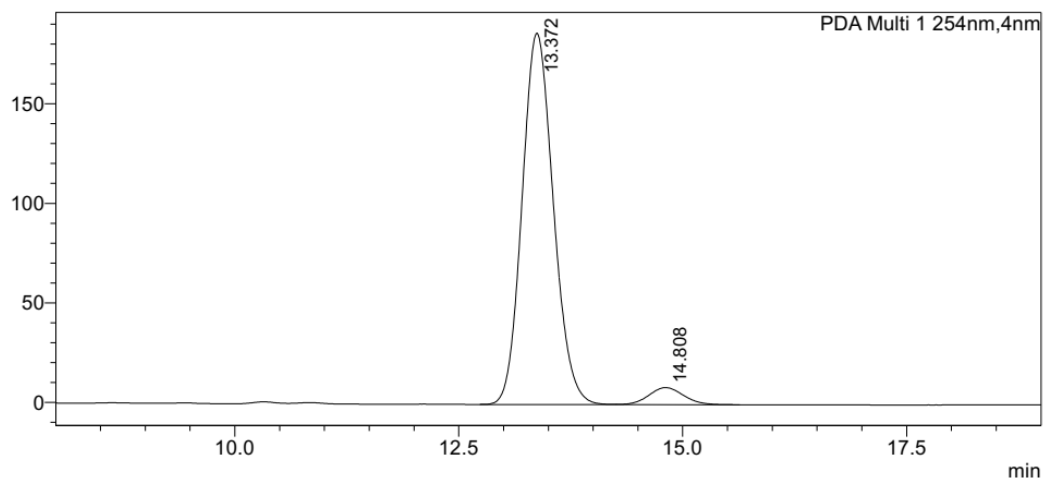
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PDA Ch1 254nm

Ret. Time	Area	Area%
13.572	1445064	50.117
15.026	1438307	49.883
	2883371	100.000

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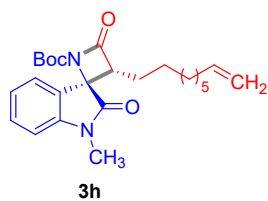
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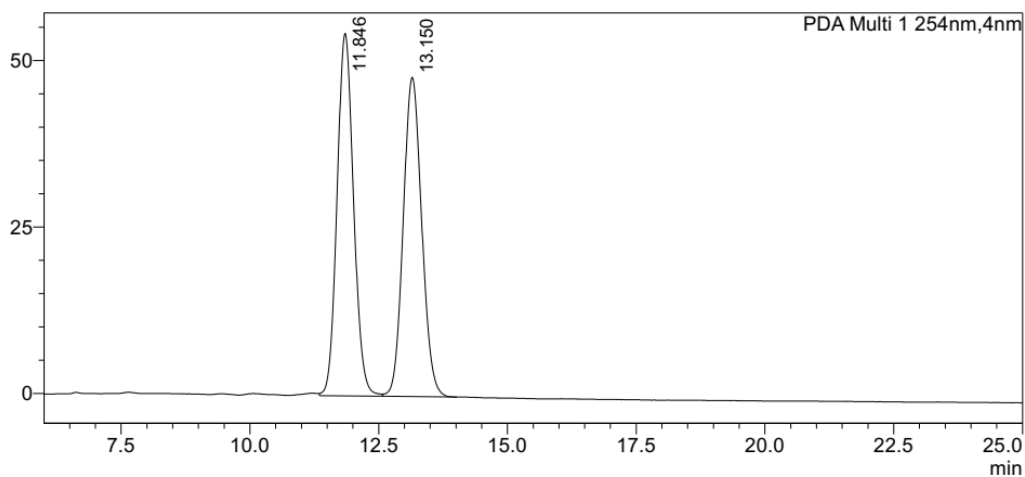
PDA Ch1 254nm

Ret. Time	Area	Area%
13.372	4527750	95.143
14.808	231143	4.857
	4758893	100.000



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mAU



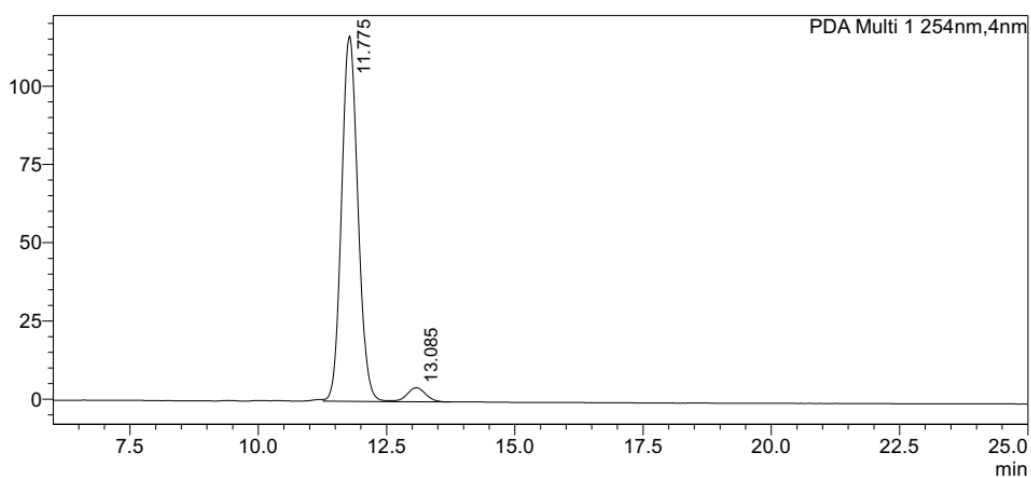
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PDA Ch1 254nm

Ret. Time	Area	Area%
11.846	1215696	50.381
13.150	1197289	49.619
	2412984	100.000

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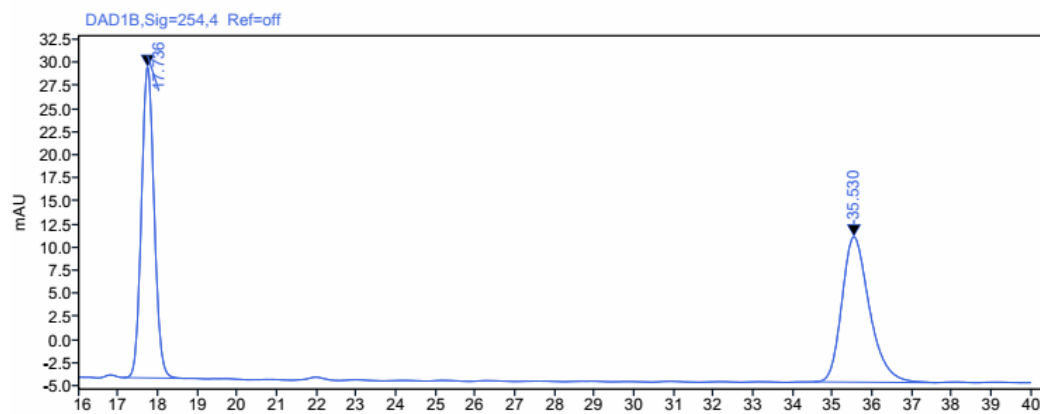
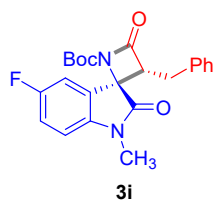
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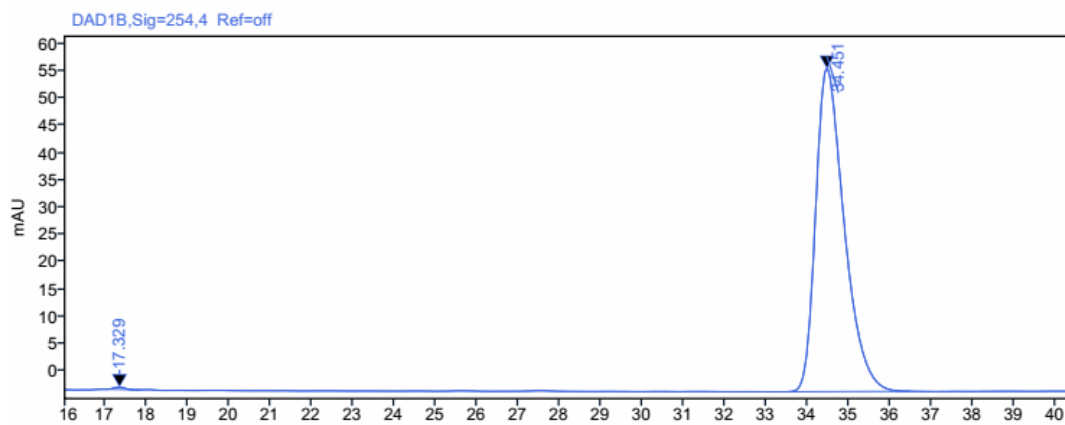
PDA Ch1 254nm

Ret. Time	Area	Area%
11.775	2583790	95.798
13.085	113344	4.202
	2697134	100.000



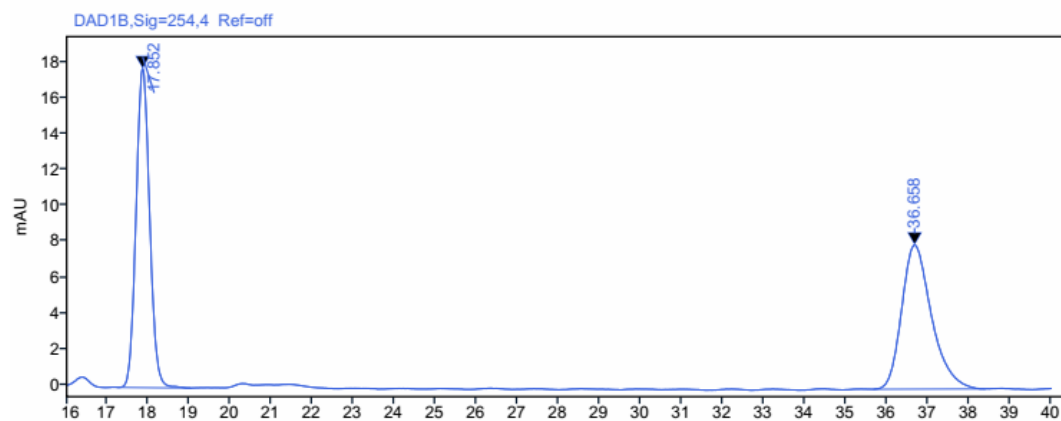
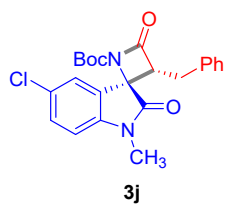
Signal: DAD1B,Sig=254,4 Ref=off

RT [min]	Width [min]	Area	Area%
17.736	1.56	750.22	49.69
35.530	3.06	759.49	50.31
Sum		1509.72	



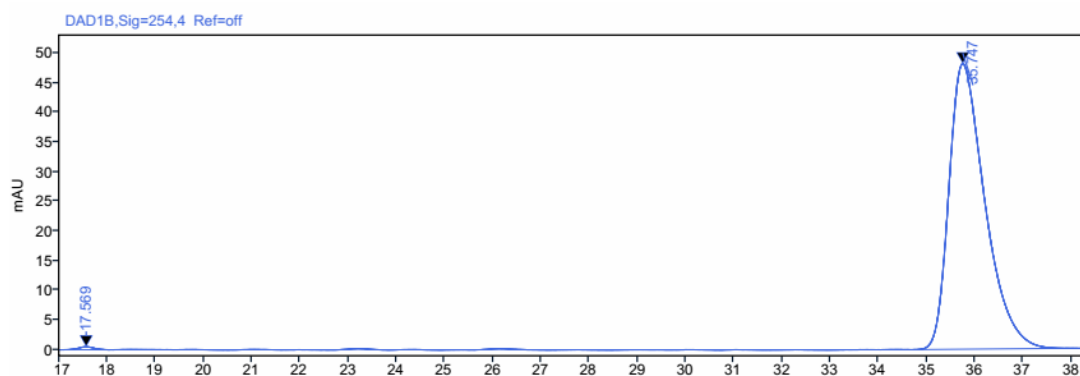
Signal: DAD1B,Sig=254,4 Ref=off

RT [min]	Width [min]	Area	Area%
17.329	0.82	7.32	0.26
34.451	2.99	2842.55	99.74
Sum		2849.87	



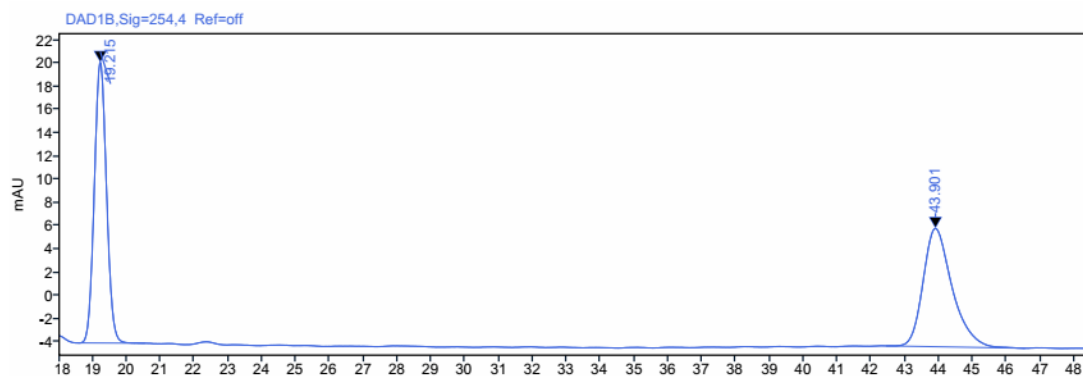
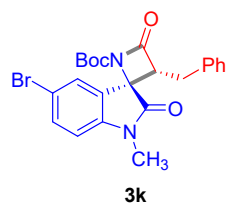
Signal: DAD1B,Sig=254,4 Ref=off

RT [min]	Width [min]	Area	Area%
17.852	1.79	408.58	50.21
36.658	2.72	405.23	49.79
Sum		813.82	



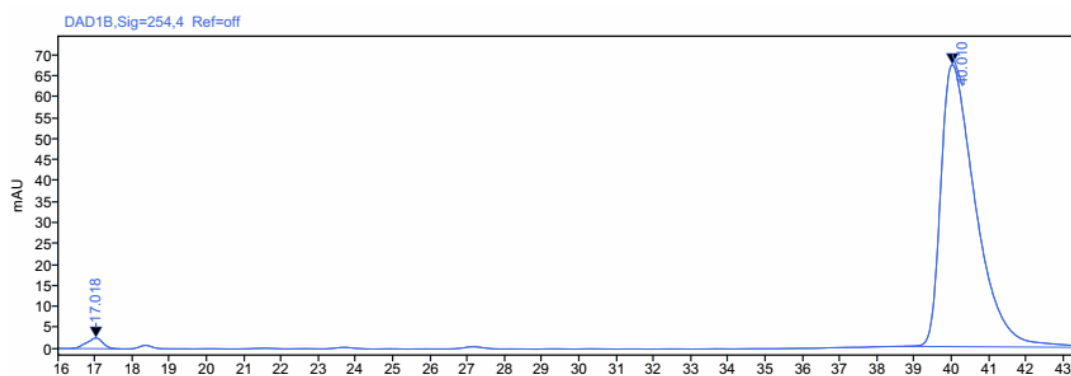
Signal: DAD1B,Sig=254,4 Ref=off

RT [min]	Width [min]	Area	Area%
17.569	0.90	10.42	0.42
35.747	3.06	2496.35	99.58
Sum		2506.77	



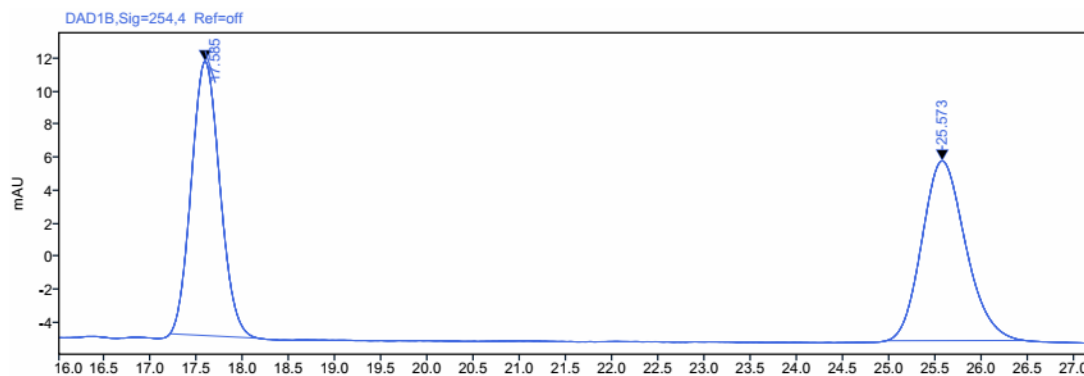
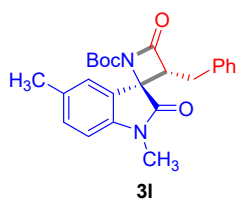
Signal: DAD1B,Sig=254,4 Ref=off

RT [min]	Width [min]	Area	Area%
19.215	2.05	604.73	49.95
43.901	4.11	605.97	50.05
Sum		1210.71	



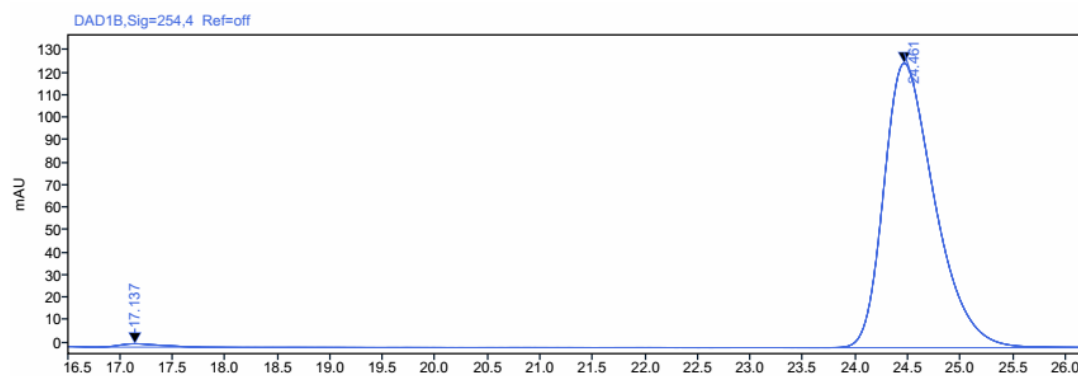
Signal: DAD1B,Sig=254,4 Ref=off

RT [min]	Width [min]	Area	Area%
17.018	1.30	76.50	1.72
40.010	5.91	4363.07	98.28
Sum		4439.57	



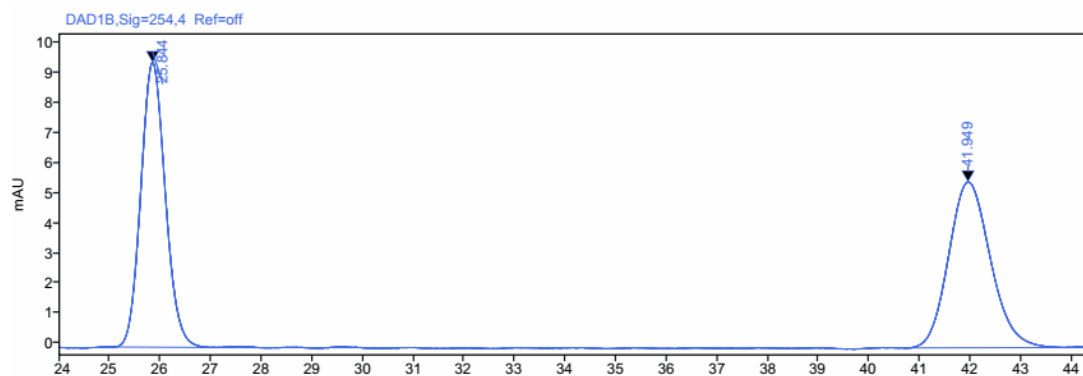
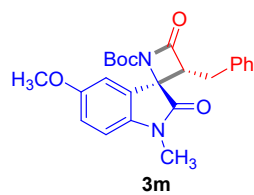
Signal: DAD1B,Sig=254,4 Ref=off

RT [min]	Width [min]	Area	Area%
17.585	0.96	357.15	49.92
25.573	1.50	358.29	50.08
Sum		715.45	



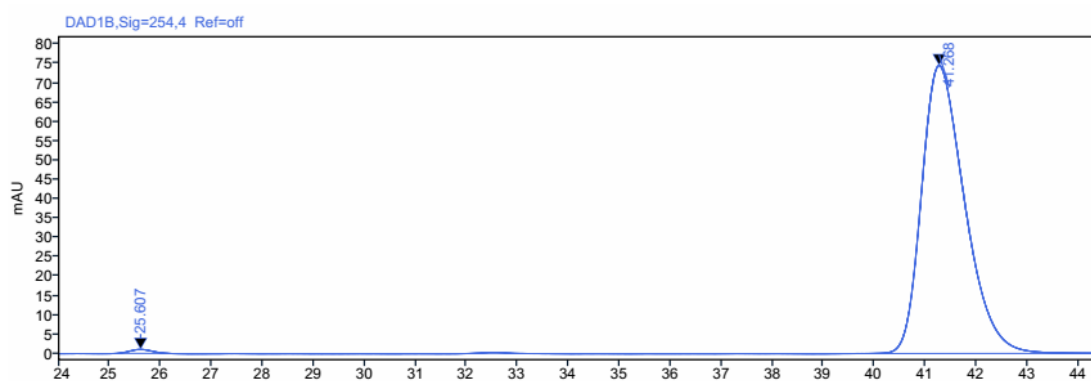
Signal: DAD1B,Sig=254,4 Ref=off

RT [min]	Width [min]	Area	Area%
17.137	1.04	40.59	0.94
24.461	3.21	4256.85	99.06
Sum		4297.44	



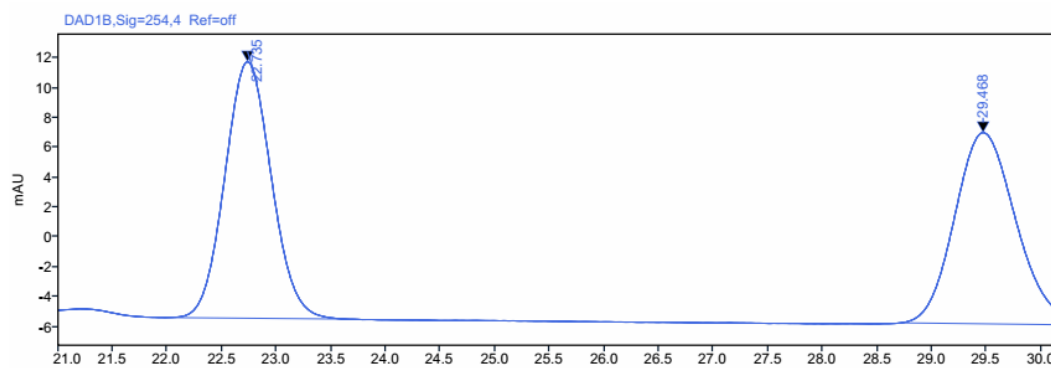
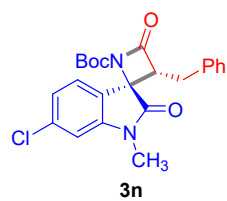
Signal: DAD1B,Sig=254,4 Ref=off

RT [min]	Width [min]	Area	Area%
25.844	2.00	317.86	50.20
41.949	3.04	315.32	49.80
Sum		633.18	



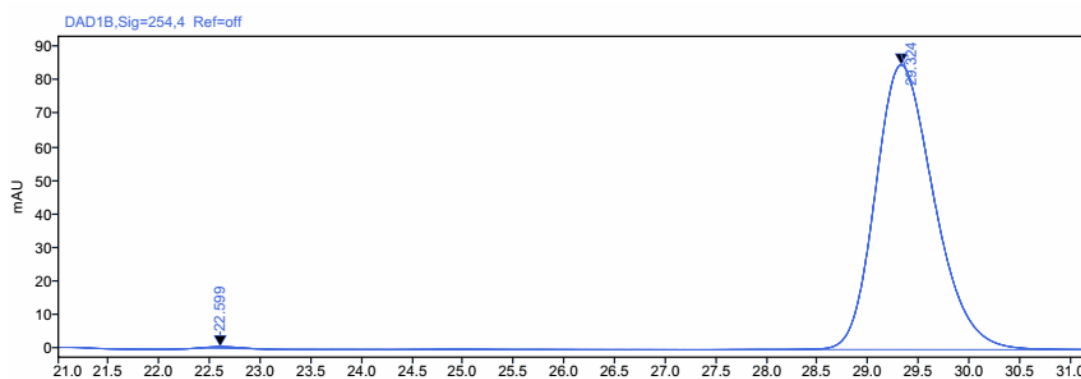
Signal: DAD1B,Sig=254,4 Ref=off

RT [min]	Width [min]	Area	Area%
25.607	1.00	30.23	0.69
41.268	4.62	4367.55	99.31
Sum		4397.78	



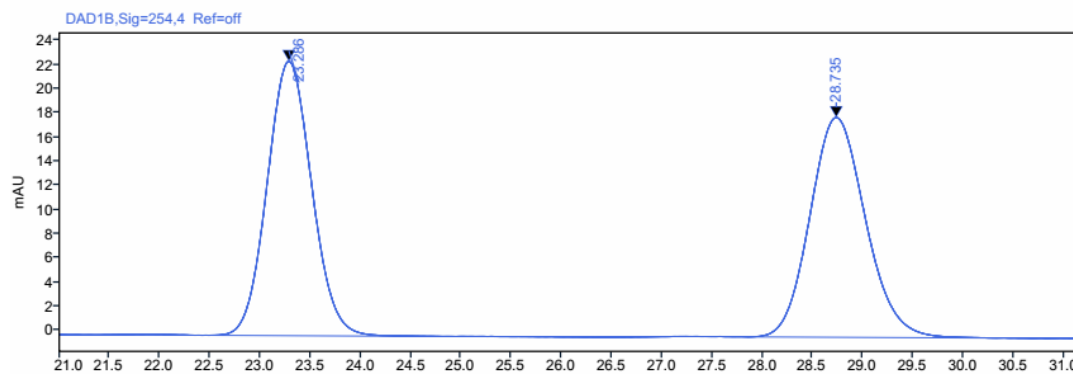
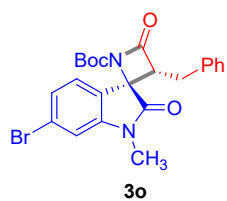
Signal: DAD1B,Sig=254,4 Ref=off

RT [min]	Width [min]	Area	Area%
22.735	1.67	509.22	50.40
29.468	2.23	501.23	49.60
Sum		1010.45	



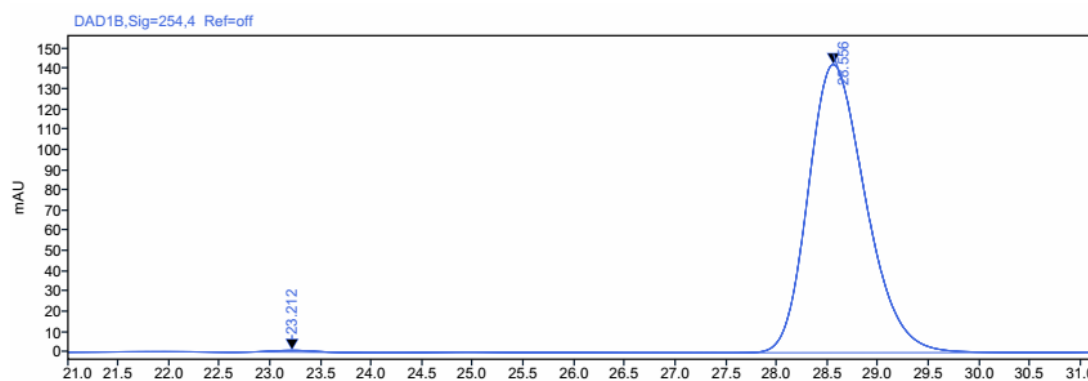
Signal: DAD1B,Sig=254,4 Ref=off

RT [min]	Width [min]	Area	Area%
22.599	0.60	10.46	0.31
29.324	3.56	3418.63	99.69
Sum		3429.09	



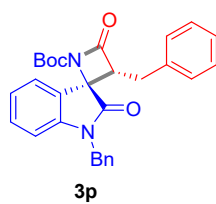
Signal: DAD1B,Sig=254,4 Ref=off

RT [min]	Width [min]	Area	Area%
23.286	2.33	701.58	50.08
28.735	2.49	699.48	49.92
Sum		1401.06	

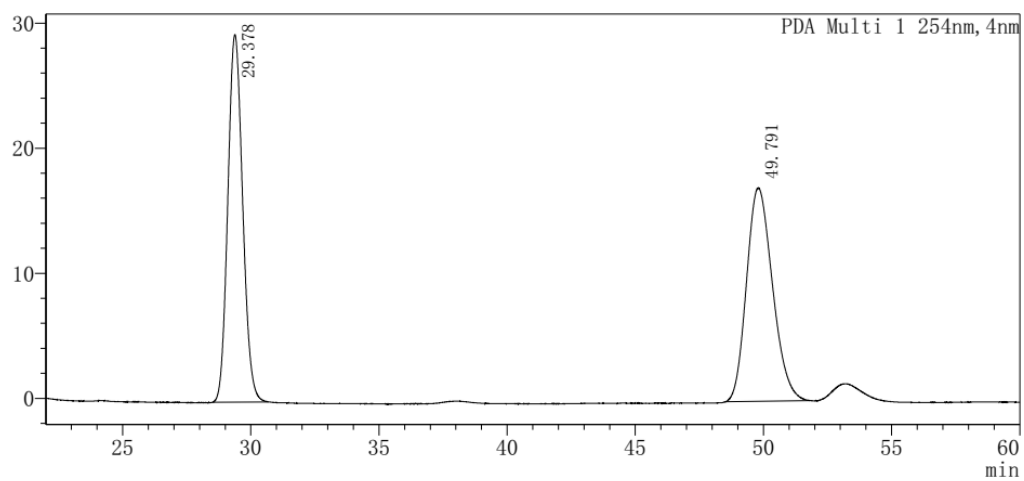


Signal: DAD1B,Sig=254,4 Ref=off

RT [min]	Width [min]	Area	Area%
23.212	1.06	24.35	0.43
28.556	3.10	5613.49	99.57
Sum		5637.84	



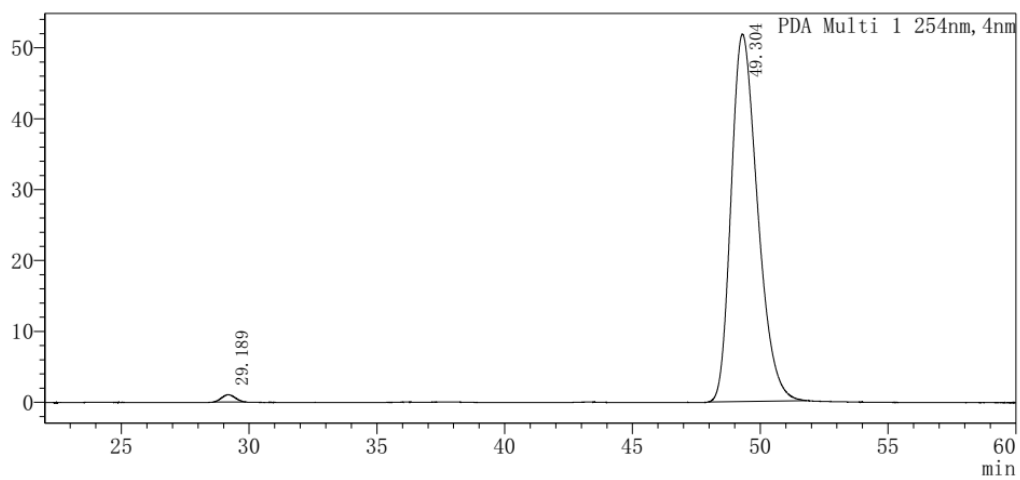
mAU



PDA Ch1 254nm

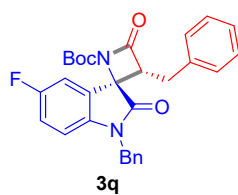
Ret. Time	Area	Area%
29.378	1181587	49.591
49.791	1201088	50.409
	2382674	100.000

mAU

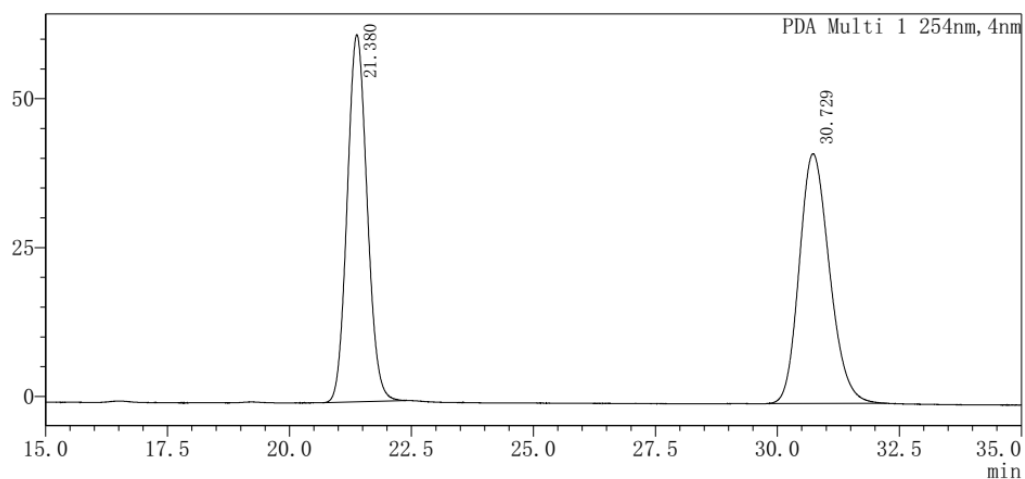


PDA Ch1 254nm

Ret. Time	Area	Area%
29.189	37742	1.002
49.304	3729143	98.998
	3766885	100.000



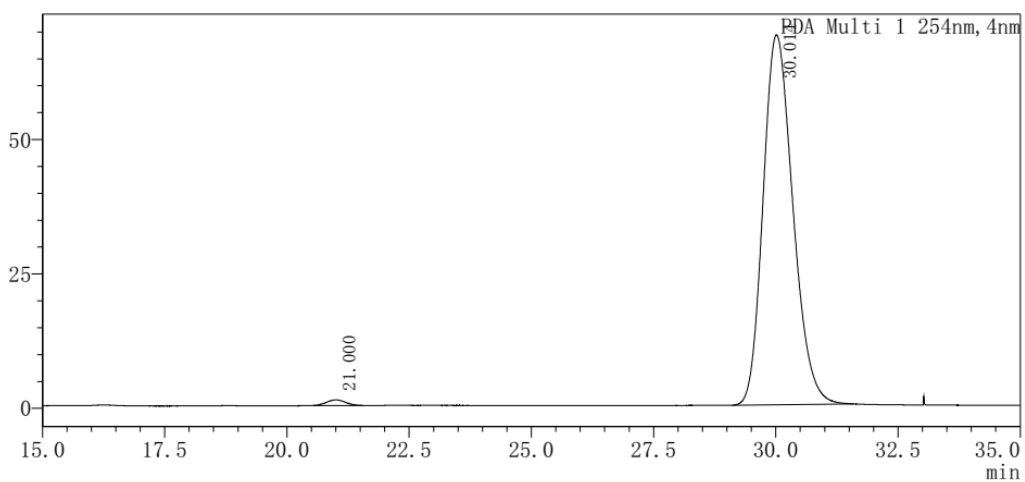
mAU



PDA Ch1 254nm

Ret. Time	Area	Area%
21.380	1751247	49.183
30.729	1809427	50.817
	3560673	100.000

mAU



PDA Ch1 254nm

Ret. Time	Area	Area%
21.000	28163	0.957
30.014	2915404	99.043
	2943567	100.000



mAU



PDA Ch1 254nm

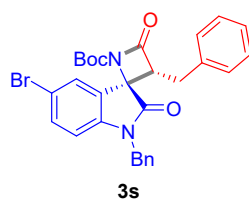
Ret. Time	Area	Area%
26.512	708890	50.670
35.716	690129	49.330
	1399019	100.000

mAU

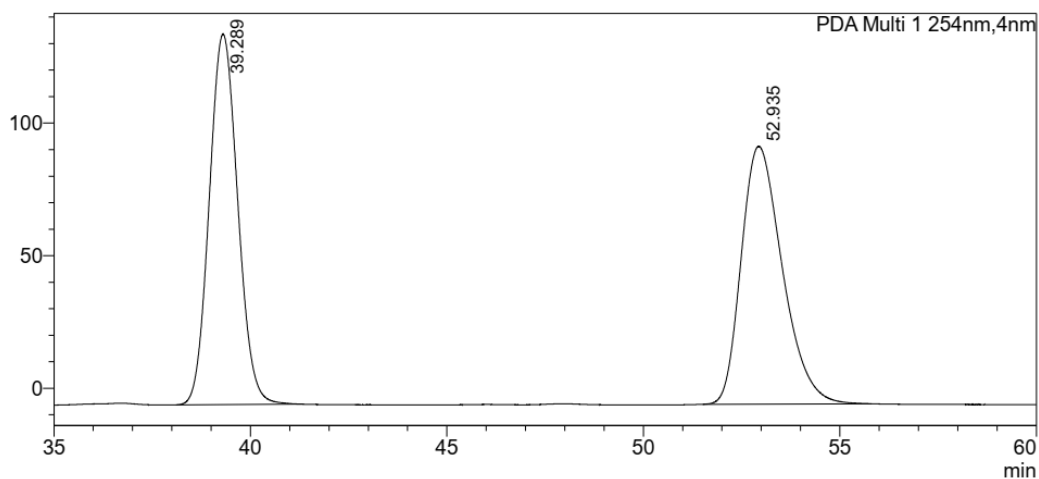


PDA Ch1 254nm

Ret. Time	Area	Area%
27.179	98782	1.012
35.594	9662778	98.988
	9761560	100.000



mAU



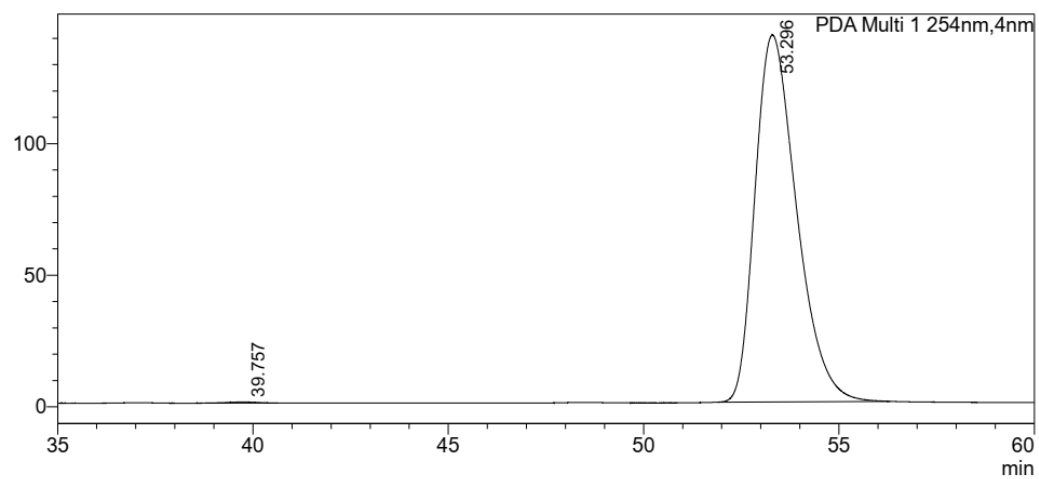
<Peak Table>

PDA Ch1 254nm

Ret. Time	Area	Area%
39.289	7035276	49.880
52.935	7069153	50.120
	14104430	100.000

<Chromatogram>

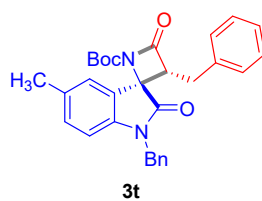
mAU



<Peak Table>

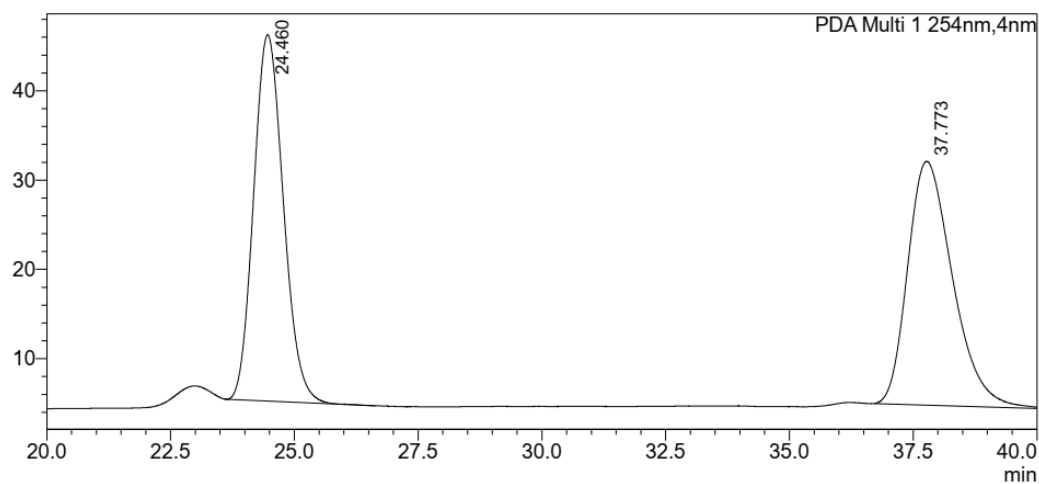
PDA Ch1 254nm

Ret. Time	Area	Area%
39.757	22885	0.221
53.296	10311954	99.779
	10334839	100.000



<Chromatogram>

mAU



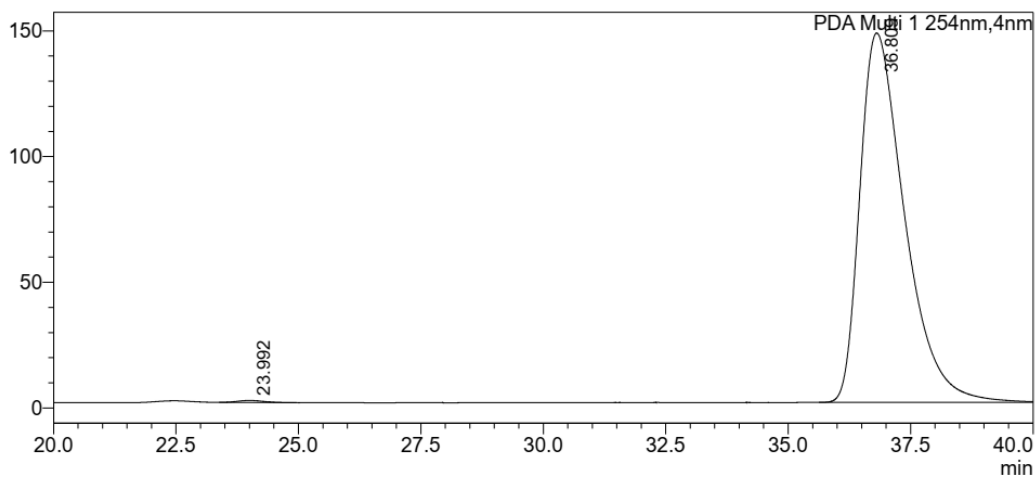
<Peak Table>

PDA Ch1 254nm

Ret. Time	Area	Area%
24.460	1713539	49.881
37.773	1721716	50.119
	3435255	100.000

<Chromatogram>

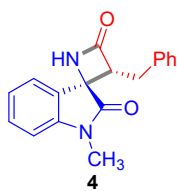
mAU



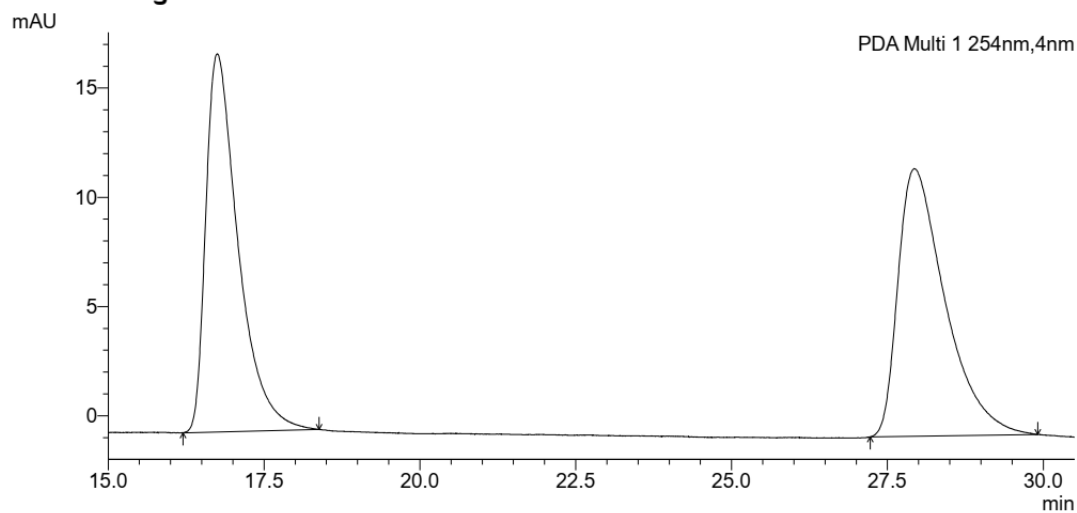
<Peak Table>

PDA Ch1 254nm

Ret. Time	Area	Area%
23.992	30872	0.330
36.809	9335270	99.670
	9366142	100.000

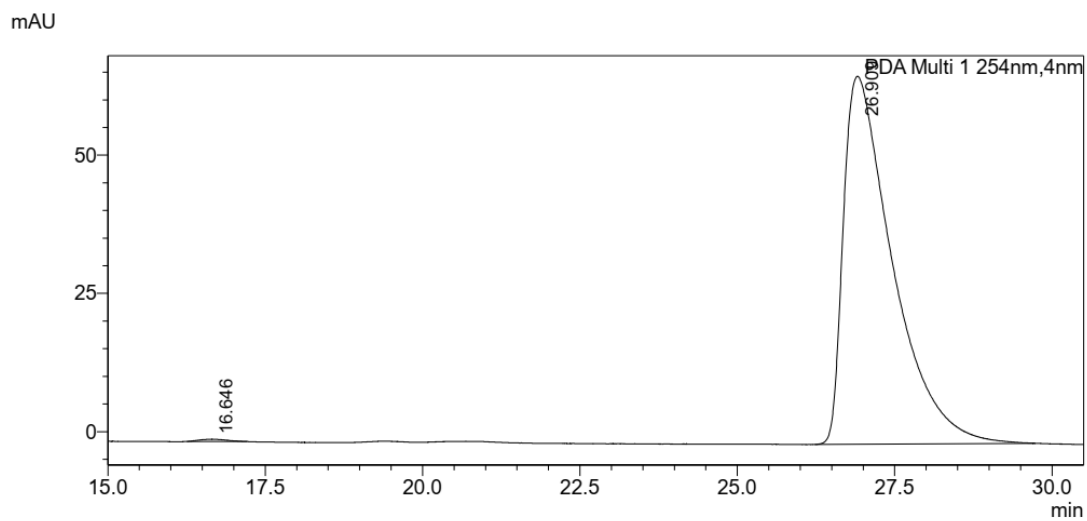


<Chromatogram>



Peak#	Ret. Time	Area	Height	Area%
1	16.751	624966	17302	49.267
2	27.928	643569	12251	50.733
Total		1268535	29553	100.000

<Chromatogram>



Peak#	Ret. Time	Area	Height	Area%
1	16.646	12361	418	0.341
2	26.909	3608146	66528	99.659
Total		3620507	66946	100.000