

Supporting Information

Asymmetric Rhodium-Catalyzed Click Cycloaddition to Access C-N Axially Chiral *N*-Triazolyl Indoles

Li Zhou^{1,†}, Yankun Li^{1,†}, Shunian Li¹, Zhenwei Shi¹, Xue Zhang¹, Chen-Ho Tung¹, and
Zhenghu Xu^{1,2,3*}

¹Key Lab of Colloid and Interface Chemistry of Ministry of Education, School of
Chemistry and Chemical Engineering, Shandong University, No. 27 South Shanda
Road, Jinan, Shandong 250100

²State Key Laboratory of Organometallic Chemistry, Shanghai Institute of Organic
Chemistry, Chinese Academy of Sciences, Shanghai 200032

³Key Laboratory of Precise Synthesis of Functional Molecules of Zhejiang Province,
School of Science, Westlake University, No. 18 Shilongshan Road, Hangzhou 310024

*Corresponding Author: xuzh@sdu.edu.cn;

[†]L. Zhou and Y. K. Li contributed equally to this work.

Table of Contents

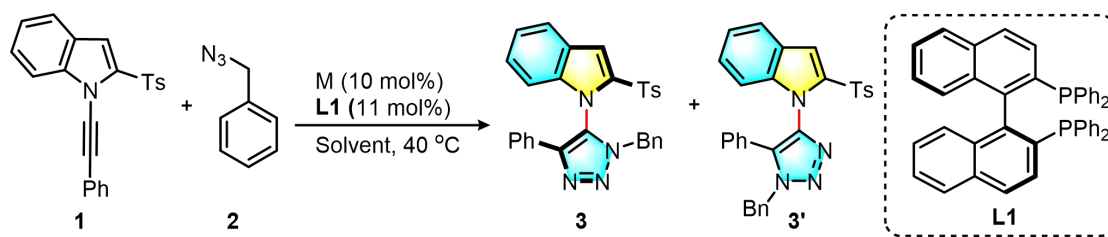
1. General information.....	S2
2. Optimization of the reaction conditions.....	S3
3. Proposed mechanism.....	S7
4. Procedure for the atroposelective click reaction.....	S7
5. Thermal racemization experiments.....	S8
6. Gram-scale experiment and synthetic applications.....	S12
7. X-ray crystallographic data for 13 and 25	S18
8. Characterization of Products 3-57	S22
9. NMR spectra.....	S105
10. References.....	S165

1. General information

The solvents used in the reaction were dried by CaH_2 or purchased from J&K or local companies unless additional notes, and all the reagents were obtained commercially and used without further purification. All the reactions were performed in the overdried glassware with magnetic stirring under nitrogen atmosphere. Column chromatography was performed with silica gel (100-200 mesh) as the stationary phase. Solvent compositions are given in (v/v). Reactions were monitored by TLC. All NMR spectra were recorded on Bruker-500 MHz spectrometer in CDCl_3 , and the chemical shifts (δ) and coupling constants (J) were expressed in ppm and Hz respectively. High resolution mass spectra (HRMS) were measured on the Bruker-Impact II instruments obtained by the Analytical Center for Structural Constituent and Physical Property in Shandong University. All substitutes were prepared according to the reported methods.¹⁻³

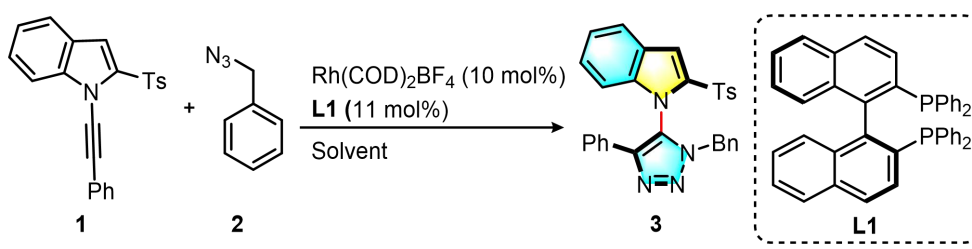
2. Optimization of the reaction conditions

Table S1. Screening of metal catalyst^[a]



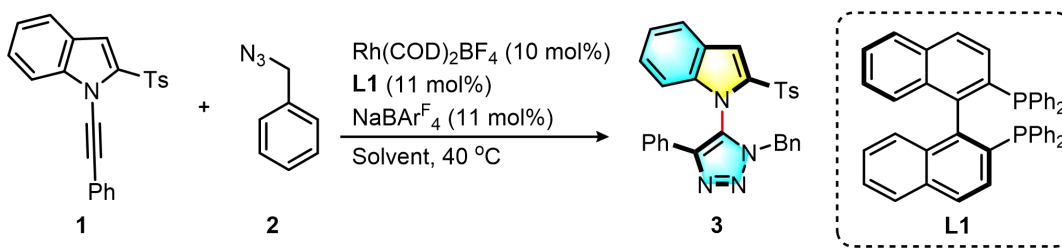
entry	metal	ligand	solvent	yield of 3 (%) ^[b]	yield of 3' (%) ^[b]	er ^[c]
1	CuI	-	DCE	-	-	-
2 ^[d]	[Ir(COD)Cl] ₂	-	MeCN	trace	45	-
3	[Rh(CO)Cl] ₂	-	MeCN	55	-	-
4 ^[e]	Rh(COD) ₂ Cl	L1	DCE	41	-	61.5:38.5
5	Rh(COD) ₂ BF ₄	L1	DCE	19	-	89.5:10.5

[a] Reaction conditions: A mixture of **1a** (0.1 mmol), **2a** (0.2 mmol), metal (10 mol%), ligand (11 mol%), solvent (2.5 mL) for 36 hours. [b] Isolated yields of **3a** were reported. [c] Determined by HPLC analysis using a chiral stationary phase. [d] [Ir(COD)Cl]₂ (5 mol%). When using iridium catalyst, the corresponding triazolyl indole **3** bearing C-N chiral axle cannot be yielded but its regio isomer **3'** can be accessible. Product **3'** has no any chiral axis, since its less steric hindrance than that of **3** leading to the result that its C-N bond between indolyl and triazolyl can rotate freely. [e] AgNTf₂ (20 mol%).

Table S2. Screening of the solvent^[a]


entry	solvent	T(°C)	yield (%) ^[b]	er ^[c]
1	DCM	25	<10	
2	DCE	40	21	89.5:10.5
3	MeCN	40	0	
4	Toluene	40	19	90:10
5	Dioxane	40	29	88.5:11.5
6	DCE:MeOH=3:1	40	24	50:50
7	Hexane	40	0	
8	Hexane:DCM = 4:1	40	30	92:8
9	Hexane:DCE = 4:1	40	52	91.5:8.5
10 ^[d]	Hexane:DCE = 4:1	40	81	91.5:8.5
11 ^[d]	Cyclohexane:DCE = 4:1	40	62	93.5:6.5

[a] Reaction conditions: A mixture of **1a** (0.1 mmol), **2a** (0.2 mmol), [Rh] (10 mol%), ligand (11 mol%), solvent (2.5 mL) for 36 hours. [b] Isolated yields of **3a** were reported. [c] Determined by HPLC analysis using a chiral stationary phase. [d] NaBAR^F₄ (11 mol%).

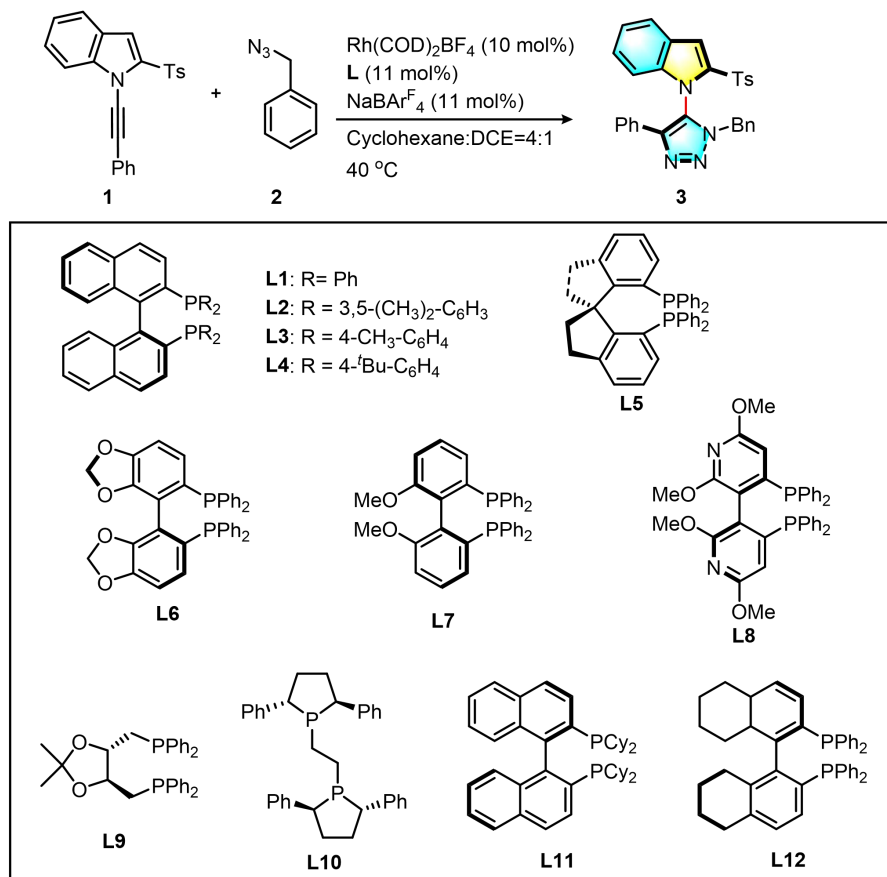
Table S3. Screening of the mix-solvent^[a]


entry	solvent	ratio	yield (%) ^[b]	er ^[c]
1	Hexane:DCE	4:1 (2 mL:0.5 mL)	81	91.5:8.5
2	Cyclohexane:DCE	4:1 (2 mL:0.5 mL)	62	93.5:6.5
3	Cyclohexane:DCE	2:1 (1.6 mL:0.8 mL)	52	92.5:7.5
4	Cyclohexane:DCE	1:1 (1.2 mL:1.2mL)	38	89:11
5	Cyclohexane:DCE	1:2 (0.8 mL:1.6 mL)	41	87.5:12.5
6	Cyclohexane:DCE	5:1 (2 mL:0.4 mL)	56	92:8
7 ^[d]	Cyclohexane:DCE	4:1 (2 mL:0.5 mL)	95	93.5:6.5

[a] Reaction conditions: A mixture of **1a** (0.1 mmol), **2a** (0.2 mmol), [Rh] (10 mol%), ligand (11

mol%), NaBAR^F₄ (11 mol%), solvent (2.5 mL) for 36 hours. [b] Isolated yields of 3a were reported. [c] Determined by HPLC analysis using a chiral stationary phase. [d] The reaction time was extended to 48 hours.

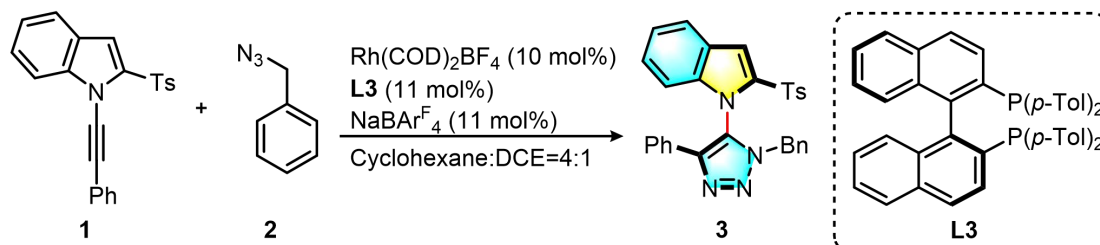
Table S4. Screening of the ligand^[a]



entry	ligand	yield/% ^[b]	er ^[c]
1	L1	95	93.5:6.5
2 ^[d]	L1	46	65.5:34.5
3	L2	89	91.5:8.5
4	L3	93	95:5
5	L4	84	94.5:5.5
6	L5	47	30:70
7	L6	67	94.5:5.5
8	L7	48	90:10
9	L8	59	3.5:96.5
10	L9	<10	-
11	L10	56	49:50
12	L11	35	15:85
13	L12	94	8.5:91.5

[a] Reaction conditions: A mixture of **1a** (0.1 mmol), **2a** (0.2 mmol), [Rh] (10 mol%), ligand (11 mol%), NaBAR₄^F (11 mol%), solvent (2.5 mL) for 48 hours. [b] Isolated yields of **3a** were reported. [c] Determined by HPLC analysis using a chiral stationary phase. [d] [Rh] (5 mol%), ligand (5.5 mol%), NaBAR₄^F (5.5 mol%)

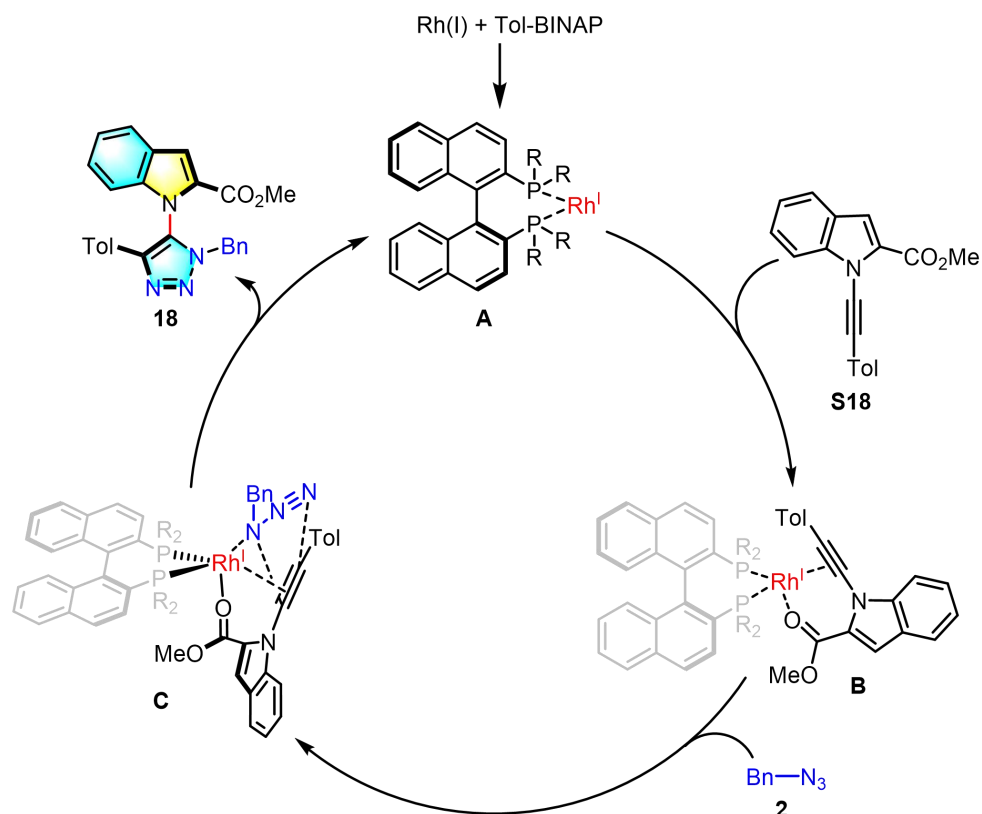
Table S5. Screening of the temperature^[a]



entry	T(°C)	yield (%) ^[b]	er ^[c]
1	25	78	94:6
2	40	93	95:5
3	50	94	93.5:6.5

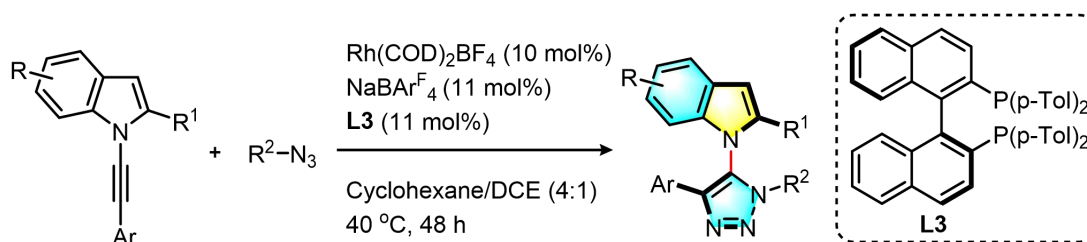
[a] Reaction conditions: A mixture of **1a** (0.1 mmol), **2a** (0.2 mmol), [Rh] (10 mol%), ligand (11 mol%), NaBAR₄^F (11 mol%), solvent (2.5 mL) for 48 hours. [b] Isolated yields of **3a** were reported. [c] Determined by HPLC analysis using a chiral stationary phase.

3. Proposed mechanism



4. Procedure for the atroposelective click reaction

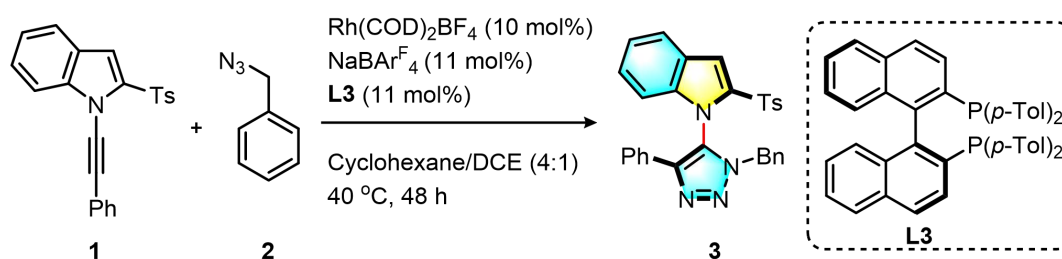
4.1 General procedure for the asymmetric synthesis of triazole



To a solution of N-alkynyl indole (0.1 mmol, 1.0 equiv.), $\text{Rh}(\text{COD})_2\text{BF}_4$ (4.0 mg, 0.010 mmol, 10 mol%), NaBARF_4 (9.7 mg, 0.011 mmol, 11 mol%) and **L3** (7.5 mg, 0.011 mmol, 11 mol%) in dried mixed solvent of cyclohexane (2.0 mL) and DCE (0.5 mL) were added azide (0.2 mmol, 2.0 equiv.) under nitrogen atmosphere. The mixture was heated to 40 °C and stirred for 48 h in a water bath. The reaction was monitored by TLC. The mixture was allowed to cool down to the room temperature and concentrated in vacuo. The residue was purified by silica gel (100-200 mesh)

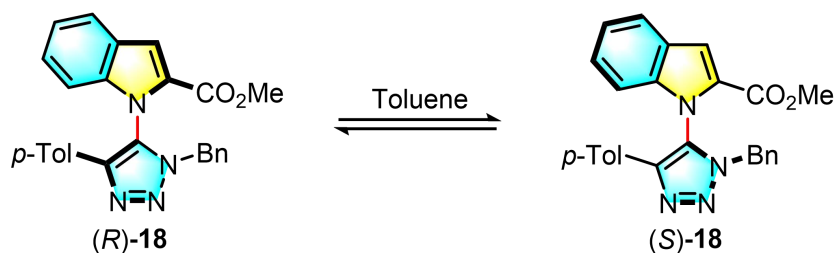
column chromatography to get the corresponding triazole.

4.2 Typical procedure for the asymmetric synthesis of **3**



To a solution of alkynyl indole **1** (37.1 mg, 0.1 mmol, 1.0 equiv.), $\text{Rh}(\text{COD})_2\text{BF}_4$ (4.0 mg, 0.010 mmol, 10 mol%), $\text{NaBAR}^{\text{F}}_4$ (9.7 mg, 0.011 mmol, 11 mol%) and **L3** (7.5 mg, 0.011 mmol, 11 mol%) in dried mixed solvent of cyclohexane (2.0 mL) and DCE (0.5 mL) were added azide **2** (25 μL , 0.2 mmol, 2.0 equiv.) by microsyringe under nitrogen atmosphere. The mixture was heated to 40 °C and stirred for 48 h in a water bath. The reaction was monitored by TLC. The mixture was allowed to cool down to the room temperature and concentrated in vacuo. The residue was purified by silica gel (100-200 mesh) column chromatography with petroleum ether/ethyl acetate (8:1) as eluent to get the corresponding triazole **3** (47.0 mg, white solid, 93% yield, 95:5 er).

5. Thermal racemization experiments



As a new type of heterobiaryls, we studied the configurational stability of **18** at various temperatures. 15 mg of **18** (96% ee) was dissolved in toluene and heated in a sealed tube at the indicated temperature for the corresponding time. At 60 °C, the configuration remains very stable and no racemization occurred after 72 hrs. At 90 °C, the enantioselectivity kept very well in 24 hrs, and slightly decreased from 96% to

92%; however, the ee value dropped very quick to 62% in 12 hrs at 120 °C and decreased to 40% in 24 hrs.

Table S6 Thermal racemization experiments

time/h	60 °C	90 °C	120 °C
	ee (%)	ee (%)	ee (%)
0	96	96	96
1	96	96	90
2	96	96	85
4	96	96	79
6	96	95	74
12	96	95	62
24	96	95	40
36	96	94	28
48	96	94	20
60	95	93	16
72	96	92	11

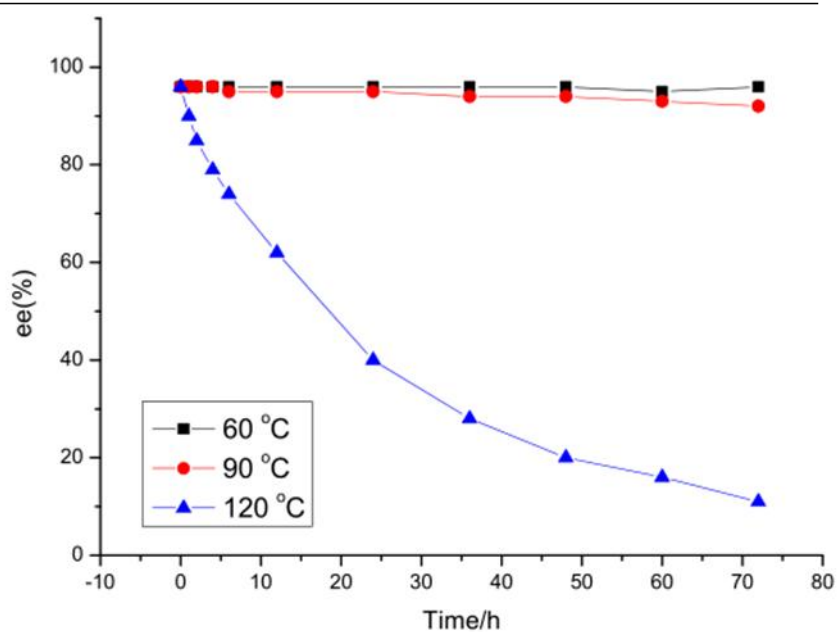


Figure S1. Thermal racemization experiments

Racemization Kinetics⁴

The variation of the enantiomeric excess (ee) with time was obtained and plotted against time by $\ln(ee_0/ee)$, where ee_0 is the initial enantiomeric excess at $t = 0$. The

gradient of the obtained graph corresponds to the rate constant of racemization, $k_{racemization}$, at that specific temperature. The rate constant for enantiomerization, $k_{enantiomerization}$, is related to the racemization rate constant according to the following equation:

$$k_{enantiomerization} = \frac{k_{racemization}}{2}$$

The half-life of racemization at that temperature can be calculated as:

$$t_{\frac{1}{2}racemization} = \frac{\ln 2}{k_{racemization}}$$

The barrier to rotation, $\Delta G^{\ddagger}_{enantiomerization}$, was subsequently calculated using the following form of the Eyring equation:

$$\Delta G^{\ddagger}_{enantiomerization} = RT_1 \cdot \ln \frac{k_B T_1}{k_{enantiomerization}}$$

Where: R = Gas constant = $8.31454 \text{ J}\cdot\text{K}^{-1}\cdot\text{mol}^{-1}$, h = Planck constant = $6.62608 \times 10^{-34} \text{ J}\cdot\text{s}$, k_B = Boltzmann constant = $1.38066 \times 10^{-23} \text{ J}\cdot\text{K}^{-1}$, and T_1 = temperature racemization studies were conducted at, in Kelvin.

Employing the assumption that the change in entropy is negligible over a short range of temperature, we can assume that ΔG^{\ddagger} does not change with temperature. It is thus possible to extrapolate the racemization constant to 25 °C, according to the following relationship:

$$\begin{aligned} k_{racemization \text{ at } 25 \text{ } ^\circ\text{C}} &= 2 k_{enantiomerization \text{ at } 25 \text{ } ^\circ\text{C}} \\ &= 2 \frac{k_B T_2}{h} e^{\left(\frac{-\Delta G^{\ddagger}_{enantiomerization}}{RT_2}\right)} \end{aligned}$$

Where $T_2 = 298.15 \text{ K}$ (25 °C).

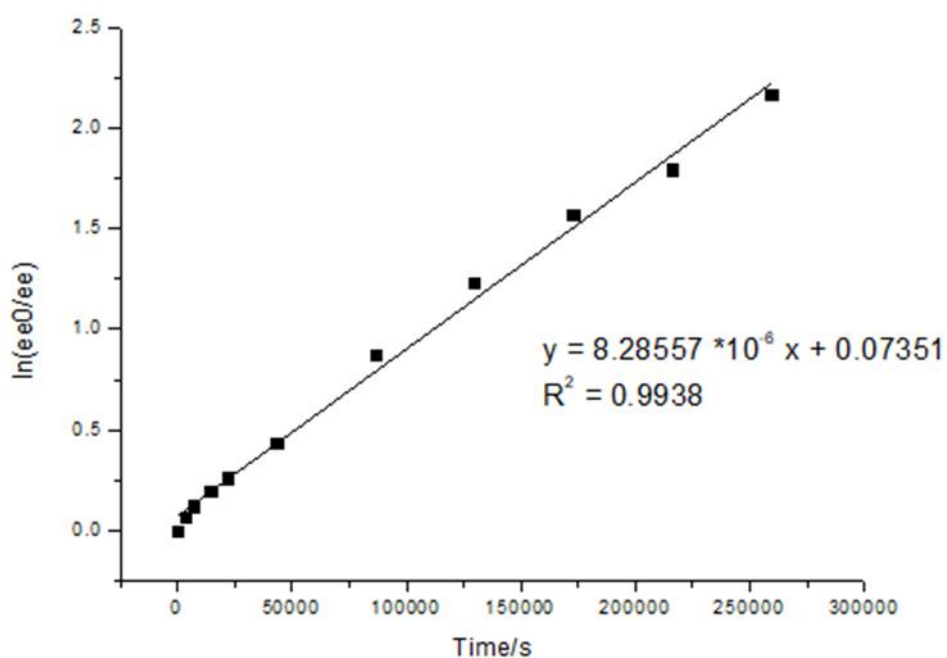
The half-life at 25 °C is calculated as follows:

$$t_{\frac{1}{2}racemization \text{ at } 25 \text{ } ^\circ\text{C}} = \frac{\ln 2}{k_{racemization \text{ at } 25 \text{ } ^\circ\text{C}}}$$

Table S7. Detail data of thermal racemization experiment (120 °C)

time/s	ee%	$\ln(ee_0/ee)$
0	96	0
3600	90	0.064539

7200	85	0.121697
14400	79	0.1949
21600	74	0.260283
43200	62	0.437214
86400	40	0.875469
129600	28	1.232144
172800	20	1.568616
216000	16	1.791759
259200	11	2.166453



$$t_{\frac{1}{2}}^{\text{racemization at } 120 \text{ } ^\circ\text{C}} = 23 \text{ h.}$$

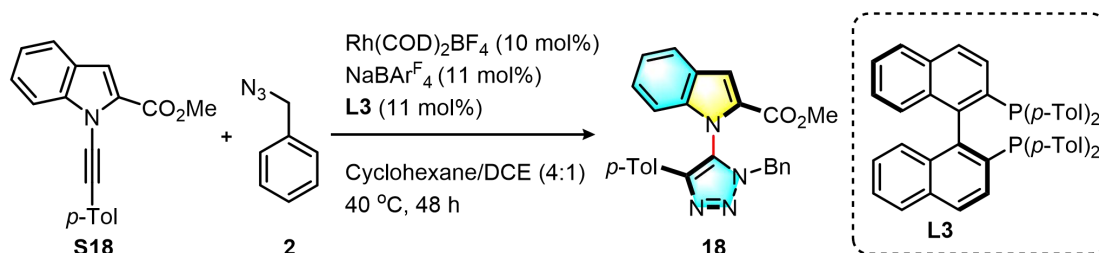
$$\Delta G^{\ddagger}_{\text{enantiomerization}} = 32.9 \text{ kcal}\cdot\text{mol}^{-1}$$

$$t_{\frac{1}{2}}^{\text{racemization at } 25 \text{ } ^\circ\text{C}} = 2363 \text{ years}$$

According to these results, and a rotation barrier of 18 at 120 °C was calculated as 32.9 kcal•mol⁻¹ which is slightly lower than that of previous C-C axial naphthyltriazoles (34.6 kcal•mol⁻¹). These data indicate that this new heterobiaryls remains good thermal stability at temperatures lower than 100 °C.

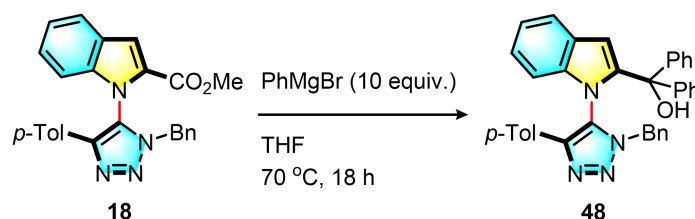
6. Gram-scale experiment and synthetic applications

6.1 Gram-scale experiment



To a solution of alkynyl indole **S18** (868.0 mg, 3.0 mmol, 1.0 equiv.), Rh(COD)₂BF₄ (134.0 mg, 0.30 mmol, 10 mol%), NaBAR^F₄ (292.5 mg, 0.33 mmol, 11 mol%) and **L3** (224.0 mg, 0.33 mmol, 11 mol%) in dried mixed solvent of cyclohexane (60.0 mL) and DCE (40.0 mL) were added azide **2** (0.75 mL, 6.0 mmol, 2.0 equiv.) by microsyringe under nitrogen atmosphere. The mixture was heated to 40 °C and stirred for 48 h in a water bath. The reaction was monitored by TLC. The mixture was allowed to cool down to the room temperature and concentrated in vacuo. The residue was purified by silica gel (100-200 mesh) column chromatography with petroleum ether/ethyl acetate (5:1) as eluent to get the corresponding triazole **18** (1.06 g, 84% yield, 99:1 er).

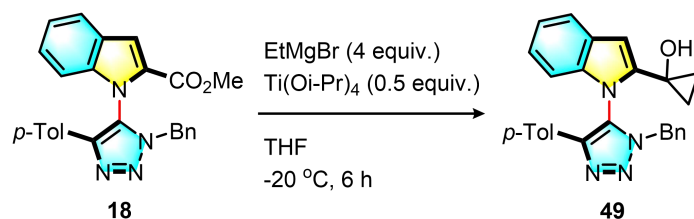
6.2 Synthesis of **48** via a Grignard reaction



To a solution of **18** (63.4 mg, 0.15 mmol, 1.0 equiv.) in dried THF (1 mL) was added PhMgBr (0.5 mL, 3M in THF, 1.50 mmol, 10 equiv.) dropwise by syringe under nitrogen atmosphere at 0 °C. The mixture was heated to 70 °C and stirred for 18 h. The reaction was monitored by TLC. After the reacts were consumed completely, the reaction was allowed to cool down to the room temperature and quenched by saturated NH₄Cl solution. The mixture was extracted by ethyl acetate (3 x 10 mL) and

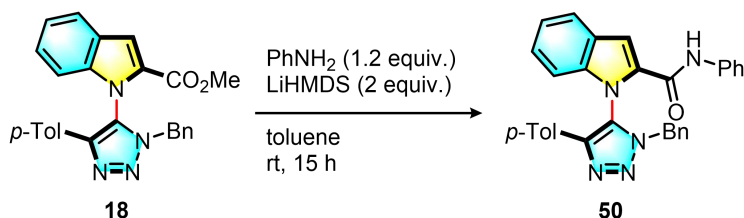
the organic phase was washed with brine. The organic phase was dried by Na_2SO_4 and concentrated in vacuo. The residue was purified by silica gel (100-200 mesh) column chromatography with petroleum ether/ethyl acetate (6:1) as the eluent to obtain **48** (62.3 mg, white solid, 76% yield, 95.5:4.5 er).

6.3 Synthesis of **49** via a Kulinkovich cyclopropanation



To a solution of **18** (84.5 mg, 0.20 mmol, 1.0 equiv.) in dried THF (1 mL) was added EtMgBr (0.8 mL, 1M in THF, 0.80 mmol, 4 equiv.) dropwise by syringe under nitrogen atmosphere at $0\text{ }^\circ\text{C}$. The mixture was cooled down to $-20\text{ }^\circ\text{C}$ and stirred for 6 h. The reaction was monitored by TLC. After the reacts were consumed completely, the reaction was allowed to warm to the room temperature and quenched by saturated NH_4Cl solution. The mixture was extracted by ethyl acetate (3 x 10 mL) and the organic phase was washed with brine. The organic phase was dried by Na_2SO_4 and concentrated in vacuo. The residue was purified by silica gel (100-200 mesh) column chromatography with petroleum ether/ethyl acetate (5:1) as the eluent to obtain **49** (36.2 mg, pale yellow solid, 43% yield, 95.5:4.5 er).

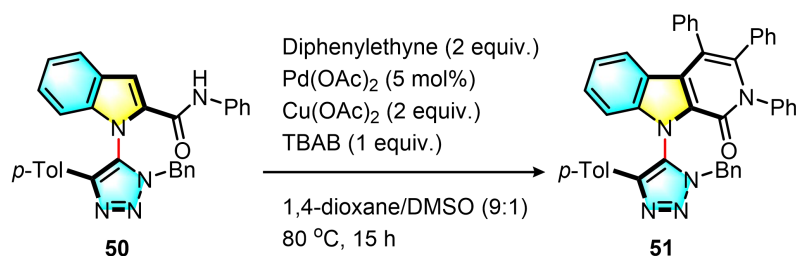
6.4 Synthesis of **50** via an amidation



To a solution of **18** (42.2 mg, 0.10 mmol, 1.0 equiv.) in dried toluene (1 mL) were added aniline (11.0 μL , 0.12 mmol, 1.2 equiv.) and LiHMDS (0.20 mL, 2M in THF, 0.20 mmol, 2.0 equiv.) dropwise by syringe under nitrogen atmosphere at the room

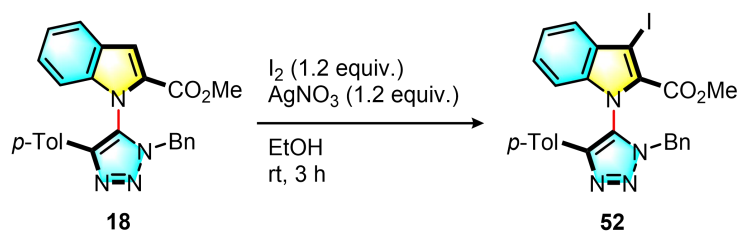
temperature. The mixture was stirred for 15 h at the ambient temperature. The reaction was monitored by TLC. After the reacts were consumed completely, the reaction was allowed to warm to the room temperature and quenched by saturated NH_4Cl solution. The mixture was extracted by ethyl acetate (3 x 5 mL) and the organic phase was washed with water and brine. The organic phase was dried by Na_2SO_4 and concentrated in vacuo. The residue was purified by silica gel (100-200 mesh) column chromatography with petroleum ether/ethyl acetate (8:1) as the eluent to obtain **50** (37.7 mg, white solid, 78% yield, 98.5:1.5 er).

6.5 Synthesis of **51** via an oxidative cyclization



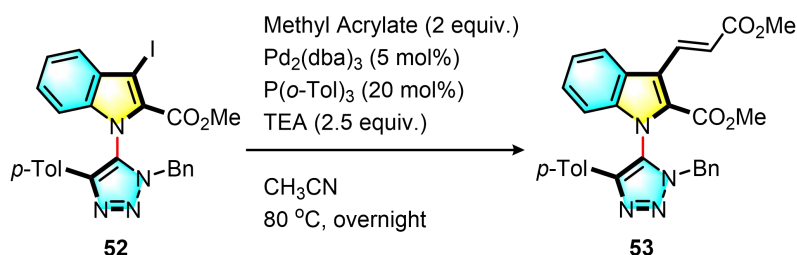
To a solution of **50** (48.4 mg, 0.10 mmol, 1.0 equiv.) and diphenylethyne (35.8 mg, 0.20 mmol, 2.0 equiv.) in a mixed solvent of 1,4-dioxane/DMSO (9:1, 2 mL) were added $\text{Pd}(\text{OAc})_2$ (1.2 mg, 0.005 mmol, 5 mol%), $\text{Cu}(\text{OAc})_2$ (39.8 mg, 0.20 mmol, 2.0 equiv.) and TBAB (32.2 mg, 0.10 mmol, 1.0 equiv.). The mixture was heated to 80 °C and stirred for 15 h. The reaction was monitored by TLC. After the reacts were consumed completely, the mixture was filtered on a pad of celite and concentrated in vacuo. The residue was purified by silica gel (100-200 mesh) column chromatography with petroleum ether/ethyl acetate (3:1) as the eluent to obtain **51** (44.2 mg, white solid, 67% yield, 96.5:3.5 er).

6.6 Synthesis of **52** via an oxidative iodination



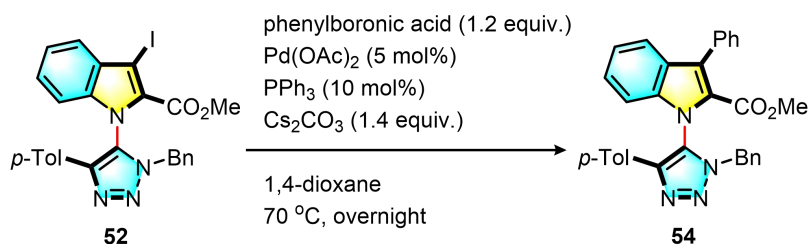
To a solution of **18** (422.5 mg, 1.0 mmol, 1.0 equiv.) in ethanol (1.5 mL) were added iodine (304.6 mg, 1.2 mmol, 1.2 equiv.) and AgNO₃ (203.8 mg, 1.2 mmol, 1.2 equiv.) under air at the room temperature. The mixture was kept in the dark and stirred at the ambient environment for 3 h. The reaction was monitored by NMR. After the reacts were consumed completely, the mixture was poured into saturated Na₂S₂O₃ solution and extracted by ethyl acetate (3 x 10 mL), and the organic phase was dried by Na₂SO₄ and concentrated in vacuo to obtain **52** (537.4 mg, white solid, 98% yield, 98:2 er).

6.7 Synthesis of **53** via a Heck coupling reaction



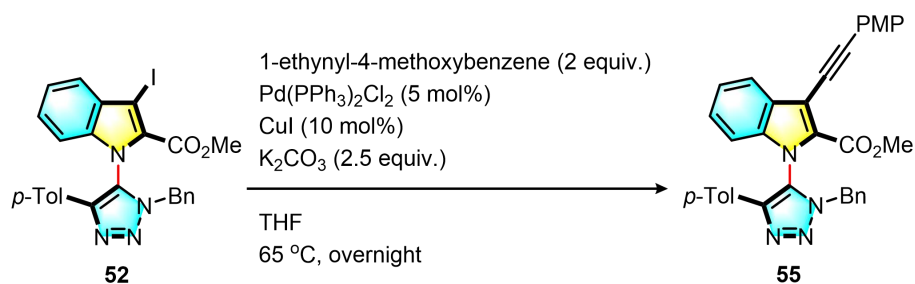
To a solution of **52** (54.8 mg, 0.10 mmol, 1.0 equiv.) in CH₃CN (1.0 mL) were added methyl acrylate (18.0 μL, 0.20 mmol, 2.0 equiv.), Pd₂(dba)₃ (4.6 mg, 0.005 mmol, 5 mol%), P(*o*-Tol)₃ (6.1 mg, 0.020 mmol, 20 mol%) and triethylamine (35.0 μL, 0.25 mmol, 2.5 equiv.) under nitrogen atmosphere. The mixture was heated to 80 °C and stirred overnight. The reaction was monitored by TLC. After the reacts were consumed completely, the mixture was poured into water and extracted by dichloromethane (3 x 5 mL). The organic phase was dried by Na₂SO₄ and concentrated in vacuo. The residue was purified by silica gel (100-200 mesh) column chromatography with petroleum ether/ethyl acetate (8:1) as the eluent to obtain **53** (46.6 mg, white solid, 92% yield, 98:2 er).

6.8 Synthesis of **54** via a Suzuki coupling reaction



To a solution of **52** (54.8 mg, 0.10 mmol, 1.0 equiv.) and phenylboronic acid (14.7 mg, 0.12 mmol, 1.2 equiv.) in 1,4-dioxane (1.0 mL) were added Pd(OAc)₂ (1.2 mg, 0.005 mmol, 5 mol%), PPh₃ (2.6 mg, 0.010 mmol, 10 mol%) and Cs₂CO₃ (45.6 mg, 0.14 mmol, 1.4 equiv.) under nitrogen atmosphere. The mixture was heated to 70 °C and stirred overnight. The reaction was monitored by TLC. After the reacts were consumed completely, the mixture was poured into water and extracted by dichloromethane (3 x 5 mL). The organic phase was dried by Na₂SO₄ and concentrated in vacuo. The residue was purified by silica gel (100-200 mesh) column chromatography with petroleum ether/ethyl acetate (6:1) as the eluent to obtain **54** (46.4 mg, white solid, 93% yield, 98:2 er).

6.9 Synthesis of **55** via a Sonogashira coupling reaction



To a solution of **52** (54.8 mg, 0.10 mmol, 1.0 equiv.) and 1-ethynyl-4-methoxybenzene (26.5 mg, 0.20 mmol, 2.0 equiv.) in THF (1.0 mL) were added and Pd(PPh₃)₂Cl₂ (3.5 mg, 0.005 mmol, 5 mol%) and CuI (1.9 mg, 0.010 mmol, 10 mol%) and K₂CO₃ (34.5 mg, 2.5 mmol, 1.4 equiv.) under nitrogen atmosphere. he mixture was heated to 65 °C and stirred overnight. The reaction was monitored by TLC. After the reacts were consumed completely, the mixture was poured into water and extracted by dichloromethane (3 x 5 mL). The organic phase was dried by Na₂SO₄

and concentrated in vacuo. The residue was purified by silica gel (100-200 mesh) column chromatography with petroleum ether/ethyl acetate (30:1) as the eluent to obtain **55** (43.6 mg, white solid, 79% yield, 97:3 er).

7. X-ray crystallographic data for **13** and **25**

A suitable crystal was selected and analyzed on a Rigaku XtaLAB Synergy diffractometer. The crystal structures have been deposited at The Cambridge Crystallographic Data Centre (CCDC: 2192307 and 2191870). These data can be obtained free of charge from The Cambridge Crystallographic Data Centre via www.ccdc.com.ac.uk/data_request/cif.

7.1 X-ray crystallographic data for **13**

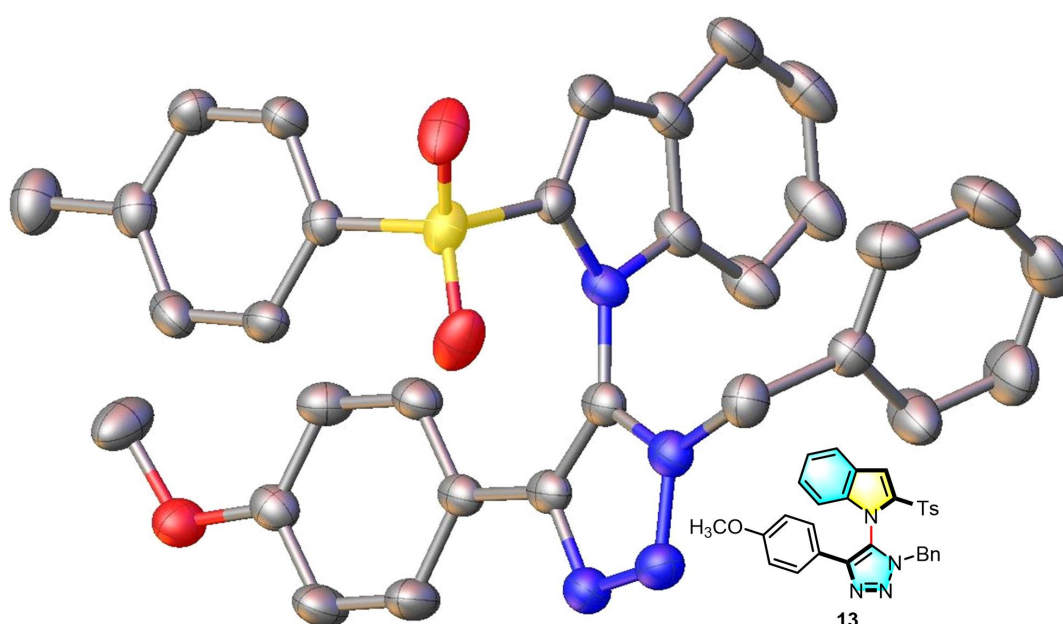


Figure S2 X-ray crystal structure of **13** (CCDC: 2192307. Thermal ellipsoids are drawn at 50% probability.)

Preparation of the crystal of **13** suitable for XRD analysis: in a tube (diameter, 0.5 cm) was added 40 mg of **13** dissolved by 2 mL dichloromethane, and then 1 mL petroleum ether and 1 mL ethyl acetate was slowly added dropwise. The crystal was recrystallized by evaporation of solvent at room temperature.

Table S8 Crystal data and structure refinement for **13**

Identification code	cu_220715C_0m
Empirical formula	C ₃₁ H ₂₆ N ₄ O ₃ S
Formula weight	534.62
Temperature/K	173.0
Crystal system	orthorhombic
Space group	P2 ₁ 2 ₁ 2 ₁
a/Å	8.2557(5)
b/Å	14.5568(9)
c/Å	21.8087(12)
α/°	90
β/°	90
γ/°	90
Volume/Å ³	2620.9(3)
Z	4
ρ _{calc} /cm ³	1.355
μ/mm ⁻¹	1.431
F(000)	1120.0
Crystal size/mm ³	0.03 × 0.03 × 0.02
Radiation	CuKα (λ = 1.54178)
2θ range for data collection/°	7.302 to 137.026
Index ranges	-9 ≤ h ≤ 9, -15 ≤ k ≤ 17, -26 ≤ l ≤ 26
Reflections collected	12512
Independent reflections	4693 [R _{int} = 0.0404, R _{sigma} = 0.0476]
Data/restraints/parameters	4693/0/354
Goodness-of-fit on F ²	1.104
Final R indexes [I>=2σ (I)]	R ₁ = 0.0350, wR ₂ = 0.0842

Final R indexes [all data]	$R_1 = 0.0400$, $wR_2 = 0.0878$
Largest diff. peak/hole / $e \text{ \AA}^{-3}$	0.33/-0.28
Flack parameter	0.020(9)

7.2 X-ray crystallographic data for **25**

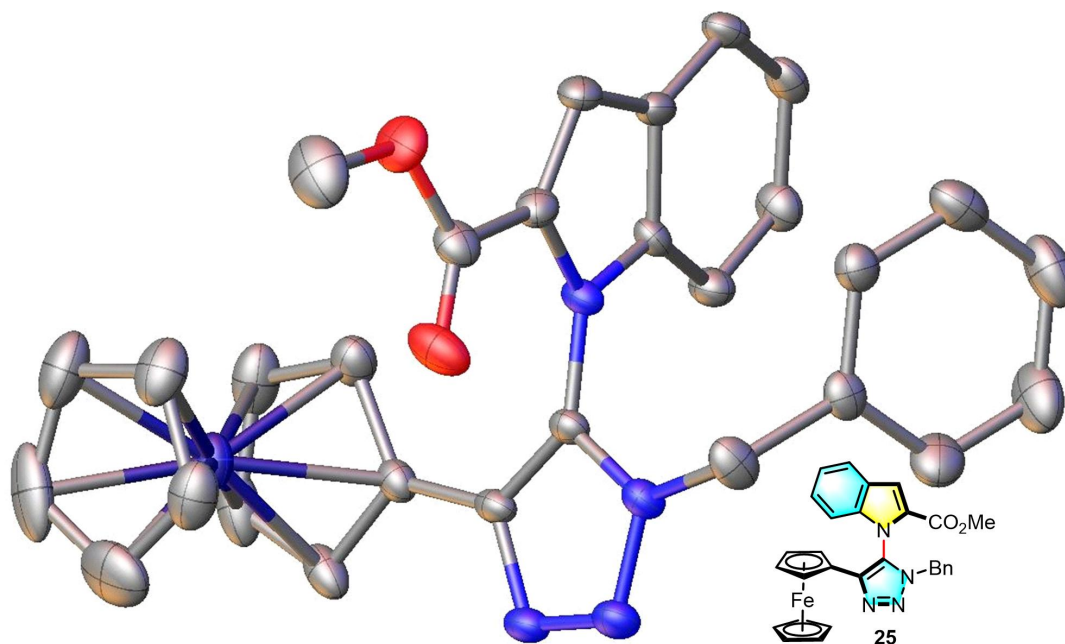


Figure S3 X-ray crystal structure of **25** (CCDC: 2191870. Thermal ellipsoids are drawn at 50% probability.)

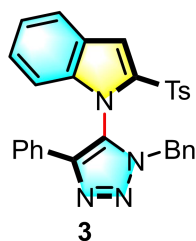
Preparation of the crystal of **25** suitable for XRD analysis: in a tube (diameter, 0.5 cm) was added 50 mg of **25** dissolved by 0.5 mL chloroform, and then 3 mL petroleum ether was slowly added dropwise. The crystal was recrystallized by evaporation of solvent at room temperature.

Table S9 Crystal data and structure refinement for **25**

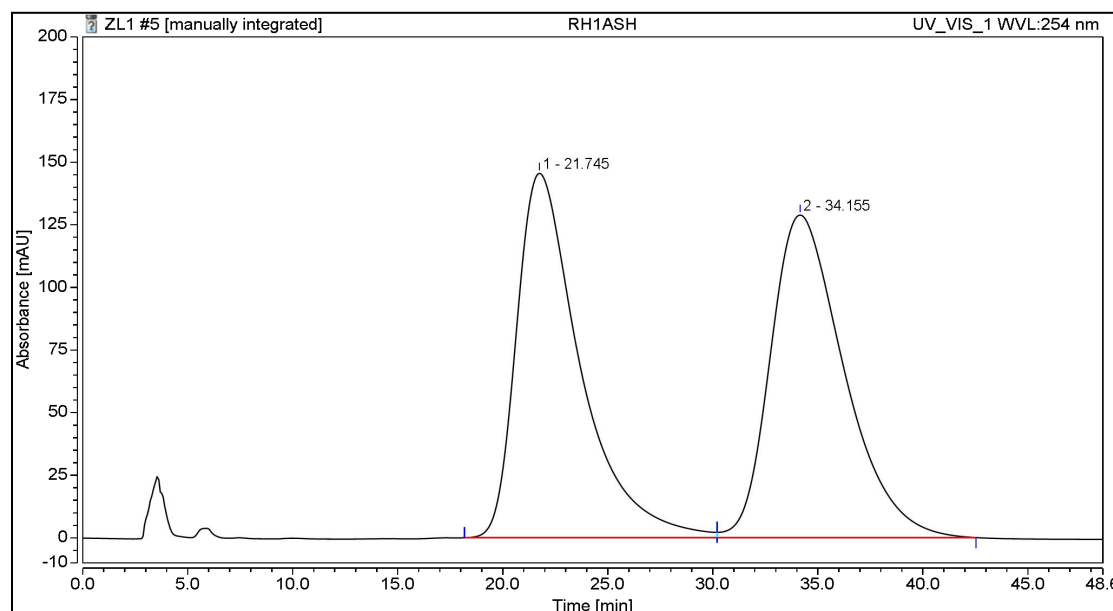
Identification code	cu_220621e_0m
Empirical formula	C ₂₉ H ₂₄ FeN ₄ O ₂

Formula weight	516.37
Temperature/K	173.0
Crystal system	monoclinic
Space group	P2 ₁
a/Å	10.5500(9)
b/Å	10.0510(8)
c/Å	12.1412(10)
α/°	90
β/°	109.660(4)
γ/°	90
Volume/Å ³	1212.38(18)
Z	2
ρ _{calc} /cm ³	1.414
μ/mm ⁻¹	5.266
F(000)	536.0
Crystal size/mm ³	0.05 × 0.04 × 0.03
Radiation	CuKα (λ = 1.54178)
2θ range for data collection/°	7.732 to 133.284
Index ranges	-12 ≤ h ≤ 12, -11 ≤ k ≤ 11, -14 ≤ l ≤ 14
Reflections collected	10500
Independent reflections	3544 [R _{int} = 0.0443, R _{sigma} = 0.0588]
Data/restraints/parameters	3544/1/327
Goodness-of-fit on F ²	1.011
Final R indexes [I ≥ 2σ (I)]	R ₁ = 0.0299, wR ₂ = 0.0688
Final R indexes [all data]	R ₁ = 0.0399, wR ₂ = 0.0706
Largest diff. peak/hole / e Å ⁻³	0.18/-0.34
Flack parameter	0.026(6)

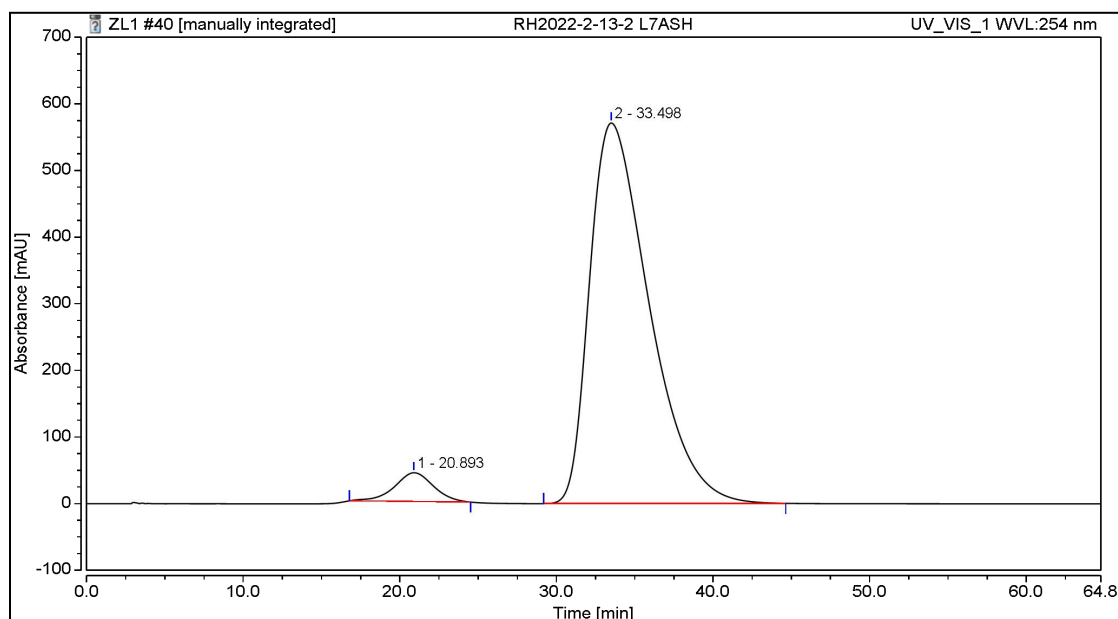
8. Characterization of Products 3-57



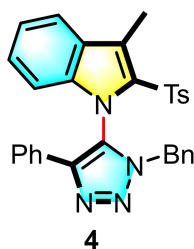
White solid, 46.8 mg, 93% yield, 95:5 er. [Chiral HPLC analysis of the product: Daicel Chiralpak AS-H 250X4.6 mm 5u column; *n*-hexane/2-propanol = 90/10, flow rate = 1.0 mL/min, λ = 254 nm, *t* (major) = 33.50 min, *t* (minor) = 22.89 min]. $[\alpha]_D^{24} = -21.1^\circ$ (*c* = 1.0, CHCl₃). **¹H NMR (500 MHz, CDCl₃)** δ 7.78 (s, 1H), 7.72 (d, *J* = 8.1 Hz, 1H), 7.28 (d, *J* = 8.9 Hz, 3H), 7.15 (t, *J* = 7.5 Hz, 1H), 7.03-6.99 (m, 2H), 6.96-6.85 (m, 7H), 6.75 (dd, *J* = 19.0, 7.8 Hz, 4H), 6.11 (d, *J* = 8.4 Hz, 1H), 5.79 (d, *J* = 15.0 Hz, 1H), 5.28 (d, *J* = 15.0 Hz, 1H), 2.04 (s, 3H). **¹³C NMR (126 MHz, CDCl₃)** δ 145.0, 142.6, 139.6, 135.9, 135.7, 133.4, 129.6, 128.6, 128.5, 128.5, 128.4, 128.1, 128.0, 127.9, 127.2, 125.7, 125.4, 124.7, 122.9, 122.9, 114.4, 111.0, 53.2, 21.6. **HRMS (ESI, *m/z*)** Calcd for C₃₀H₂₅N₄O₂S (M+H)⁺: 505.1693; Found: 505.1683.



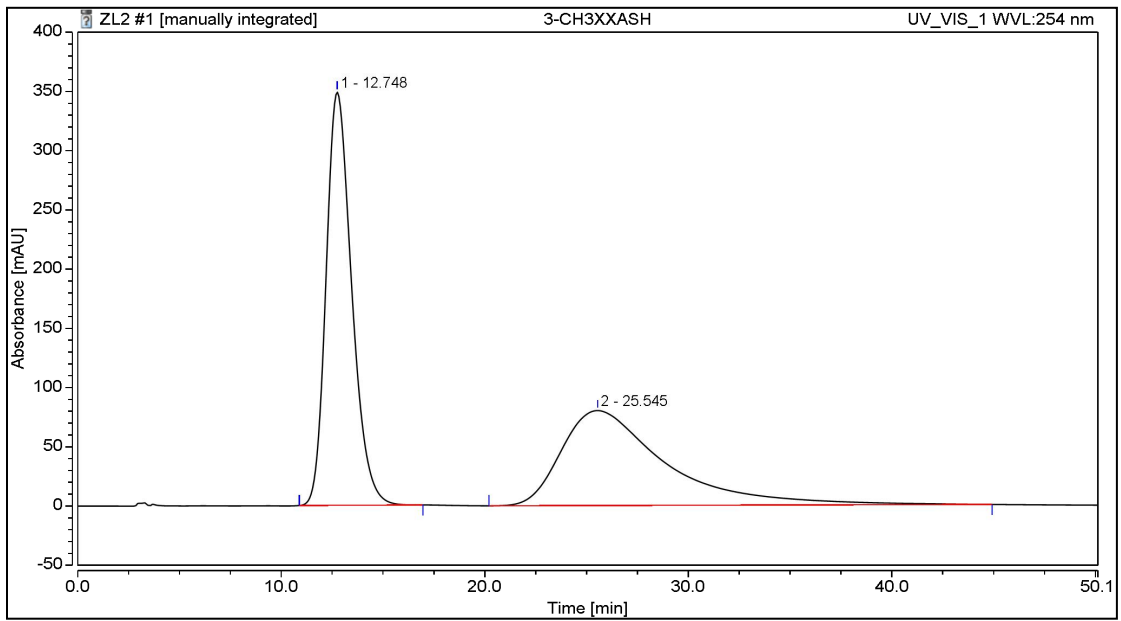
Integration Results						
No.	Peak Name	Retention Time min	Area mAU*min	Height mAU	Relative Area %	Relative Height %
1		21.745	510.149	145.506	49.39	53.05
2		34.155	522.829	128.800	50.61	46.95
Total:			1032.978	274.306	100.00	100.00



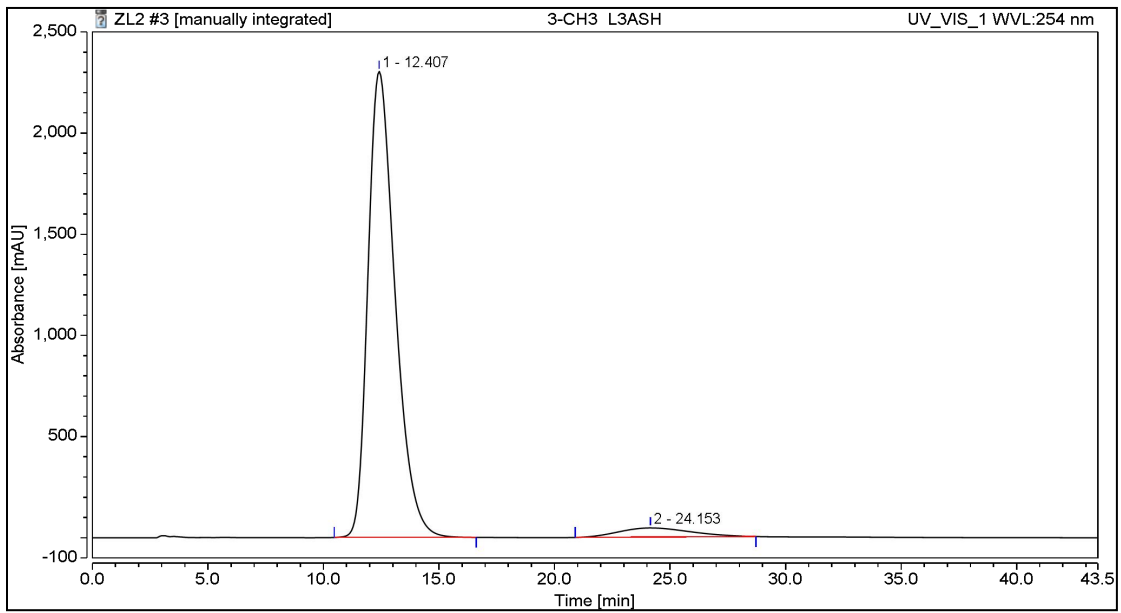
Integration Results						
No.	Peak Name	Retention Time min	Area mAU*min	Height mAU	Relative Area %	Relative Height %
1		20.893	124.289	43.156	4.71	7.02
2		33.498	2515.127	571.339	95.29	92.98
Total:			2639.416	614.495	100.00	100.00



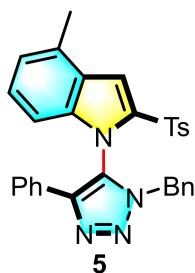
White solid, 42.9 mg, 83% yield, 95:5 er. [Chiral HPLC analysis of the product: Daicel Chiralpak AS-H 250X4.6 mm 5u column; *n*-hexane/2-propanol = 95/5, flow rate = 1.0 mL/min, $\lambda = 254$ nm, t (major) = 12.41 min, t (minor) = 24.15 min]. $[\alpha]_D^{25} = -71.2^\circ$ ($c = 0.7$, CHCl_3). **$^1\text{H NMR}$ (500 MHz, CDCl_3)** δ 7.69 (d, $J = 8.1$ Hz, 1H), 7.27-7.23 (m, 2H), 7.14 (t, $J = 7.4$ Hz, 1H), 7.04-6.85 (m, 9H), 6.77 (dd, $J = 17.4, 8.3$ Hz, 4H), 6.12 (d, $J = 8.4$ Hz, 1H), 5.74 (d, $J = 15.0$ Hz, 1H), 5.24 (d, $J = 15.0$ Hz, 1H), 2.93 (s, 3H), 2.06 (s, 3H). **$^{13}\text{C NMR}$ (126 MHz, CDCl_3)** δ 144.6, 142.4, 138.4, 137.4, 133.6, 130.4, 129.5, 128.9, 128.5, 128.5, 128.4, 128.1, 127.8, 127.6, 127.5, 127.2, 126.6, 124.9, 124.8, 122.3, 121.0, 111.0, 53.0, 21.5, 10.3. **HRMS (ESI, m/z)** Calcd for $\text{C}_{31}\text{H}_{27}\text{N}_4\text{O}_2\text{S}$ ($\text{M}+\text{H}$) $^+$: 519.1849; Found: 519.1863.



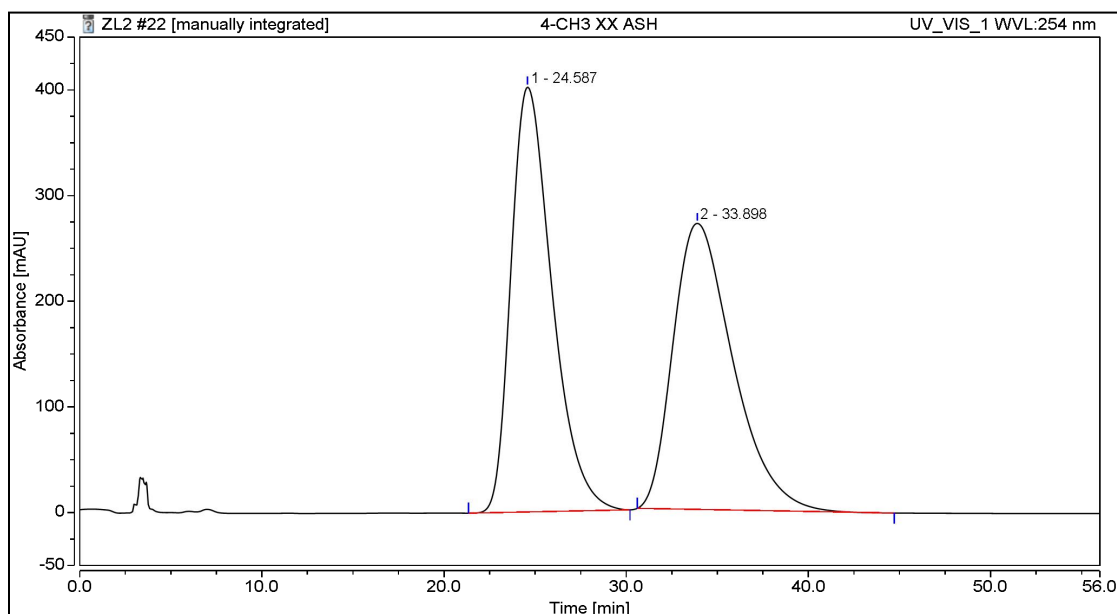
Integration Results						
No.	Peak Name	Retention Time min	Area mAU*min	Height mAU	Relative Area %	Relative Height %
1		12.748	508.948	348.933	51.77	81.31
2		25.545	474.240	80.218	48.23	18.69
Total:			983.188	429.151	100.00	100.00



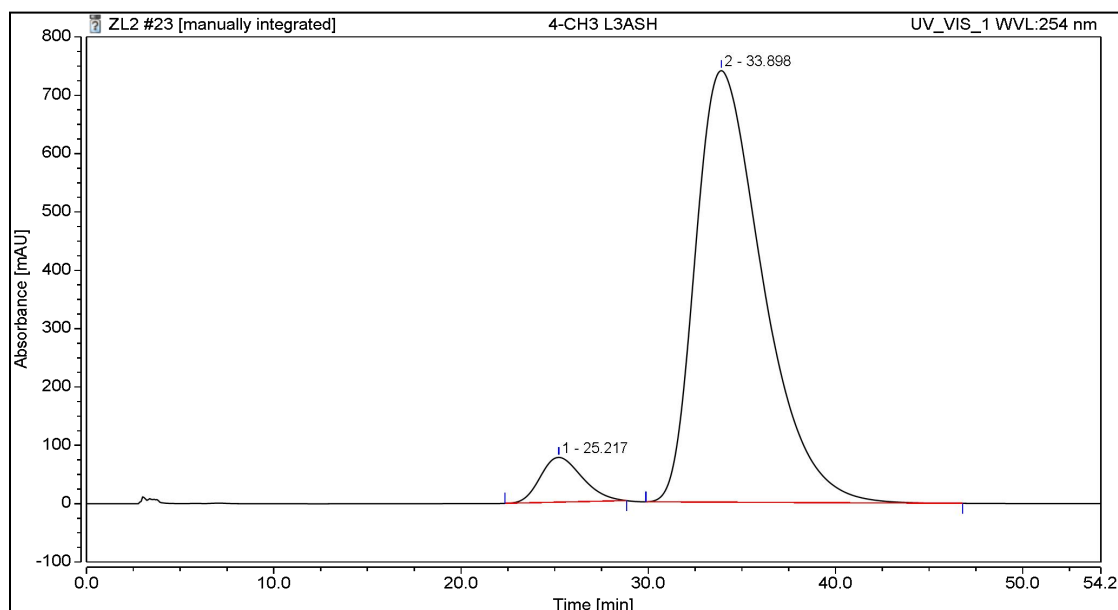
Integration Results						
No.	Peak Name	Retention Time min	Area mAU*min	Height mAU	Relative Area %	Relative Height %
1		12.407	3133.689	2303.978	95.04	98.08
2		24.153	163.374	45.093	4.96	1.92
Total:			3297.063	2349.072	100.00	100.00



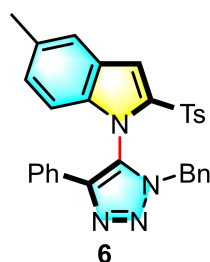
White solid, 38.3 mg, 74% yield, 94:6 er. [Chiral HPLC analysis of the product: Daicel Chiralpak AS-H 250X4.6 mm 5u column; *n*-hexane/2-propanol = 95/5, flow rate = 1.0 mL/min, $\lambda = 254$ nm, t (major) = 33.90 min, t (minor) = 25.22 min]. $[\alpha]_D^{26} = -14.3^\circ$ ($c = 0.8$, CHCl_3). **$^1\text{H NMR}$ (500 MHz, CDCl_3)** δ 7.81 (s, 1H), 7.28 (d, $J = 8.3$ Hz, 2H), 7.05-6.92 (m, 5H), 6.91-6.81 (m, 5H), 6.76 (t, $J = 8.3$ Hz, 4H), 5.98 (d, $J = 8.4$ Hz, 1H), 5.74 (d, $J = 15.0$ Hz, 1H), 5.23 (d, $J = 15.0$ Hz, 1H), 2.64 (s, 3H), 2.05 (s, 3H). **$^{13}\text{C NMR}$ (126 MHz, CDCl_3)** δ 144.9, 142.5, 139.7, 135.9, 135.3, 133.5, 132.8, 129.6, 128.6, 128.5, 128.4, 128.1, 128.0, 127.9, 127.5, 125.9, 125.6, 124.8, 123.1, 113.1, 108.6, 53.1, 21.5, 18.6. **HRMS (ESI, m/z)** Calcd for $\text{C}_{31}\text{H}_{27}\text{N}_4\text{O}_2\text{S}$ ($\text{M}+\text{H}$) $^+$: 519.1849; Found: 519.1864.



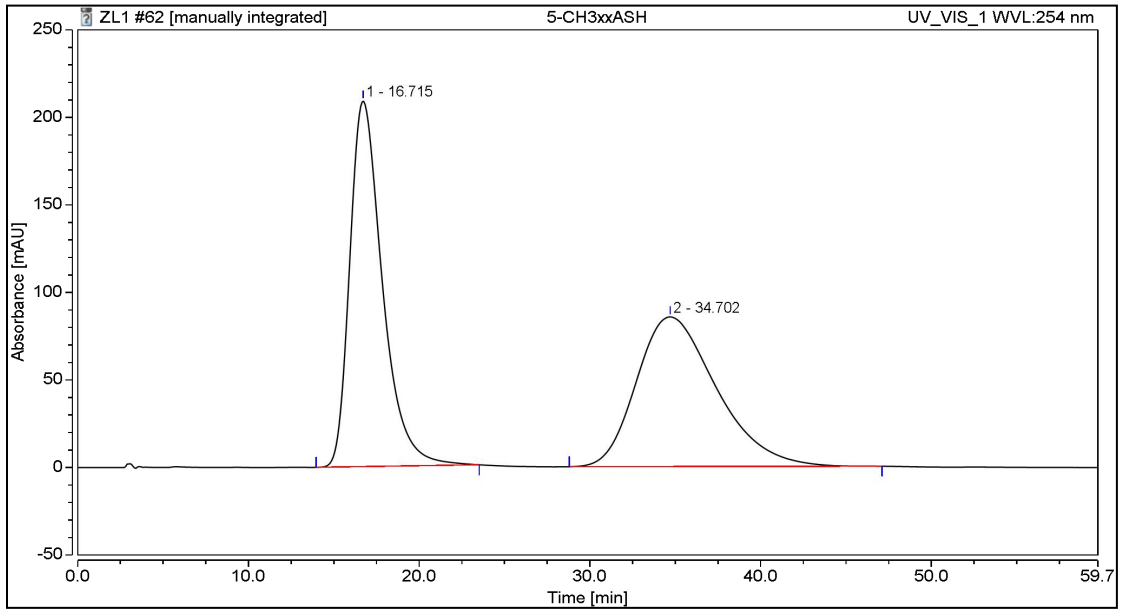
Integration Results						
No.	Peak Name	Retention Time min	Area mAU*min	Height mAU	Relative Area %	Relative Height %
1		24.587	1048.879	402.066	50.42	59.76
2		33.898	1031.457	270.719	49.58	40.24
Total:			2080.337	672.785	100.00	100.00



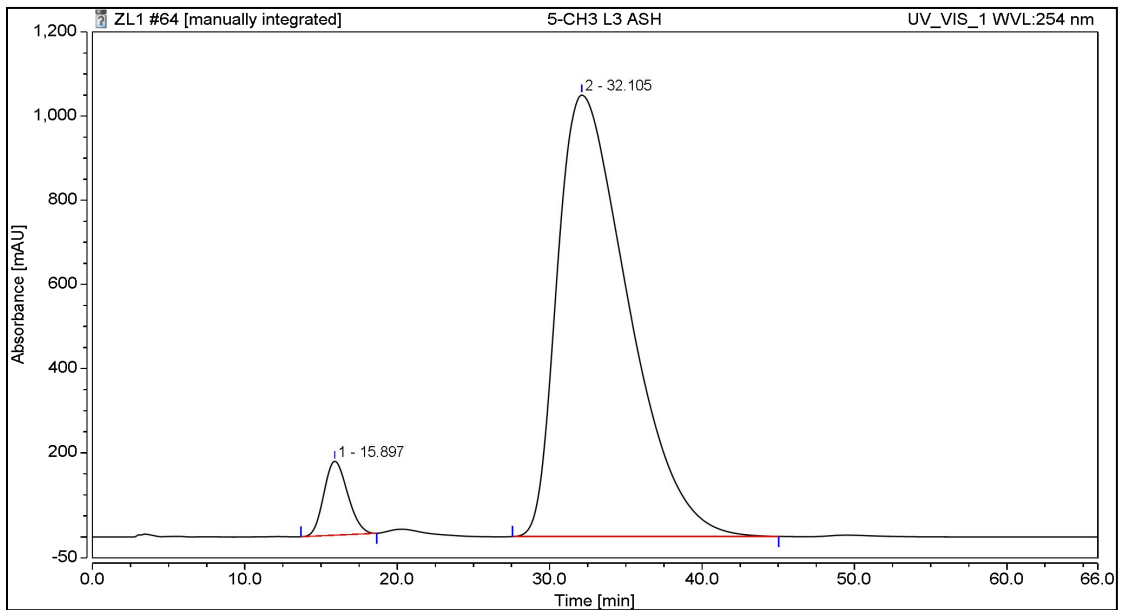
Integration Results						
No.	Peak Name	Retention Time min	Area mAU*min	Height mAU	Relative Area %	Relative Height %
1		25.217	198.613	76.747	6.07	9.40
2		33.898	3076.101	739.744	93.93	90.60
Total:			3274.714	816.491	100.00	100.00



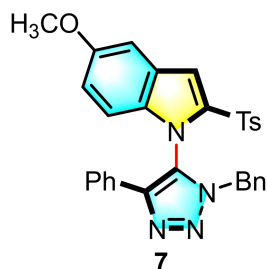
White solid, 45.1 mg, 87% yield, 94.5:5.5 er. [Chiral HPLC analysis of the product: Daicel Chiralpak AS-H 250X4.6 mm 5u column; *n*-hexane/2-propanol = 90/10, flow rate = 1.0 mL/min, $\lambda = 254$ nm, t (major) = 32.11 min, t (minor) = 15.90 min]. $[\alpha]_D^{26} = -47.3^\circ$ ($c = 0.9$, CHCl_3). **$^1\text{H NMR}$ (500 MHz, CDCl_3)** δ 7.69 (s, 1H), 7.49 (s, 1H), 7.26 (d, $J = 8.2$ Hz, 2H), 7.06-6.96 (m, 4H), 6.90-6.85 (m, 4H), 6.75 (dd, $J = 12.3, 8.2$ Hz, 5H), 6.04 (d, $J = 8.5$ Hz, 1H), 5.75 (d, $J = 15.0$ Hz, 1H), 5.25 (d, $J = 15.0$ Hz, 1H), 2.38 (s, 3H), 2.04 (s, 3H). **$^{13}\text{C NMR}$ (126 MHz, CDCl_3)** δ 144.9, 142.6, 138.2, 136.0, 135.9, 133.6, 132.6, 129.6, 129.1, 128.7, 128.6, 128.5, 128.4, 128.1, 128.0, 127.9, 125.949, 125.8, 124.8, 122.3, 114.1, 110.8, 53.1, 21.5, 21.4. **HRMS (ESI, m/z)** Calcd for $\text{C}_{31}\text{H}_{27}\text{N}_4\text{O}_2\text{S}$ ($\text{M}+\text{H}$) $^+$: 519.1849; Found: 519.1853.



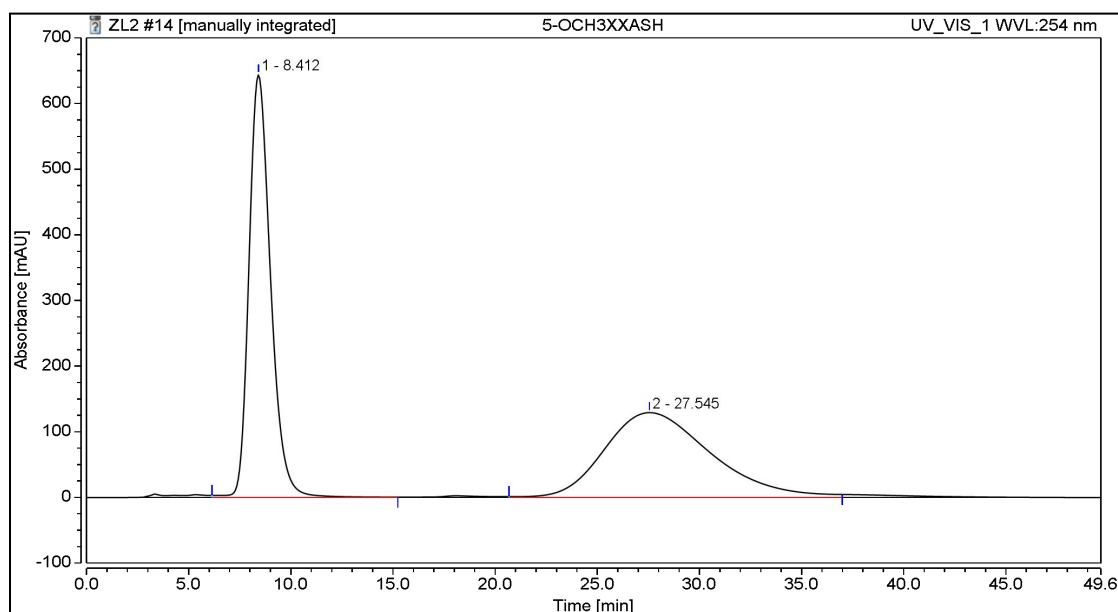
Integration Results						
No.	Peak Name	Retention Time min	Area mAU*min	Height mAU	Relative Area %	Relative Height %
1		16.715	462.910	208.894	49.93	70.95
2		34.702	464.197	85.522	50.07	29.05
Total:			927.107	294.416	100.00	100.00



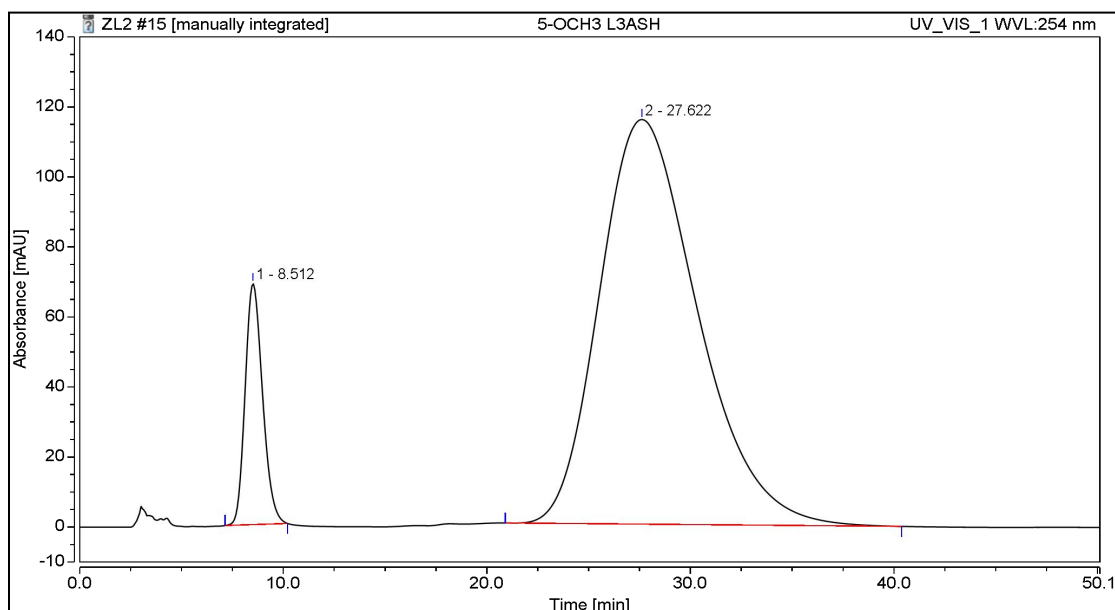
Integration Results						
No.	Peak Name	Retention Time min	Area mAU*min	Height mAU	Relative Area %	Relative Height %
1		15.897	318.701	175.885	5.34	14.36
2		32.105	5649.173	1049.148	94.66	85.64
Total:			5967.874	1225.033	100.00	100.00



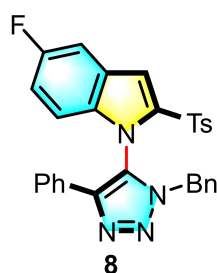
White solid, 38.9 mg, 73% yield, 90.5:9.5 er. [Chiral HPLC analysis of the product: Daicel Chiralpak AS-H 250X4.6 mm 5u column; *n*-hexane/2-propanol = 60/40, flow rate = 1.0 mL/min, λ = 254 nm, *t* (major) = 27.62 min, *t* (minor) = 8.51 min]. $[\alpha]_D^{26} = -16.4^\circ$ (*c* = 0.7, CHCl₃). **¹H NMR (500 MHz, CDCl₃)** δ 7.68 (s, 1H), 7.26 (d, *J* = 8.5 Hz, 2H), 7.10 (d, *J* = 2.4 Hz, 1H), 7.06 (t, *J* = 7.4 Hz, 1H), 7.02-7.00 (m, 3H), 6.92-6.84 (m, 4H), 6.74 (dd, *J* = 22.8, 8.3 Hz, 4H), 6.57 (dd, *J* = 9.1, 2.4 Hz, 1H), 6.00 (d, *J* = 9.1 Hz, 1H), 5.77 (d, *J* = 15.0 Hz, 1H), 5.28 (d, *J* = 15.0 Hz, 1H), 3.83 (s, 3H), 2.04 (s, 3H). **¹³C NMR (126 MHz, CDCl₃)** δ 156.2, 144.9, 142.6, 136.2, 135.9, 134.8, 133.6, 129.6, 128.6, 128.6, 128.5, 128.5, 128.1, 128.0, 127.9, 126.1, 125.8, 124.8, 118.4, 114.0, 112.0, 103.3, 55.9, 53.1, 21.5. **HRMS (ESI, *m/z*)** Calcd for C₃₁H₂₇N₄O₃S (M+H)⁺: 535.1798; Found: 535.1813.



Integration Results						
No.	Peak Name	Retention Time min	Area mAU*min	Height mAU	Relative Area %	Relative Height %
1		8.412	791.281	644.023	50.30	83.27
2		27.545	781.919	129.393	49.70	16.73
Total:			1573.200	773.416	100.00	100.00

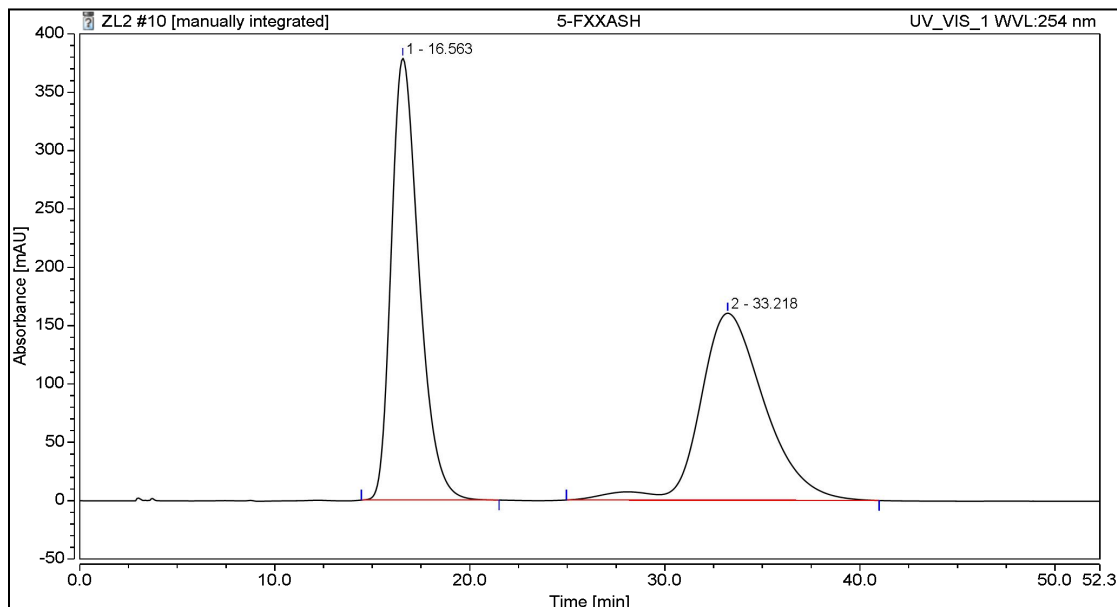


Integration Results						
No.	Peak Name	Retention Time min	Area mAU*min	Height mAU	Relative Area %	Relative Height %
1		8.512	68.387	68.854	9.58	37.33
2		27.622	645.248	115.589	90.42	62.67
Total:			713.636	184.442	100.00	100.00

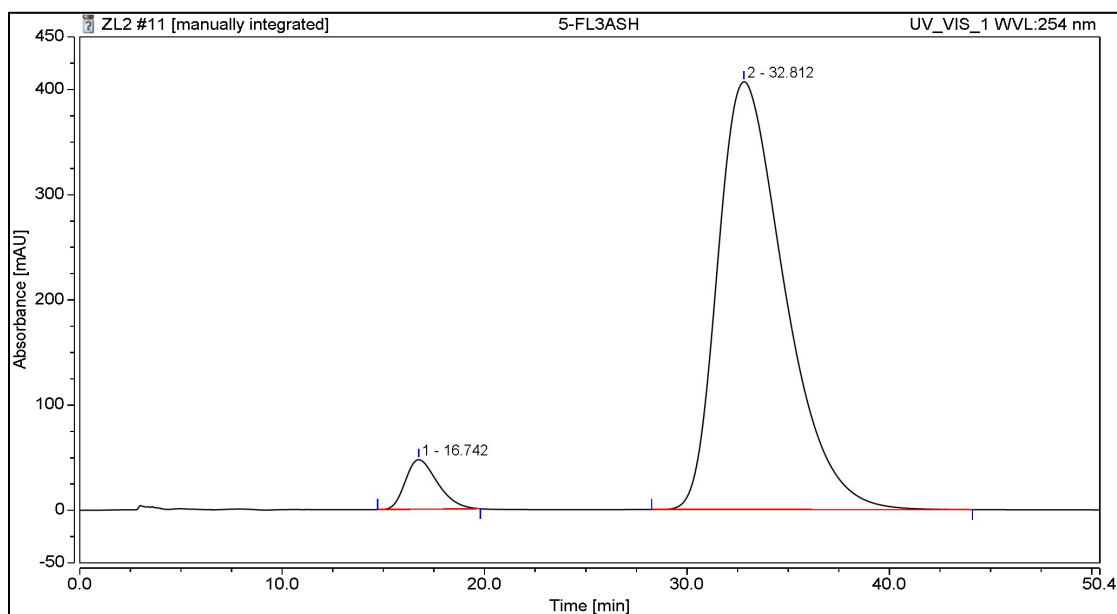


White solid, 39.6 mg, 76% yield, 94.5:5.5 er. [Chiral HPLC analysis of the product: Daicel Chiralpak AS-H 250X4.6 mm 5u column; *n*-hexane/2-propanol = 90/10, flow rate = 1.0 mL/min, $\lambda = 254$ nm, t (major) = 32.81 min, t (minor) = 16.74 min]. $[\alpha]_D^{26} = -43.5^\circ$ ($c = 0.9$, CHCl_3). **$^1\text{H NMR}$ (500 MHz, CDCl_3)** δ 7.72 (s, 1H), 7.35 (dd, $J = 8.5, 2.4$ Hz, 1H), 7.27 (d, $J = 8.5$ Hz, 2H), 7.05 - 7.00 (m, 2H), 6.96 (t, $J = 7.6$ Hz, 2H), 6.89 - 6.86 (m, 4H), 6.78 (d, $J = 8.2$ Hz, 2H), 6.71 (d, $J = 9.0$ Hz, 2H), 6.64 (td, $J = 9.0, 2.4$ Hz, 1H), 6.01 (dd, $J = 9.1, 4.1$ Hz, 1H), 5.81 (d, $J = 15.0$ Hz, 1H), 5.30 (d, $J = 15.0$ Hz, 1H), 2.05 (s, 3H). **$^{13}\text{C NMR}$ (126 MHz, CDCl_3)** δ 160.1, 158.2, 145.2, 142.7, 137.7, 136.0, 135.5, 133.4, 129.7, 128.7, 128.6, 128.4, 128.4, 128.2, 128.0, 125.9, 125.8, 125.5, 124.7, 116.3, 116.0, 113.9, 113.8, 112.3, 112.2, 107.7, 107.5, 53.3, 21.5. **$^{19}\text{F NMR}$ (471 MHz,**

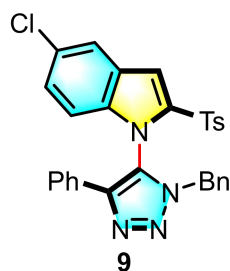
CDCl_3 δ -119.57. HRMS (ESI, m/z) Calcd for $\text{C}_{30}\text{H}_{24}\text{FN}_4\text{O}_2\text{S}$ (M+H)⁺: 523.1599; Found: 523.1612.



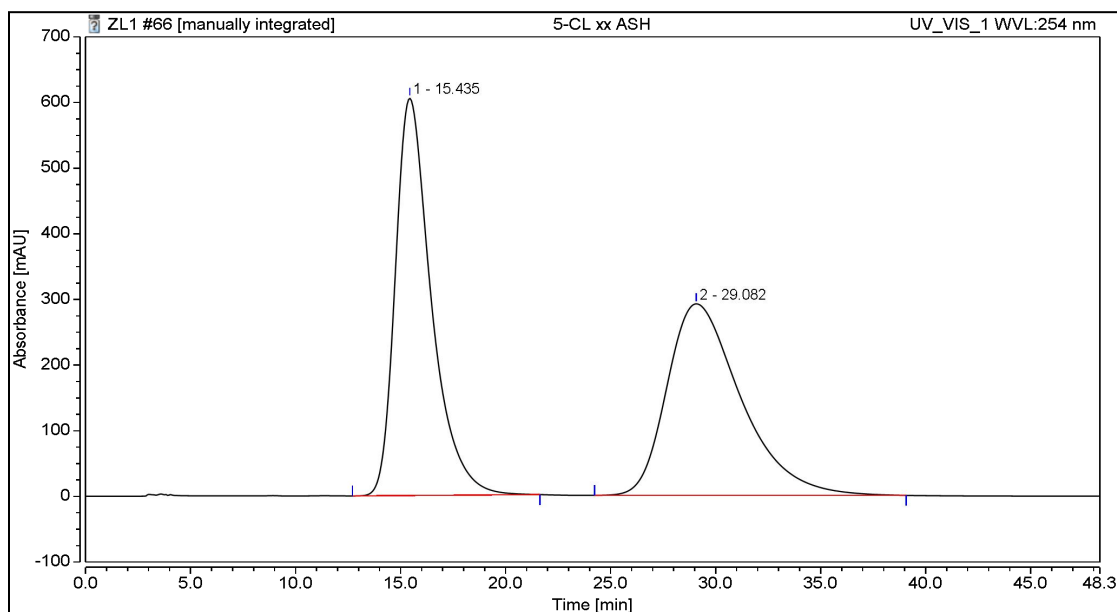
Integration Results						
No.	Peak Name	Retention Time min	Area mAU*min	Height mAU	Relative Area %	Relative Height %
1		16.563	625.068	378.632	50.45	70.25
2		33.218	613.929	160.318	49.55	29.75
Total:			1238.997	538.951	100.00	100.00



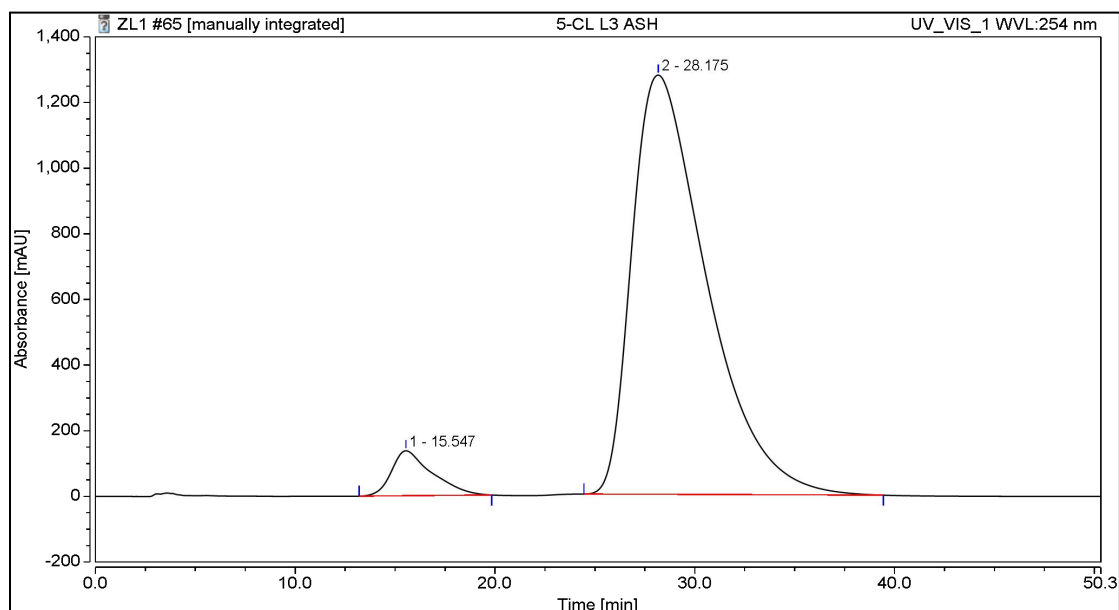
Integration Results						
No.	Peak Name	Retention Time min	Area mAU*min	Height mAU	Relative Area %	Relative Height %
1		16.742	86.736	47.162	5.29	10.39
2		32.812	1552.392	406.777	94.71	89.61
Total:			1639.128	453.939	100.00	100.00



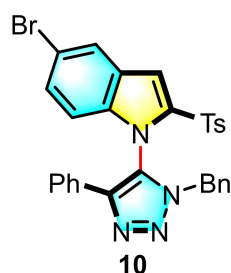
White solid, 47.3 mg, 88% yield, 94.5:5.5 er. [Chiral HPLC analysis of the product: Daicel Chiralpak AS-H 250X4.6 mm 5u column; *n*-hexane/2-propanol = 90/10, flow rate = 1.0 mL/min, λ = 254 nm, *t* (major) = 28.18 min, *t* (minor) = 15.55 min]. $[\alpha]_D^{27} = -29.2^\circ$ (*c* = 0.8, CHCl₃). **¹H NMR (500 MHz, CDCl₃)** δ 7.72-7.67 (m, 2H), 7.28-7.25 (m, 2H), 7.03 (dt, *J* = 15.0, 7.4 Hz, 2H), 6.96 (t, *J* = 7.6 Hz, 2H), 6.91-6.82 (m, 5H), 6.78 (d, *J* = 8.2 Hz, 2H), 6.70 (d, *J* = 7.4 Hz, 2H), 6.00 (d, *J* = 8.9 Hz, 1H), 5.81 (d, *J* = 15.0 Hz, 1H), 5.29 (d, *J* = 15.0 Hz, 1H), 2.05 (s, 3H). **¹³C NMR (126 MHz, CDCl₃)** δ 145.3, 142.8, 137.9, 137.5, 135.4, 133.4, 129.7, 128.8, 128.7, 128.6, 128.4, 128.4, 128.2, 128.0, 127.6, 126.4, 125.3, 124.7, 122.2, 113.4, 112.2, 53.4, 21.5. **HRMS (ESI, *m/z*)** Calcd for C₃₀H₂₄ClN₄O₂S (M+H)⁺: 539.1303; Found: 539.1300.



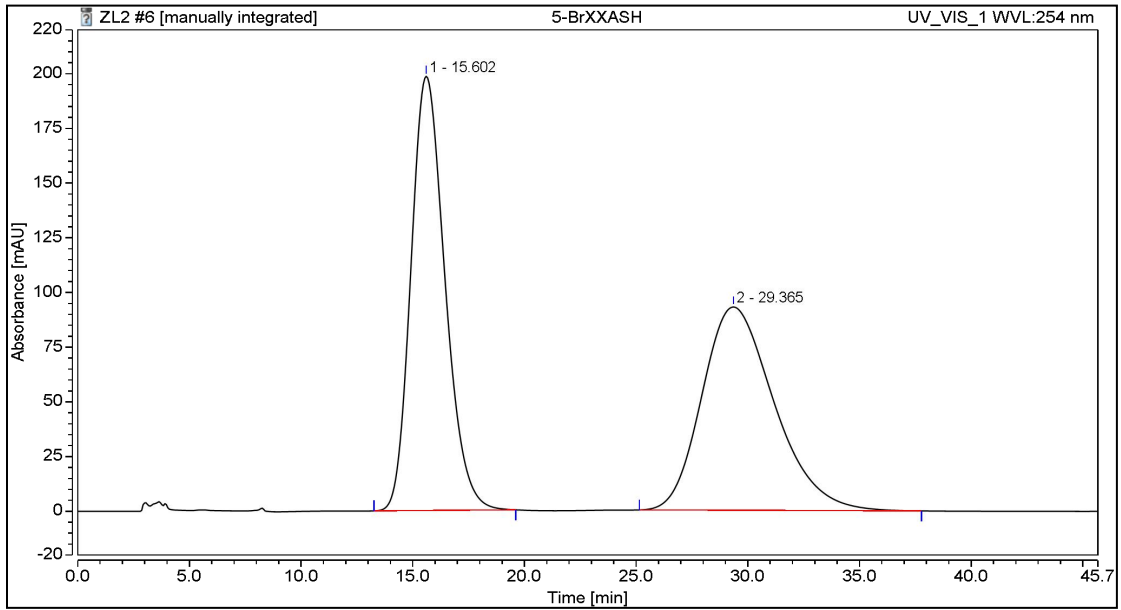
Integration Results						
No.	Peak Name	Retention Time min	Area mAU*min	Height mAU	Relative Area %	Relative Height %
1		15.435	1202.491	605.186	50.26	67.47
2		29.082	1190.210	291.804	49.74	32.53
Total:			2392.701	896.991	100.00	100.00



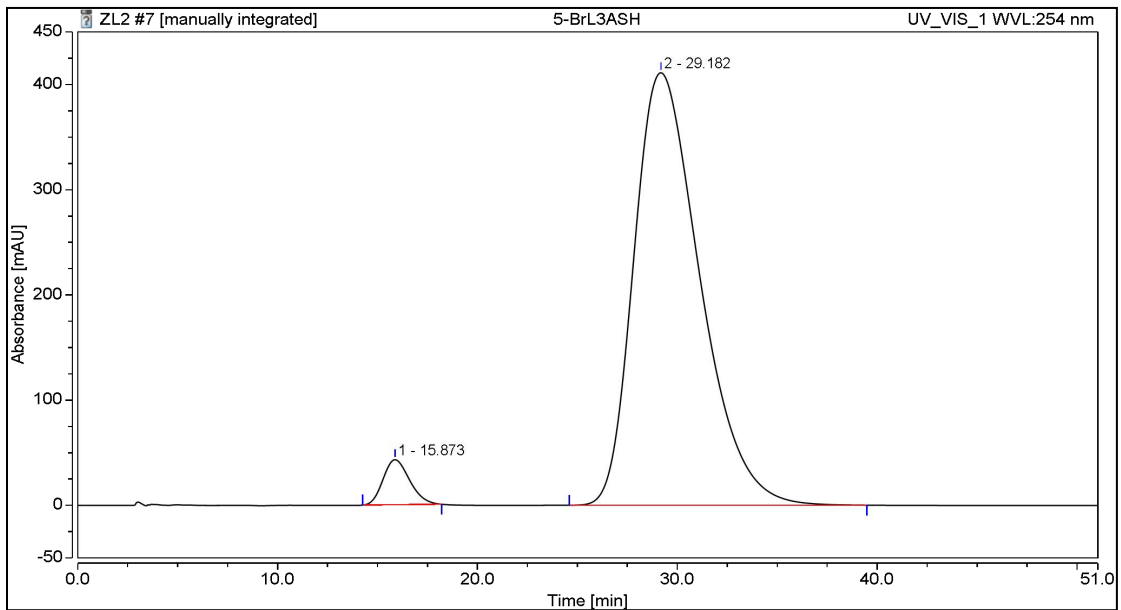
Integration Results						
No.	Peak Name	Retention Time min	Area mAU*min	Height mAU	Relative Area %	Relative Height %
1		15.547	321.673	137.085	5.50	9.69
2		28.175	5528.951	1277.709	94.50	90.31
Total:			5850.624	1414.794	100.00	100.00



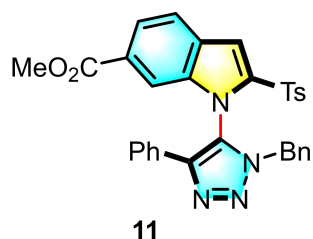
White solid, 36.7 mg, 63% yield, 96:4 er. [Chiral HPLC analysis of the product: Daicel Chiralpak AS-H 250X4.6 mm 5u column; *n*-hexane/2-propanol = 90/10, flow rate = 1.0 mL/min, $\lambda = 254$ nm, t (major) = 29.18 min, t (minor) = 15.87 min]. $[\alpha]_D^{27} = -30.8^\circ$ ($c = 0.5$, CHCl_3). **$^1\text{H NMR}$ (500 MHz, CDCl_3)** δ 7.85 (d, $J = 1.6$ Hz, 1H), 7.69 (s, 1H), 7.26 (d, $J = 8.3$ Hz, 2H), 7.08-7.00 (m, 2H), 6.99-6.93 (m, 3H), 6.91-6.84 (m, 4H), 6.78 (d, $J = 8.1$ Hz, 2H), 6.71 (d, $J = 8.1$ Hz, 2H), 5.95 (d, $J = 8.9$ Hz, 1H), 5.81 (d, $J = 15.0$ Hz, 1H), 5.28 (d, $J = 15.0$ Hz, 1H), 2.05 (s, 3H). **$^{13}\text{C NMR}$ (126 MHz, CDCl_3)** δ 145.3, 142.8, 138.2, 137.4, 135.4, 133.4, 130.2, 129.7, 128.7, 128.6, 128.4, 128.3, 128.2, 128.0, 127.0, 125.3, 125.2, 124.7, 116.2, 113.3, 112.5, 53.4, 21.5. **HRMS (ESI, m/z)** Calcd for $\text{C}_{30}\text{H}_{24}\text{BrN}_4\text{O}_2\text{S}$ ($\text{M}+\text{H}$) $^+$: 583.0798, 583.0777; Found: 583.0792, 583.0774.



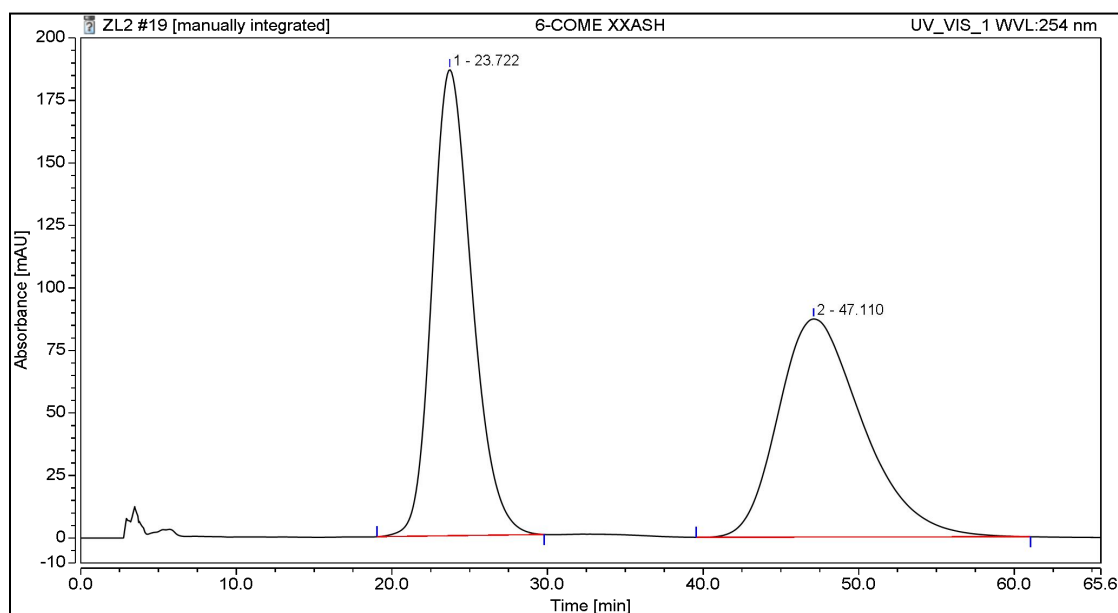
Integration Results						
No.	Peak Name	Retention Time min	Area mAU*min	Height mAU	Relative Area %	Relative Height %
1		15.602	350.324	198.494	50.13	68.12
2		29.365	348.474	92.916	49.87	31.88
Total:			698.797	291.410	100.00	100.00



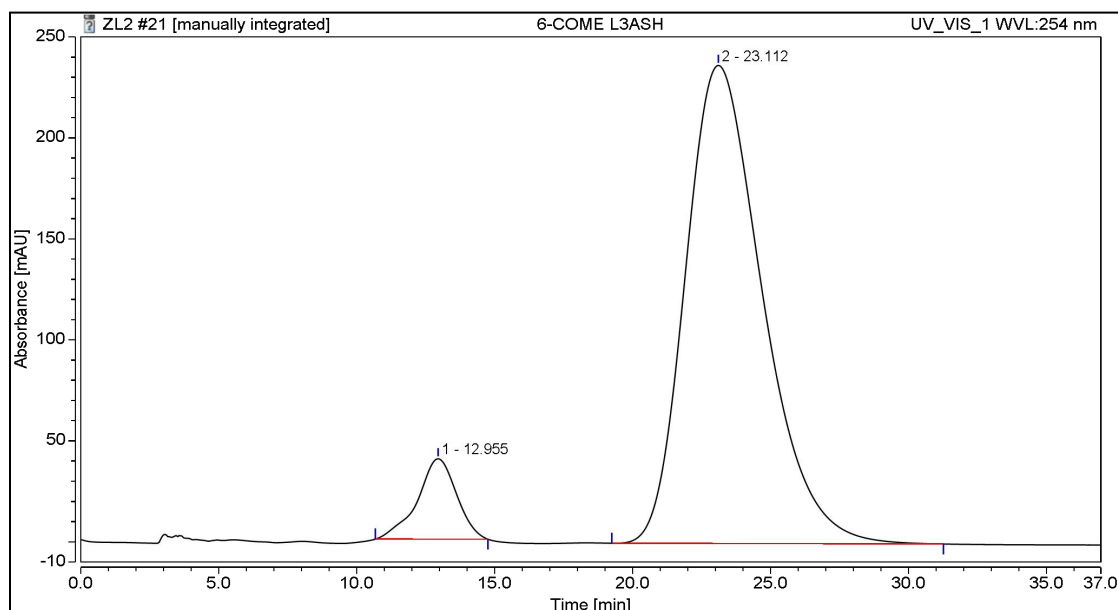
Integration Results						
No.	Peak Name	Retention Time min	Area mAU*min	Height mAU	Relative Area %	Relative Height %
1		15.873	66.001	42.854	4.03	9.44
2		29.182	1572.435	411.161	95.97	90.56
Total:			1638.436	454.015	100.00	100.00



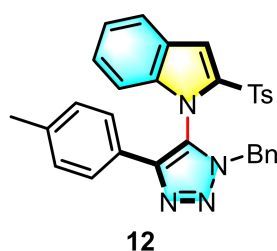
White solid, 29.2 mg, 52% yield, 92:8 er. [Chiral HPLC analysis of the product: Daicel Chiralpak AS-H 250X4.6 mm 5u column; *n*-hexane/2-propanol = 80/20, flow rate = 1.0 mL/min, $\lambda = 254$ nm, t (major) = 23.11 min, t (minor) = 12.96 min]. $[\alpha]_D^{26} = -85.0^\circ$ ($c = 0.5$, CHCl_3). $^1\text{H NMR}$ (500 MHz, CDCl_3) δ 7.82-7.71 (m, 3H), 7.28 (d, $J = 8.2$ Hz, 2H), 7.01 (t, $J = 7.4$ Hz, 1H), 6.92-6.81 (m, 7H), 6.79 (d, $J = 8.1$ Hz, 2H), 6.73 (d, $J = 7.7$ Hz, 2H), 6.69 (s, 1H), 5.85 (d, $J = 15.0$ Hz, 1H), 5.27 (d, $J = 15.0$ Hz, 1H), 3.75 (s, 3H), 2.06 (s, 3H). $^{13}\text{C NMR}$ (126 MHz, CDCl_3) δ 165.2, 144.4, 142.1, 138.0, 137.9, 134.3, 132.3, 128.7, 127.8, 127.6, 127.6, 127.5, 127.3, 127.2, 127.2, 127.1, 124.2, 123.8, 122.628, 121.718, 112.7, 112.2, 52.5, 51.1, 20.6. **HRMS (ESI, m/z)** Calcd for $\text{C}_{32}\text{H}_{27}\text{N}_4\text{O}_4\text{S}$ ($\text{M}+\text{H}$) $^+$: 563.1748; Found: 563.1740.



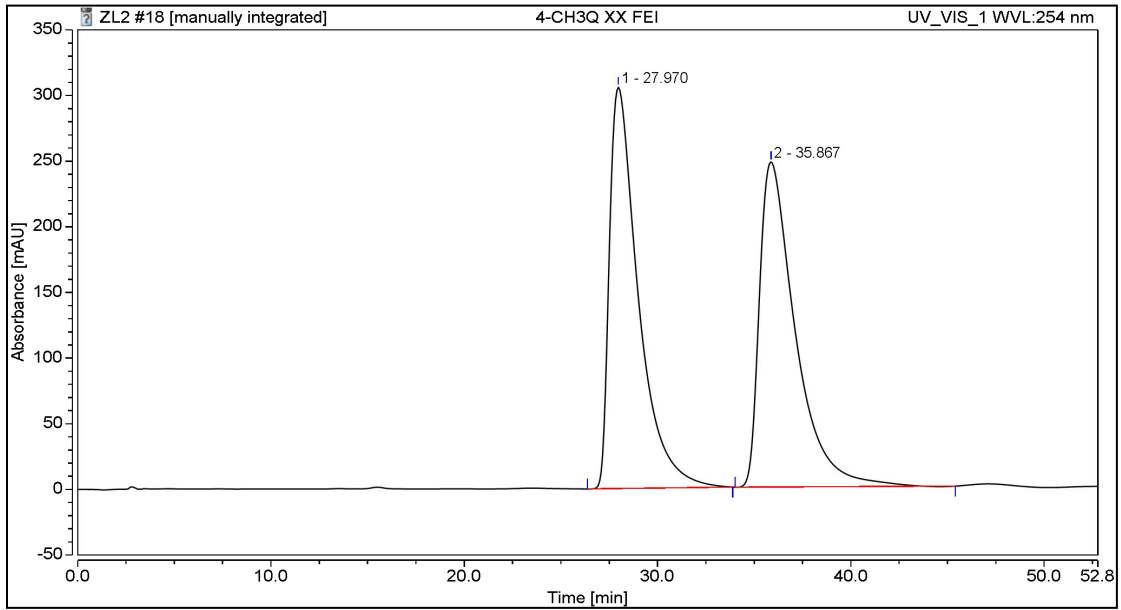
Integration Results						
No.	Peak Name	Retention Time min	Area mAU*min	Height mAU	Relative Area %	Relative Height %
1		23.722	553.142	186.416	50.17	68.12
2		47.110	549.297	87.249	49.83	31.88
Total:			1102.440	273.665	100.00	100.00



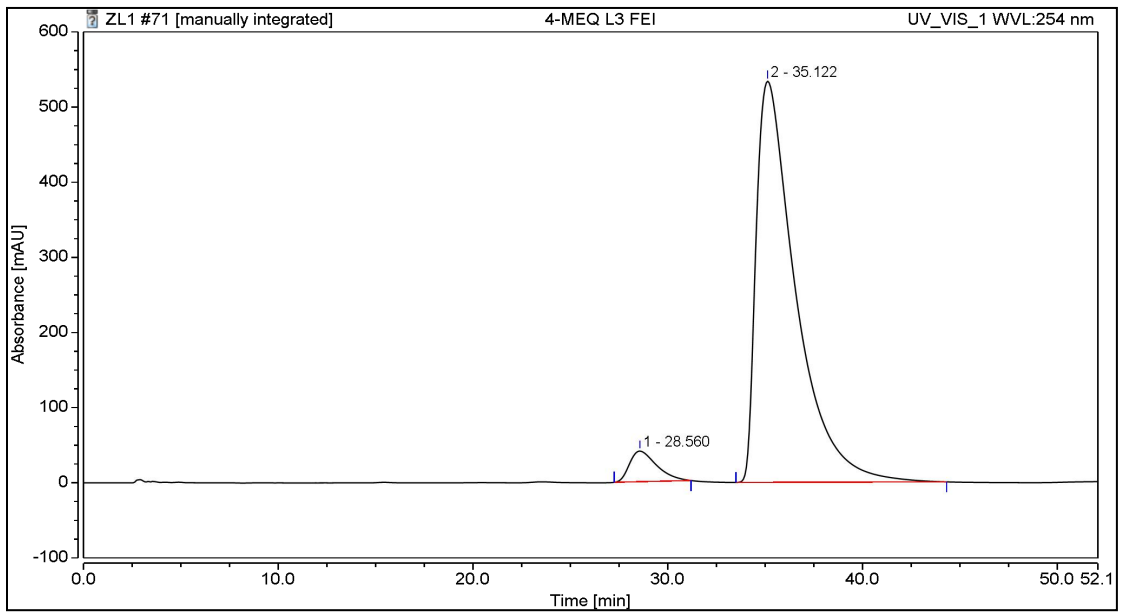
Integration Results						
No.	Peak Name	Retention Time min	Area mAU*min	Height mAU	Relative Area %	Relative Height %
1		12.955	65.576	39.823	7.92	14.40
2		23.112	762.873	236.745	92.08	85.60
Total:			828.449	276.569	100.00	100.00



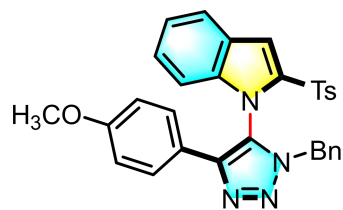
White solid, 41.9 mg, 81% yield, 95:5 er. [Chiral HPLC analysis of the product: Phenomenex 00G-4457-E0 250X4.6 mm 5u column; *n*-hexane/2-propanol = 85/15, flow rate = 1.0 mL/min, λ = 254 nm, t (major) = 35.12 min, t (minor) = 28.56 min]. $[\alpha]_D^{26} = -60.7^\circ$ ($c = 0.7$, CHCl_3). **$^1\text{H NMR}$ (500 MHz, CDCl_3)** δ 7.76 (s, 1H), 7.70 (d, $J = 8.1$ Hz, 1H), 7.27 (d, $J = 8.3$ Hz, 2H), 7.13 (t, $J = 7.6$ Hz, 1H), 7.00 (t, $J = 7.3$ Hz, 1H), 6.96-6.84 (m, 5H), 6.78 (d, $J = 8.1$ Hz, 2H), 6.68 (d, $J = 8.2$ Hz, 2H), 6.61 (d, $J = 8.3$ Hz, 2H), 6.11 (d, $J = 8.4$ Hz, 1H), 5.76 (d, $J = 15.0$ Hz, 1H), 5.25 (d, $J = 15.0$ Hz, 1H), 2.16 (s, 3H), 2.05 (s, 3H). **$^{13}\text{C NMR}$ (126 MHz, CDCl_3)** δ 144.8, 142.8, 139.7, 137.9, 136.1, 135.9, 133.5, 129.6, 128.8, 128.6, 128.4, 128.0, 127.2, 125.9, 125.5, 125.4, 124.8, 122.9, 122.9, 114.3, 111.1, 53.2, 21.4, 21.2. **HRMS (ESI, m/z)** Calcd for $\text{C}_{31}\text{H}_{27}\text{N}_4\text{O}_2\text{S}$ ($\text{M}+\text{H}$) $^+$: 519.1849; Found: 519.1838.



Integration Results						
No.	Peak Name	Retention Time min	Area mAU*min	Height mAU	Relative Area %	Relative Height %
1		27.970	529.372	305.697	49.91	55.24
2		35.867	531.188	247.689	50.09	44.76
Total:			1060.561	553.386	100.00	100.00

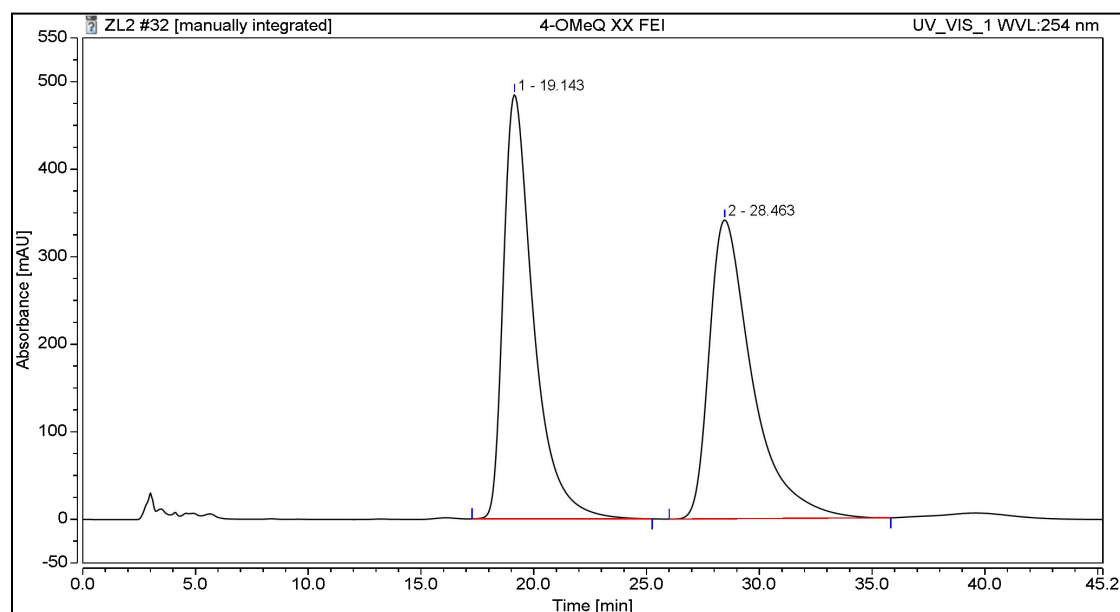


Integration Results						
No.	Peak Name	Retention Time min	Area mAU*min	Height mAU	Relative Area %	Relative Height %
1		28.560	65.952	40.793	4.99	7.10
2		35.122	1255.327	533.941	95.01	92.90
Total:			1321.279	574.733	100.00	100.00

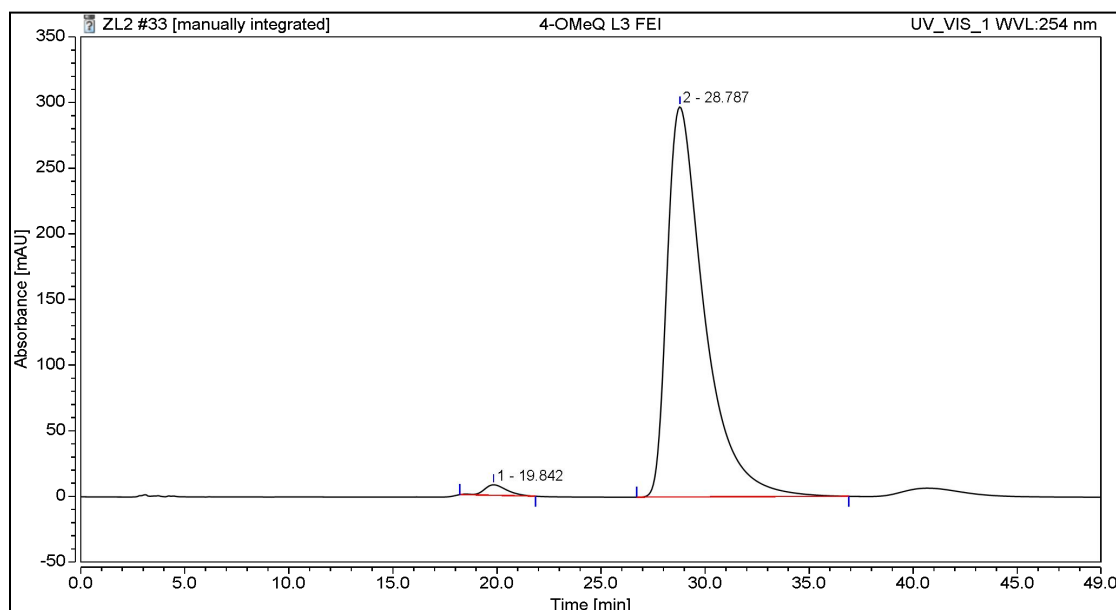


13

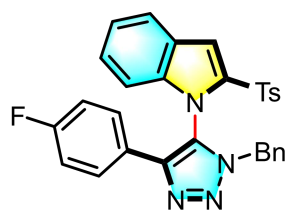
White solid, 47.5 mg, 89% yield, 98.5:1.5 er. [Chiral HPLC analysis of the product: Phenomenex 00G-4457-E0 250X4.6 mm 5u column; *n*-hexane/2-propanol = 70/30, flow rate =1.0 mL/min, λ = 254 nm, t (major) = 28.79 min, t (minor) = 19.84 min]. $[\alpha]_D^{26} = -83.6^\circ$ ($c = 1.1$, CHCl_3). **$^1\text{H NMR}$ (500 MHz, CDCl_3)** δ 7.76 (s, 1H), 7.71 (d, $J = 8.1$ Hz, 1H), 7.28 (d, $J = 8.3$ Hz, 2H), 7.14 (t, $J = 7.5$ Hz, 1H), 7.00 (t, $J = 7.3$ Hz, 1H), 6.97-6.84 (m, 5H), 6.80 (d, $J = 8.1$ Hz, 2H), 6.67 (d, $J = 8.9$ Hz, 2H), 6.40 (d, $J = 8.9$ Hz, 2H), 6.12 (d, $J = 8.4$ Hz, 1H), 5.75 (d, $J = 15.0$ Hz, 1H), 5.24 (d, $J = 15.0$ Hz, 1H), 3.65 (s, 3H), 2.08 (s, 3H). **$^{13}\text{C NMR}$ (126 MHz, CDCl_3)** δ 159.5, 144.9, 142.6, 139.7, 136.1, 135.8, 133.5, 129.6, 128.5, 128.4, 128.0, 127.2, 126.2, 125.5, 124.8, 122.9, 122.9, 121.4, 114.3, 113.6, 111.1, 55.2, 53.1, 21.4. **HRMS (ESI, m/z)** Calcd for $\text{C}_{31}\text{H}_{27}\text{N}_4\text{O}_3\text{S}$ ($\text{M}+\text{H}$) $^+$: 535.1798; Found: 535.1786.



Integration Results						
No.	Peak Name	Retention Time min	Area mAU*min	Height mAU	Relative Area %	Relative Height %
1		19.143	748.754	484.775	49.82	58.67
2		28.463	754.276	341.497	50.18	41.33
Total:			1503.030	826.272	100.00	100.00



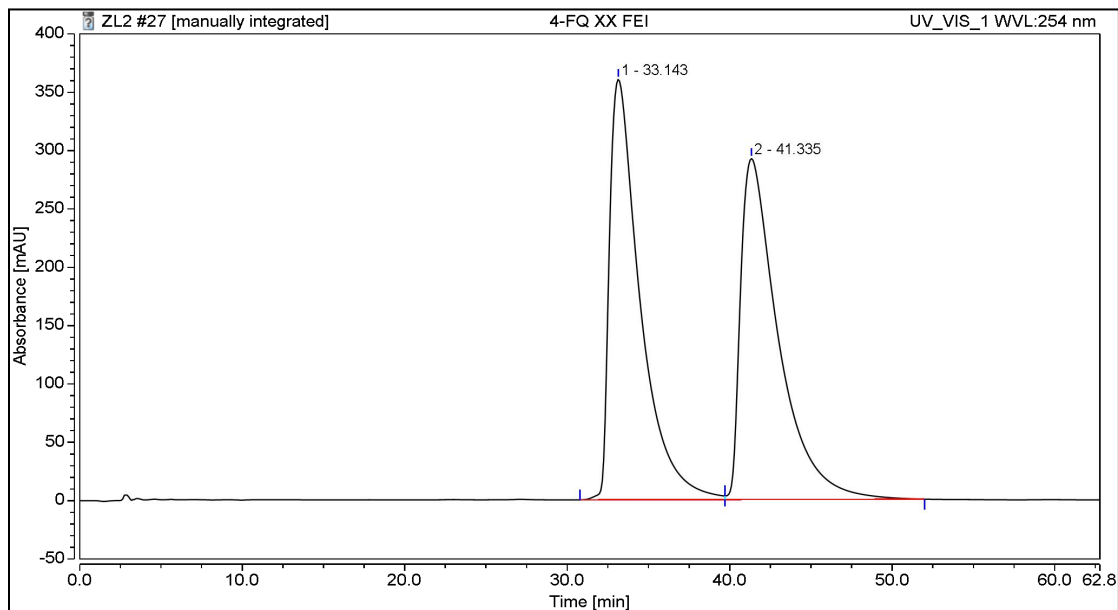
Integration Results						
No.	Peak Name	Retention Time min	Area mAU*min	Height mAU	Relative Area %	Relative Height %
1		19.842	10.146	8.026	1.62	2.63
2		28.787	615.625	297.212	98.38	97.37
Total:			625.771	305.238	100.00	100.00



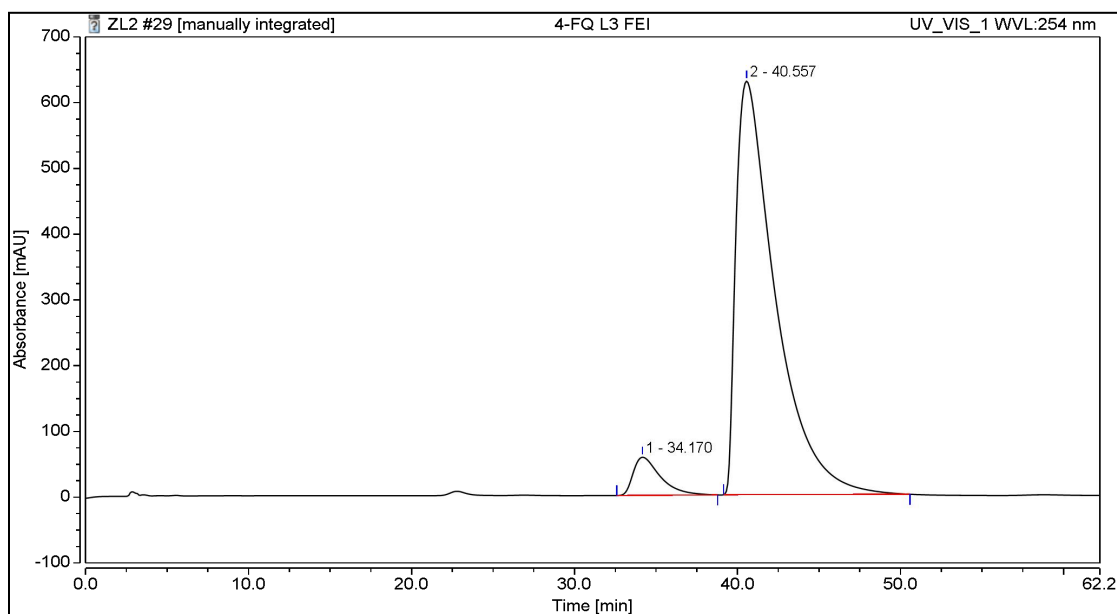
14

White solid, 41.2 mg, 79% yield, 94:6 er. [Chiral HPLC analysis of the product: Phenomenex 00G-4457-E0 250X4.6 mm 5u column; *n*-hexane/2-propanol = 90/10, flow rate = 1.0 mL/min, λ = 254 nm, *t* (major) = 40.56 min, *t* (minor) = 34.17 min]. $[\alpha]_D^{26} = -71.5^\circ$ (*c* = 0.7, CHCl₃). **¹H NMR (500 MHz, CDCl₃)** δ 7.77 (s, 1H), 7.72 (d, *J* = 8.1 Hz, 1H), 7.29 (d, *J* = 8.3 Hz, 2H), 7.15 (t, *J* = 7.5 Hz, 1H), 7.01 (t, *J* = 7.3 Hz, 1H), 6.93 (q, *J* = 6.9, 6.1 Hz, 3H), 6.84 (dd, *J* = 20.9, 7.8 Hz, 4H), 6.76-6.69 (m, 2H), 6.57 (t, *J* = 8.7 Hz, 2H), 6.11 (d, *J* = 8.4 Hz, 1H), 5.76 (d, *J* = 15.0 Hz, 1H), 5.25 (d, *J* = 15.0 Hz, 1H), 2.11 (s, 3H). **¹³C NMR (126 MHz, CDCl₃)** δ 163.5, 161.6, 145.1, 141.9, 139.6, 136.1, 136.0, 133.4, 129.6, 128.6, 128.5, 128.4, 128.0, 127.3, 126.7, 126.7, 125.5, 125.0, 123.1, 123.0, 115.2, 115.1, 114.5, 111.0, 53.3, 21.4. **¹⁹F NMR (471 MHz, CDCl₃)** δ

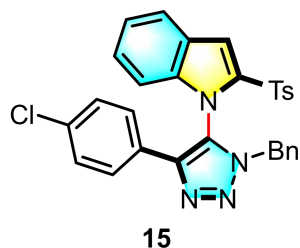
-113.10. HRMS (ESI, m/z) Calcd for C₃₀H₂₄FN₄O₂S (M+H)⁺: 523.1599; Found: 523.1584.



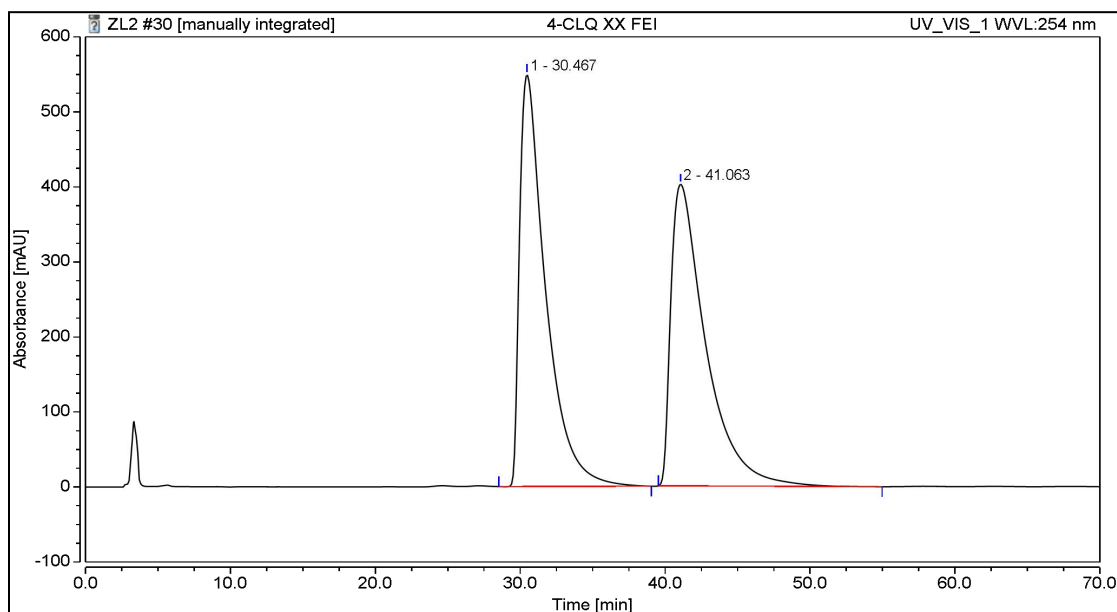
Integration Results						
No.	Peak Name	Retention Time min	Area mAU*min	Height mAU	Relative Area %	Relative Height %
1		33.143	789.486	360.345	50.02	55.22
2		41.335	788.721	292.189	49.98	44.78
Total:			1578.208	652.533	100.00	100.00



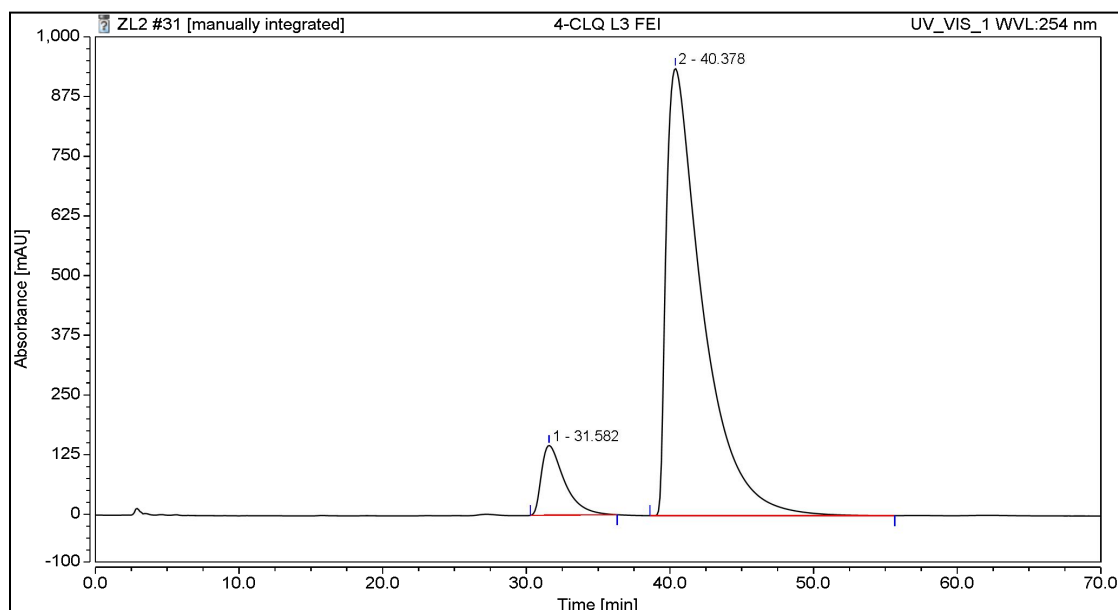
Integration Results						
No.	Peak Name	Retention Time min	Area mAU*min	Height mAU	Relative Area %	Relative Height %
1		34.170	112.486	58.062	5.99	8.45
2		40.557	1765.578	629.068	94.01	91.55
Total:			1878.063	687.131	100.00	100.00



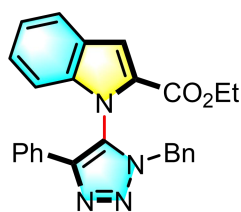
White solid, 47.3 mg, 88% yield, 91:9 er. [Chiral HPLC analysis of the product: Phenomenex 00G-4457-E0 250X4.6 mm 5u column; *n*-hexane/2-propanol = 90/10, flow rate =1.0 mL/min, λ = 254 nm, *t* (major) = 40.38 min, *t* (minor) = 31.58 min]. $[\alpha]_D^{26} = -72.0^\circ$ (*c* = 0.7, CHCl₃). **¹H NMR (500 MHz, CDCl₃)** δ 7.77 (s, 1H), 7.72 (d, *J* = 8.1 Hz, 1H), 7.28 (d, *J* = 8.3 Hz, 2H), 7.16 (t, *J* = 7.5 Hz, 1H), 7.01 (t, *J* = 7.3 Hz, 1H), 6.97-6.90 (m, 3H), 6.89-6.78 (m, 6H), 6.67 (d, *J* = 8.6 Hz, 2H), 6.10 (d, *J* = 8.4 Hz, 1H), 5.77 (d, *J* = 15.0 Hz, 1H), 5.25 (d, *J* = 15.0 Hz, 1H), 2.12 (s, 3H). **¹³C NMR (126 MHz, CDCl₃)** δ 145.2, 141.7, 139.5, 136.0, 135.9, 134.0, 133.3, 129.6, 128.6, 128.5, 128.4, 128.4, 128.0, 127.4, 127.2, 126.0, 125.9, 125.5, 123.1, 123.0, 114.6, 110.9, 53.3, 21.5. **HRMS (ESI, *m/z*)** Calcd for C₃₀H₂₄ClN₄O₂S (M+H)⁺: 539.1303; Found: 539.1290.



Integration Results						
No.	Peak Name	Retention Time min	Area mAU*min	Height mAU	Relative Area %	Relative Height %
1		30.467	1144.063	549.026	50.59	57.72
2		41.063	1117.506	402.147	49.41	42.28
Total:			2261.569	951.173	100.00	100.00

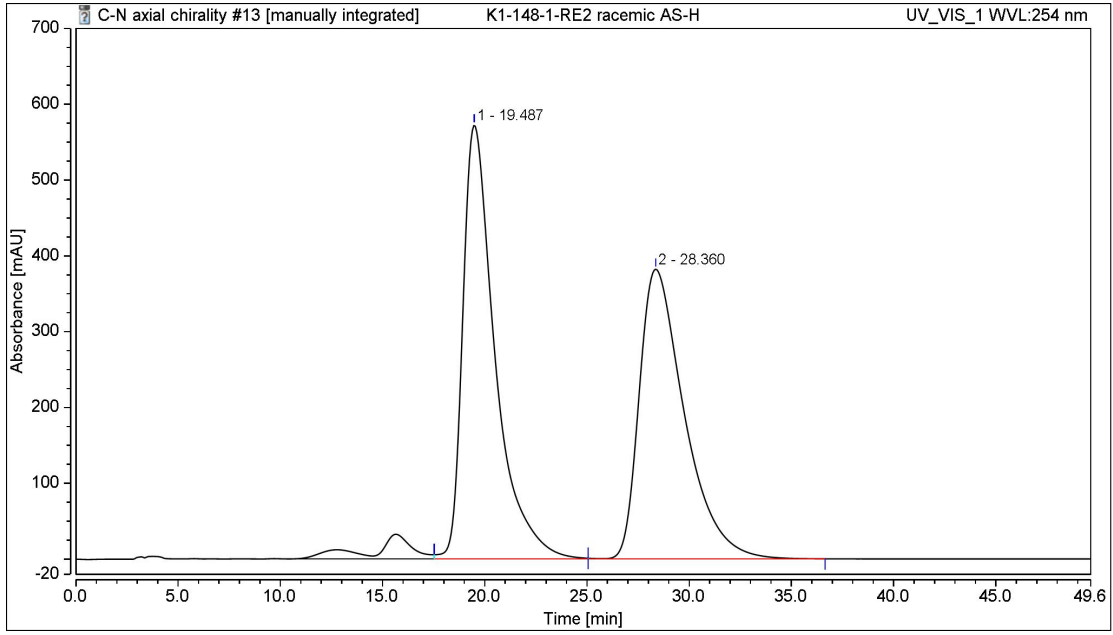


Integration Results						
No.	Peak Name	Retention Time min	Area mAU*min	Height mAU	Relative Area %	Relative Height %
1		31.582	271.999	146.177	9.01	13.50
2		40.378	2745.507	936.922	90.99	86.50
Total:			3017.506	1083.099	100.00	100.00

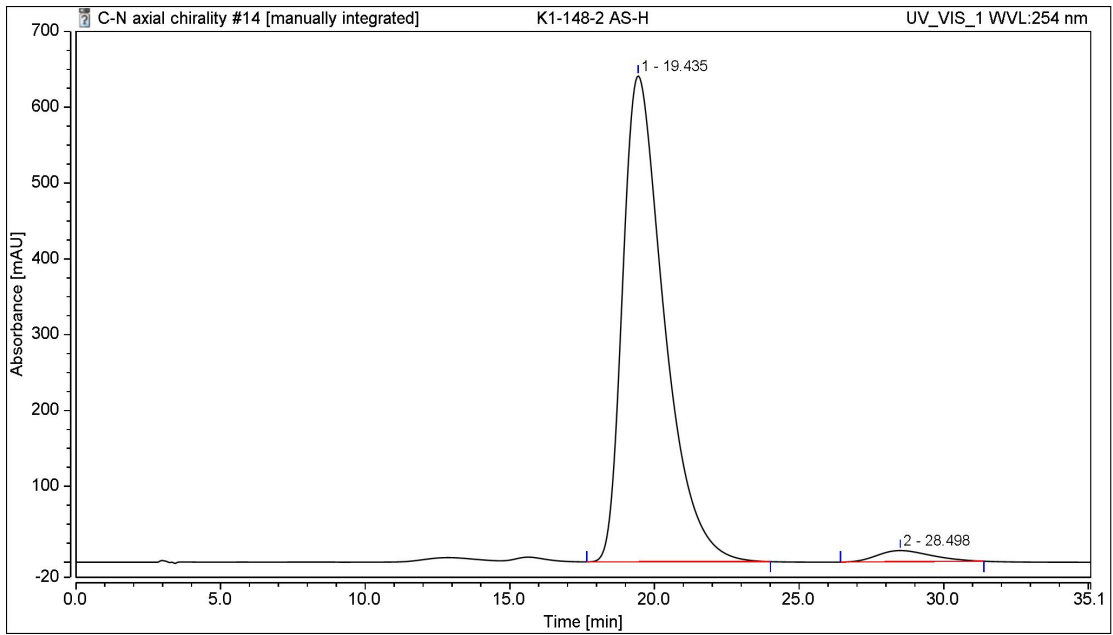


16

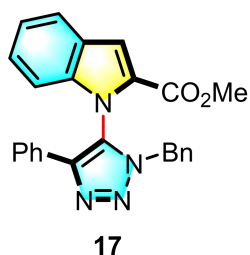
White solid, 37.2 mg, 88% yield, 97:3 er. [Chiral HPLC analysis of the product: Daicel Chiralpak AS-H 250X4.6 mm 5u column; *n*-hexane/2-propanol = 90/10, flow rate = 1.0 mL/min, λ = 254 nm, *t* (major) = 19.44 min, *t* (minor) = 28.50 min]. $[\alpha]_D^{26} = -103.0^\circ$ (*c* = 1.0, CHCl₃). **¹H NMR (500 MHz, CDCl₃)** δ 7.74 (d, *J* = 8.1 Hz, 1H), 7.60 (s, 1H), 7.35-7.28 (m, 2H), 7.24-7.10 (m, 6H), 7.10-7.04 (m, 2H), 6.91 (d, *J* = 7.0 Hz, 2H), 6.60 (d, *J* = 8.3 Hz, 1H), 5.24 (d, *J* = 15.0 Hz, 1H), 5.19 (d, *J* = 15.0 Hz, 1H), 4.03 (dq, *J* = 10.7, 7.0 Hz, 1H), 3.91 (dq, *J* = 10.7, 7.2 Hz, 1H), 1.05 (t, *J* = 7.2 Hz, 3H). **¹³C NMR (126 MHz, CDCl₃)** δ 158.9, 141.3, 138.1, 132.3, 128.4, 127.8, 127.8, 127.7, 127.5, 127.4, 127.2, 127.2, 125.9, 125.8, 124.4, 121.8, 121.6, 113.3, 109.9, 60.0, 51.3, 12.8. **HRMS (ESI, *m/z*)** Calcd for C₂₆H₂₃N₄O₂ (M+H)⁺: 423.1816; Found: 423.1803.



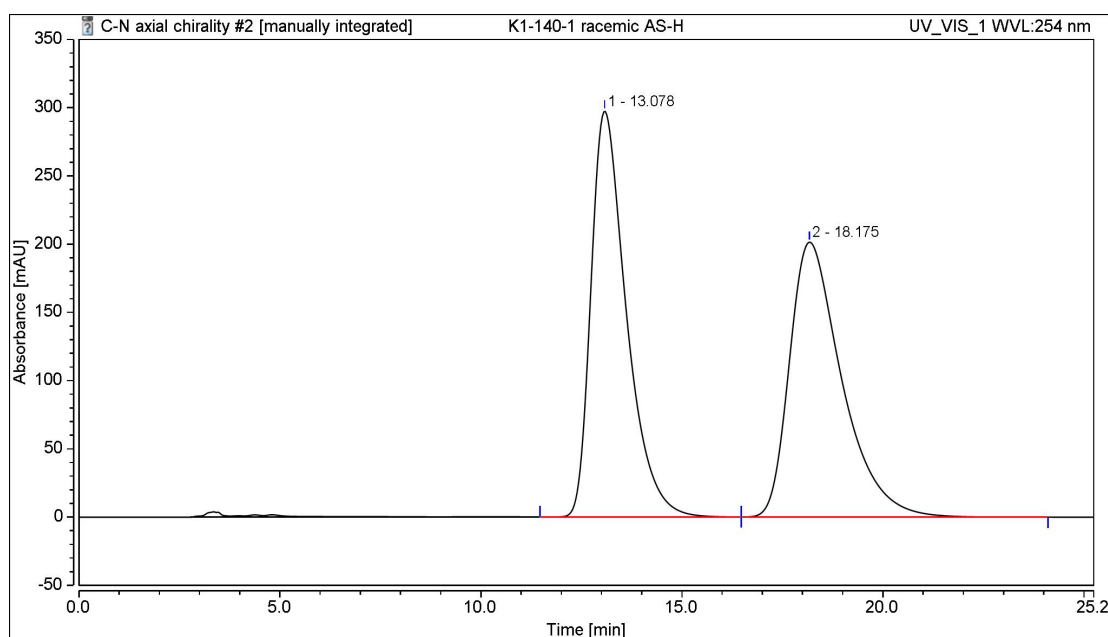
Integration Results						
No.	Peak Name	Retention Time min	Area mAU*min	Height mAU	Relative Area %	Relative Height %
1		19.487	1044.411	572.187	51.71	59.96
2		28.360	975.394	382.081	48.29	40.04
Total:			2019.804	954.268	100.00	100.00



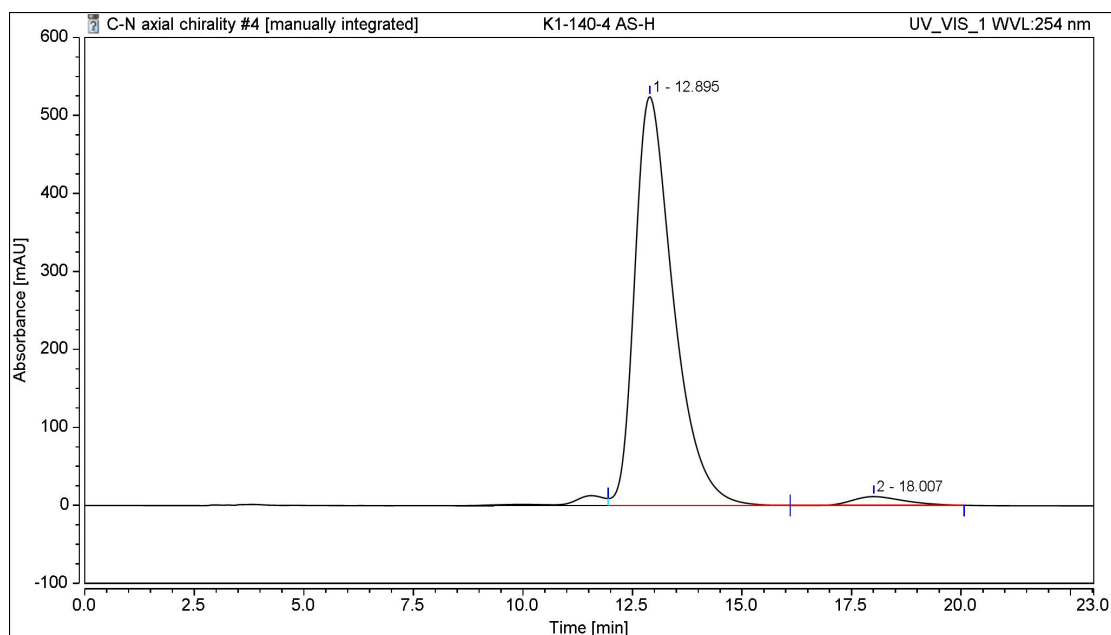
Integration Results						
No.	Peak Name	Retention Time min	Area mAU*min	Height mAU	Relative Area %	Relative Height %
1		19.435	1063.450	640.979	97.08	97.75
2		28.498	31.933	14.731	2.92	2.25
Total:			1095.383	655.710	100.00	100.00



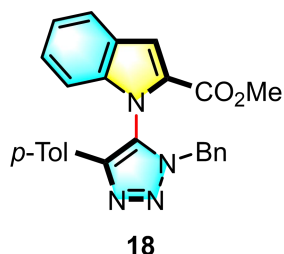
White solid, 39.6 mg, 97% yield, 97:3 er. [Chiral HPLC analysis of the product: Daicel Chiralpak AS-H 250X4.6 mm 5u column; *n*-hexane/2-propanol = 80/20, flow rate = 1.0 mL/min, $\lambda = 254$ nm, t (major) = 12.90 min, t (minor) = 18.00 min]. $[\alpha]_D^{26} = -122.1^\circ$ ($c = 0.9$, CHCl_3). **$^1\text{H NMR}$ (500 MHz, CDCl_3)** δ 7.74 (d, $J = 7.9$ Hz, 1H), 7.55 (s, 1H), 7.33-7.27 (m, 2H), 7.23-7.19 (m, 1H), 7.19-7.10 (m, 5H), 7.10-7.04 (m, 2H), 6.90 (dt, $J = 7.1, 1.3$ Hz, 2H), 6.59 (dd, $J = 8.4, 1.1$ Hz, 1H), 5.23 (s, 2H), 3.58 (s, 3H). **$^{13}\text{C NMR}$ (126 MHz, CDCl_3)** δ 159.4, 141.3, 138.2, 132.3, 128.4, 127.7, 127.5, 127.5, 127.3, 127.2, 127.2, 125.9, 125.7, 124.4, 121.8, 121.6, 113.2, 109.9, 51.3, 50.9. **HRMS (ESI, m/z)** Calcd for $\text{C}_{25}\text{H}_{21}\text{N}_4\text{O}_2$ ($\text{M}+\text{H}$) $^+$: 409.1659; Found: 409.1659.



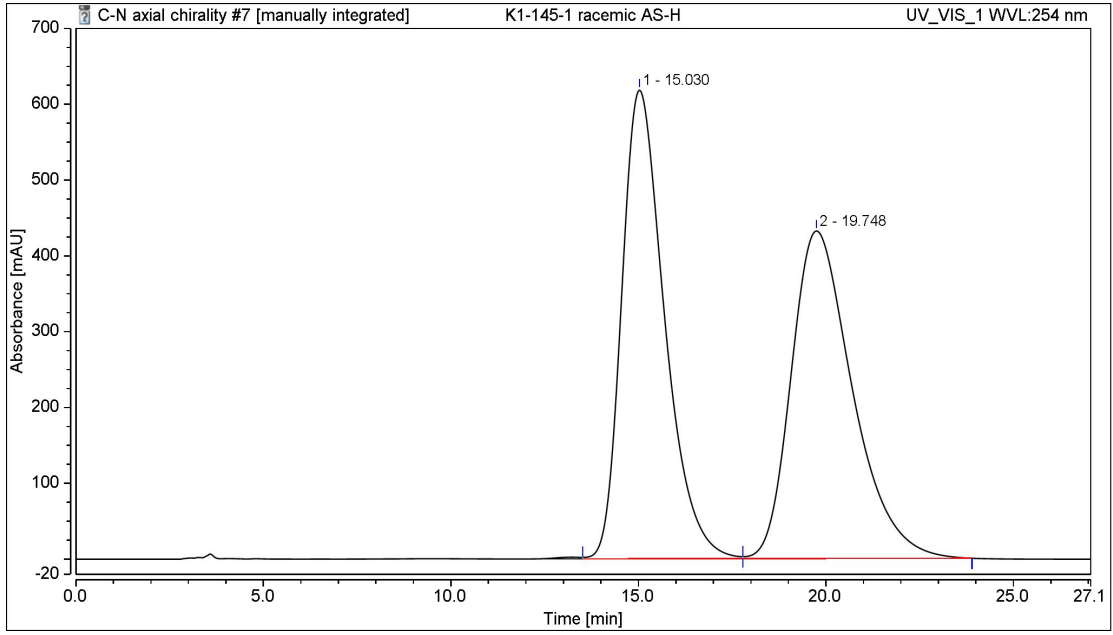
Integration Results						
No.	Peak Name	Retention Time min	Area mAU*min	Height mAU	Relative Area %	Relative Height %
1		13.078	304.096	297.546	50.03	59.62
2		18.175	303.677	201.552	49.97	40.38
Total:			607.773	499.097	100.00	100.00



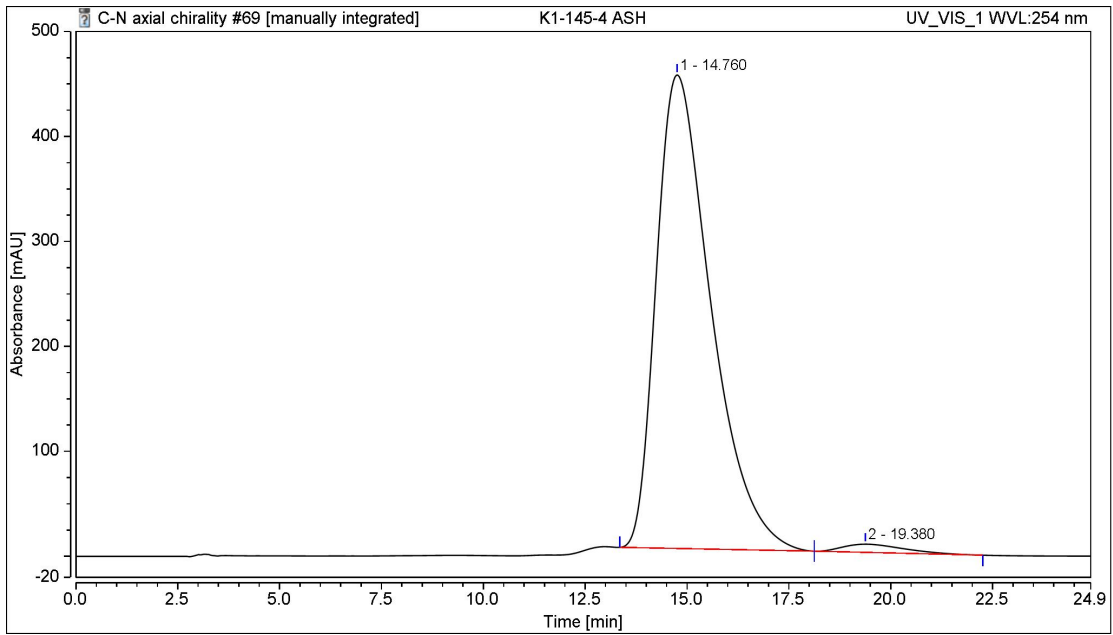
Integration Results						
No.	Peak Name	Retention Time min	Area mAU*min	Height mAU	Relative Area %	Relative Height %
1		12.895	536.308	524.364	97.22	97.90
2		18.007	15.351	11.221	2.78	2.10
Total:			551.659	535.585	100.00	100.00



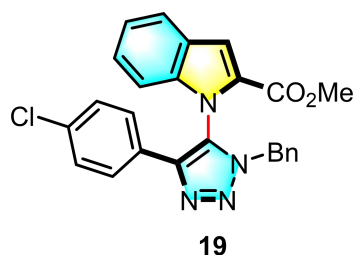
White solid, 40.1 mg, 95% yield, 98:2 er. [Chiral HPLC analysis of the product: Daicel Chiralpak AS-H 250X4.6 mm 5u column; *n*-hexane/2-propanol = 80/20, flow rate = 1.0 mL/min, λ = 254 nm, t (major) = 14.76 min, t (minor) = 19.38 min]. $[\alpha]_D^{24} = -138.5^\circ$ ($c = 0.7$, CHCl_3). **$^1\text{H NMR}$ (500 MHz, CDCl_3)** δ 7.73 (d, $J = 8.1$ Hz, 1H), 7.55 (s, 1H), 7.19 (dd, $J = 16.0, 7.9$ Hz, 3H), 7.15-7.09 (m, 2H), 7.09-7.03 (m, 2H), 6.97 (d, $J = 8.2$ Hz, 2H), 6.90 (d, $J = 7.3$ Hz, 2H), 6.58 (d, $J = 8.4$ Hz, 1H), 5.22 (s, 2H), 3.57 (s, 3H), 2.22 (s, 3H). **$^{13}\text{C NMR}$ (126 MHz, CDCl_3)** δ 159.4, 141.4, 138.2, 137.1, 132.4, 128.4, 127.4, 127.3, 127.2, 127.1, 125.9, 125.7, 125.5, 124.3, 121.8, 121.5, 113.2, 109.9, 51.3, 50.8, 20.1. **HRMS (ESI, m/z)** Calcd for $\text{C}_{26}\text{H}_{23}\text{N}_4\text{O}_2$ ($\text{M}+\text{H}$) $^+$: 423.1816; Found: 423.1824.



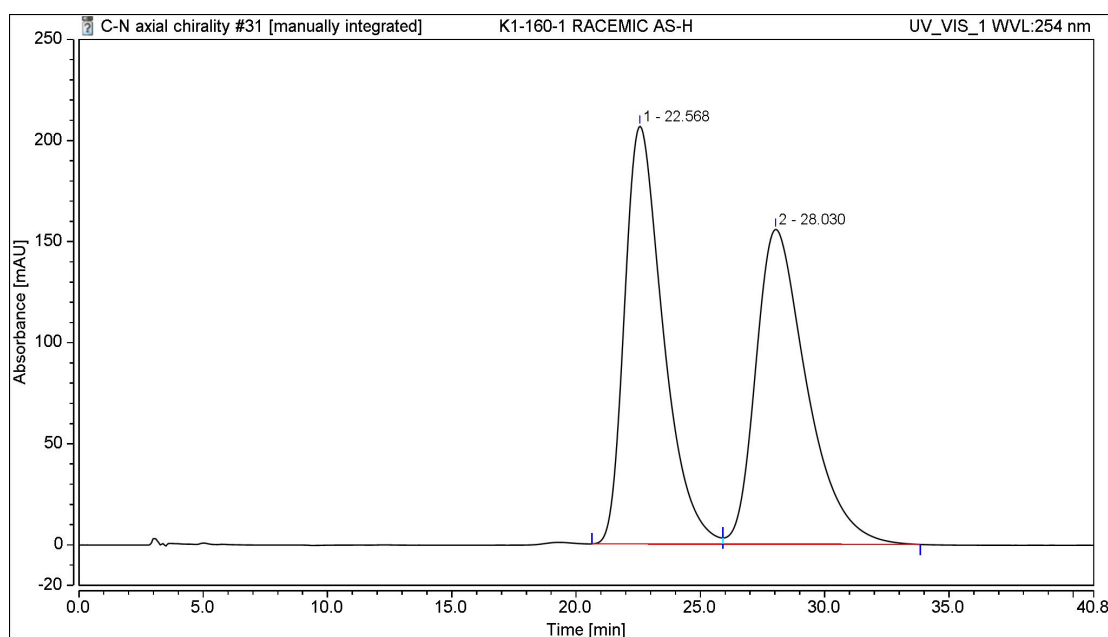
Integration Results						
No.	Peak Name	Retention Time min	Area mAU*min	Height mAU	Relative Area %	Relative Height %
1		15.030	817.110	618.224	50.03	58.86
2		19.748	816.085	432.063	49.97	41.14
Total:			1633.195	1050.287	100.00	100.00



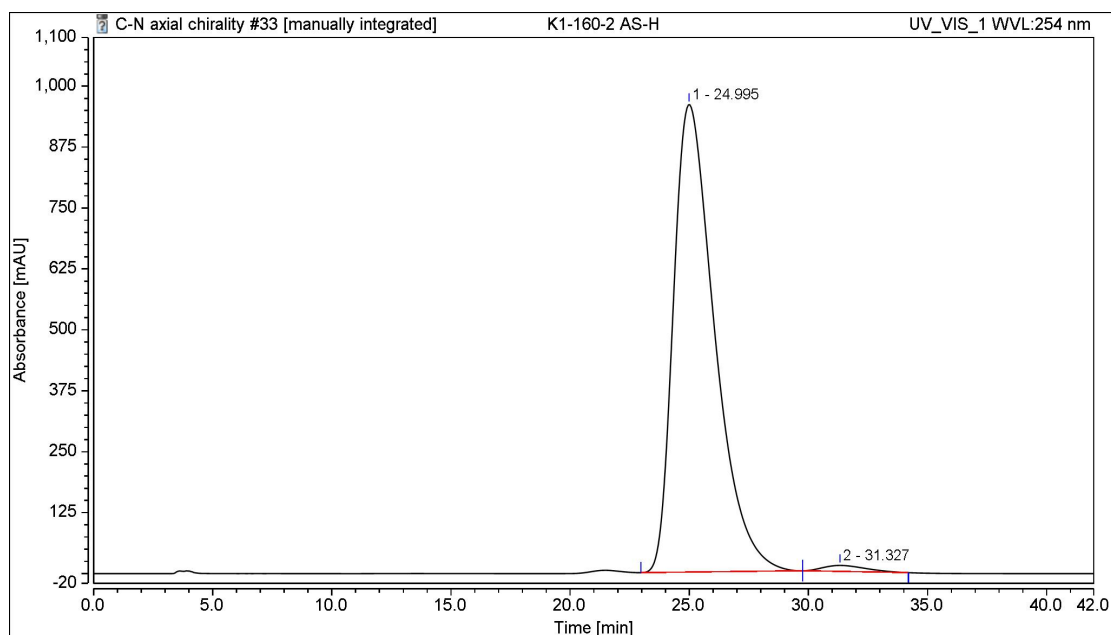
Integration Results						
No.	Peak Name	Retention Time min	Area mAU*min	Height mAU	Relative Area %	Relative Height %
1		14.760	701.418	451.134	98.08	98.29
2		19.380	13.718	7.839	1.92	1.71
Total:			715.136	458.972	100.00	100.00



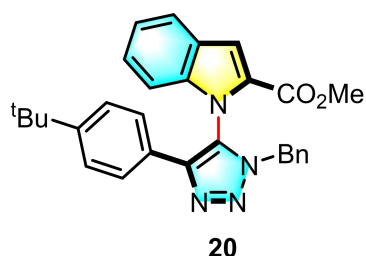
White solid, 43.8 mg, 99% yield, 98.5:1.5 er. [Chiral HPLC analysis of the product: Daicel Chiralpak AS-H 250X4.6 mm 5u column; *n*-hexane/2-propanol = 90/10, flow rate = 1.0 mL/min, λ = 254 nm, *t* (major) = 25.00 min, *t* (minor) = 31.33 min]. $[\alpha]_D^{26} = -150.5^\circ$ (*c* = 1.5, CHCl₃). **¹H NMR (500 MHz, CDCl₃)** δ 7.74 (d, *J* = 8.1 Hz, 1H), 7.55 (s, 1H), 7.22 (dd, *J* = 7.9, 5.8 Hz, 3H), 7.17-7.10 (m, 4H), 7.07 (t, *J* = 7.4 Hz, 2H), 6.89 (d, *J* = 7.3 Hz, 2H), 6.56 (d, *J* = 8.4 Hz, 1H), 5.23 (s, 2H), 3.60 (s, 3H). **¹³C NMR (126 MHz, CDCl₃)** δ 159.4, 140.4, 138.1, 133.1, 132.2, 127.9, 127.7, 127.5, 127.4, 127.2, 127.1, 126.9, 126.0, 125.8, 125.6, 121.9, 121.8, 113.3, 109.7, 51.4, 50.9. **HRMS (ESI, *m/z*)** Calcd for C₂₅H₂₀ClN₄O₂ (M+H)⁺: 443.1269; Found: 443.1264.



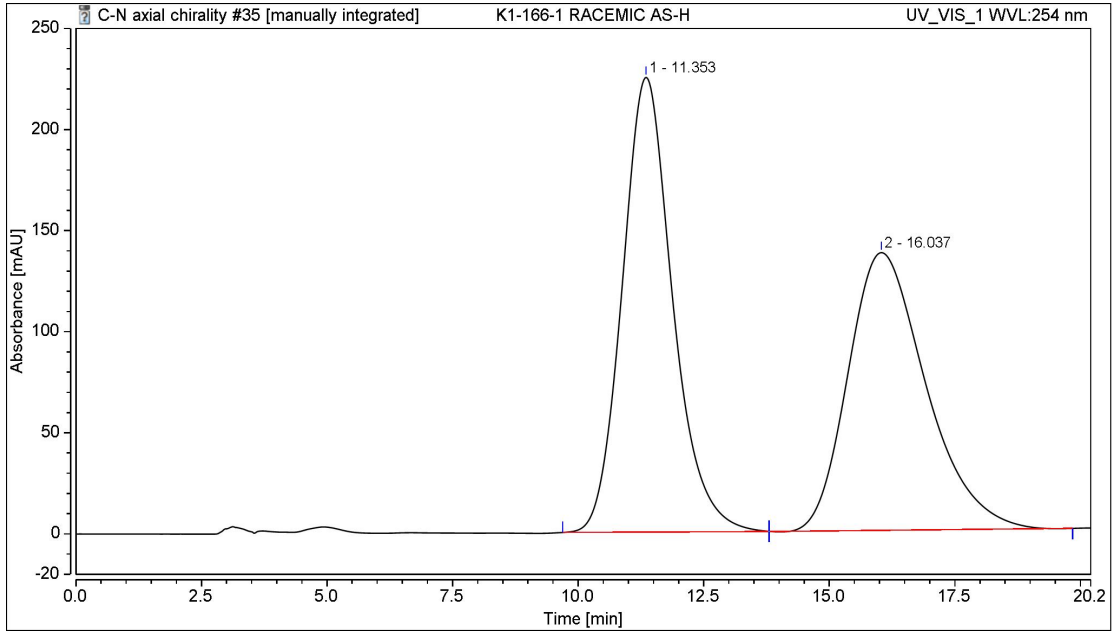
Integration Results						
No.	Peak Name	Retention Time min	Area mAU*min	Height mAU	Relative Area %	Relative Height %
1		22.568	371.844	206.617	50.09	57.02
2		28.030	370.434	155.734	49.91	42.98
Total:			742.277	362.351	100.00	100.00



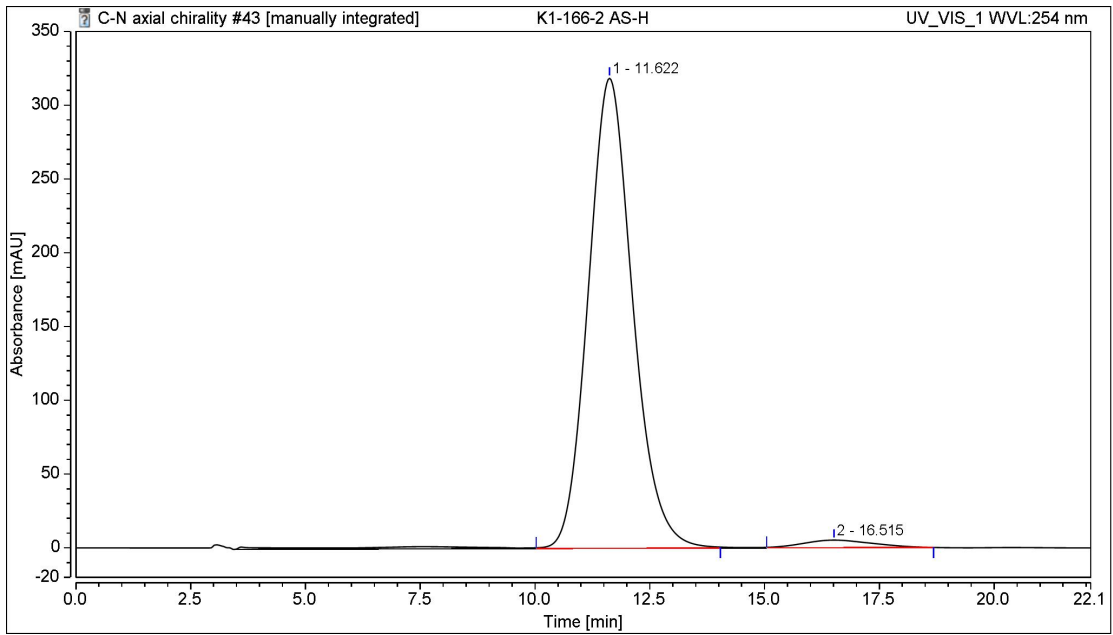
Integration Results						
No.	Peak Name	Retention Time min	Area mAU*min	Height mAU	Relative Area %	Relative Height %
1		24.995	1917.227	959.612	98.68	98.74
2		31.327	25.549	12.248	1.32	1.26
Total:			1942.776	971.860	100.00	100.00



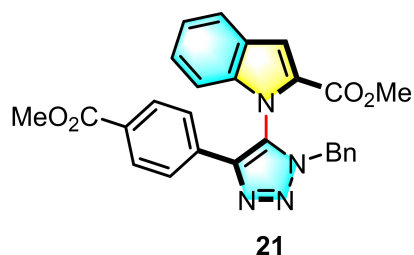
White solid, 44.6 mg, 96% yield, 97.5:2.5 er. [Chiral HPLC analysis of the product: Daicel Chiralpak AS-H 250X4.6 mm 5u column; *n*-hexane/2-propanol = 90/10, flow rate = 1.0 mL/min, λ = 254 nm, t (major) = 11.62 min, t (minor) = 16.52 min]. $[\alpha]_D^{26} = -138.8^\circ$ ($c = 1.4$, CHCl_3). $^1\text{H NMR}$ (500 MHz, CDCl_3) δ 7.74 (d, $J = 8.1$ Hz, 1H), 7.57 (s, 1H), 7.26-7.22 (m, 2H), 7.22-7.16 (m, 3H), 7.16-7.10 (m, 2H), 7.07 (t, $J = 7.4$ Hz, 2H), 6.91 (d, $J = 7.3$ Hz, 2H), 6.59 (d, $J = 8.4$ Hz, 1H), 5.22 (s, 2H), 3.58 (s, 3H), 1.21 (s, 9H). $^{13}\text{C NMR}$ (126 MHz, CDCl_3) δ 159.4, 150.2, 141.3, 138.3, 132.4, 127.4, 127.3, 127.3, 127.2, 127.1, 125.9, 125.7, 125.5, 124.6, 124.0, 121.8, 121.5, 113.1, 110.0, 51.3, 50.8, 33.5, 30.1. HRMS (ESI, m/z , m/z) Calcd for $\text{C}_{29}\text{H}_{29}\text{N}_4\text{O}_2$ ($\text{M}+\text{H}$) $^+$: 465.2285; Found: 465.2282.



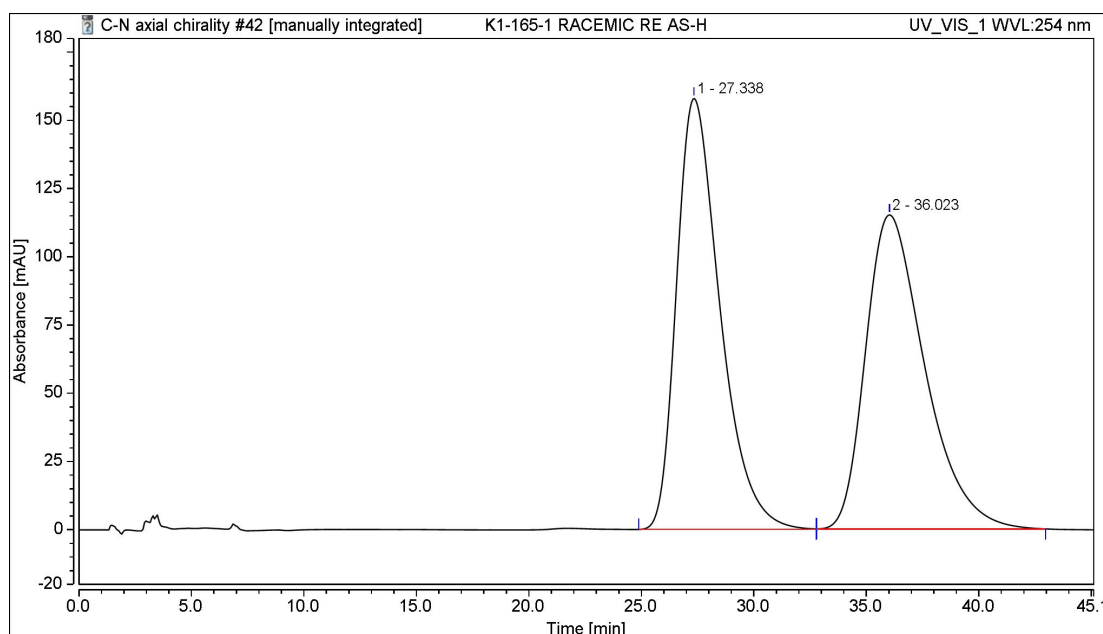
Integration Results						
No.	Peak Name	Retention Time min	Area mAU*min	Height mAU	Relative Area %	Relative Height %
1		11.353	261.306	224.954	51.47	62.08
2		16.037	246.368	137.401	48.53	37.92
Total:			507.674	362.356	100.00	100.00



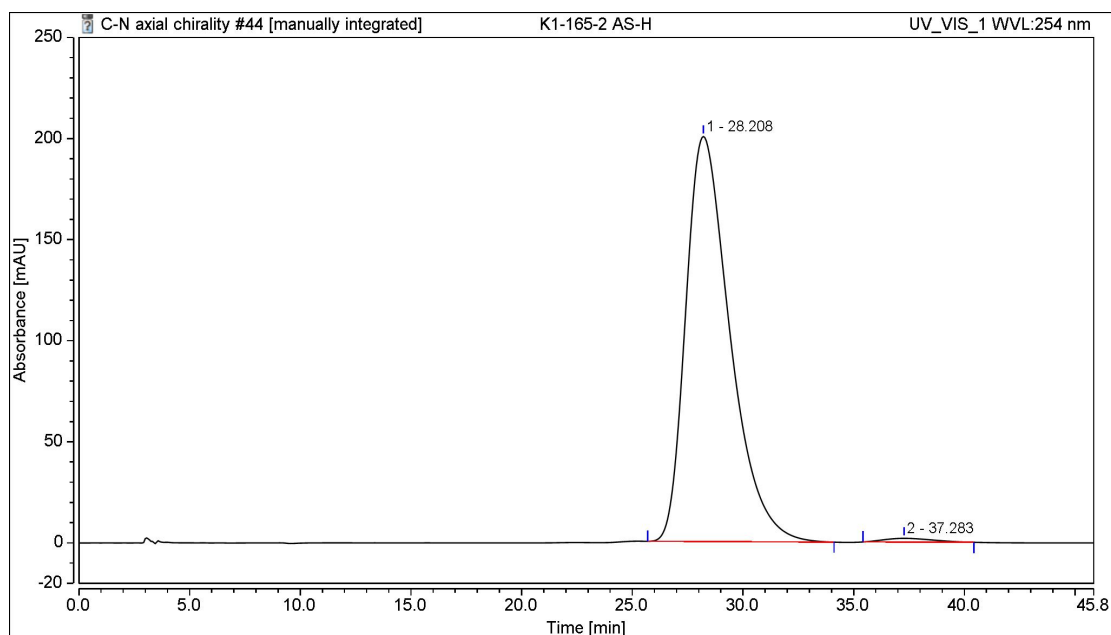
Integration Results						
No.	Peak Name	Retention Time min	Area mAU*min	Height mAU	Relative Area %	Relative Height %
1		11.622	357.320	318.637	97.51	98.40
2		16.515	9.118	5.178	2.49	1.60
Total:			366.437	323.815	100.00	100.00



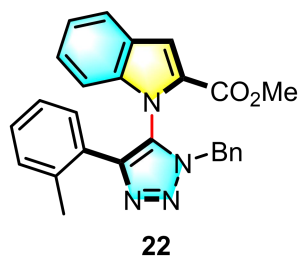
White solid, 46.2 mg, 99% yield, 99:1 er. [Chiral HPLC analysis of the product: Daicel Chiralpak AS-H 250X4.6 mm 5u column; *n*-hexane/2-propanol = 90/10, flow rate = 1.0 mL/min, λ = 254 nm, *t* (major) = 28.20 min, *t* (minor) = 37.28 min]. $[\alpha]_D^{26} = -197.5^\circ$ (*c* = 1.6, CHCl₃). **¹H NMR (500 MHz, CDCl₃)** δ 7.83 (d, *J* = 8.4 Hz, 2H), 7.74 (d, *J* = 8.1 Hz, 1H), 7.56 (s, 1H), 7.34 (d, *J* = 8.5 Hz, 2H), 7.22 (t, *J* = 7.5 Hz, 1H), 7.17-7.10 (m, 2H), 7.07 (t, *J* = 7.6 Hz, 2H), 6.90 (d, *J* = 7.5 Hz, 2H), 6.56 (d, *J* = 8.4 Hz, 1H), 5.25 (s, 2H), 3.82 (s, 3H), 3.60 (s, 3H). **¹³C NMR (126 MHz, CDCl₃)** δ 165.6, 159.4, 140.3, 138.1, 132.7, 132.2, 129.0, 128.6, 128.5, 127.5, 127.4, 127.2, 127.1, 126.1, 125.8, 124.2, 122.0, 121.8, 113.4, 109.7, 51.4, 51.0, 50.9. **HRMS (ESI, *m/z*)** Calcd for C₂₇H₂₃N₄O₄ (M+H)⁺: 467.1714; Found: 467.1711.



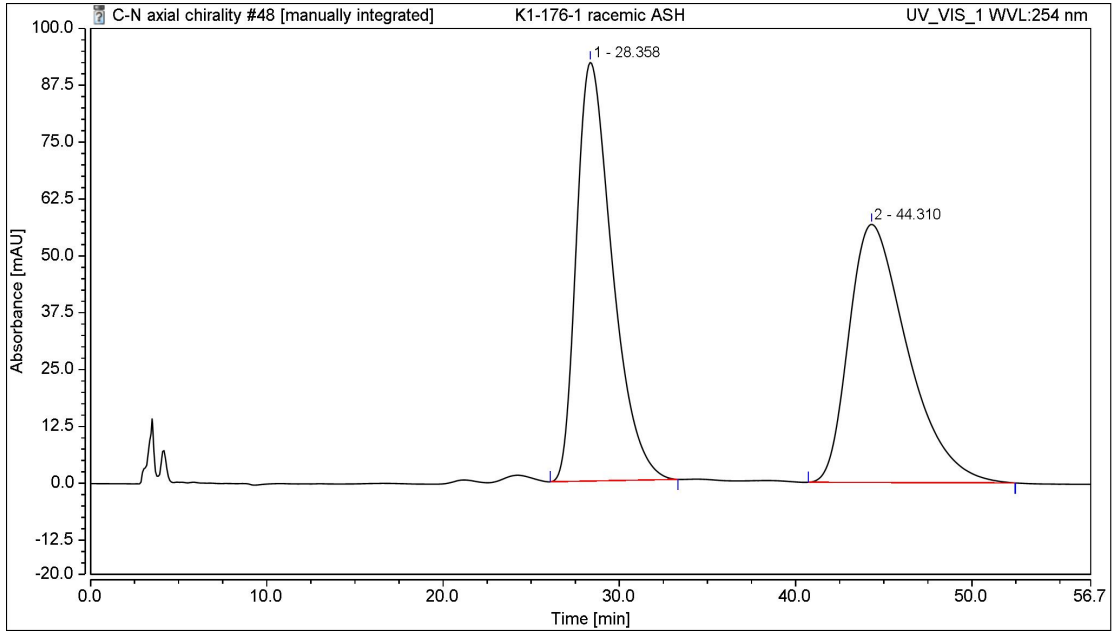
Integration Results						
No.	Peak Name	Retention Time min	Area mAU*min	Height mAU	Relative Area %	Relative Height %
1		27.338	353.414	157.901	50.15	57.83
2		36.023	351.275	115.126	49.85	42.17
Total:			704.690	273.028	100.00	100.00



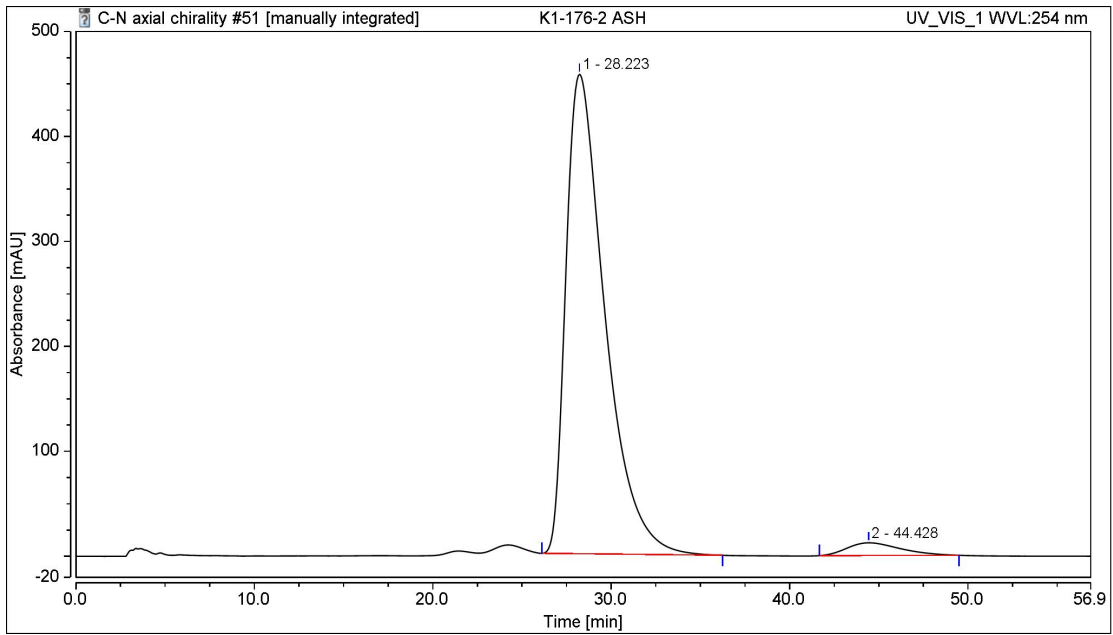
Integration Results						
No.	Peak Name	Retention Time min	Area mAU*min	Height mAU	Relative Area %	Relative Height %
1		28.208	464.106	200.370	99.00	99.09
2		37.283	4.700	1.842	1.00	0.91
Total:			468.806	202.211	100.00	100.00



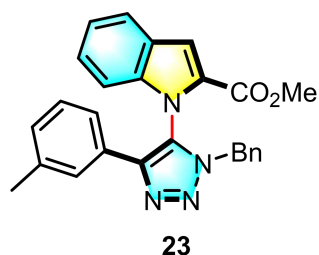
White solid, 36.3 mg, 86% yield, 96.5:3.5 er. [Chiral HPLC analysis of the product: Daicel Chiralpak AS-H 250X4.6 mm 5u column; *n*-hexane/2-propanol = 90/10, flow rate = 1.0 mL/min, λ = 254 nm, *t* (major) = 28.22 min, *t* (minor) = 44.43 min]. $[\alpha]_D^{26} = -49.9^\circ$ (*c* = 1.2, CHCl₃). **¹H NMR (500 MHz, CDCl₃)** δ 7.65 (dd, *J* = 6.2, 3.0 Hz, 1H), 7.41 (s, 1H), 7.19-7.05 (m, 7H), 6.93-6.86 (m, 4H), 6.65 (dd, *J* = 6.2, 3.3 Hz, 1H), 5.27 (d, *J* = 14.8 Hz, 1H), 5.22 (d, *J* = 14.8 Hz, 1H), 3.61 (s, 3H), 2.35 (s, 3H). **¹³C NMR (126 MHz, CDCl₃)** δ 159.5, 142.9, 138.7, 136.5, 132.3, 129.5, 128.8, 128.0, 127.5, 127.4, 127.3, 127.2, 125.7, 125.5, 124.5, 121.8, 121.4, 112.9, 109.7, 51.5, 50.8, 19.4. **HRMS (ESI, *m/z*)** Calcd for C₂₆H₂₃N₄O₂ (M+H)⁺: 423.1816; Found: 423.1829.



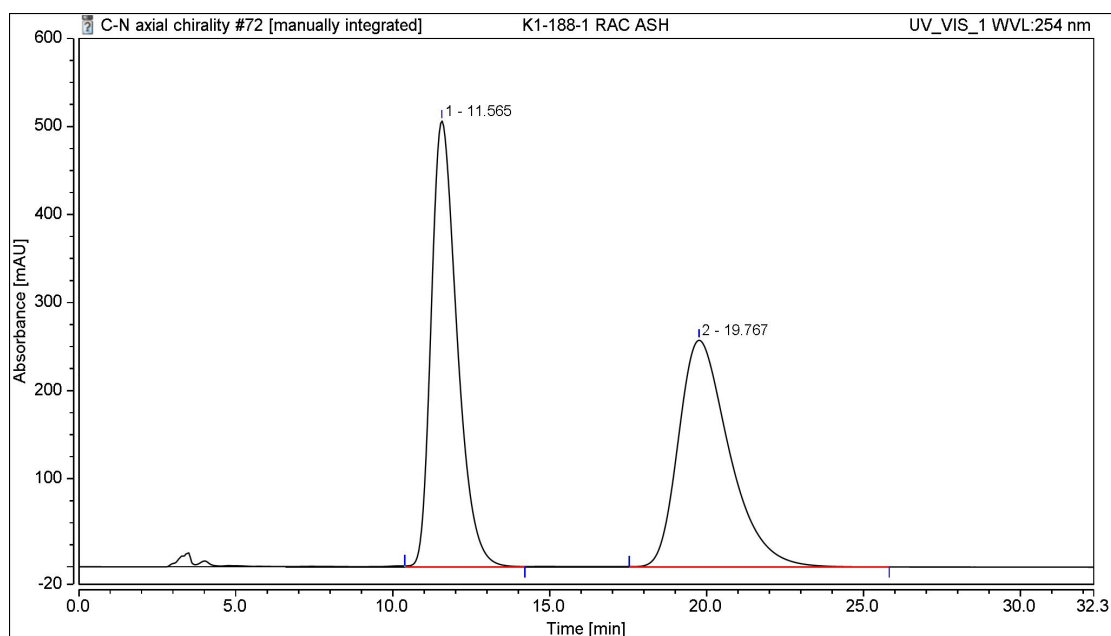
Integration Results						
No.	Peak Name	Retention Time min	Area mAU*min	Height mAU	Relative Area %	Relative Height %
1		28.358	217.073	92.041	49.82	61.86
2		44.310	218.629	56.745	50.18	38.14
Total:			435.702	148.787	100.00	100.00



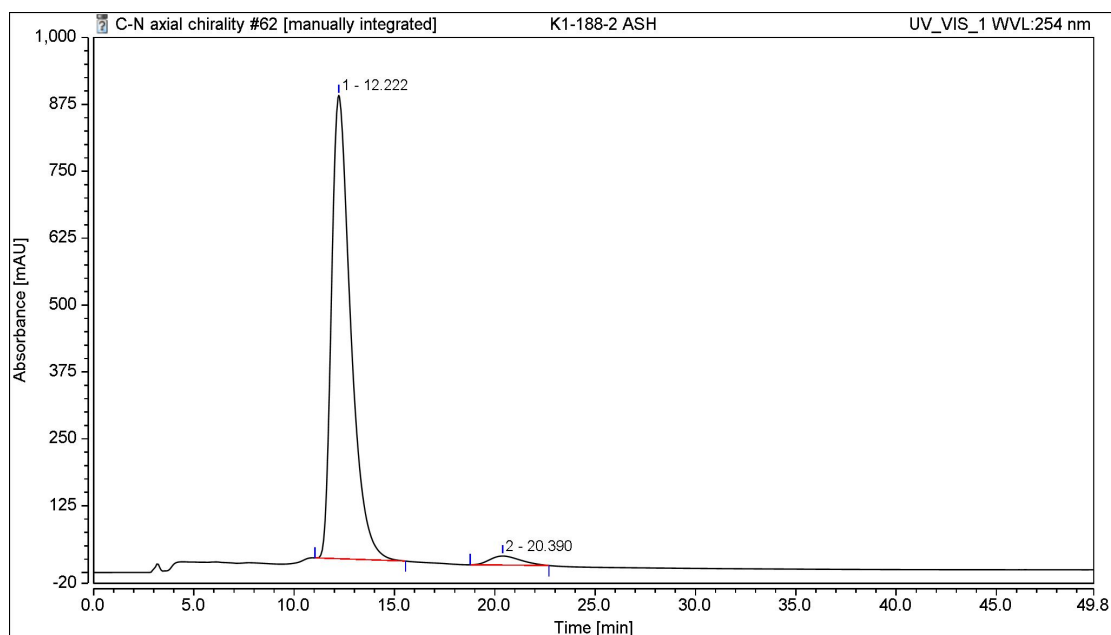
Integration Results						
No.	Peak Name	Retention Time min	Area mAU*min	Height mAU	Relative Area %	Relative Height %
1		28.223	1155.721	456.839	96.51	97.42
2		44.428	41.781	12.111	3.49	2.58
Total:			1197.502	468.950	100.00	100.00



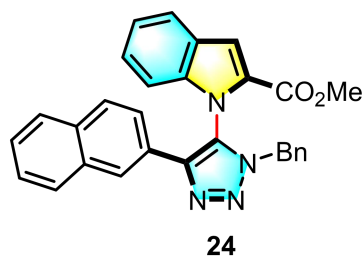
White solid, 33.8 mg, 80% yield, 97:3 er. [Chiral HPLC analysis of the product: Daicel Chiralpak AS-H 250X4.6 mm 5u column; *n*-hexane/2-propanol = 80/20, flow rate = 1.0 mL/min, $\lambda = 254$ nm, t (major) = 12.22 min, t (minor) = 20.39 min]. $[\alpha]_D^{26} = -74.0^\circ$ ($c = 2.0$, CHCl_3). **$^1\text{H NMR}$ (500 MHz, CDCl_3)** δ 7.73 (d, $J = 7.9$ Hz, 1H), 7.56 (s, 1H), 7.34 (s, 1H), 7.20 (t, $J = 7.6$ Hz, 1H), 7.13 (td, $J = 7.2, 2.1$ Hz, 2H), 7.07 (t, $J = 7.3$ Hz, 2H), 6.99 (d, $J = 6.4$ Hz, 2H), 6.91 (d, $J = 7.2$ Hz, 2H), 6.85 (t, $J = 4.4$ Hz, 1H), 6.58 (d, $J = 8.4$ Hz, 1H), 5.24 (s, 2H), 3.58 (s, 3H), 2.19 (s, 3H). **$^{13}\text{C NMR}$ (126 MHz, CDCl_3)** δ 159.4, 141.4, 138.3, 137.2, 132.4, 128.2, 128.0, 127.5, 127.5, 127.5, 127.3, 127.3, 127.2, 125.9, 125.7, 125.4, 121.8, 121.6, 121.2, 113.2, 109.9, 51.3, 50.8, 20.3. **HRMS (ESI, m/z)** Calcd for $\text{C}_{26}\text{H}_{23}\text{N}_4\text{O}_2$ ($\text{M}+\text{H}$) $^+$: 423.1816; Found: 423.1811.



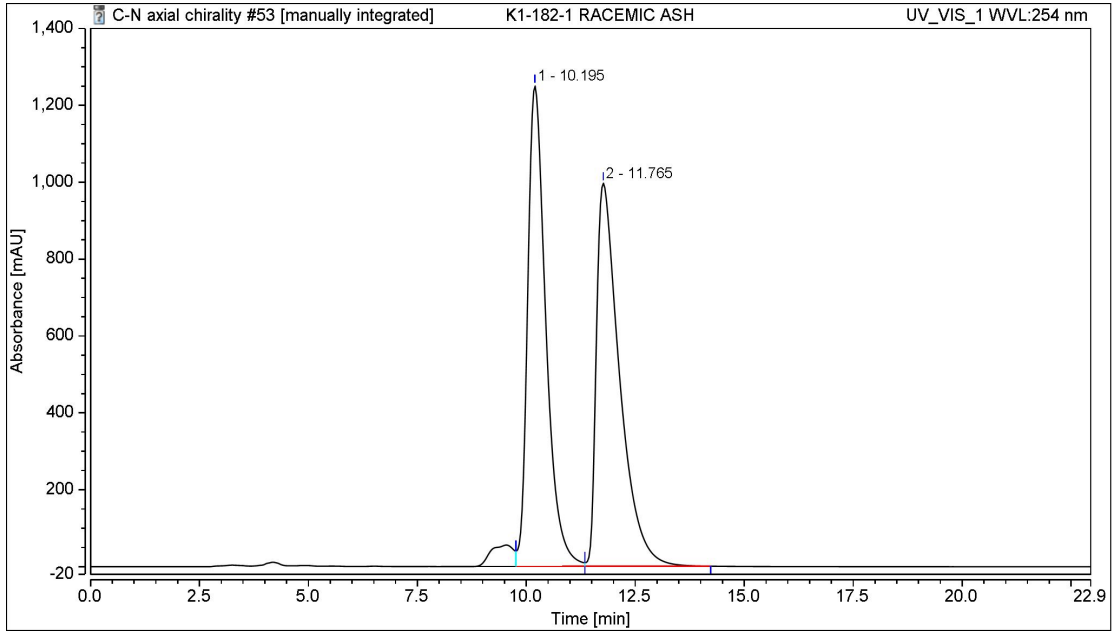
Integration Results						
No.	Peak Name	Retention Time min	Area mAU*min	Height mAU	Relative Area %	Relative Height %
1		11.565	483.400	506.594	50.00	66.31
2		19.767	483.424	257.436	50.00	33.69
Total:			966.823	764.030	100.00	100.00



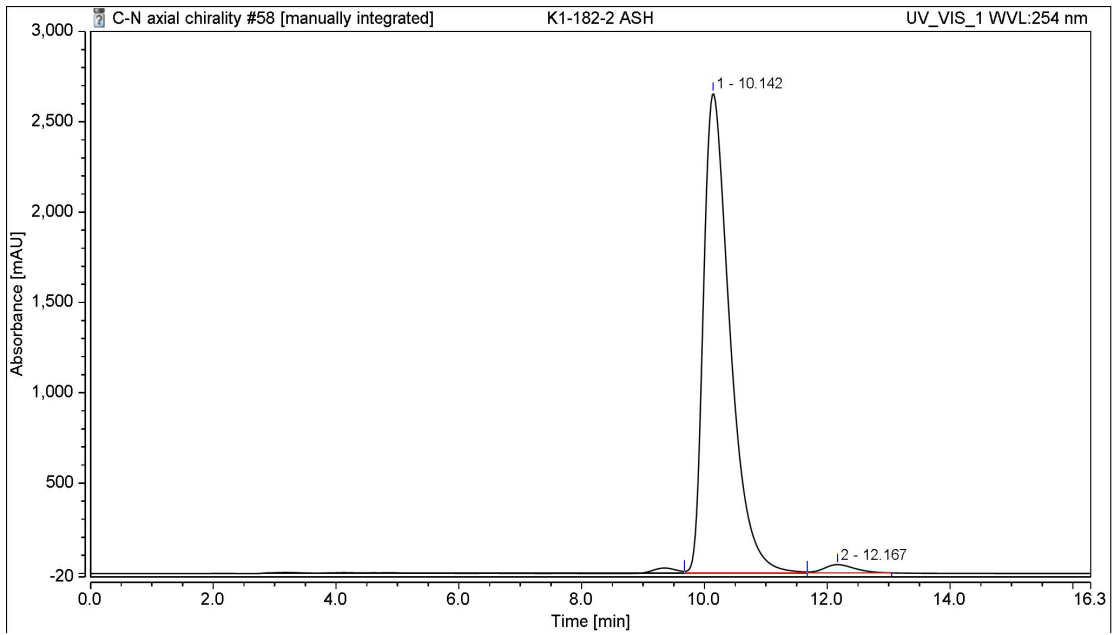
Integration Results						
No.	Peak Name	Retention Time min	Area mAU*min	Height mAU	Relative Area %	Relative Height %
1		12.222	960.617	865.905	96.91	98.08
2		20.390	30.592	16.987	3.09	1.92
Total:			991.209	882.892	100.00	100.00



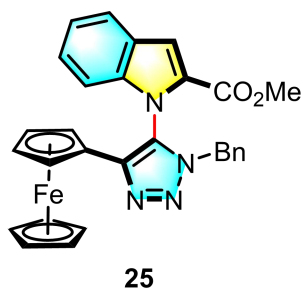
White solid, 44.9 mg, 98% yield, 98:2 yield. [Chiral HPLC analysis of the product: Daicel Chiralpak AS-H 250X4.6 mm 5u column; *n*-hexane/2-propanol = 80/20, flow rate = 1.0 mL/min, λ = 254 nm, t (major) = 10.14 min, t (minor) = 12.17 min]. $[\alpha]_D^{26} = -220.4^\circ$ ($c = 1.4$, CHCl_3). **$^1\text{H NMR}$ (500 MHz, CDCl_3)** δ 7.77 (d, $J = 8.1$ Hz, 1H), 7.73 (s, 1H), 7.68 (d, $J = 7.3$ Hz, 1H), 7.63 (d, $J = 8.7$ Hz, 1H), 7.60 (s, 1H), 7.55 (d, $J = 7.3$ Hz, 1H), 7.43-7.33 (m, 3H), 7.22 (t, $J = 7.3$ Hz, 1H), 7.13 (td, $J = 7.1, 1.9$ Hz, 2H), 7.09 (t, $J = 7.4$ Hz, 2H), 6.95 (d, $J = 7.2$ Hz, 2H), 6.63 (d, $J = 8.4$ Hz, 1H), 5.29 (s, 2H), 3.58 (s, 3H). **$^{13}\text{C NMR}$ (126 MHz, CDCl_3)** δ 159.4, 141.0, 138.6, 138.5, 137.2, 131.9, 128.9, 128.4, 127.4, 127.2, 126.2, 125.8, 125.4, 124.5, 122.2, 122.1, 121.7, 113.2, 110.2, 51.0, 20.1. **HRMS (ESI, m/z)** Calcd for $\text{C}_{29}\text{H}_{23}\text{N}_4\text{O}_2$ ($\text{M}+\text{H}$) $^+$: 459.1816; Found: 459.1824.



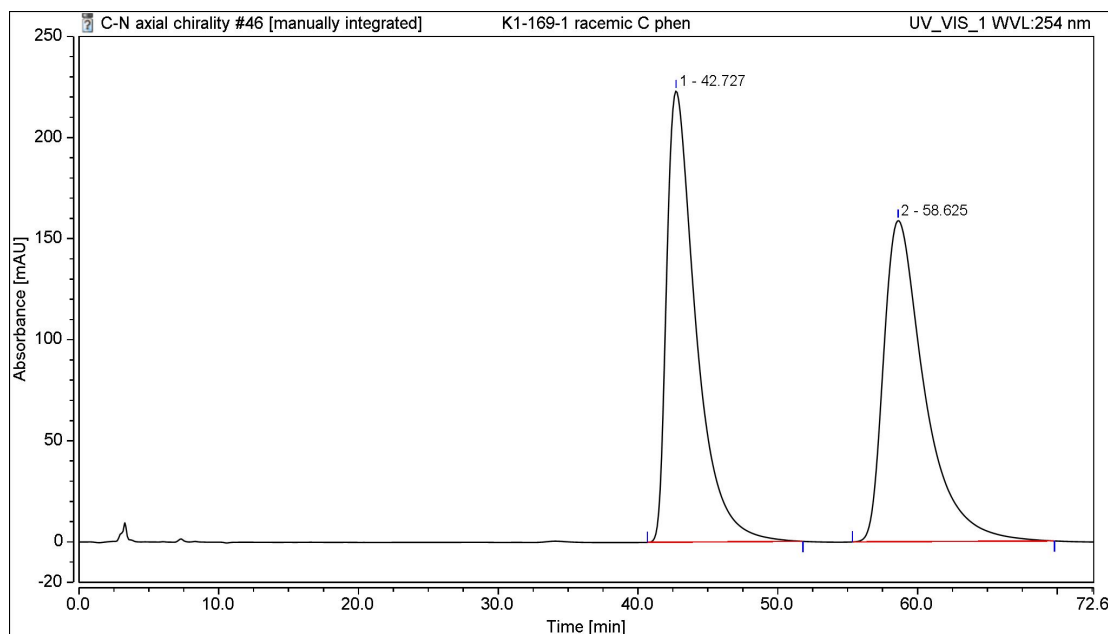
Integration Results						
No.	Peak Name	Retention Time min	Area mAU*min	Height mAU	Relative Area %	Relative Height %
1		10.195	607.064	1250.628	49.74	55.65
2		11.765	613.343	996.832	50.26	44.35
Total:			1220.407	2247.460	100.00	100.00



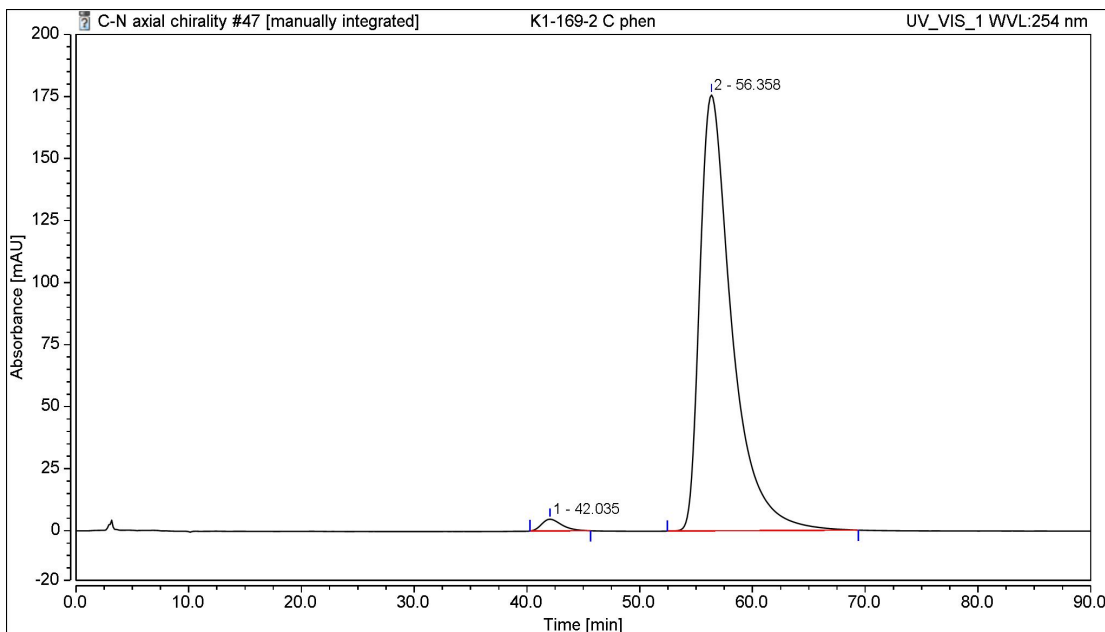
Integration Results						
No.	Peak Name	Retention Time min	Area mAU*min	Height mAU	Relative Area %	Relative Height %
1		10.142	1326.548	2655.841	98.00	98.29
2		12.167	27.134	46.121	2.00	1.71
Total:			1353.683	2701.962	100.00	100.00



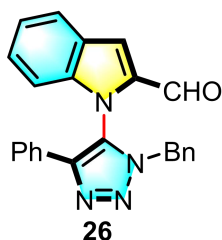
Brownish red solid, 50.6 mg, 98% yield, 98.5:1.5 er. [Chiral HPLC analysis of the product: Phenomenex 00G-4457-E0 250X4.6 mm 5u column; *n*-hexane/2-propanol = 90/10, flow rate = 1.0 mL/min, λ = 254 nm, *t* (major) = 56.36 min, *t* (minor) = 42.04 min]. $[\alpha]_D^{26} = -125.3^\circ$ (*c* = 1.7, CHCl₃). ¹H NMR (500 MHz, CDCl₃) δ 7.73 (d, *J* = 8.1 Hz, 1H), 7.58 (d, *J* = 1.1 Hz, 1H), 7.21-7.17 (m, 1H), 7.13-7.07 (m, 2H), 7.04 (td, *J* = 6.6, 1.7 Hz, 2H), 6.93 (d, *J* = 6.9 Hz, 2H), 6.47 (dd, *J* = 8.4, 0.9 Hz, 1H), 5.41 (d, *J* = 14.8 Hz, 1H), 5.17 (d, *J* = 14.8 Hz, 1H), 4.37 (dt, *J* = 2.6, 1.3 Hz, 1H), 4.09 (td, *J* = 2.6, 1.4 Hz, 1H), 3.99 (td, *J* = 2.6, 1.4 Hz, 1H), 3.94 (s, 5H), 3.72 (s, 3H), 3.69 (dt, *J* = 2.6, 1.3 Hz, 1H). ¹³C NMR (126 MHz, CDCl₃) δ 159.7, 141.8, 138.6, 132.6, 127.4, 127.4, 127.3, 127.2, 125.9, 125.7, 125.6, 121.7, 121.5, 112.9, 110.0, 72.3, 68.3, 67.6, 67.6, 65.0, 64.4, 51.3, 50.9. HRMS (ESI, *m/z*) Calcd for C₂₉H₂₅FeN₄O₂ (M+H)⁺: 517.1321; Found: 517.1334.



Integration Results						
No.	Peak Name	Retention Time min	Area mAU*min	Height mAU	Relative Area %	Relative Height %
1		42.727	542.974	223.229	50.20	58.42
2		58.625	538.570	158.865	49.80	41.58
Total:			1081.544	382.093	100.00	100.00

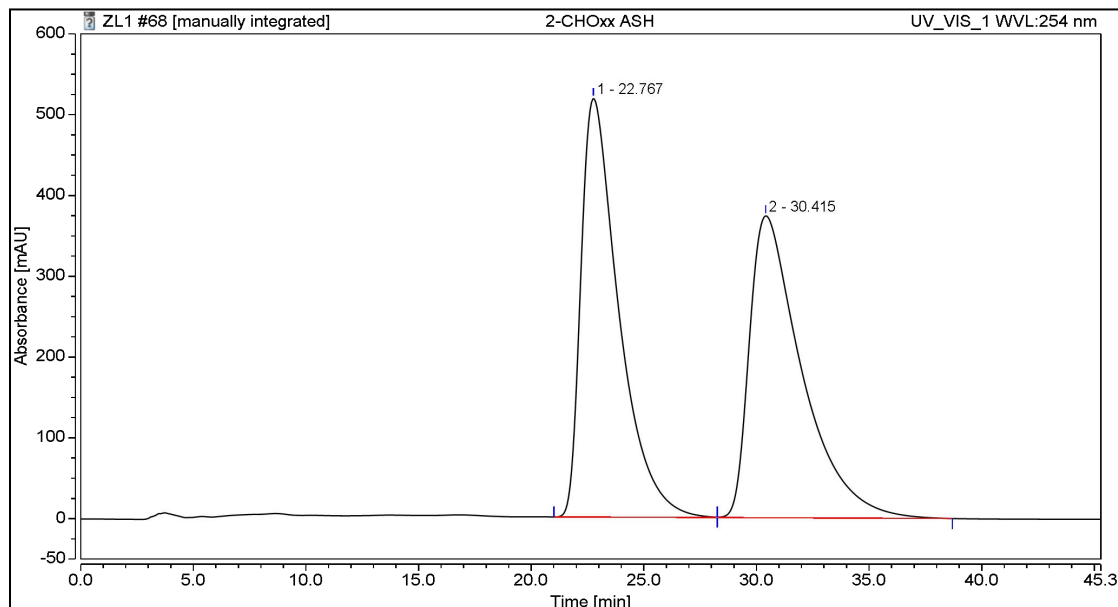


Integration Results						
No.	Peak Name	Retention Time min	Area mAU*min	Height mAU	Relative Area %	Relative Height %
1		42.035	9.856	4.744	1.67	2.63
2		56.358	579.342	175.688	98.33	97.37
Total:			589.198	180.432	100.00	100.00

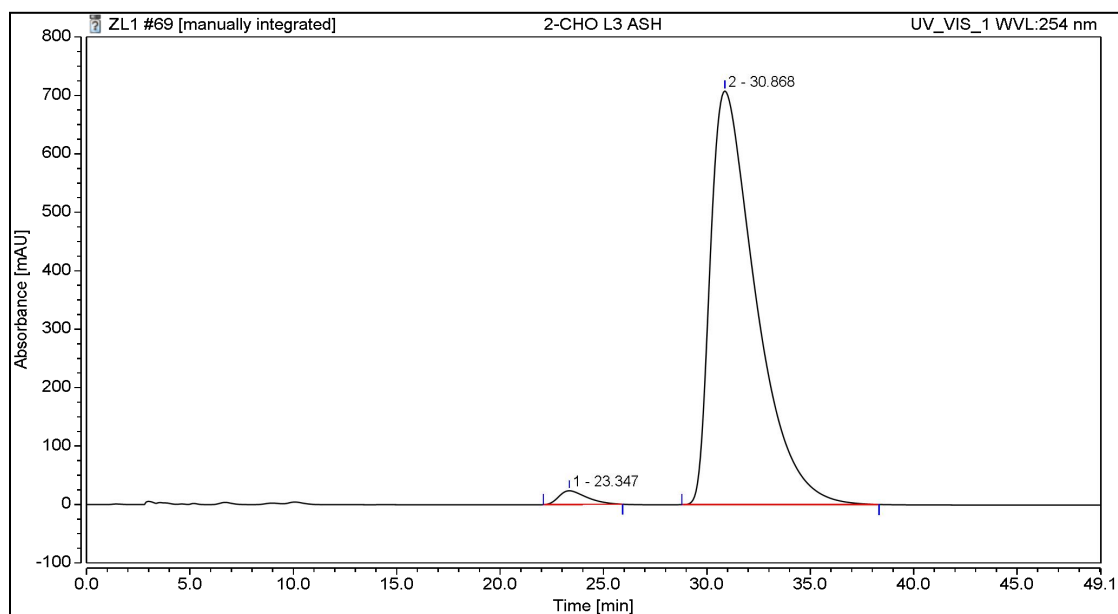


White solid, 37.0 mg, 98% yield, 98:2 er. [Chiral HPLC analysis of the product: Daicel Chiralpak AS-H 250X4.6 mm 5u column; *n*-hexane/2-propanol = 85/15, flow rate = 1.0 mL/min, λ = 254 nm, t (major) = 30.87 min, t (minor) = 23.35 min]. $[\alpha]_D^{26} = -194.4^\circ$ ($c = 1.1$, CHCl_3). $^1\text{H NMR}$ (500 MHz, CDCl_3) δ 9.65 (s, 1H), 7.78 (d, $J = 7.8$ Hz, 1H), 7.51 (s, 1H), 7.30-7.13 (m, 7H), 7.09 (t, $J = 7.3$ Hz, 1H), 7.03 (t, $J = 7.4$ Hz, 2H), 6.84 (d, $J = 7.3$ Hz, 2H), 6.61 (d, $J = 8.2$ Hz, 1H), 5.35 (d, $J = 14.9$ Hz, 1H), 5.17 (d, $J = 14.9$ Hz, 1H). $^{13}\text{C NMR}$ (126 MHz, CDCl_3) δ 180.4, 142.4, 139.9, 135.7, 133.3, 129.4, 128.8, 128.6,

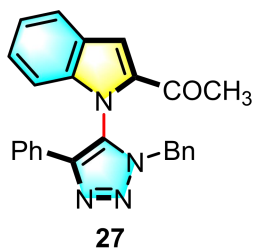
128.5, 128.5, 128.1, 128.0, 127.0, 125.6, 123.7, 123.1, 119.2, 111.1, 52.7. HRMS (ESI, m/z) Calcd for C₂₄H₁₉N₄O (M+H)⁺: 379.1553; Found: 379.1537.



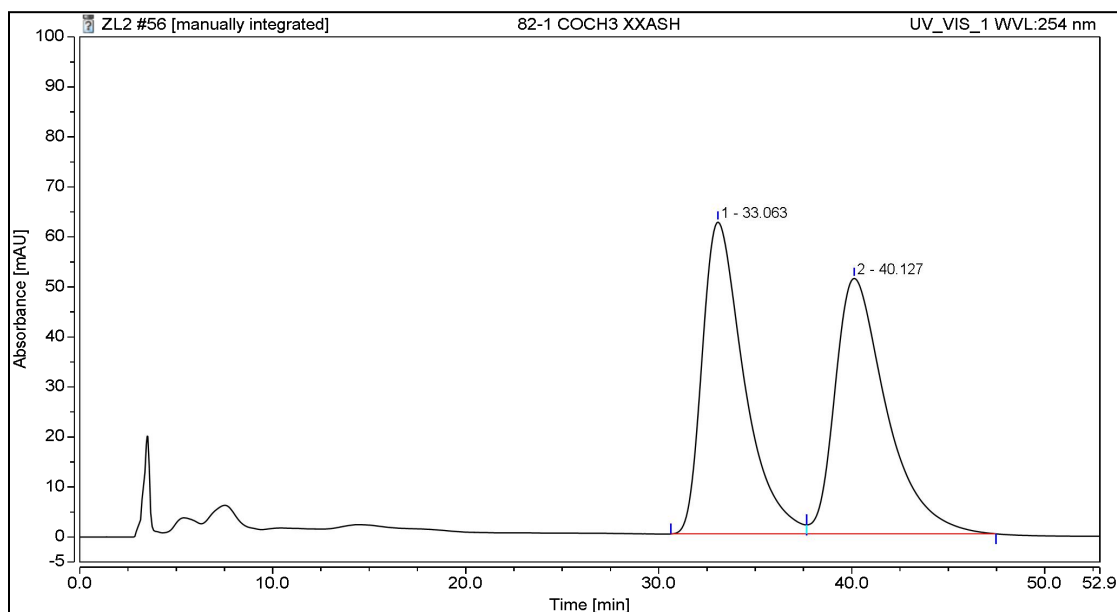
Integration Results						
No.	Peak Name	Retention Time min	Area mAU*min	Height mAU	Relative Area %	Relative Height %
1		22.767	1007.468	518.256	50.05	58.10
2		30.415	1005.392	373.793	49.95	41.90
Total:			2012.860	892.050	100.00	100.00



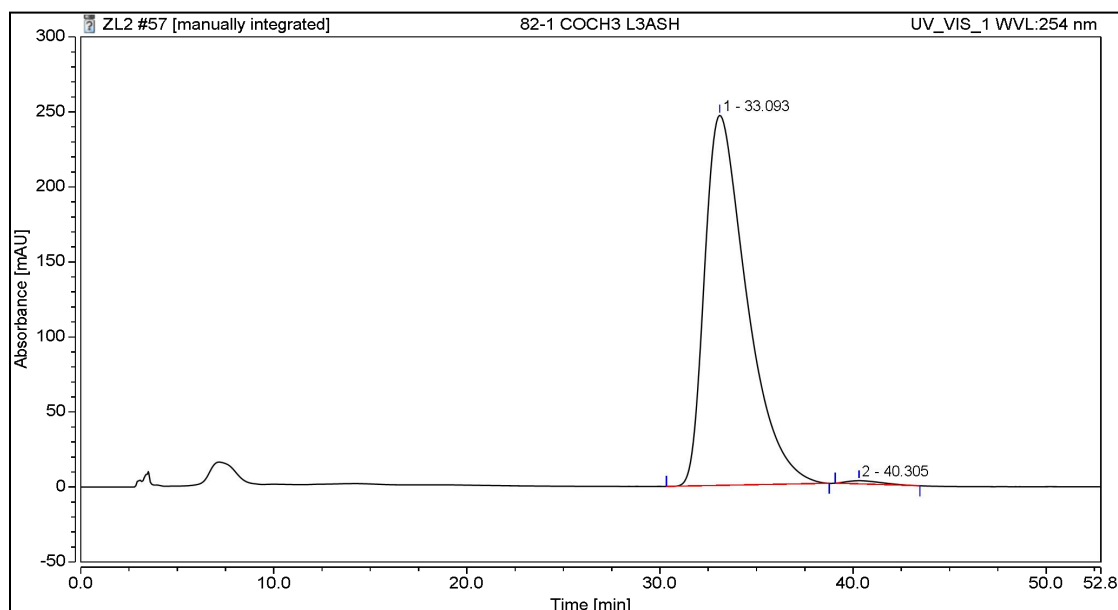
Integration Results						
No.	Peak Name	Retention Time min	Area mAU*min	Height mAU	Relative Area %	Relative Height %
1		23.347	36.737	23.572	2.00	3.22
2		30.868	1799.594	707.831	98.00	96.78
Total:			1836.330	731.402	100.00	100.00



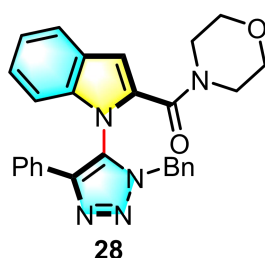
White solid, 36.4 mg, 96% yield, 99:1 er. [Chiral HPLC analysis of the product: Daicel Chiralpak AS-H 250X4.6 mm 5u column; *n*-hexane/2-propanol = 90/10, flow rate = 1.0 mL/min, λ = 254 nm, t (major) = 33.09 min, t (minor) = 40.31 min]. $[\alpha]_D^{26} = -161.8^\circ$ (c = 1.0, CHCl₃). **¹H NMR (500 MHz, CDCl₃)** δ 7.73 (d, *J* = 7.9 Hz, 1H), 7.49 (s, 1H), 7.26-7.24 (m, 2H), 7.19 (t, *J* = 7.0 Hz 1H), 7.15-7.08 (m, 5H), 7.03 (t, *J* = 7.4 Hz, 2H), 6.86 (d, *J* = 7.3 Hz, 2H), 6.52 (d, *J* = 8.3 Hz, 1H), 5.31 (d, *J* = 14.9 Hz, 1H), 5.12 (d, *J* = 14.9 Hz, 1H), 2.42 (s, 3H). **¹³C NMR (126 MHz, CDCl₃)** δ 189.0, 141.9, 139.6, 135.3, 133.5, 129.7, 129.3, 128.7, 128.6, 128.4, 128.3, 128.2, 127.8, 126.8, 125.5, 123.2, 122.8, 115.1, 111.1, 52.5, 27.0. **HRMS (ESI, m/z)** Calcd for C₂₅H₂₁N₄O (M+H)⁺: 393.1710; Found: 393.1704.



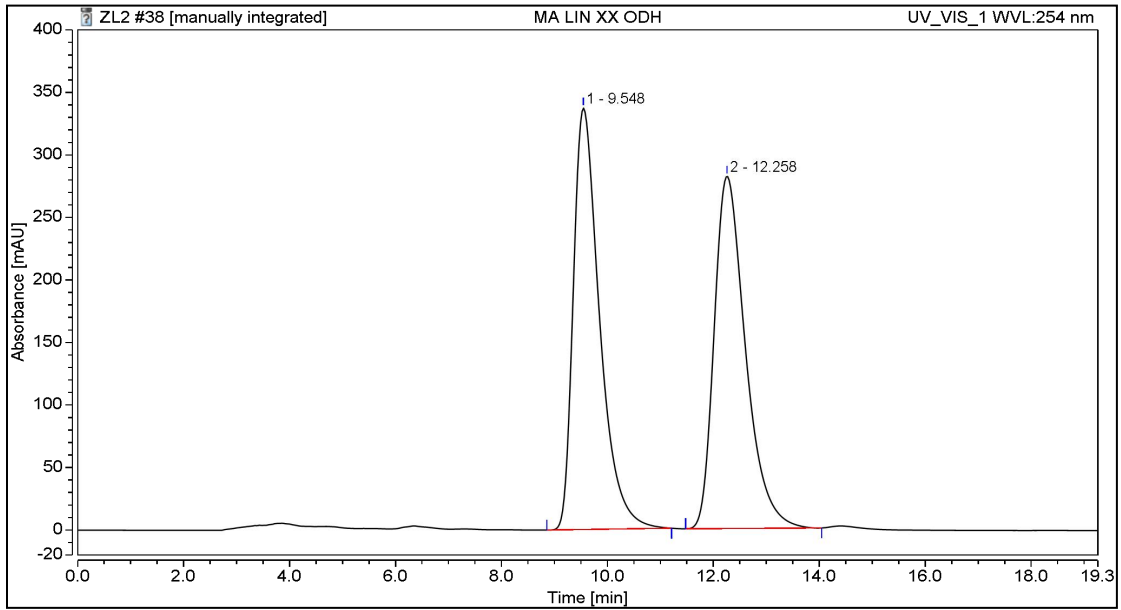
Integration Results						
No.	Peak Name	Retention Time min	Area mAU*min	Height mAU	Relative Area %	Relative Height %
1		33.063	156.720	62.363	49.91	54.97
2		40.127	157.280	51.091	50.09	45.03
Total:			314.000	113.454	100.00	100.00



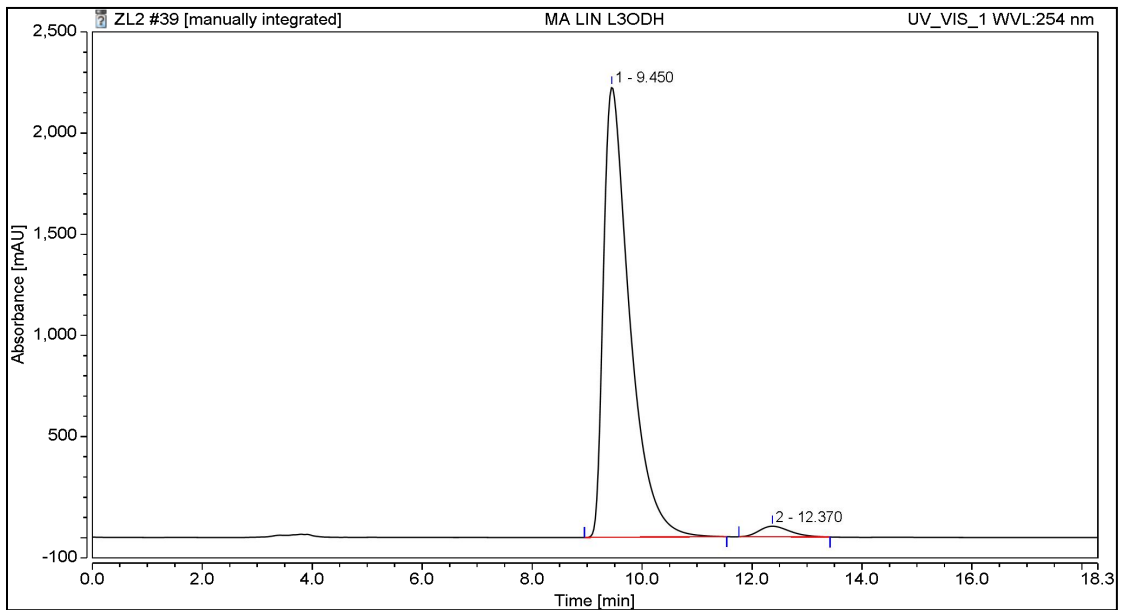
Integration Results						
No.	Peak Name	Retention Time min	Area mAU*min	Height mAU	Relative Area %	Relative Height %
1		33.093	623.523	246.692	99.28	99.15
2		40.305	4.501	2.119	0.72	0.85
Total:			628.024	248.811	100.00	100.00



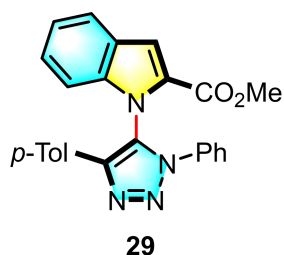
White solid, 44.9 mg, 97% yield, 97:3 er. [Chiral HPLC analysis of the product: Daicel Chiralcel OD-H 250X4.6 mm 5u column; *n*-hexane/2-propanol = 70/30, flow rate = 1.0 mL/min, $\lambda = 254$ nm, t (major) = 12.37 min, t (minor) = 9.45 min]. $[\alpha]_D^{26} = -65.1^\circ$ ($c = 1.0$, CHCl_3). **$^1\text{H NMR}$ (500 MHz, CDCl_3)** δ 7.66 (d, $J = 8.0$ Hz, 1H), 7.18-7.13 (m, 7H), 7.11-7.05 (m, 4H), 6.97 (t, $J = 8.2$ Hz, 1H), 6.85 (s, 1H), 6.35 (d, $J = 9.0$ Hz, 1H), 5.69 (d, $J = 14.9$ Hz, 1H), 5.37 (d, $J = 14.9$ Hz, 1H), 4.08-3.00 (m, 8H). **$^{13}\text{C NMR}$ (126 MHz, CDCl_3)** δ 161.3, 142.6, 138.4, 134.0, 131.9, 129.6, 128.9, 128.7, 128.6, 128.5, 128.5, 128.4, 126.8, 125.6, 125.4, 122.4, 121.9, 111.0, 107.8, 66.6, 52.5. **HRMS (ESI, m/z)** Calcd for $\text{C}_{28}\text{H}_{26}\text{N}_5\text{O}_2$ ($\text{M}+\text{H}$) $^+$: 464.2081; Found: 464.2074.



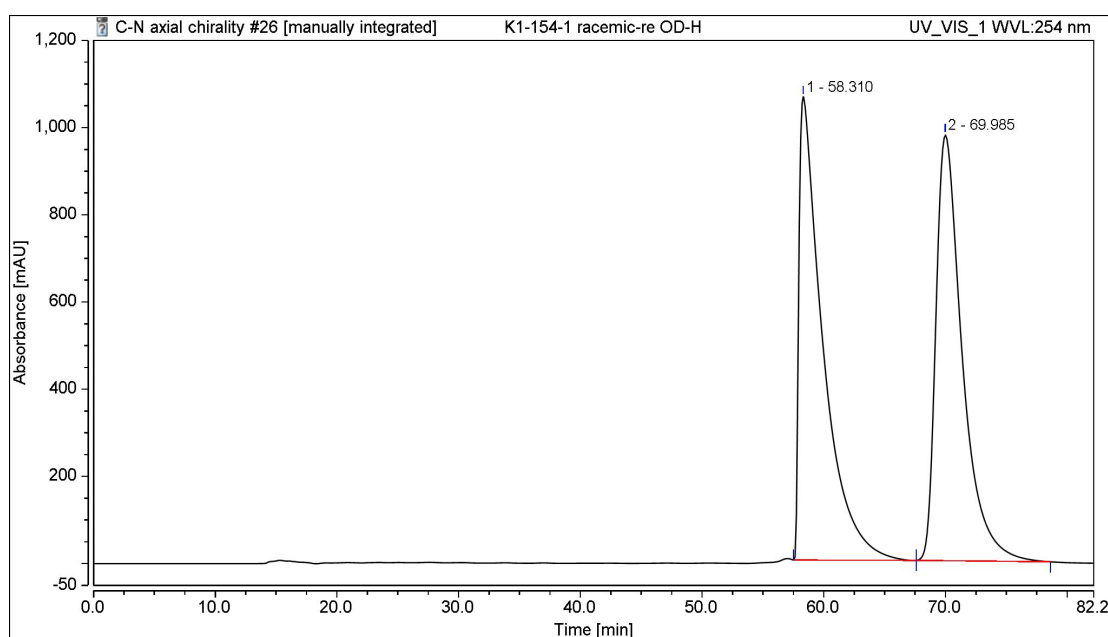
Integration Results						
No.	Peak Name	Retention Time min	Area mAU*min	Height mAU	Relative Area %	Relative Height %
1		9.548	193.632	337.147	50.12	54.46
2		12.258	192.681	281.877	49.88	45.54
Total:			386.313	619.024	100.00	100.00



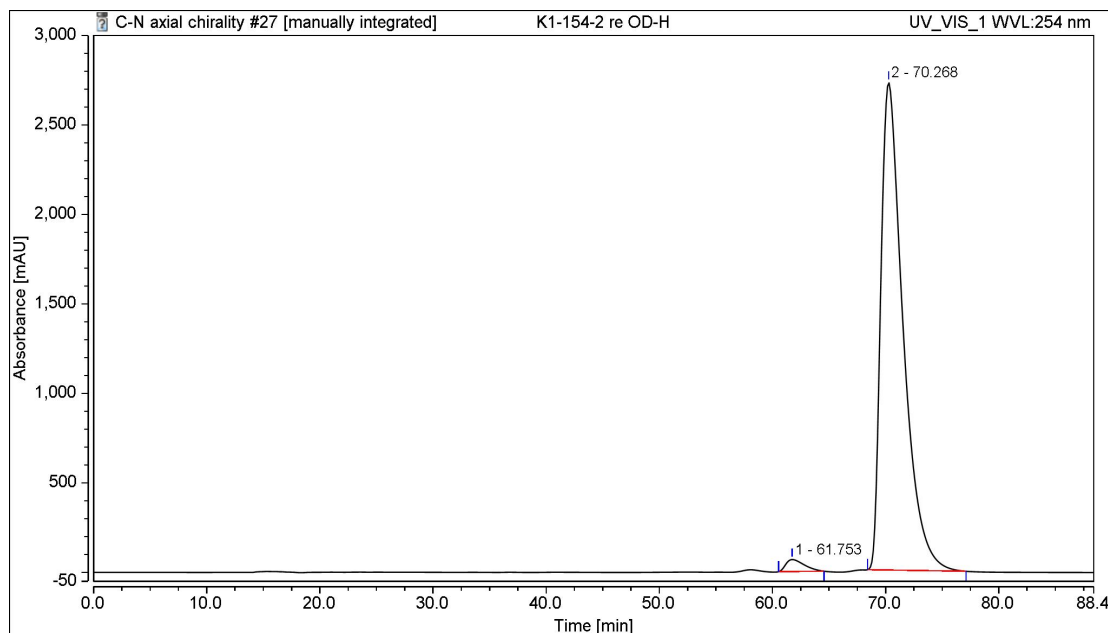
Integration Results						
No.	Peak Name	Retention Time min	Area mAU*min	Height mAU	Relative Area %	Relative Height %
1		9.450	1228.696	2226.605	97.29	97.69
2		12.370	34.281	52.637	2.71	2.31
Total:			1262.977	2279.242	100.00	100.00



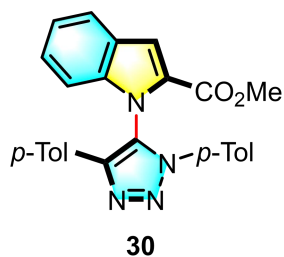
White solid, 40.0 mg, 98% yield, 98:2 er. [Chiral HPLC analysis of the product: Daicel Chiralcel OD-H 250X4.6 mm 5u column; n-hexane/2-propanol = 90/10, flow rate = 0.2 mL/min, $\lambda = 254$ nm, t (major) = 70.27 min, t (minor) = 61.75 min]. $[\alpha]_D^{26} = -99.0^\circ$ (c = 0.9, CHCl₃). **¹H NMR (500 MHz, CDCl₃)** δ 7.75 (d, *J* = 7.9 Hz, 1H), 7.48 (s, 1H), 7.36-7.24 (m, 7H), 7.19 (d, *J* = 8.1 Hz, 2H), 7.04-7.01 (m, 3H), 3.64 (s, 3H), 2.26 (s, 3H). **¹³C NMR (126 MHz, CDCl₃)** δ 159.4, 141.1, 138.5, 137.3, 134.4, 128.5, 128.3, 128.3, 127.4, 127.3, 126.2, 125.9, 125.3, 124.5, 122.4, 122.1, 121.8, 113.3, 110.2, 51.0, 20.2. **HRMS (ESI, m/z)** Calcd for C₂₅H₂₁N₄O₂ (M+H)⁺: 409.1659; Found: 409.1658.



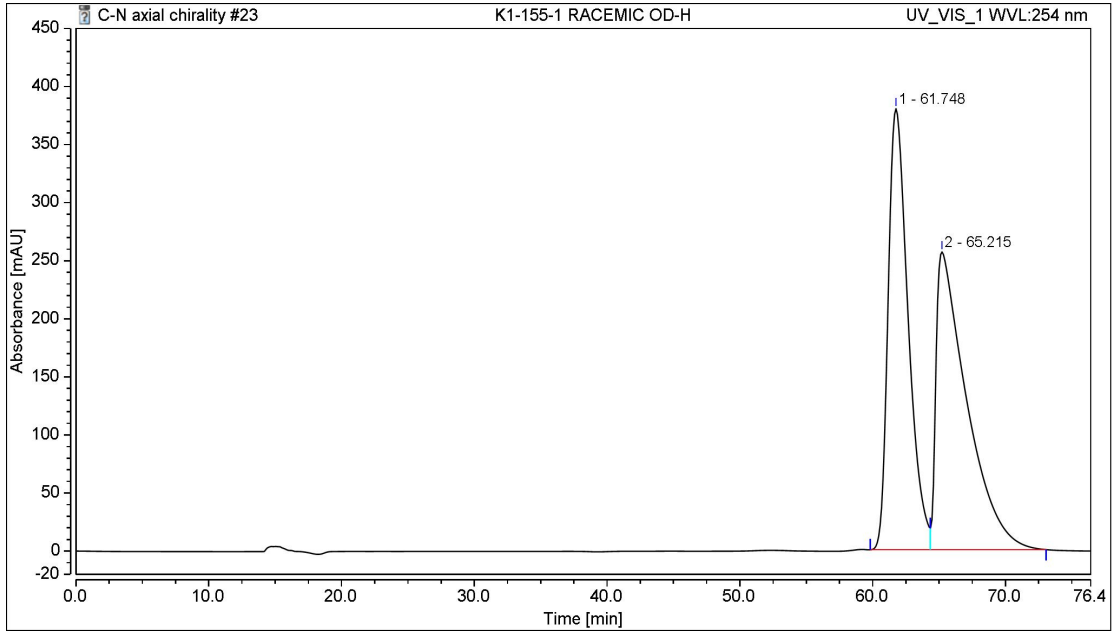
Integration Results						
No.	Peak Name	Retention Time min	Area mAU*min	Height mAU	Relative Area %	Relative Height %
1		58.310	2411.646	1063.042	49.61	52.12
2		69.985	2449.099	976.574	50.39	47.88
Total:			4860.745	2039.616	100.00	100.00



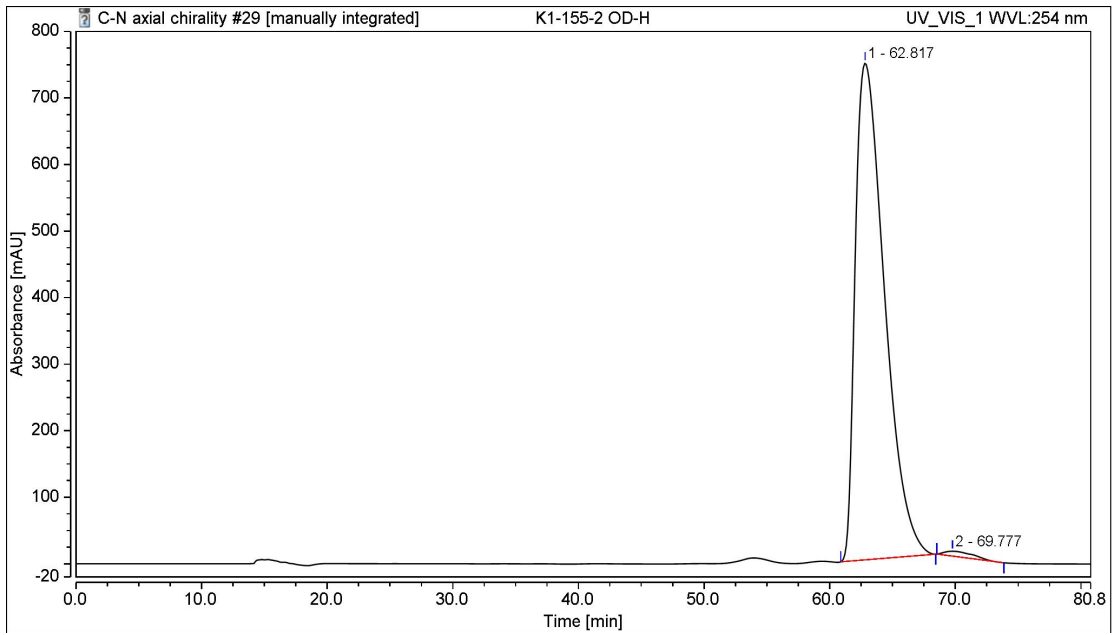
Integration Results						
No.	Peak Name	Retention Time min	Area mAU*min	Height mAU	Relative Area %	Relative Height %
1		61.753	126.252	67.076	2.00	2.40
2		70.268	6194.434	2724.741	98.00	97.60
Total:			6320.686	2791.816	100.00	100.00



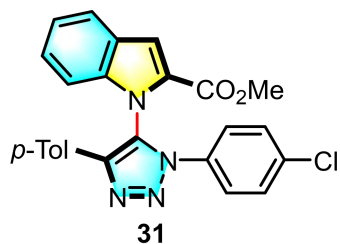
White solid, 41.0 mg, 97% yield, 99:1 er. [Chiral HPLC analysis of the product: Daicel Chiralcel OD-H 250X4.6 mm 5u column; n-hexane/2-propanol = 90/10, flow rate = 0.2 mL/min, $\lambda = 254$ nm, t (major) = 62.82 min, t (minor) = 69.78 min]. $[\alpha]_D^{26} = -67.4^\circ$ (c = 1.2, CHCl₃). **¹H NMR (500 MHz, CDCl₃)** δ 7.75 (d, *J* = 7.9 Hz, 1H), 7.48 (s, 1H), 7.33 (t, *J* = 7.7 Hz, 1H), 7.28-7.24 (m, 3H), 7.09-7.00 (m, 7H), 3.65 (s, 3H), 2.28 (s, 3H), 2.25 (s, 3H). **¹³C NMR (126 MHz, CDCl₃)** δ 159.4, 141.0, 138.6, 138.5, 137.2, 131.9, 128.9, 128.4, 127.4, 127.2, 126.2, 125.8, 125.4, 124.5, 122.2, 122.1, 121.7, 113.2, 110.2, 51.0, 20.2, 20.1. **HRMS (ESI, m/z)** Calcd for C₂₆H₂₃N₄O₂ (M+H)⁺: 423.1816; Found: 423.1820.



Integration Results						
No.	Peak Name	Retention Time min	Area mAU*min	Height mAU	Relative Area %	Relative Height %
1		61.748	663.429	379.842	49.13	59.69
2		65.215	686.818	256.504	50.87	40.31
Total:			1350.247	636.346	100.00	100.00

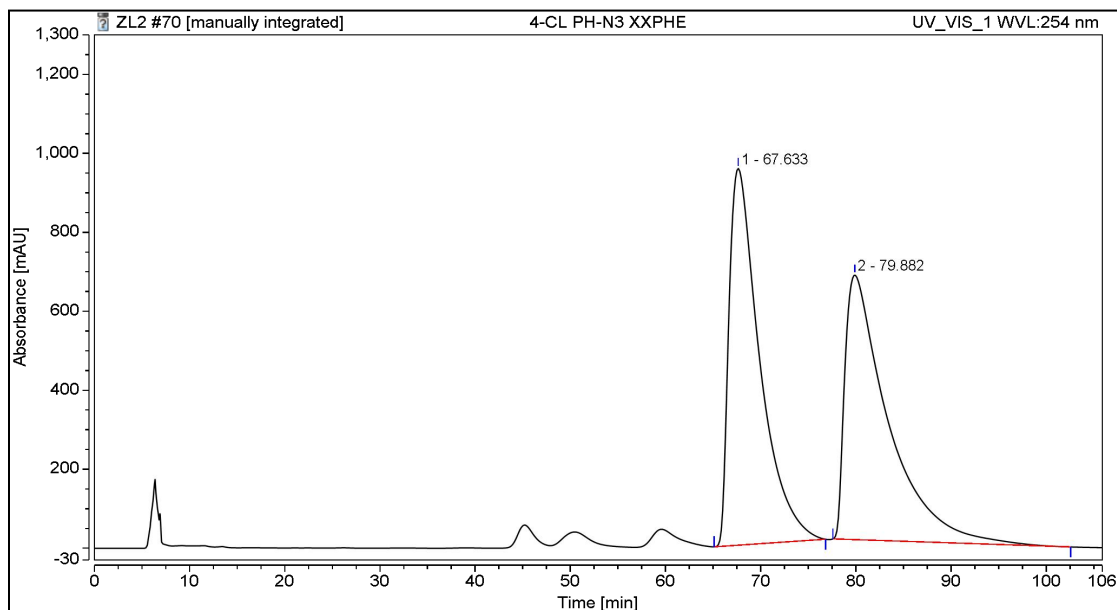


Integration Results						
No.	Peak Name	Retention Time min	Area mAU*min	Height mAU	Relative Area %	Relative Height %
1		62.817	2015.548	746.573	98.95	99.01
2		69.777	21.393	7.445	1.05	0.99
Total:			2036.941	754.018	100.00	100.00

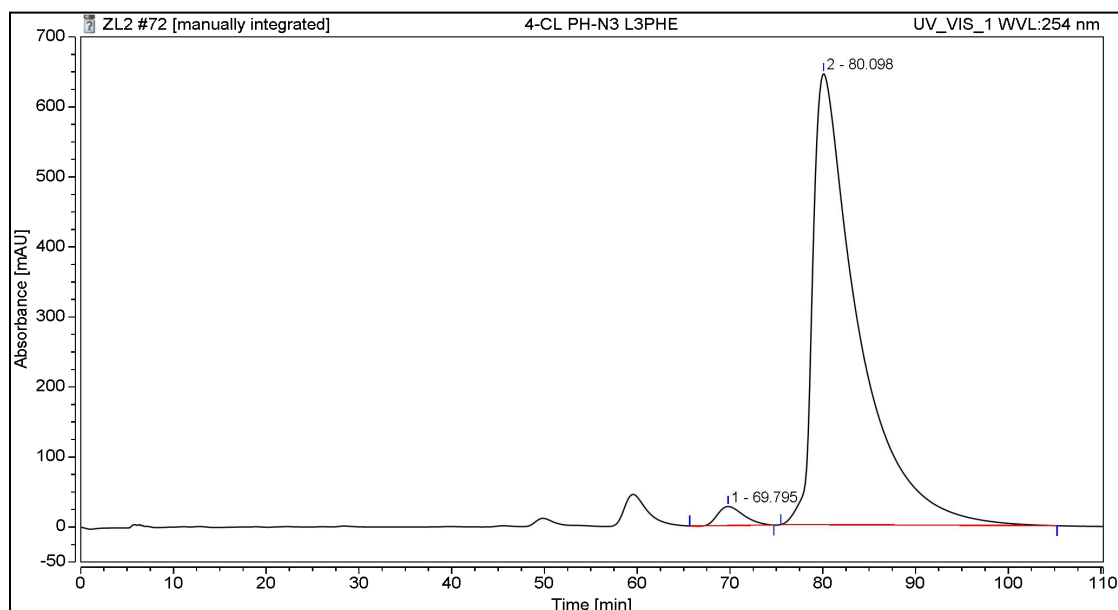


White solid, 38.9 mg, 88% yield, 97.5:2.5 er. [Chiral HPLC analysis of the product: Phenomenex 00G-4457-E0 250X4.6 mm 5u column; *n*-hexane/2-propanol = 90/10, flow rate = 0.5 mL/min, λ = 254 nm, *t* (major) = 80.10 min, *t* (minor) = 69.80 min].

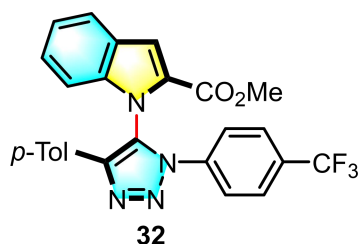
$[\alpha]_D^{25} = -55.0^\circ$ ($c = 0.6$, CHCl_3). **$^1\text{H NMR}$ (500 MHz, CDCl_3)** δ 7.76 (d, $J = 7.9$ Hz, 1H), 7.49 (s, 1H), 7.33 (t, $J = 7.6$ Hz, 1H), 7.28 (d, $J = 7.6$ Hz, 1H), 7.24-7.22 (m, 4H), 7.13 (d, $J = 8.8$ Hz, 2H), 7.02 (t, $J = 7.7$ Hz, 3H), 3.65 (s, 3H), 2.24 (s, 3H). **$^{13}\text{C NMR}$ (126 MHz, CDCl_3)** δ 160.6, 142.5, 139.6, 138.6, 135.5, 134.0, 129.7, 129.7, 128.4, 128.3, 127.5, 127.1, 126.3, 125.7, 124.7, 123.4, 123.1, 114.5, 111.2, 52.2, 21.3. **HRMS (ESI, m/z)** Calcd for $\text{C}_{25}\text{H}_{20}\text{ClN}_4\text{O}_2$ ($\text{M}+\text{H}$) $^+$: 443.1269; Found: 443.1261.



Integration Results						
No.	Peak Name	Retention Time min	Area mAU*min	Height mAU	Relative Area %	Relative Height %
1		67.633	3566.677	954.444	50.37	58.74
2		79.882	3513.940	670.283	49.63	41.26
Total:			7080.618	1624.726	100.00	100.00

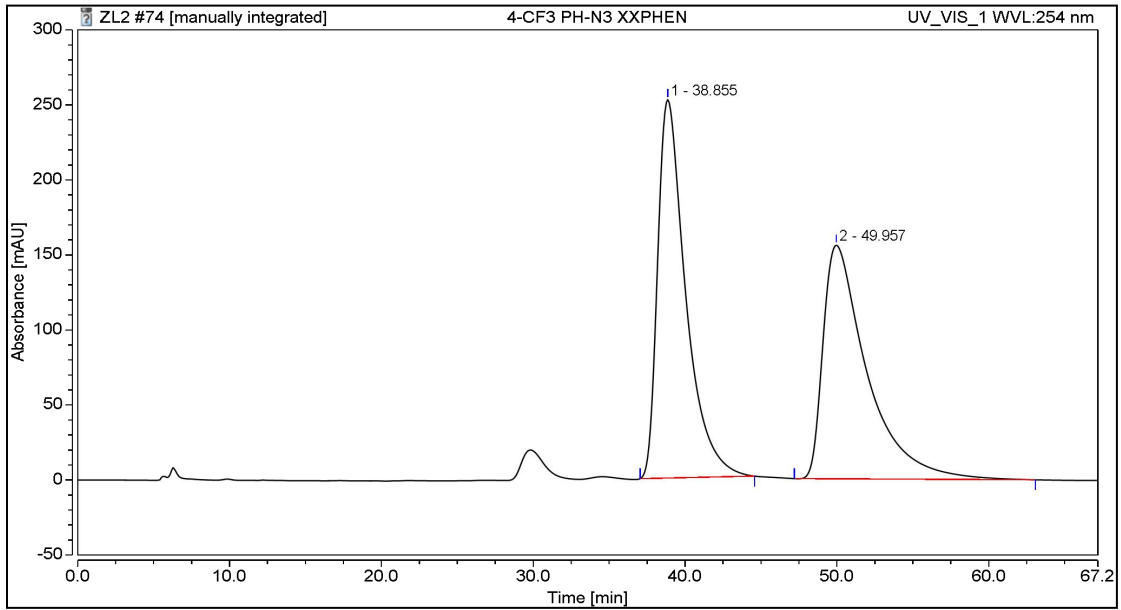


Integration Results						
No.	Peak Name	Retention Time min	Area mAU*min	Height mAU	Relative Area %	Relative Height %
1		69.795	88.150	27.264	2.37	4.06
2		80.098	3633.417	644.477	97.63	95.94
Total:			3721.567	671.741	100.00	100.00

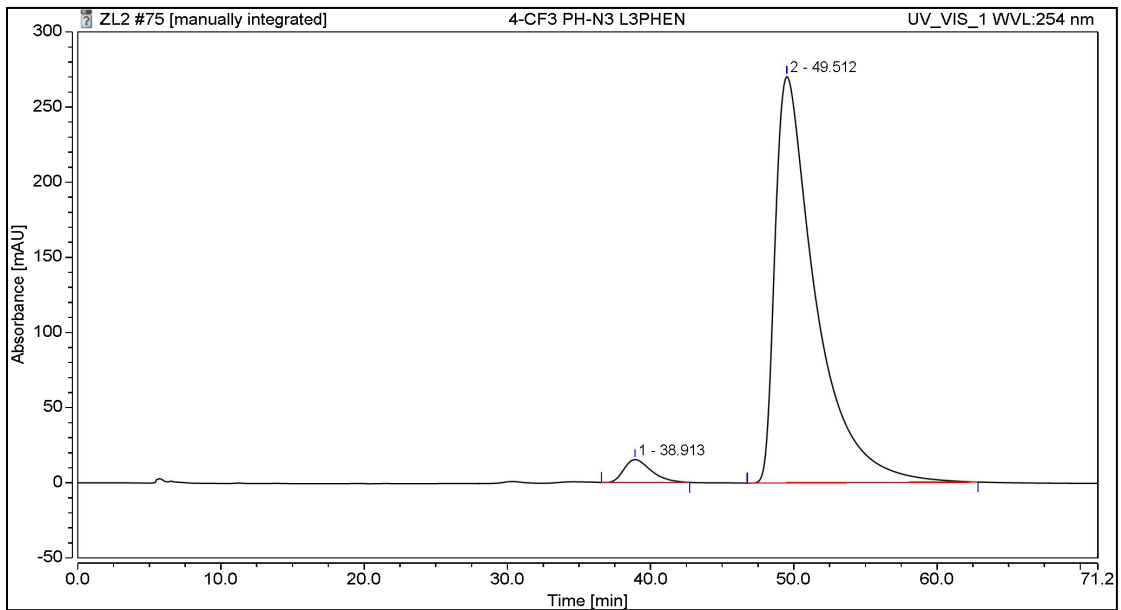


White solid, 43.8 mg, 92% yield, 96.5:3.5 er. [Chiral HPLC analysis of the product: Phenomenex 00G-4457-E0 250X4.6 mm 5u column; *n*-hexane/2-propanol = 90/10, flow rate = 0.5 mL/min, λ = 254 nm, *t* (major) = 40.51 min, *t* (minor) = 38.91 min].

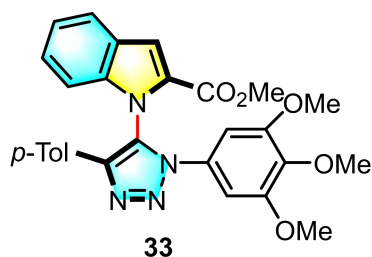
$[\alpha]_D^{25} = -73.0^\circ$ ($c = 0.8$, CHCl_3). **$^1\text{H NMR}$ (500 MHz, CDCl_3)** δ 7.79 (d, $J = 7.9$ Hz, 1H), 7.59-7.50 (m, 3H), 7.34 (d, $J = 8.4$ Hz, 3H), 7.30 (t, $J = 7.4$ Hz, 1H), 7.23 (d, $J = 8.2$ Hz, 2H), 7.06-7.01 (m, 3H), 3.65 (s, 3H), 2.25 (s, 3H). **$^{13}\text{C NMR}$ (126 MHz, CDCl_3)** δ 160.5, 142.8, 139.5, 138.8, 138.4, 131.4, 131.2, 129.7, 128.3, 128.3, 127.7, 127.1, 126.8, 126.8, 126.1, 125.7, 124.7, 123.5, 123.3, 123.2, 122.5, 114.7, 111.2, 52.2, 21.3. **$^{19}\text{F NMR}$ (471 MHz, CDCl_3)** δ -62.81. **HRMS (ESI, m/z)** Calcd for $\text{C}_{26}\text{H}_{20}\text{F}_3\text{N}_4\text{O}_2$ ($\text{M}+\text{H}$) $^+$: 477.1533; Found: 477.1519.



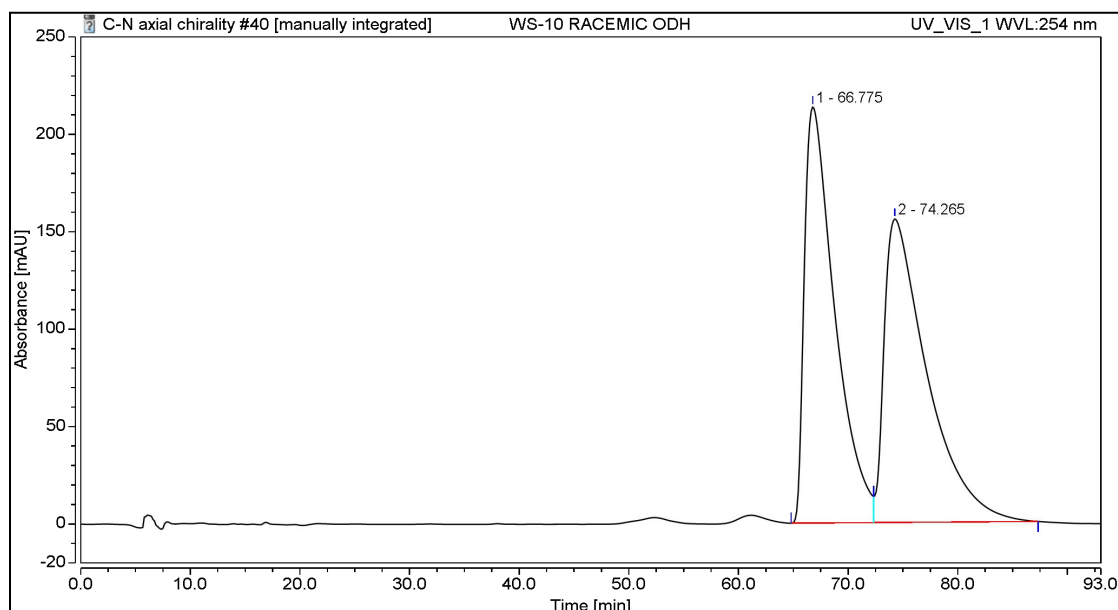
Integration Results						
No.	Peak Name	Retention Time min	Area mAU*min	Height mAU	Relative Area %	Relative Height %
1		38.855	540.109	252.272	50.90	61.83
2		49.957	521.102	155.737	49.10	38.17
Total:			1061.211	408.009	100.00	100.00



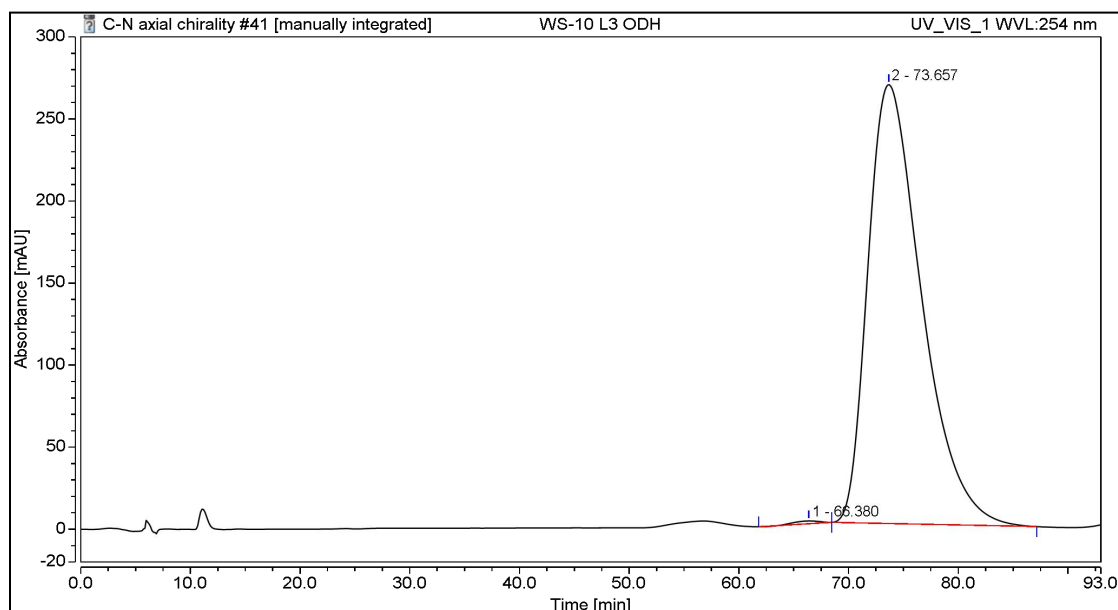
Integration Results						
No.	Peak Name	Retention Time min	Area mAU*min	Height mAU	Relative Area %	Relative Height %
1		38.913	33.344	15.172	3.63	5.31
2		49.512	886.280	270.395	96.37	94.69
Total:			919.624	285.567	100.00	100.00



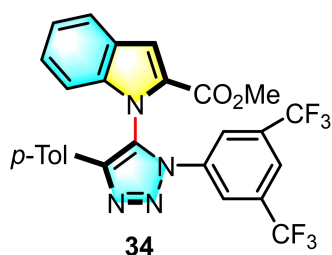
White solid, 44.8 mg, 90% yield, 99.5:0.5 er. [Chiral HPLC analysis of the product: Daicel Chiralcel OD-H 250X4.6 mm 5u column; *n*-hexane/2-propanol = 95/5, flow rate = 0.5 mL/min, λ = 254 nm, t (major) = 77.36 min, t (minor) = 66.38 min]. $[\alpha]_D^{26} = -46.9^\circ$ ($c = 1.1$, CHCl_3). **$^1\text{H NMR}$ (500 MHz, CDCl_3)** δ 7.76 (d, $J = 8.0$ Hz, 1H), 7.48 (s, 1H), 7.39 - 7.36 (m, 3H), 7.31-7.26 (m, 1H), 7.13 (d, $J = 8.3$ Hz, 1H), 7.06 (d, $J = 8.1$ Hz, 2H), 6.37 (s, 2H), 3.77 (s, 3H), 3.67 (s, 3H), 3.45 (s, 6H), 2.27 (s, 3H). **$^{13}\text{C NMR}$ (126 MHz, CDCl_3)** δ 160.5, 153.5, 142.5, 139.9, 138.6, 130.8, 129.7, 128.6, 128.2, 127.4, 127.1, 126.5, 123.3, 123.0, 114.2, 111.4, 100.7, 61.0, 56.0, 52.1, 21.4. **HRMS (ESI, m/z)** Calcd for $\text{C}_{28}\text{H}_{27}\text{N}_4\text{O}_5$ ($\text{M}+\text{H}$) $^+$: 499.1976; Found: 499.1961.



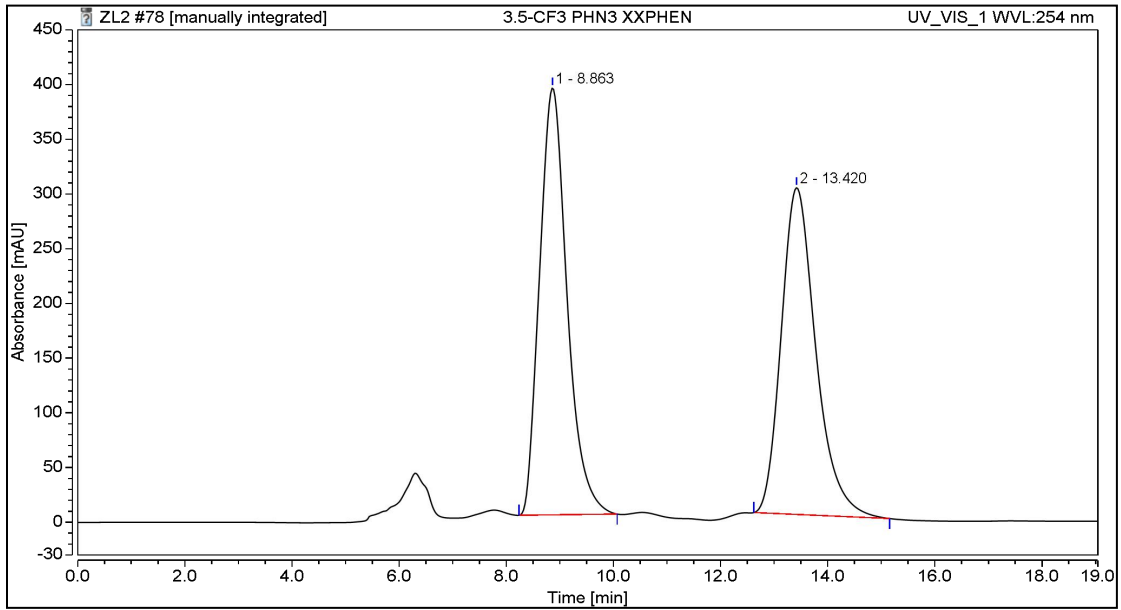
Integration Results						
No.	Peak Name	Retention Time min	Area mAU*min	Height mAU	Relative Area %	Relative Height %
1		66.775	685.215	213.653	49.21	57.83
2		74.265	707.275	155.817	50.79	42.17
Total:			1392.490	369.469	100.00	100.00



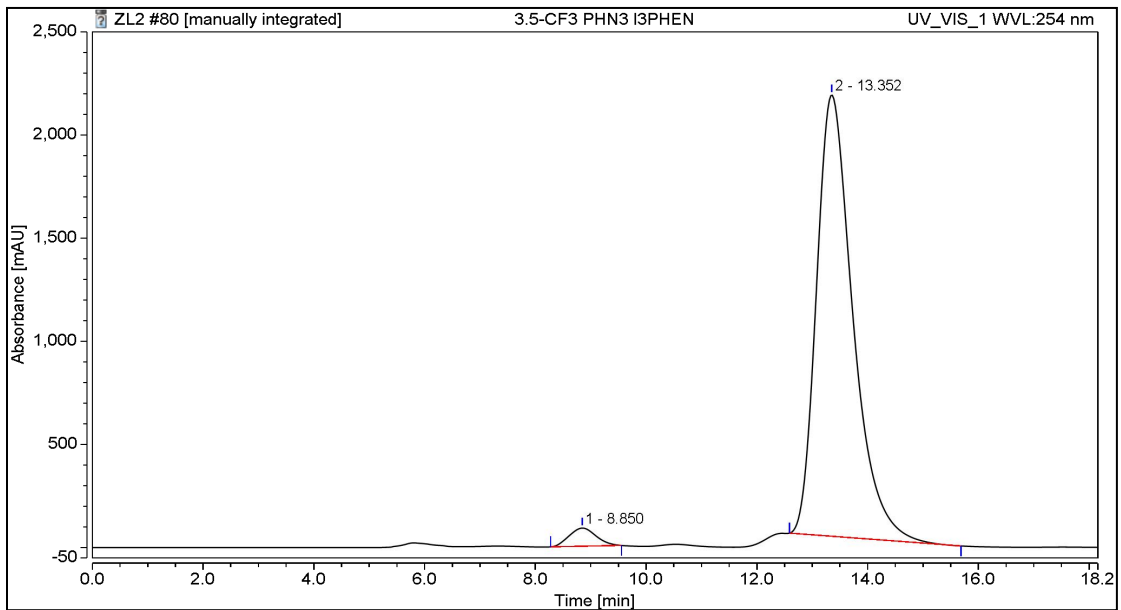
Integration Results						
No.	Peak Name	Retention Time min	Area mAU*min	Height mAU	Relative Area %	Relative Height %
1		66.380	4.779	1.727	0.31	0.64
2		73.657	1517.630	267.505	99.69	99.36
Total:			1522.409	269.231	100.00	100.00



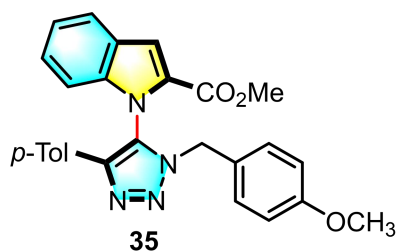
White solid, 49.5 mg, 91% yield, 97:3 er. [Chiral HPLC analysis of the product: Phenomenex 00G-4457-E0 250X4.6 mm 5u column; *n*-hexane/2-propanol = 90/10, flow rate = 0.5 mL/min, λ = 254 nm, *t* (major) = 13.35 min, *t* (minor) = 8.85 min]. $[\alpha]_D^{26} = -88.3^\circ$ (*c* = 0.9, CHCl₃). **¹H NMR (500 MHz, CDCl₃)** δ 7.81 (d, *J* = 8.2 Hz, 2H), 7.61 (s, 2H), 7.53 (s, 1H), 7.39 (t, *J* = 7.7 Hz, 1H), 7.35-7.32 (m, 3H), 7.07 (d, *J* = 8.2 Hz, 3H), 3.67 (s, 3H), 2.28 (s, 3H). **¹³C NMR (126 MHz, CDCl₃)** δ 160.7, 143.0, 139.5, 139.1, 136.7, 133.7, 133.4, 133.1, 132.8, 129.8, 128.5, 128.1, 128.0, 127.2, 125.9, 125.8, 123.7, 123.5, 123.3, 123.3, 122.9, 121.4, 115.0, 111.0, 52.3, 21.4. **¹⁹F NMR (471 MHz, CDCl₃)** δ -63.37. **HRMS (ESI, *m/z*)** Calcd for C₂₇H₁₉F₆N₄O₂ (M+H)⁺: 545.1407; Found: 545.1395.



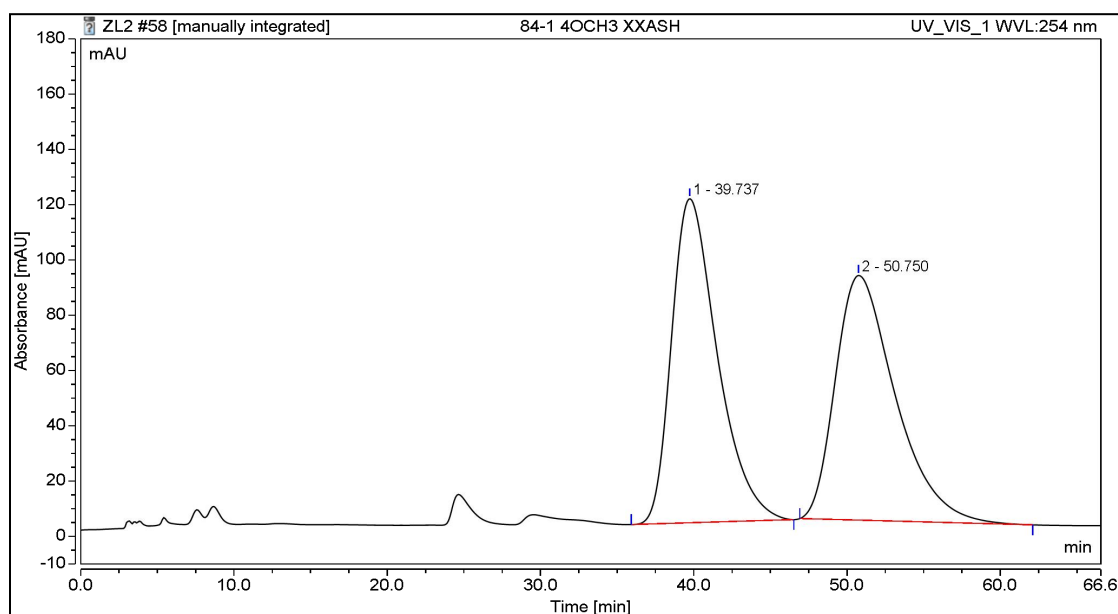
Integration Results						
No.	Peak Name	Retention Time min	Area mAU*min	Height mAU	Relative Area %	Relative Height %
1		8.863	231.922	390.331	50.96	56.65
2		13.420	223.212	298.693	49.04	43.35
Total:			455.134	689.024	100.00	100.00



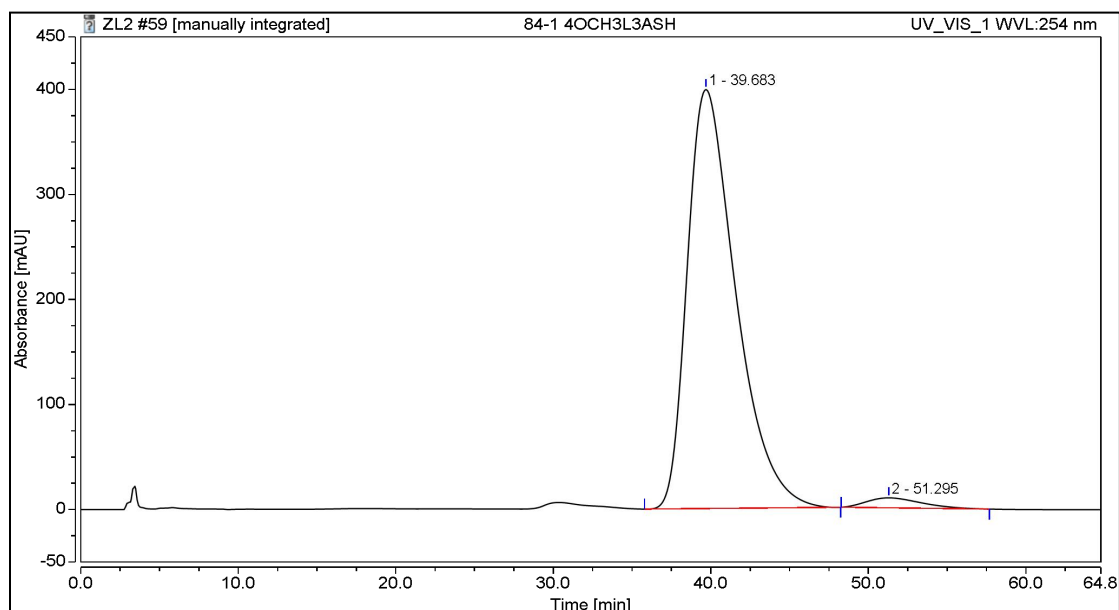
Integration Results						
No.	Peak Name	Retention Time min	Area mAU*min	Height mAU	Relative Area %	Relative Height %
1		8.850	49.817	88.095	2.97	3.95
2		13.352	1625.013	2140.351	97.03	96.05
Total:			1674.830	2228.447	100.00	100.00



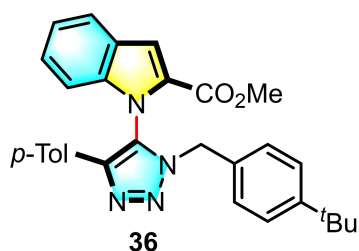
White solid, 43.4 mg, 96% yield, 97.5:2.5 er. [Chiral HPLC analysis of the product: Daicel Chiralpak AS-H 250X4.6 mm 5u column; *n*-hexane/2-propanol = 90/10, flow rate = 1.0 mL/min, λ = 254 nm, *t* (major) = 39.68 min, *t* (minor) = 50.30 min]. $[\alpha]_D^{26} = -196.5^\circ$ (*c* = 1.0, CHCl₃). **¹H NMR (500 MHz, CDCl₃)** δ 7.74 (d, *J* = 8.0 Hz, 1H), 7.56 (s, 1H), 7.20 (dd, *J* = 15.9, 7.8 Hz, 3H), 7.13 (t, *J* = 7.7 Hz, 1H), 6.96 (d, *J* = 8.1 Hz, 2H), 6.80 (d, *J* = 8.6 Hz, 2H), 6.56 (t, *J* = 7.6 Hz, 3H), 5.20 (d, *J* = 15.0 Hz, 1H), 5.14 (d, *J* = 15.0 Hz, 1H), 3.67 (s, 3H), 3.60 (s, 3H), 2.22 (s, 3H). **¹³C NMR (126 MHz, CDCl₃)** δ 160.5, 159.7, 142.5, 139.4, 138.2, 129.7, 129.5, 128.4, 128.1, 126.9, 126.8, 126.7, 125.6, 125.4, 122.9, 122.6, 114.2, 113.9, 111.1, 55.3, 52.0, 52.0, 21.3. **HRMS (ESI, *m/z*)** Calcd for C₂₇H₂₅N₄O₃ (M+H)⁺: 453.1921; Found: 453.1914.



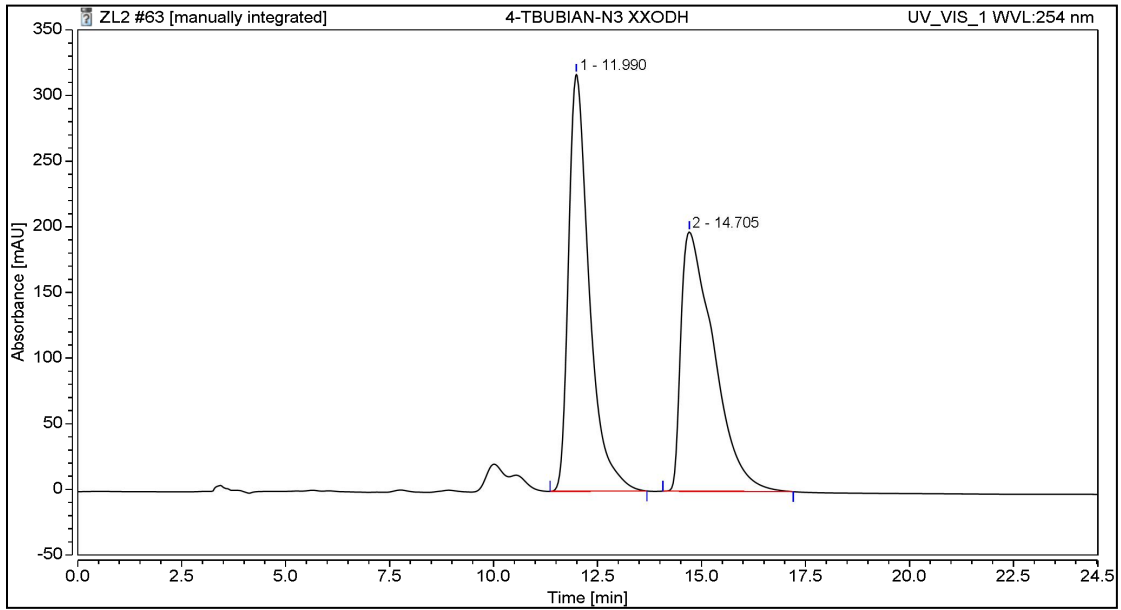
Integration Results						
No.	Peak Name	Retention Time min	Area mAU*min	Height mAU	Relative Area %	Relative Height %
1		39.737	406.063	117.266	50.29	56.98
2		50.750	401.307	88.536	49.71	43.02
Total:			807.369	205.802	100.00	100.00



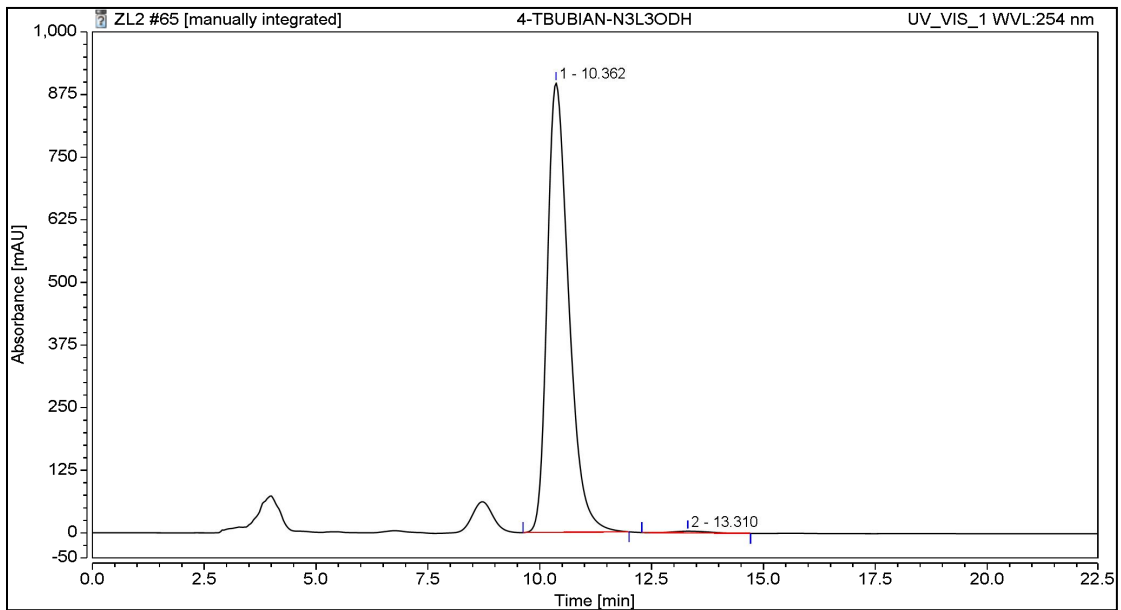
Integration Results						
No.	Peak Name	Retention Time min	Area mAU*min	Height mAU	Relative Area %	Relative Height %
1		39.683	1423.872	398.988	97.38	97.67
2		51.295	38.292	9.517	2.62	2.33
Total:			1462.164	408.505	100.00	100.00



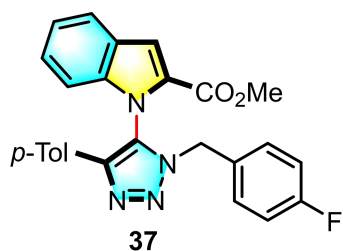
White solid, 43.5 mg, 91% yield, 99.5:0.5 er. [Chiral HPLC analysis of the product: Daicel Chiralcel OD-H 250X4.6 mm 5u column; *n*-hexane/2-propanol = 90/10, flow rate = 1.0 mL/min, λ = 254 nm, t (major) = 10.36 min, t (minor) = 13.31 min]. $[\alpha]_D^{26} = -205.8^\circ$ ($c = 0.9$, CHCl_3). $^1\text{H NMR}$ (500 MHz, CDCl_3) δ 7.71 (d, $J = 8.0$ Hz, 1H), 7.55 (s, 1H), 7.17 (t, $J = 7.6$ Hz, 3H), 7.09-7.01 (m, 3H), 6.97 (d, $J = 8.1$ Hz, 2H), 6.80 (d, $J = 8.3$ Hz, 2H), 6.52 (d, $J = 8.4$ Hz, 1H), 5.29 (d, $J = 14.5$ Hz, 1H), 5.15 (d, $J = 14.5$ Hz, 1H), 3.61 (s, 3H), 2.22 (s, 3H), 1.19 (s, 9H). $^{13}\text{C NMR}$ (126 MHz, CDCl_3) δ 160.6, 151.5, 142.5, 139.4, 138.2, 130.5, 129.5, 128.3, 128.3, 128.0, 126.9, 126.8, 126.8, 125.4, 125.4, 122.8, 122.8, 114.3, 111.1, 52.3, 52.0, 34.6, 31.3, 21.3. **HRMS (ESI, m/z)** Calcd for $\text{C}_{30}\text{H}_{31}\text{N}_4\text{O}_2$ ($\text{M}+\text{H}$) $^+$: 479.2442; Found: 479.2435.



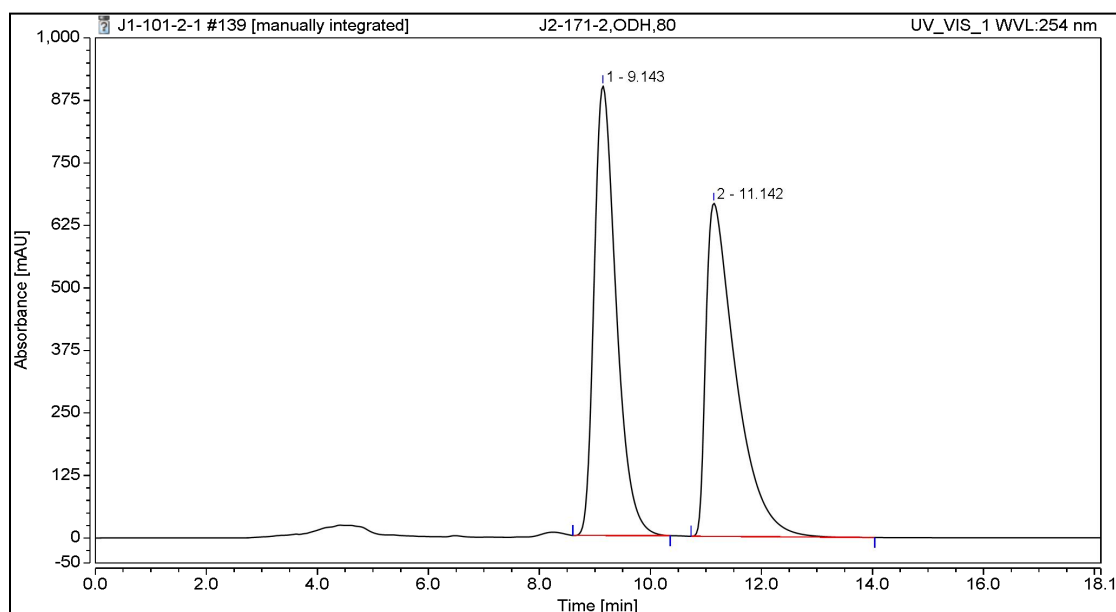
Integration Results						
No.	Peak Name	Retention Time min	Area mAU*min	Height mAU	Relative Area %	Relative Height %
1		11.990	183.730	317.604	50.44	61.65
2		14.705	180.517	197.561	49.56	38.35
Total:			364.247	515.165	100.00	100.00



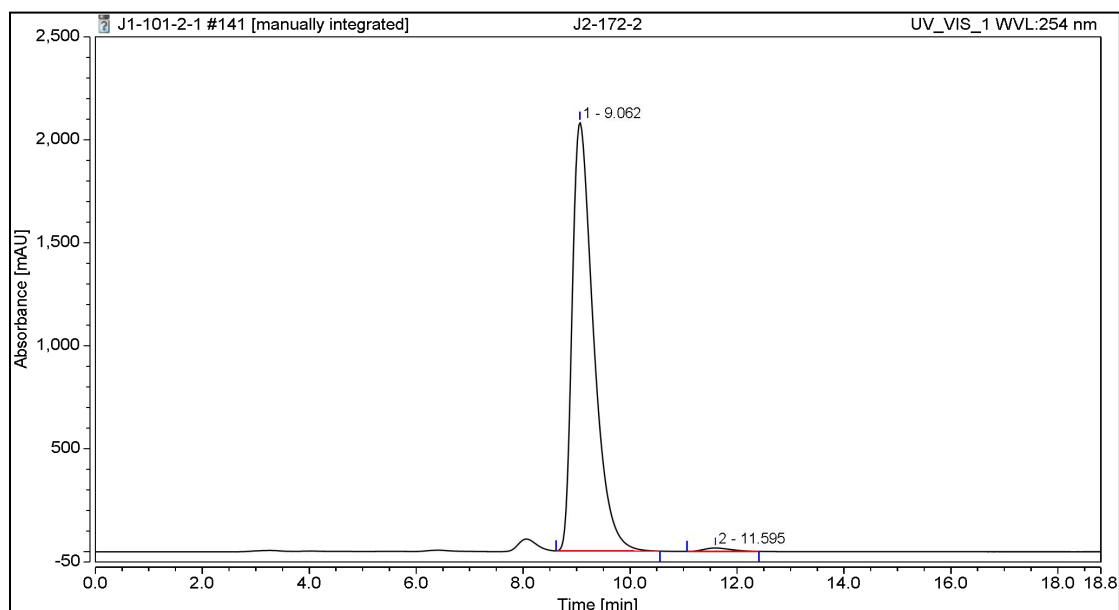
Integration Results						
No.	Peak Name	Retention Time min	Area mAU*min	Height mAU	Relative Area %	Relative Height %
1		10.362	501.652	897.439	99.41	99.63
2		13.310	2.969	3.360	0.59	0.37
Total:			504.621	900.799	100.00	100.00



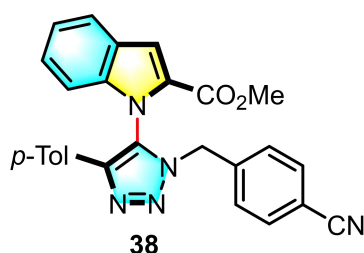
White solid, 41.8 mg, 95% yield, 99:1 er. [Chiral HPLC analysis of the product: Daicel Chiralcel OD-H 250X4.6 mm 5u column; *n*-hexane/2-propanol = 80/20, flow rate = 1.0 mL/min, λ = 254 nm, t (major) = 9.06 min, t (minor) = 11.60 min]. $[\alpha]_D^{26} = -143.0^\circ$ (c = 1.0, CHCl₃). **¹H NMR (500 MHz, CDCl₃)** δ 7.74 (d, *J* = 8.0 Hz, 1H), 7.56 (s, 1H), 7.22 (t, *J* = 7.5 Hz, 1H), 7.19-7.13 (m, 3H), 6.97 (d, *J* = 8.1 Hz, 2H), 6.87 (dd, *J* = 8.6, 5.3 Hz, 2H), 6.74 (t, *J* = 8.6 Hz, 2H), 6.56 (d, *J* = 8.3 Hz, 1H), 5.23 (d, *J* = 14.9 Hz, 1H), 5.17 (d, *J* = 14.9 Hz, 1H), 3.63 (s, 3H), 2.22 (s, 3H). **¹³C NMR (126 MHz, CDCl₃)** δ 163.8, 161.8, 160.6, 142.6, 139.4, 138.3, 130.3, 130.2, 129.5, 129.4, 128.3, 128.2, 127.1, 126.8, 126.6, 125.4, 123.0, 122.8, 115.6, 115.4, 114.3, 111.0, 52.0, 51.7, 21.3. **¹⁹F NMR (471 MHz, CDCl₃)** δ -113.38. **HRMS (ESI, m/z)** Calcd for C₂₆H₂₂FN₄O₂ (M+H)⁺: 441.1721; Found: 441.1708.



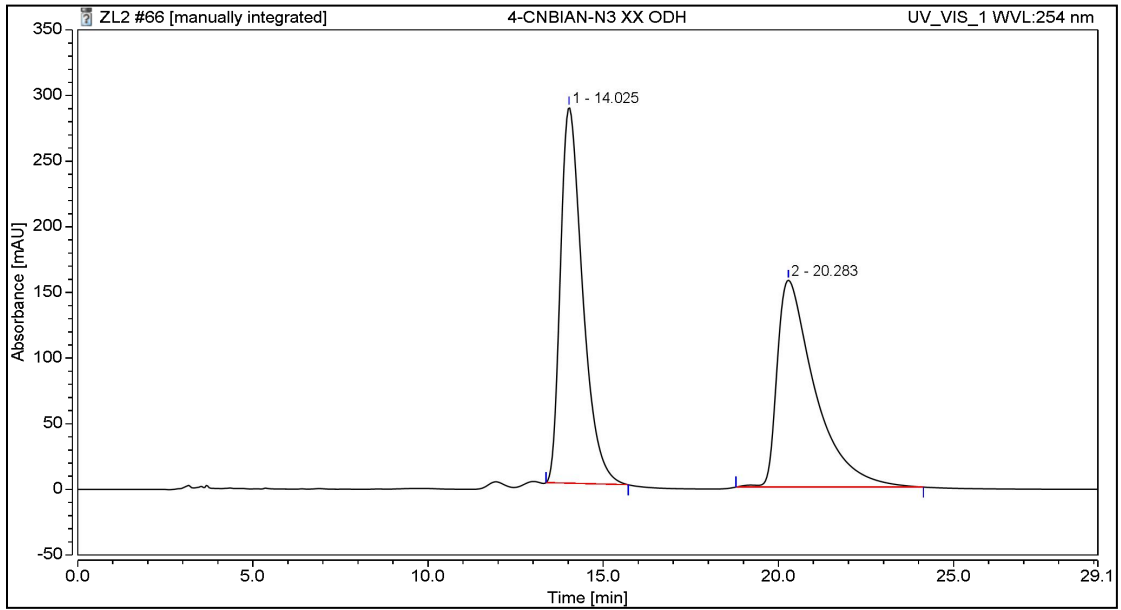
Integration Results						
No.	Peak Name	Retention Time min	Area mAU*min	Height mAU	Relative Area %	Relative Height %
1		9.143	413.720	899.222	49.90	57.44
2		11.142	415.340	666.376	50.10	42.56
Total:			829.060	1565.598	100.00	100.00



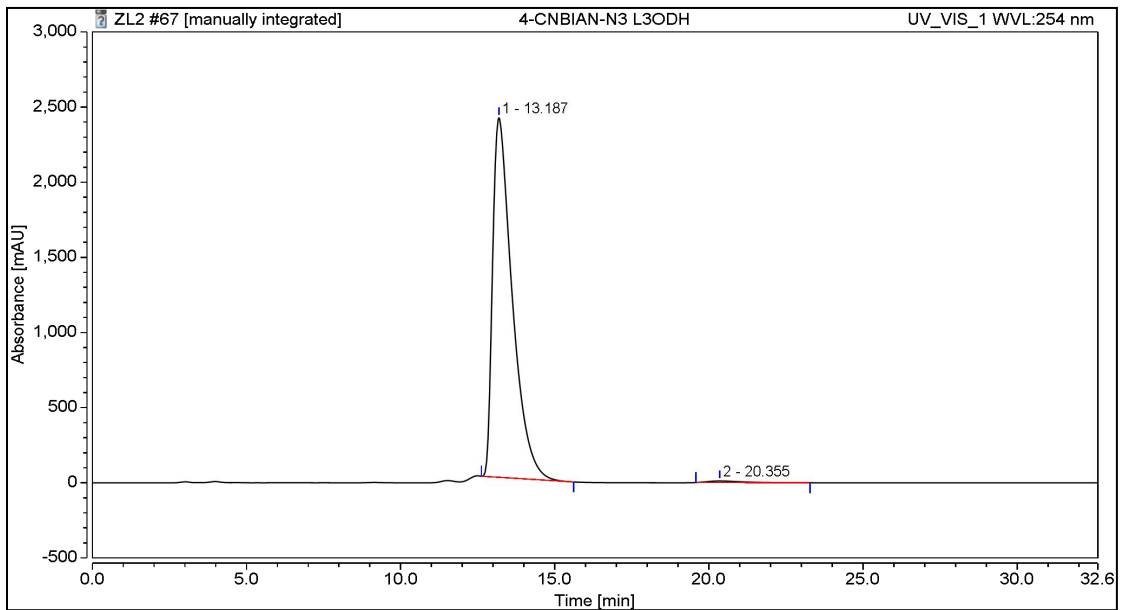
Integration Results						
No.	Peak Name	Retention Time min	Area mAU*min	Height mAU	Relative Area %	Relative Height %
1		9.062	959.903	2082.009	98.99	99.21
2		11.595	9.761	16.674	1.01	0.79
Total:			969.664	2098.683	100.00	100.00



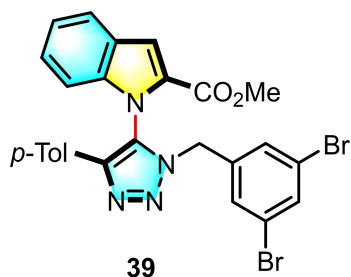
White solid, 41.8 mg, 83% yield, 99:1 er. [Chiral HPLC analysis of the product: Daicel Chiralcel OD-H 250X4.6 mm 5u column; *n*-hexane/2-propanol = 70/30, flow rate = 1.0 mL/min, λ = 254 nm, *t* (major) = 20.36 min, *t* (minor) = 13.19 min]. $[\alpha]_D^{26} = -155.5^\circ$ (*c* = 1.0, CHCl₃). **¹H NMR (500 MHz, CDCl₃)** δ 7.73 (d, *J* = 8.0 Hz, 1H), 7.54 (s, 1H), 7.34 (d, *J* = 8.3 Hz, 2H), 7.23 (t, *J* = 7.2 Hz, 1H), 7.18-7.12 (m, 3H), 7.00 (dd, *J* = 21.4, 8.2 Hz, 4H), 6.52 (d, *J* = 8.4 Hz, 1H), 5.35 (d, *J* = 15.0 Hz, 1H), 5.21 (d, *J* = 15.0 Hz, 1H), 3.67 (s, 3H), 2.23 (s, 3H). **¹³C NMR (126 MHz, CDCl₃)** δ 160.6, 142.7, 139.2, 138.6, 138.5, 132.3, 129.6, 129.0, 128.3, 128.2, 127.2, 126.9, 126.3, 125.5, 123.1, 123.0, 118.1, 114.4, 112.5, 110.8, 52.1, 51.7, 21.3. **HRMS (ESI, *m/z*)** Calcd for C₂₇H₂₂N₅O₂ (M+H)⁺: 448.1768; Found: 448.1762.



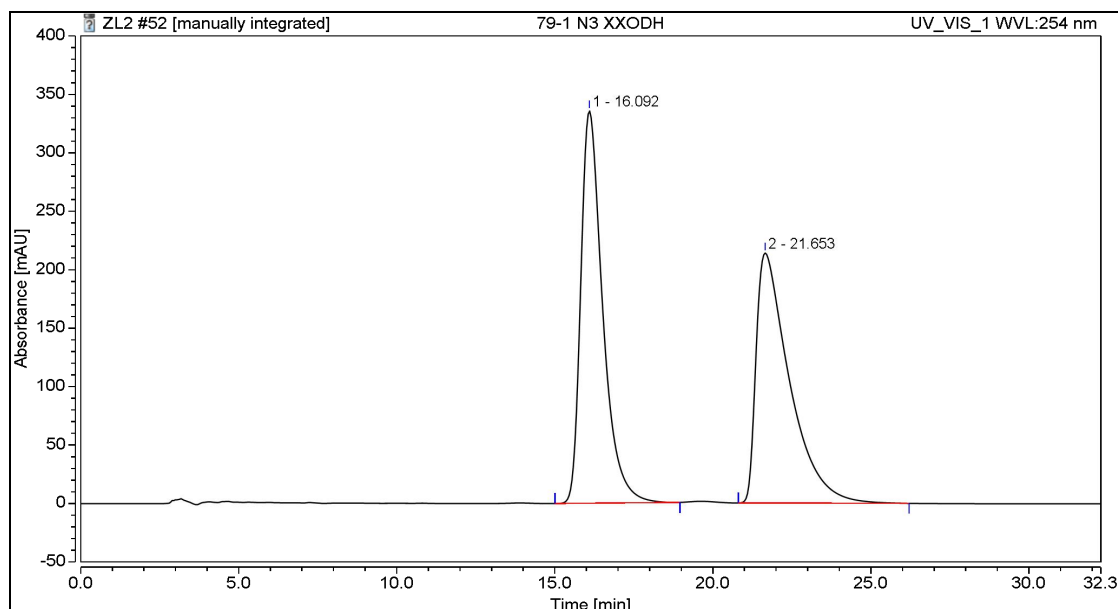
Integration Results						
No.	Peak Name	Retention Time min	Area mAU*min	Height mAU	Relative Area %	Relative Height %
1		14.025	210.390	286.429	51.62	64.50
2		20.283	197.173	157.622	48.38	35.50
Total:			407.563	444.051	100.00	100.00



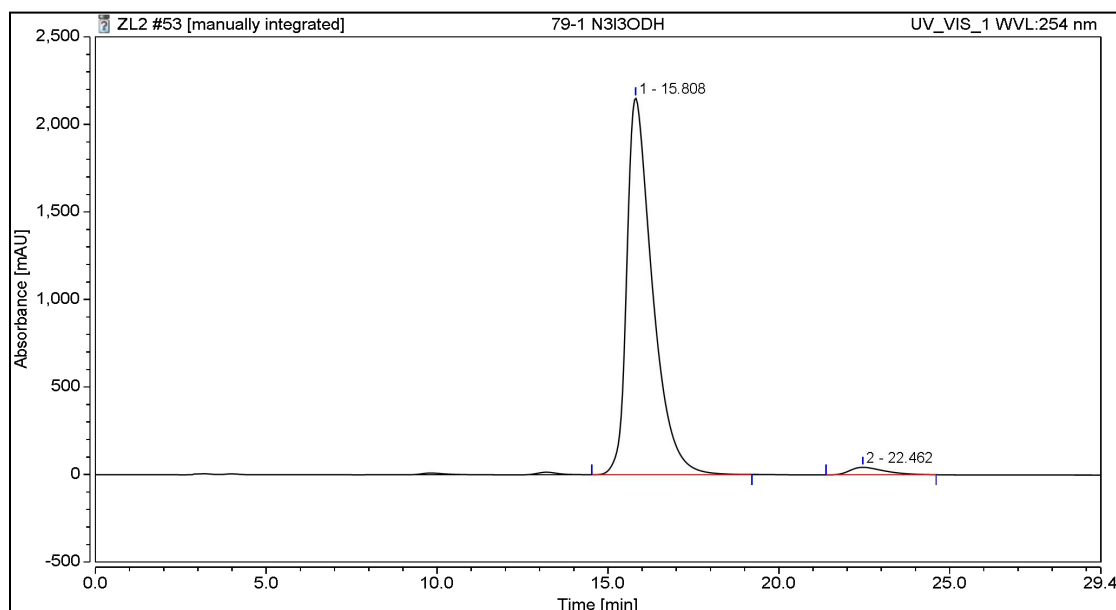
Integration Results						
No.	Peak Name	Retention Time min	Area mAU*min	Height mAU	Relative Area %	Relative Height %
1		13.187	1766.737	2393.232	99.22	99.56
2		20.355	13.822	10.461	0.78	0.44
Total:			1780.559	2403.694	100.00	100.00



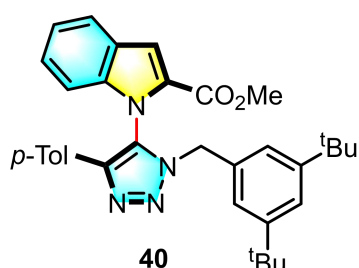
White solid, 53.4 mg, 92% yield, 97.5:2.5 er. [Chiral HPLC analysis of the product: Daicel Chiralcel OD-H 250X4.6 mm 5u column; *n*-hexane/2-propanol = 90/10, flow rate = 1.0 mL/min, λ = 254 nm, *t* (major) = 15.81 min, *t* (minor) = 22.46 min]. $[\alpha]_D^{25} = -83.5^\circ$ (*c* = 1.1, CHCl₃). **¹H NMR (500 MHz, CDCl₃)** δ 7.76 (d, *J* = 7.2 Hz, 1H), 7.58 (s, 1H), 7.33 (s, 1H), 7.24-7.18 (m, 4H), 6.99 (d, *J* = 8.1 Hz, 2H), 6.92 (d, *J* = 1.4 Hz, 2H), 6.58 (d, *J* = 8.1 Hz, 1H), 5.25 (d, *J* = 15.0 Hz, 1H), 5.09 (d, *J* = 15.0 Hz, 1H), 3.70 (s, 3H), 2.23 (s, 3H). **¹³C NMR (126 MHz, CDCl₃)** δ 160.6, 142.7, 139.1, 138.5, 136.8, 134.1, 130.2, 129.6, 128.3, 128.1, 127.2, 126.8, 126.4, 125.5, 123.2, 123.1, 123.0, 114.5, 110.6, 52.2, 51.3, 21.3. **HRMS (ESI, *m/z*)** Calcd for C₂₆H₂₁Br₂N₄O₂ (M+H)⁺: 579.0026, 581.0005; Found: 579.0040, 581.0004.



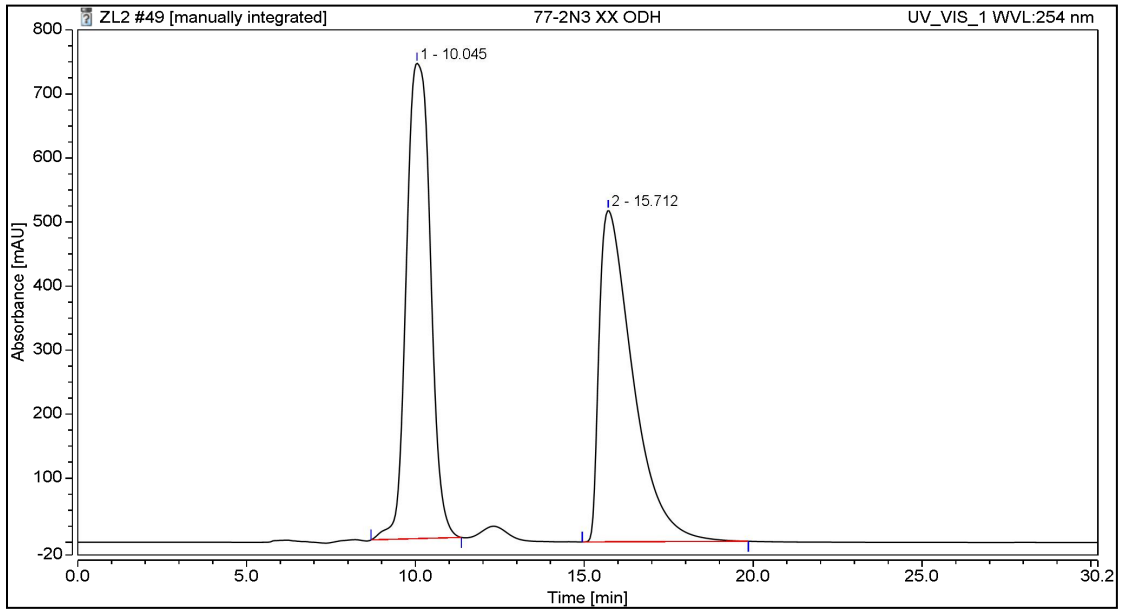
Integration Results						
No.	Peak Name	Retention Time min	Area mAU*min	Height mAU	Relative Area %	Relative Height %
1		16.092	269.912	335.744	50.83	61.08
2		21.653	261.144	213.906	49.17	38.92
Total:			531.056	549.651	100.00	100.00



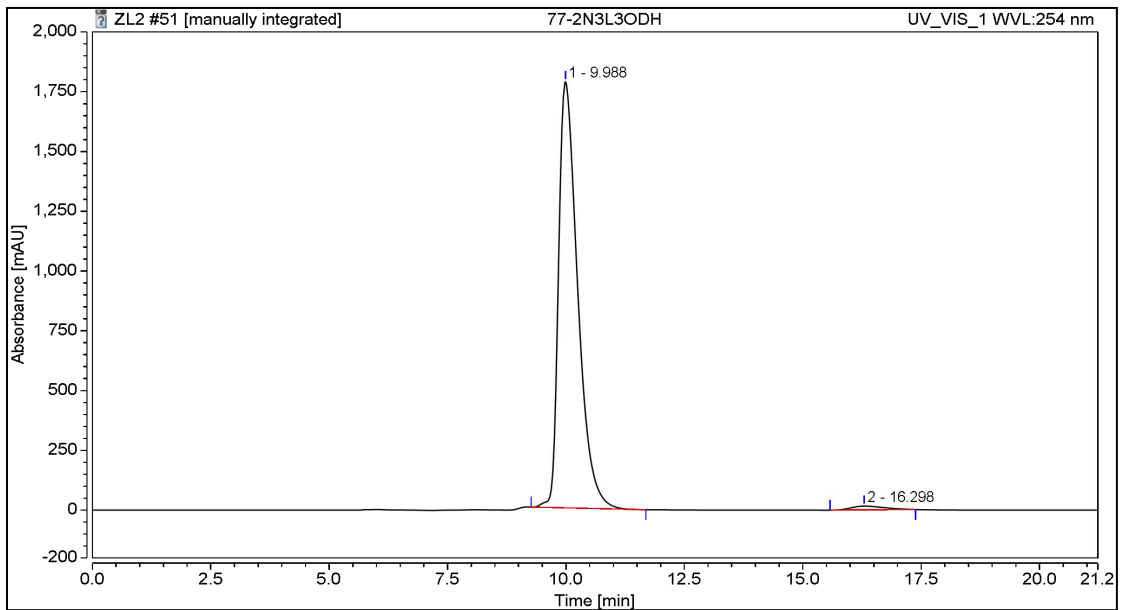
Integration Results						
No.	Peak Name	Retention Time min	Area mAU*min	Height mAU	Relative Area %	Relative Height %
1		15.808	1878.216	2154.039	97.36	98.04
2		22.462	50.939	43.067	2.64	1.96
Total:			1929.155	2197.106	100.00	100.00



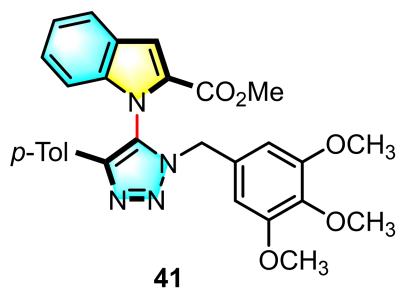
White solid, 48.5 mg, 91% yield, 98.5:1.5 er. [Chiral HPLC analysis of the product: Daicel Chiralcel OD-H 250X4.6 mm 5u column; *n*-hexane/2-propanol = 90/10, flow rate = 0.5 mL/min, λ = 254 nm, t (major) = 10.00 min, t (minor) = 16.30 min]. $[\alpha]_D^{26} = -217.8^\circ$ ($c = 0.9$, CHCl_3). $^1\text{H NMR}$ (500 MHz, CDCl_3) δ 7.69 (d, $J = 8.0$ Hz, 1H), 7.55 (s, 1H), 7.18-7.09 (m, 4H), 7.05 (t, $J = 8.1$ Hz, 1H), 6.95 (d, $J = 8.1$ Hz, 2H), 6.76 (d, $J = 1.6$ Hz, 2H), 6.47 (d, $J = 8.3$ Hz, 1H), 5.36 (d, $J = 14.7$ Hz, 1H), 5.18 (d, $J = 14.7$ Hz, 1H), 3.60 (s, 3H), 2.21 (s, 3H), 1.13 (s, 18H). $^{13}\text{C NMR}$ (126 MHz, CDCl_3) δ 160.6, 151.3, 142.3, 139.4, 138.1, 132.8, 129.5, 128.4, 128.3, 126.9, 126.8, 126.7, 125.3, 122.9, 122.7, 122.6, 122.4, 114.3, 111.1, 53.2, 52.0, 34.7, 31.3, 21.3. **HRMS (ESI, m/z)** Calcd for $\text{C}_{34}\text{H}_{39}\text{N}_4\text{O}_2$ ($\text{M}+\text{H}$) $^+$: 535.3068; Found: 535.3061.



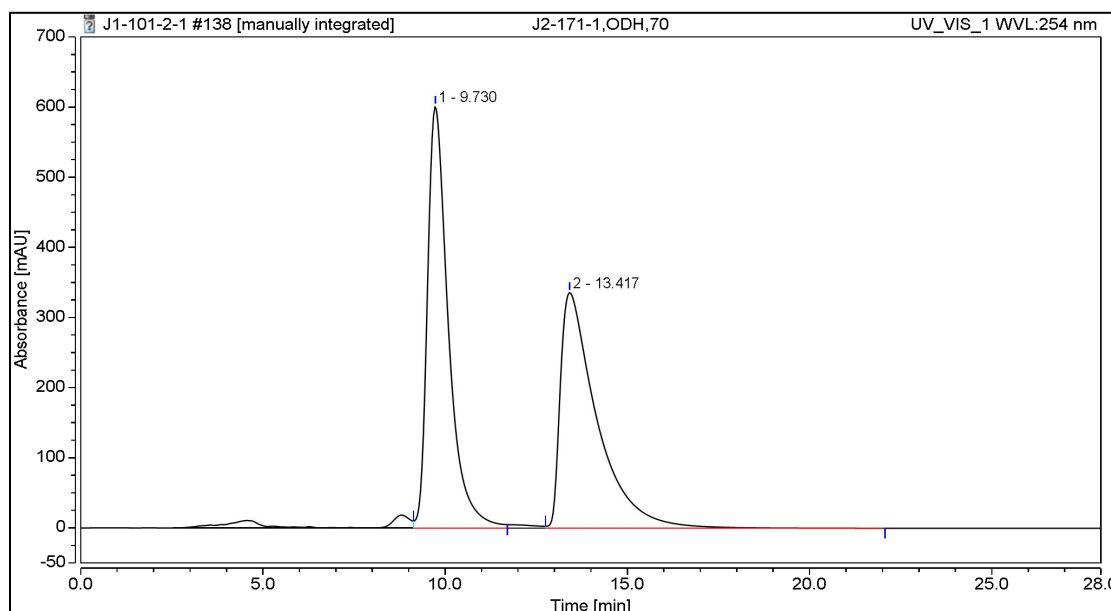
Integration Results						
No.	Peak Name	Retention Time min	Area mAU*min	Height mAU	Relative Area %	Relative Height %
1		10.045	617.997	742.478	50.79	58.92
2		15.712	598.722	517.649	49.21	41.08
Total:			1216.720	1260.126	100.00	100.00



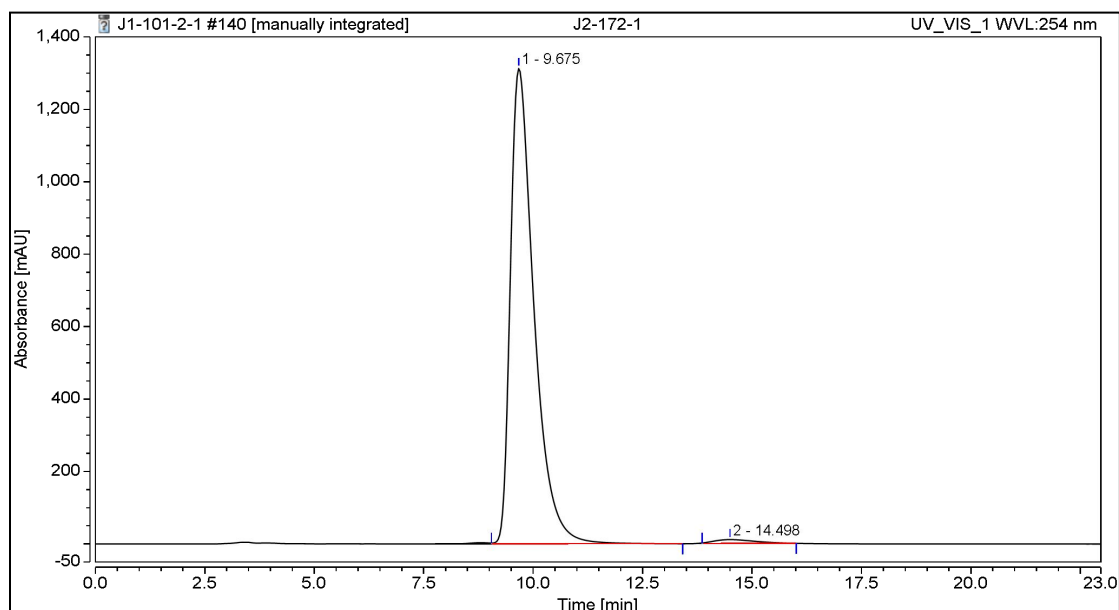
Integration Results						
No.	Peak Name	Retention Time min	Area mAU*min	Height mAU	Relative Area %	Relative Height %
1		9.988	833.985	1782.681	98.46	99.11
2		16.298	13.020	16.033	1.54	0.89
Total:			847.004	1798.713	100.00	100.00



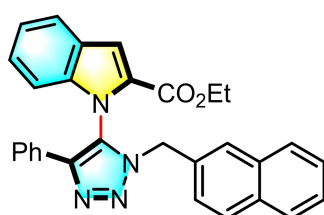
White solid, 40.1 mg, 88% yield, 98.5:1.5 er. [Chiral HPLC analysis of the product: Daicel Chiralcel OD-H 250X4.6 mm 5u column; *n*-hexane/2-propanol = 70/30, flow rate = 1.0 mL/min, λ = 254 nm, *t* (major) = 9.68 min, *t* (minor) = 14.50 min]. $[\alpha]_D^{26} = -102.3^\circ$ (*c* = 1.1, CHCl₃). **¹H NMR (500 MHz, CDCl₃)** δ 7.73 (d, *J* = 7.9 Hz, 1H), 7.53 (s, 1H), 7.23-7.13 (m, 4H), 6.97 (d, *J* = 8.1 Hz, 2H), 6.57 (d, *J* = 8.2 Hz, 1H), 6.05 (s, 2H), 5.22 (d, *J* = 14.7 Hz, 1H), 5.13 (d, *J* = 14.7 Hz, 1H), 3.70 (s, 3H), 3.66 (s, 3H), 3.58 (s, 6H), 2.22 (s, 3H). **¹³C NMR (126 MHz, CDCl₃)** δ 160.5, 153.2, 142.7, 139.4, 138.3, 138.1, 129.5, 128.8, 128.4, 128.1, 127.0, 126.7, 126.6, 125.4, 122.9, 122.8, 114.0, 111.1, 105.5, 60.8, 55.9, 53.0, 52.1, 21.3. **HRMS (ESI, *m/z*)** Calcd for C₂₉H₂₉N₄O₅ (M+H)⁺: 513.2132; Found: 513.2125.



Integration Results						
No.	Peak Name	Retention Time min	Area mAU*min	Height mAU	Relative Area %	Relative Height %
1		9.730	400.704	601.229	50.69	64.16
2		13.417	389.835	335.863	49.31	35.84
Total:			790.540	937.093	100.00	100.00

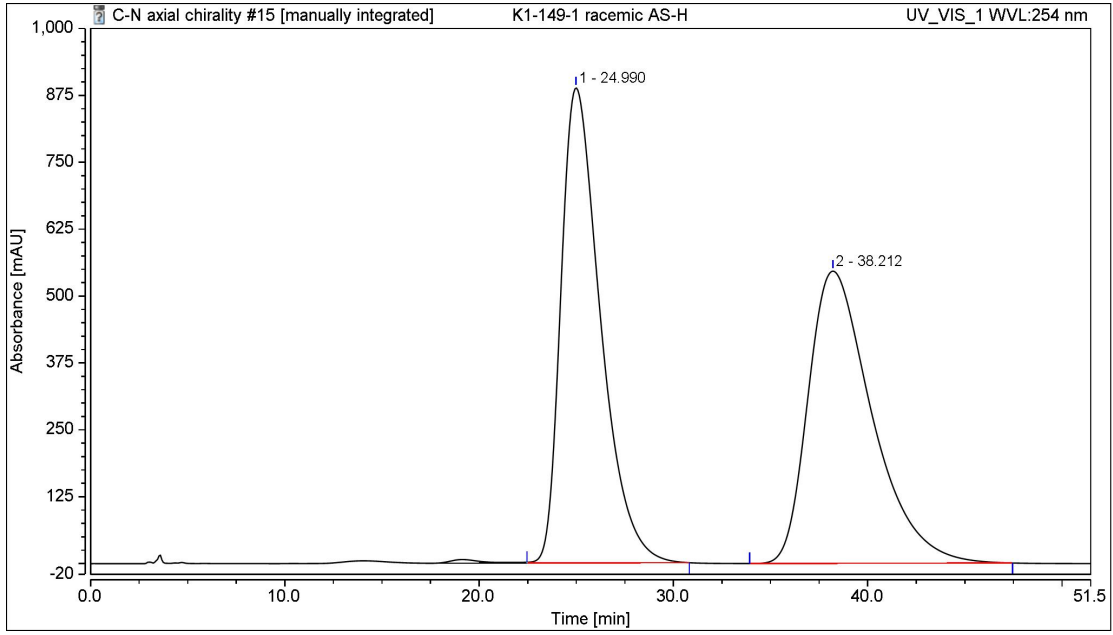


Integration Results						
No.	Peak Name	Retention Time min	Area mAU*min	Height mAU	Relative Area %	Relative Height %
1		9.675	818.613	1313.054	98.60	99.20
2		14.498	11.593	10.604	1.40	0.80
Total:			830.205	1323.658	100.00	100.00

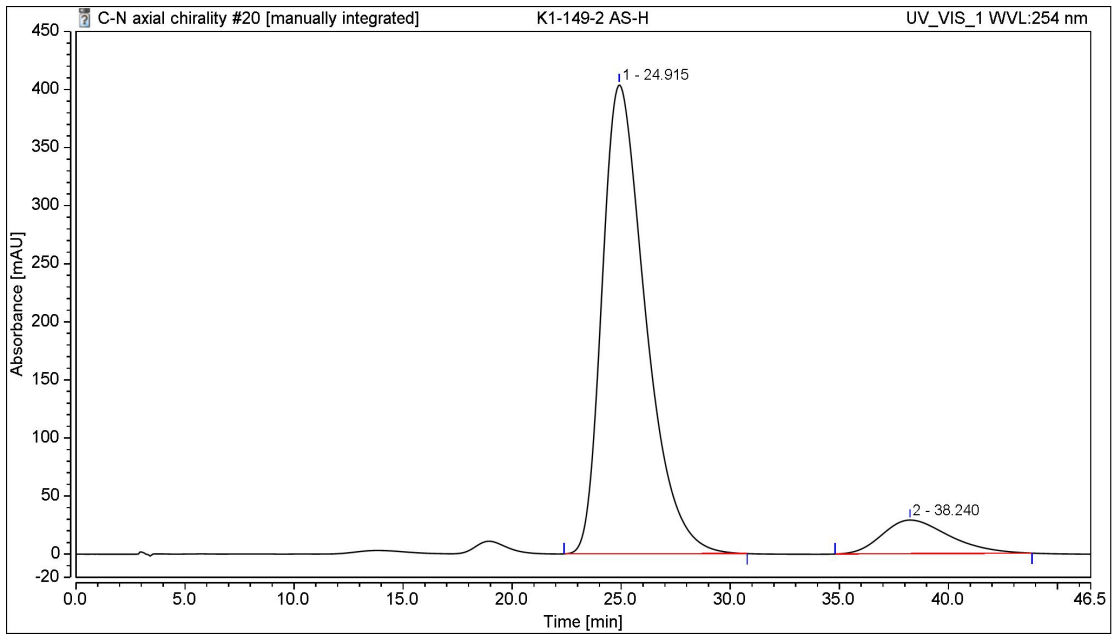


42

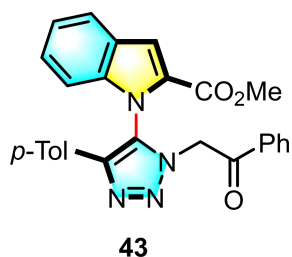
White solid, 43.5 mg, 92% yield, 90:10 er. [Chiral HPLC analysis of the product: Daicel Chiralpak AS-H 250X4.6 mm 5u column; *n*-hexane/2-propanol = 90/10, flow rate = 1.0 mL/min, λ = 254 nm, *t* (major) = 24.92 min, *t* (minor) = 38.24 min]. $[\alpha]_D^{26} = -20.0^\circ$ (*c* = 1.4, CHCl₃). **¹H NMR (500 MHz, CDCl₃)** δ 7.70 (d, *J* = 8.1 Hz, 2H), 7.61 (d, *J* = 8.4 Hz, 1H), 7.55 (s, 1H), 7.50 (dd, *J* = 7.3, 2.3 Hz, 1H), 7.44-7.38 (m, 2H), 7.36-7.31 (m, 2H), 7.21-7.14 (m, 4H), 7.13 (s, 1H), 7.09 (t, *J* = 7.6 Hz, 1H), 6.97 (t, *J* = 7.8 Hz, 1H), 6.56 (d, *J* = 8.4 Hz, 1H), 5.40 (d, *J* = 14.5 Hz, 1H), 5.34 (d, *J* = 14.5 Hz, 1H), 3.78 (q, *J* = 7.1 Hz, 2H), 0.96 (t, *J* = 7.2 Hz, 3H). **¹³C NMR (126 MHz, CDCl₃)** δ 158.8, 141.4, 138.1, 132.0, 131.8, 129.5, 128.4, 127.8, 127.8, 127.7, 127.5, 127.2, 126.8, 126.7, 126.4, 125.7, 125.7, 125.4, 125.2, 124.6, 124.4, 121.7, 121.5, 113.2, 109.7, 59.8, 51.6, 12.7. **HRMS (ESI, *m/z*)** Calcd for C₃₀H₂₅N₄O₂ (M+H)⁺: 473.1972; Found: 473.1953.



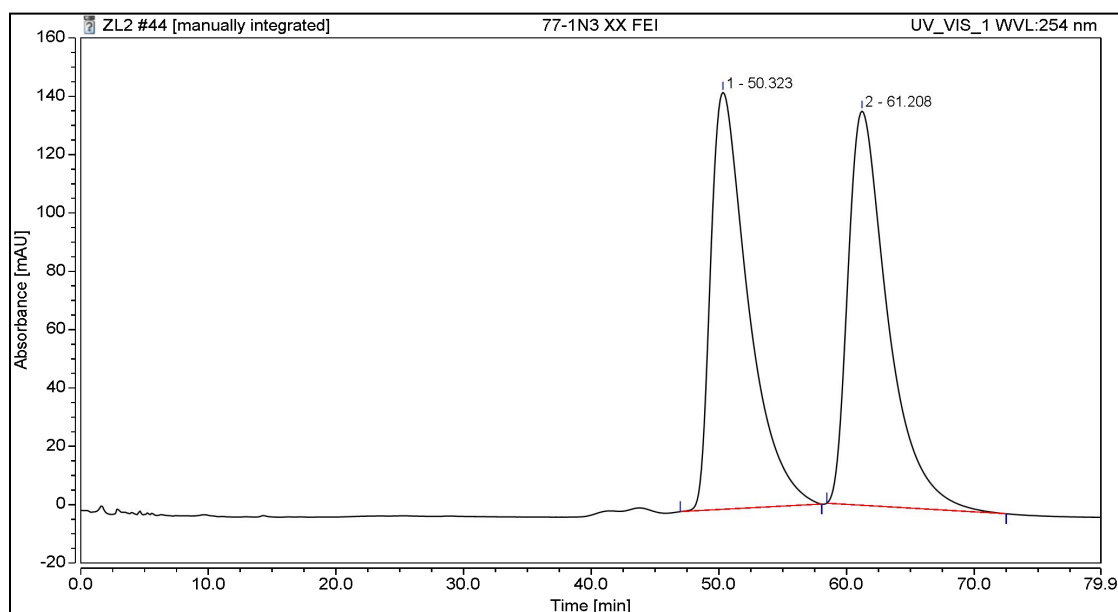
Integration Results						
No.	Peak Name	Retention Time min	Area mAU*min	Height mAU	Relative Area %	Relative Height %
1		24.990	2092.208	887.713	50.19	61.91
2		38.212	2076.071	546.119	49.81	38.09
Total:			4168.279	1433.832	100.00	100.00



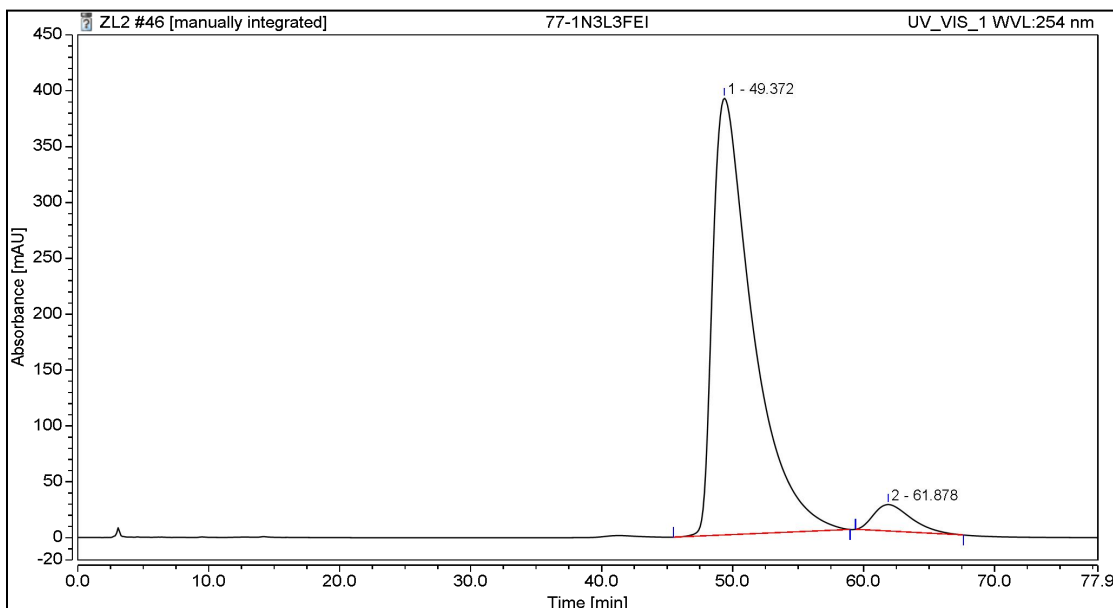
Integration Results						
No.	Peak Name	Retention Time min	Area mAU*min	Height mAU	Relative Area %	Relative Height %
1		24.915	930.720	403.730	90.02	93.30
2		38.240	103.138	28.973	9.98	6.70
Total:			1033.858	432.703	100.00	100.00



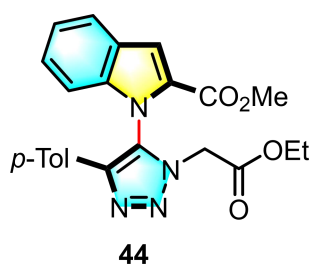
White solid, 39.6 mg, 88% yield, 94.5:5.5 er. [Chiral HPLC analysis of the product: Phenomenex 00G-4457-E0 250X4.6 mm 5u column; *n*-hexane/2-propanol = 80/20, flow rate = 1.0 mL/min, λ = 254 nm, *t* (major) = 49.37 min, *t* (minor) = 61.88 min]. $[\alpha]_D^{26} = -65.6^\circ$ (*c* = 0.9, CHCl₃). **¹H NMR (500 MHz, CDCl₃)** δ 7.77 (d, *J* = 7.6 Hz, 2H), 7.69 (d, *J* = 7.9 Hz, 1H), 7.58-7.52 (m, 2H), 7.40 (t, *J* = 7.8 Hz, 2H), 7.29 (d, *J* = 7.8 Hz, 1H), 7.21 (t, *J* = 7.5 Hz, 1H), 7.12 (d, *J* = 8.3 Hz, 1H), 7.06 (d, *J* = 8.1 Hz, 2H), 6.96 (d, *J* = 8.1 Hz, 2H), 5.88 (d, *J* = 17.5 Hz, 1H), 5.44 (d, *J* = 17.5 Hz, 1H), 3.78 (s, 3H), 2.22 (s, 3H). **¹³C NMR (126 MHz, CDCl₃)** δ 189.9, 161.1, 142.2, 140.2, 138.3, 134.3, 134.2, 129.7, 129.5, 129.0, 128.6, 128.2, 127.4, 127.1, 126.5, 125.4, 123.0, 122.8, 115.0, 112.5, 53.7, 52.3, 21.3. **HRMS (ESI, *m/z*)** Calcd for C₂₇H₂₃N₄O₃ (M+H)⁺: 451.1765; Found: 451.1751.



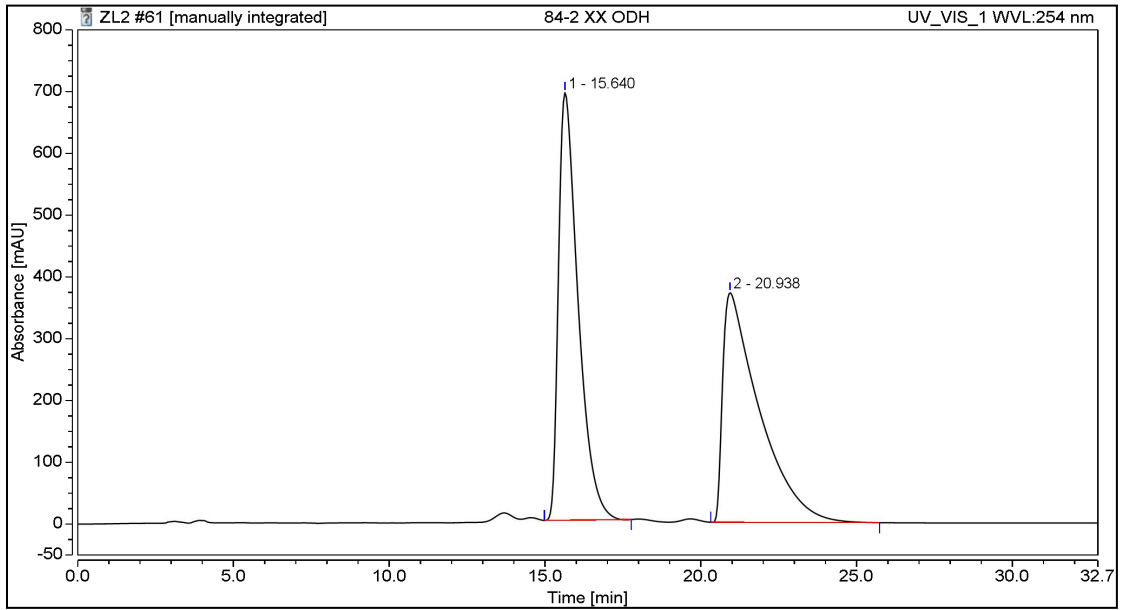
Integration Results						
No.	Peak Name	Retention Time min	Area mAU*min	Height mAU	Relative Area %	Relative Height %
1		50.323	487.913	142.939	49.92	51.40
2		61.208	489.410	135.125	50.08	48.60
Total:			977.323	278.064	100.00	100.00



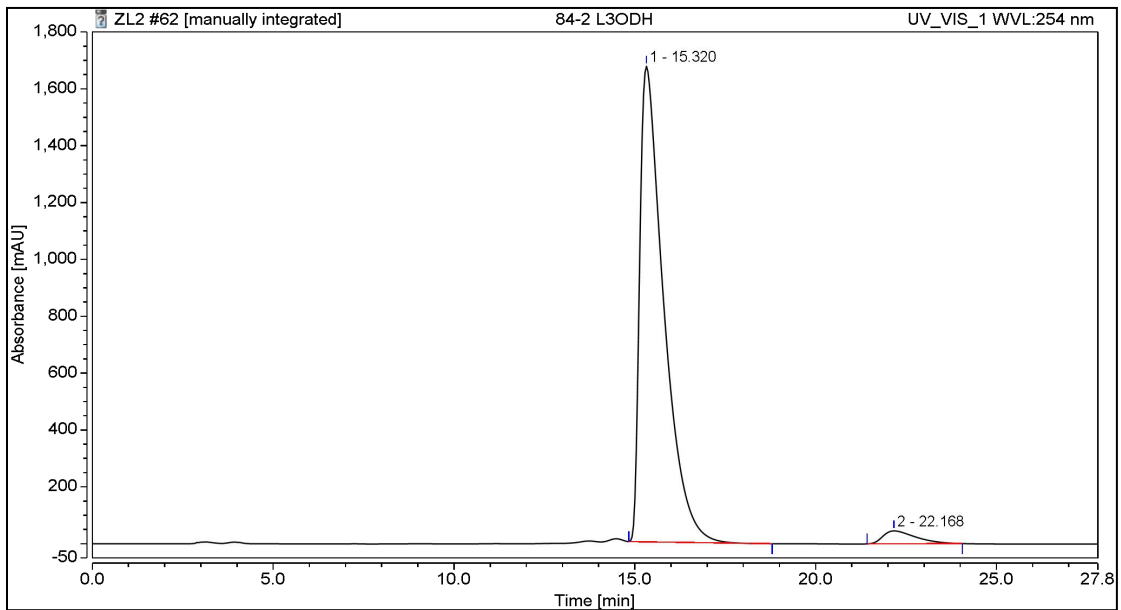
Integration Results						
No.	Peak Name	Retention Time min	Area mAU*min	Height mAU	Relative Area %	Relative Height %
1		49.372	1384.856	390.914	94.60	94.29
2		61.878	78.994	23.662	5.40	5.71
Total:			1463.850	414.576	100.00	100.00



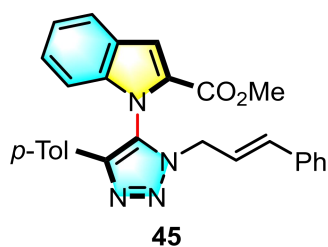
White solid, 37.2 mg, 89% yield, 96.5:3.5 er. [Chiral HPLC analysis of the product: Daicel Chiralcel OD-H 250X4.6 mm 5u column; *n*-hexane/2-propanol = 90/10, flow rate = 1.0 mL/min, λ = 254 nm, t (major) = 15.32 min, t (minor) = 22.17 min]. $[\alpha]_D^{26} = -243.2^\circ$ ($c = 1.0$, CHCl_3). $^1\text{H NMR}$ (500 MHz, CDCl_3) δ 7.76 (d, $J = 7.6$ Hz, 1H), 7.60 (s, 1H), 7.31-7.23 (m, 2H), 7.08 (d, $J = 8.2$ Hz, 2H), 7.04 (d, $J = 7.5$ Hz, 1H), 6.97 (d, $J = 8.1$ Hz, 2H), 5.12 (d, $J = 17.4$ Hz, 1H), 4.77 (d, $J = 17.4$ Hz, 1H), 3.98 (q, $J = 7.1$ Hz, 2H), 3.77 (s, 3H), 2.22 (s, 3H), 1.07 (t, $J = 7.1$ Hz, 3H). $^{13}\text{C NMR}$ (126 MHz, CDCl_3) δ 165.8, 161.0, 142.0, 139.9, 138.4, 129.5, 129.1, 128.5, 127.2, 127.1, 126.3, 125.4, 123.1, 123.0, 114.9, 112.2, 62.4, 52.3, 48.8, 21.3, 13.9. **HRMS (ESI, m/z)** Calcd for $\text{C}_{23}\text{H}_{23}\text{N}_4\text{O}_4$ ($\text{M}+\text{H}$) $^+$: 419.1714; Found: 419.1716.



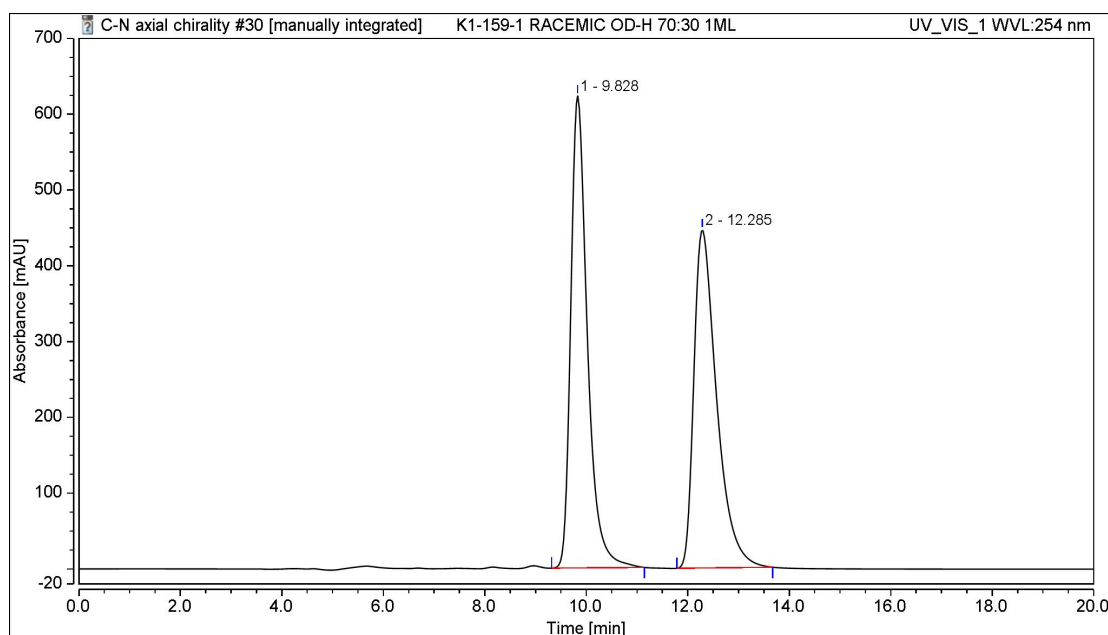
Integration Results						
No.	Peak Name	Retention Time min	Area mAU*min	Height mAU	Relative Area %	Relative Height %
1		15.640	505.521	692.498	49.99	65.07
2		20.938	505.726	371.810	50.01	34.93
Total:			1011.248	1064.308	100.00	100.00



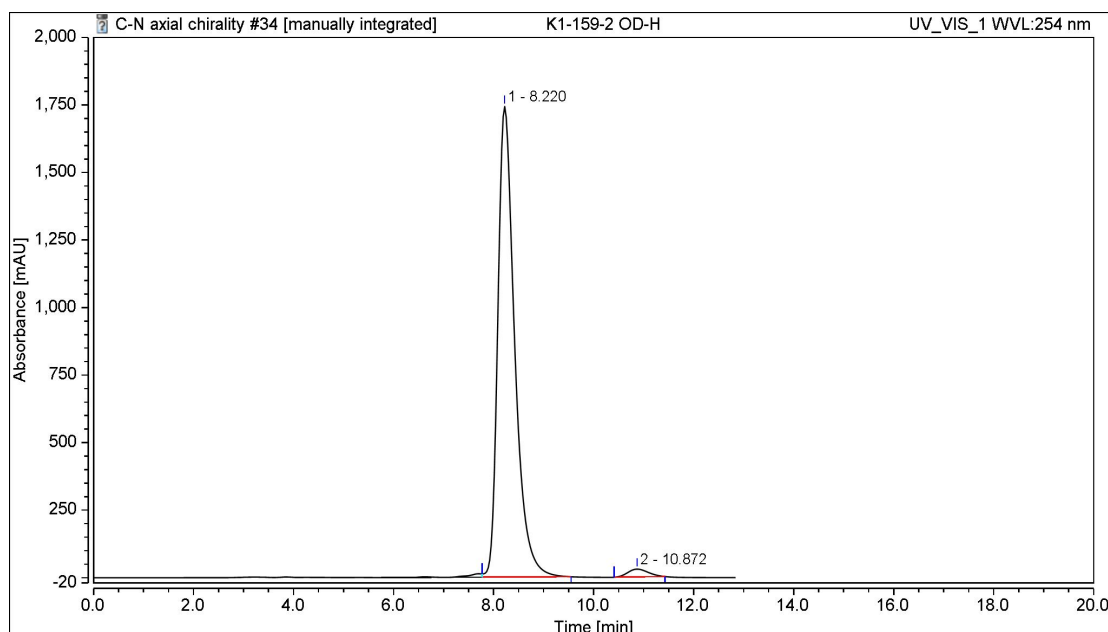
Integration Results						
No.	Peak Name	Retention Time min	Area mAU*min	Height mAU	Relative Area %	Relative Height %
1		15.320	1283.973	1672.974	96.44	97.35
2		22.168	47.369	45.458	3.56	2.65
Total:			1331.341	1718.433	100.00	100.00



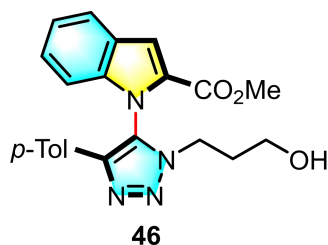
White solid, 43.5 mg, 97% yield, 98:2 er. [Chiral HPLC analysis of the product: Daicel Chiralcel OD-H 250X4.6 mm 5u column; n-hexane/2-propanol = 70/30, flow rate = 1.0 mL/min, $\lambda = 254$ nm, t (major) = 8.22 min, t (minor) = 10.87 min]. $[\alpha]_D^{23} = -72.3^\circ$ (c = 1.4, CHCl₃) **¹H NMR (500 MHz, CDCl₃)** δ 7.75 (d, *J* = 6.7 Hz, 1H), 7.56 (s, 1H), 7.27-7.19 (m, 7H), 7.05 (dd, *J* = 7.5, 2.1 Hz, 2H), 7.00 (d, *J* = 8.2 Hz, 2H), 6.91 (d, *J* = 8.1 Hz, 1H), 6.11-6.01 (m, 2H), 4.90-4.83 (m, 1H), 4.81-4.74 (m, 1H), 3.59 (s, 3H), 2.24 (s, 3H). **¹³C NMR (126 MHz, CDCl₃)** δ 159.6, 141.3, 138.5, 137.1, 134.4, 134.1, 128.4, 127.5, 127.4, 127.2, 126.1, 125.9, 125.6, 125.5, 124.3, 122.0, 121.7, 120.1, 113.1, 110.1, 50.9, 49.5, 20.2. **HRMS (ESI, m/z)** Calcd for C₂₈H₂₅N₄O₂ (M+H)⁺: 449.1972; Found: 449.1968.



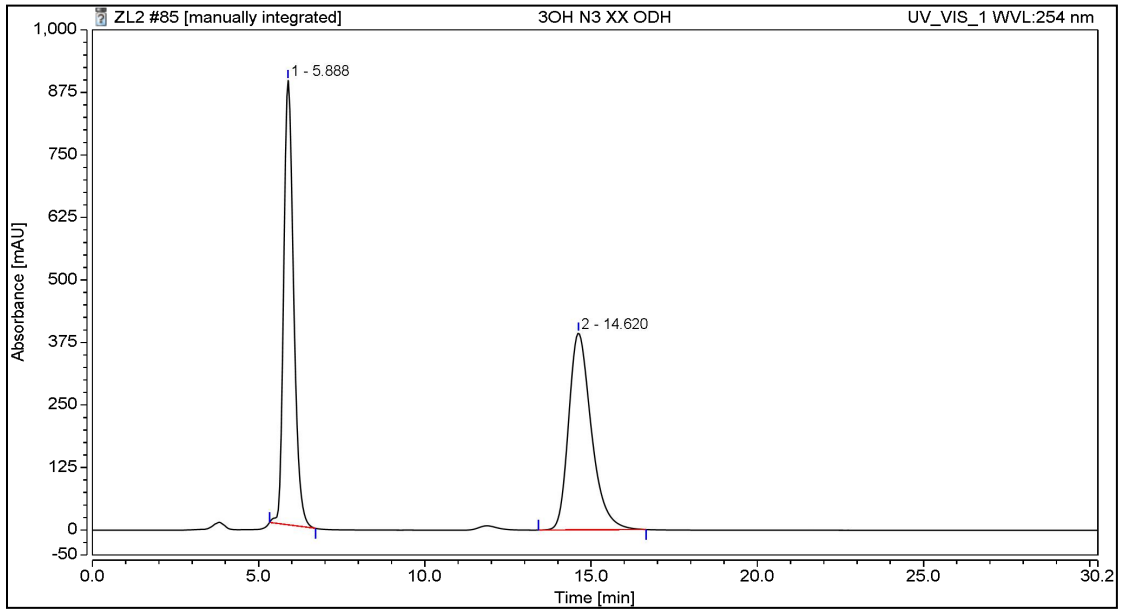
Integration Results						
No.	Peak Name	Retention Time min	Area mAU*min	Height mAU	Relative Area %	Relative Height %
1		9.828	235.733	622.749	50.47	58.26
2		12.285	231.329	446.203	49.53	41.74
Total:			467.062	1068.953	100.00	100.00



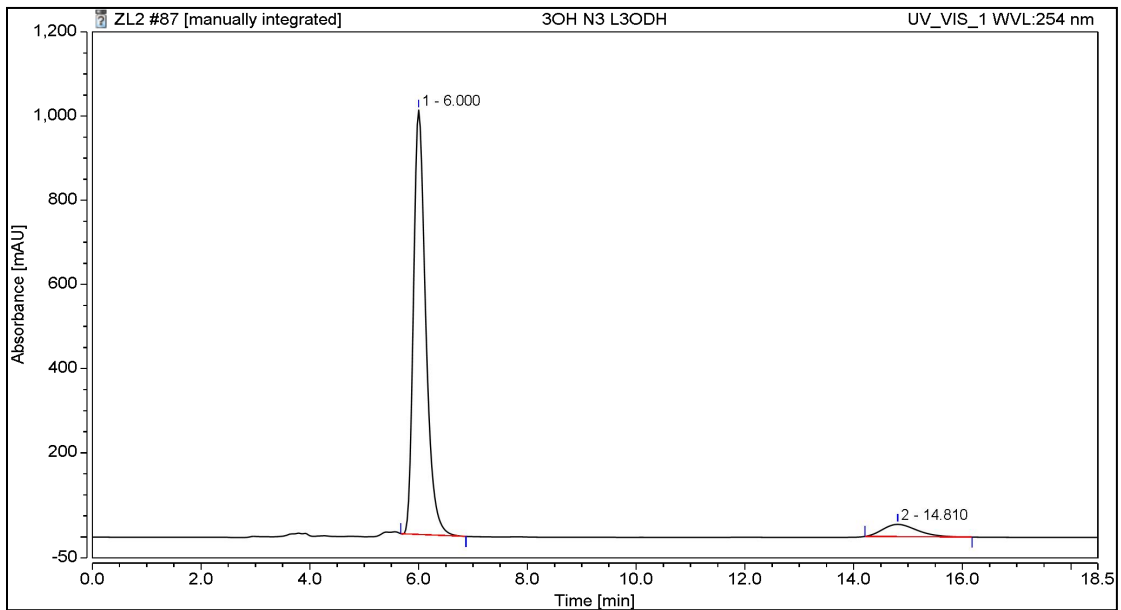
Integration Results						
No.	Peak Name	Retention Time min	Area mAU*min	Height mAU	Relative Area %	Relative Height %
1		8.220	678.279	1742.082	98.01	98.36
2		10.872	13.744	29.019	1.99	1.64
Total:			692.023	1771.101	100.00	100.00



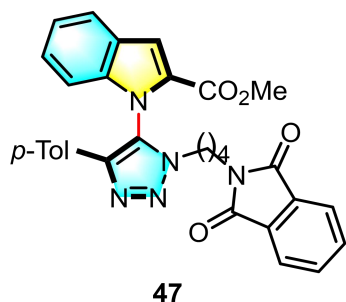
White solid, 32.7 mg, 84% yield, 92.5:7.5 er. [Chiral HPLC analysis of the product: Daicel Chiralcel OD-H 250X4.6 mm 5u column; *n*-hexane/2-propanol = 70/30, flow rate = 1.0 mL/min, λ = 254 nm, t (major) = 6.00 min, t (minor) = 14.81 min]. $[\alpha]_D^{26} = -262.3^\circ$ ($c = 0.9$, CHCl_3). **$^1\text{H NMR}$ (500 MHz, CDCl_3)** δ 7.79 (d, $J = 7.5$ Hz, 1H), 7.61 (s, 1H), 7.34-7.26 (m, 2H), 7.11 (d, $J = 8.2$ Hz, 2H), 6.97 (d, $J = 8.0$ Hz, 2H), 6.92 (d, $J = 7.4$ Hz, 1H), 4.24-4.08 (m, 2H), 3.74 (s, 3H), 3.64 (t, $J = 5.8$ Hz, 2H), 2.22 (s, 3H), 2.06-1.93 (m, 2H). **$^{13}\text{C NMR}$ (126 MHz, CDCl_3)** δ 161.0, 142.0, 139.8, 138.3, 129.5, 128.6, 128.5, 127.4, 127.1, 126.5, 125.3, 123.3, 123.0, 114.6, 111.0, 59.0, 52.3, 44.5, 31.5, 21.3. **HRMS (ESI, m/z)** Calcd for $\text{C}_{22}\text{H}_{23}\text{N}_4\text{O}_3$ ($\text{M}+\text{H}$) $^+$: 391.1765; Found: 391.1741.



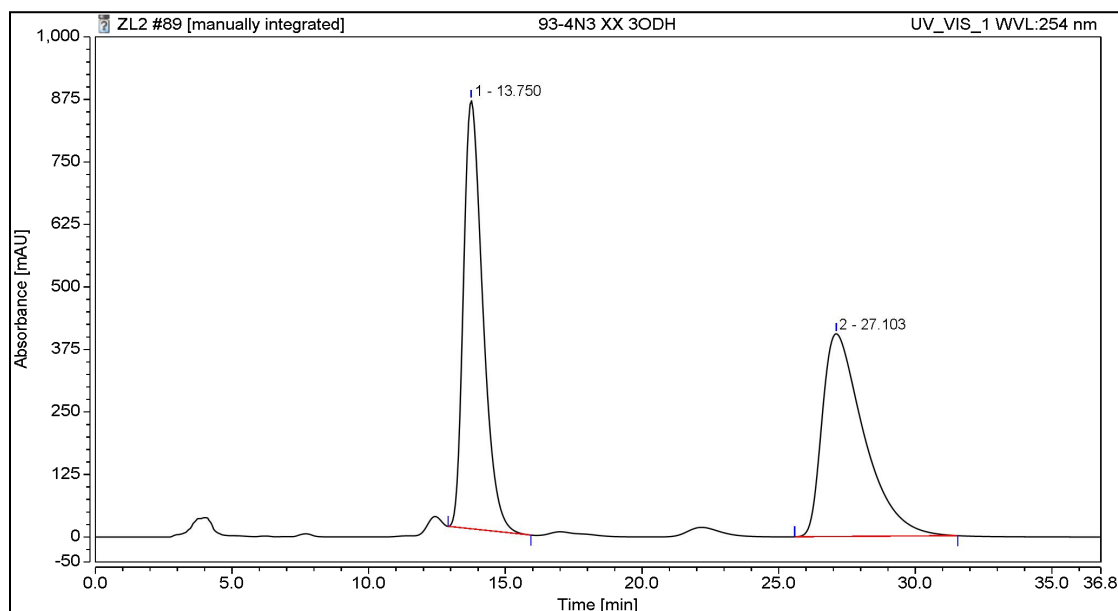
Integration Results						
No.	Peak Name	Retention Time min	Area mAU*min	Height mAU	Relative Area %	Relative Height %
1		5.888	309.027	888.528	49.75	69.31
2		14.620	312.108	393.503	50.25	30.69
Total:			621.135	1282.032	100.00	100.00



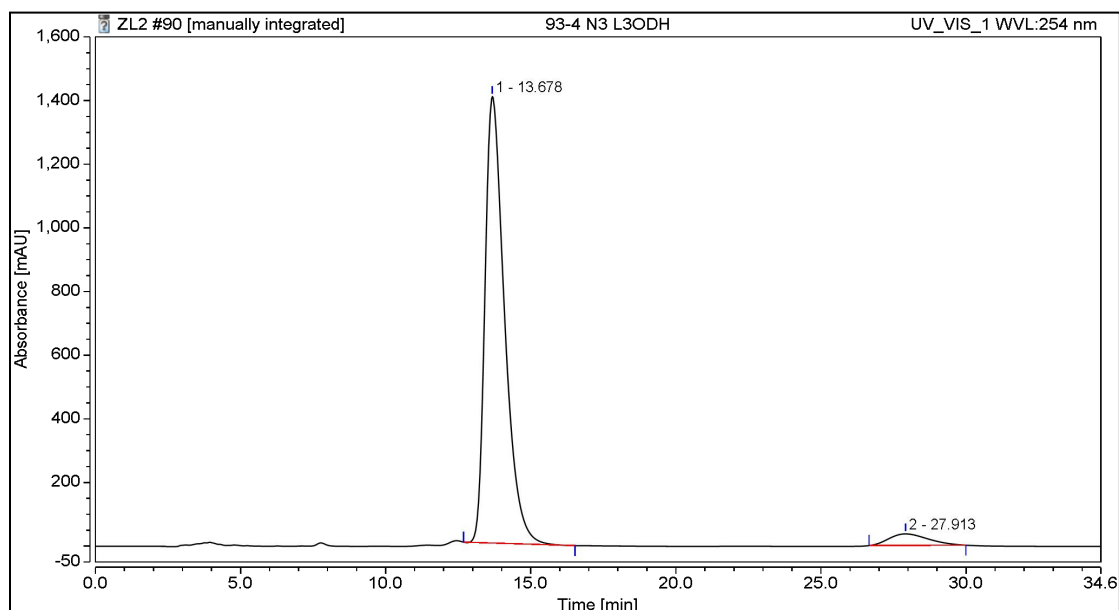
Integration Results						
No.	Peak Name	Retention Time min	Area mAU*min	Height mAU	Relative Area %	Relative Height %
1		6.000	263.287	1008.657	92.48	97.19
2		14.810	21.400	29.125	7.52	2.81
Total:			284.687	1037.782	100.00	100.00



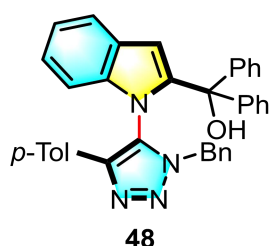
White solid, 46.3 mg, 87% yield, 95:5 er. [Chiral HPLC analysis of the product: Daicel Chiralcel OD-H 250X4.6 mm 5u column; *n*-hexane/2-propanol = 70/30, flow rate = 1.0 mL/min, λ = 254 nm, t (major) = 13.68 min, t (minor) = 27.91 min]. $[\alpha]_D^{26} = -184.4^\circ$ ($c = 1.2$, CHCl_3). **$^1\text{H NMR}$ (500 MHz, CDCl_3)** δ 7.79 (dd, $J = 5.2, 3.1$ Hz, 2H), 7.75 (d, $J = 7.9$ Hz, 1H), 7.70 (dd, $J = 5.3, 3.0$ Hz, 2H), 7.59 (s, 1H), 7.26 (t, $J = 7.5$ Hz, 1H), 7.20 (t, $J = 7.4$ Hz, 1H), 7.11 (d, $J = 8.0$ Hz, 2H), 6.96 (d, $J = 8.0$ Hz, 2H), 6.89 (d, $J = 8.2$ Hz, 1H), 4.17-4.01 (m, 2H), 3.75 (s, 3H), 3.56 (t, $J = 6.7$ Hz, 2H), 2.22 (s, 3H), 1.80-1.59 (m, 4H). **$^{13}\text{C NMR}$ (126 MHz, CDCl_3)** δ 168.3, 160.8, 142.0, 139.7, 138.2, 134.0, 132.1, 129.5, 128.5, 128.3, 127.4, 127.0, 126.7, 125.4, 123.3, 123.2, 122.9, 114.5, 111.0, 52.2, 47.3, 37.0, 26.4, 25.7, 21.3. **HRMS (ESI, m/z)** Calcd for $\text{C}_{31}\text{H}_{28}\text{N}_5\text{O}_4$ ($\text{M}+\text{H}$) $^+$: 534.2136; Found: 534.2131.



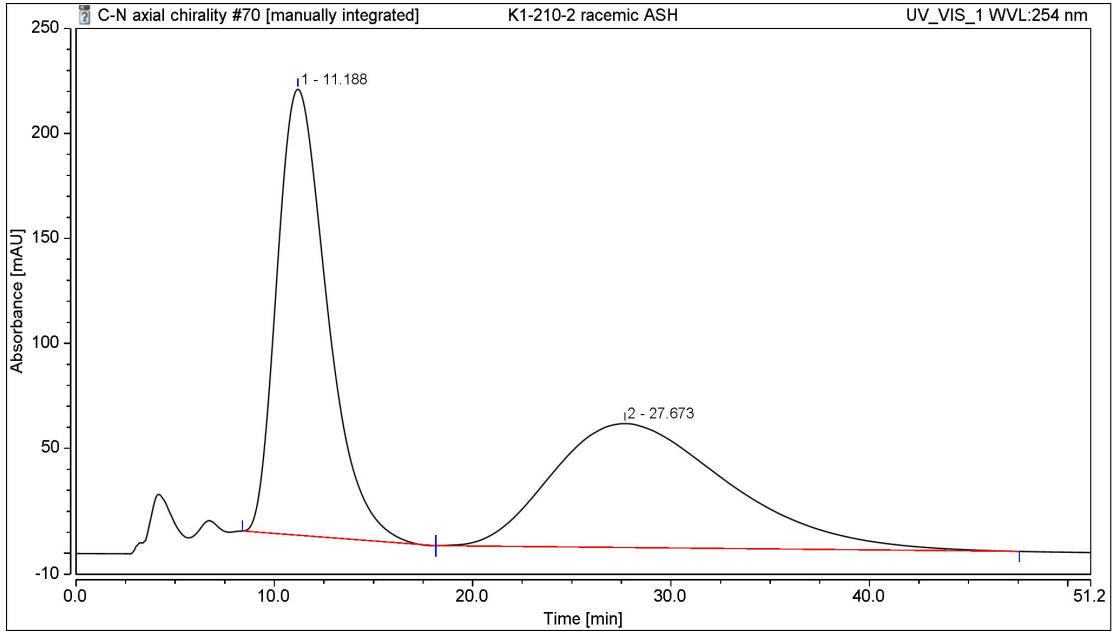
Integration Results						
No.	Peak Name	Retention Time min	Area mAU*min	Height mAU	Relative Area %	Relative Height %
1		13.750	703.499	856.581	49.51	67.87
2		27.103	717.504	405.582	50.49	32.13
Total:			1421.003	1262.163	100.00	100.00



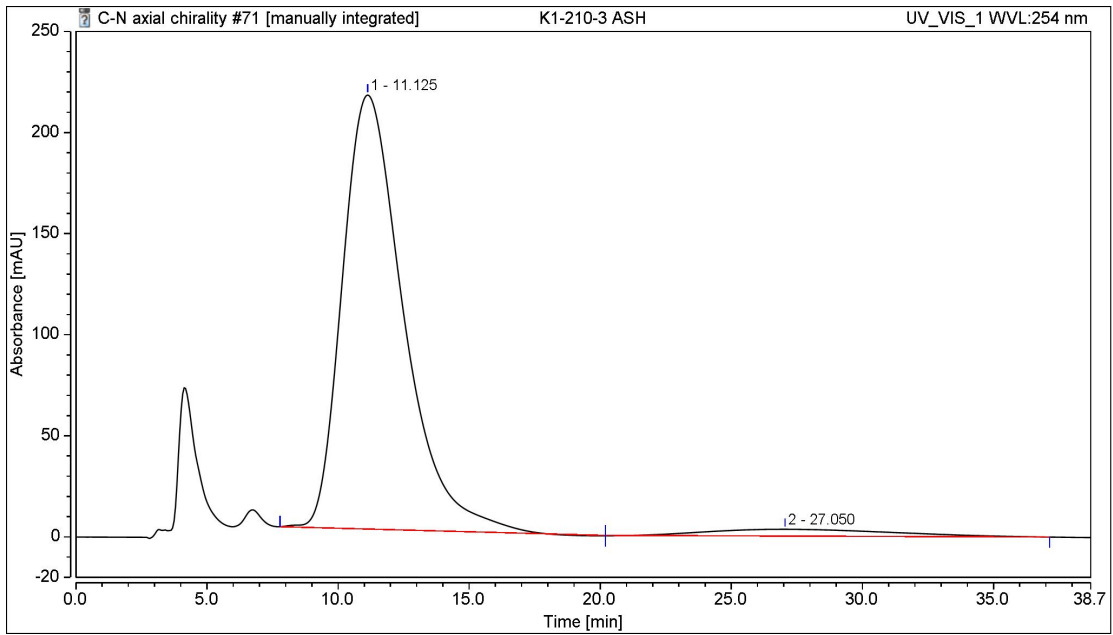
Integration Results						
No.	Peak Name	Retention Time min	Area mAU*min	Height mAU	Relative Area %	Relative Height %
1		13.678	1095.763	1403.428	95.06	97.48
2		27.913	56.923	36.334	4.94	2.52
Total:			1152.686	1439.761	100.00	100.00



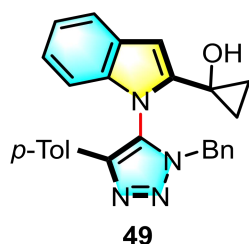
White solid, 41.5 mg, 76% yield, 95.5:4.5 er. [Chiral HPLC analysis of the product: Daicel Chiralpak AS-H 250X4.6 mm 5u column; *n*-hexane/2-propanol = 80/20, flow rate = 1.0 mL/min, λ = 254 nm, t (major) = 11.12 min, t (minor) = 27.05 min]. $[\alpha]_D^{26} = -7.8^\circ$ ($c = 1.2$, CHCl_3). **$^1\text{H NMR}$ (500 MHz, CDCl_3)** δ 7.53 (d, $J = 7.9$ Hz, 1H), 7.43-7.34 (m, 5H), 7.13-6.96 (m, 11H), 6.92-6.80 (m, 5H), 6.28 (s, 1H), 6.21 (d, $J = 8.2$ Hz, 1H), 5.10 (d, $J = 15.0$ Hz, 1H), 4.55 (d, $J = 15.0$ Hz, 1H), 2.63 (s, 1H), 2.26 (s, 3H). **$^{13}\text{C NMR}$ (126 MHz, CDCl_3)** δ 144.8, 144.5, 143.4, 142.8, 139.6, 137.7, 134.1, 129.1, 128.9, 128.6, 128.4, 128.3, 128.3, 128.2, 127.9, 127.9, 127.8, 127.0, 126.0, 123.8, 121.5, 120.9, 110.6, 109.1, 79.4, 51.6, 21.3. **HRMS (ESI, m/z)** Calcd for $\text{C}_{37}\text{H}_{31}\text{N}_4\text{O}$ ($\text{M}+\text{H}$) $^+$: 547.2492; Found: 547.2478.



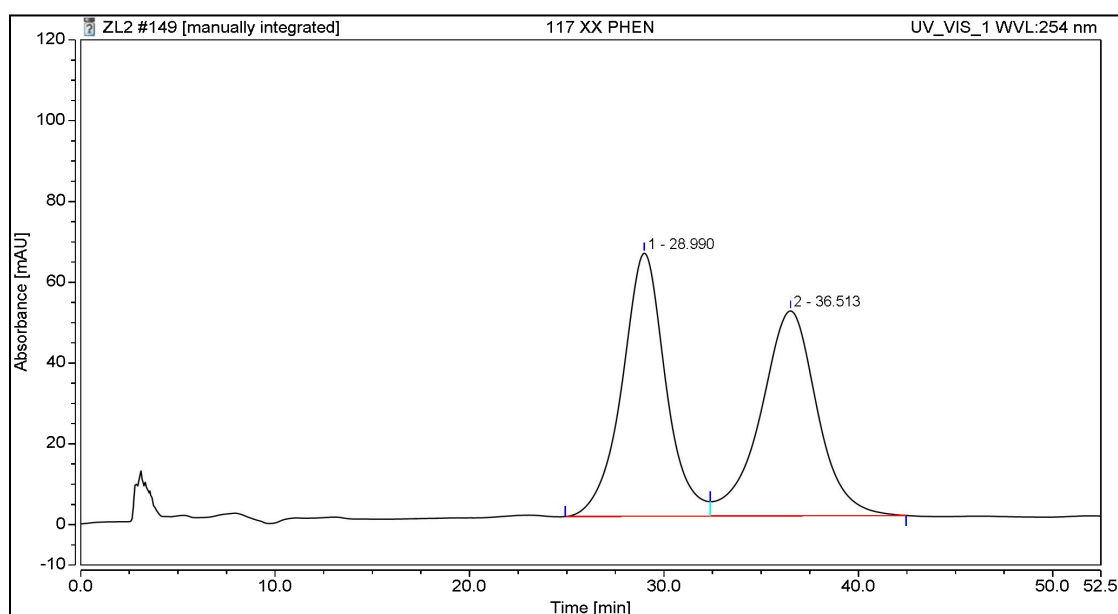
Integration Results						
No.	Peak Name	Retention Time min	Area mAU*min	Height mAU	Relative Area %	Relative Height %
1		11.188	623.547	212.448	50.57	78.26
2		27.673	609.601	59.025	49.43	21.74
Total:			1233.148	271.473	100.00	100.00



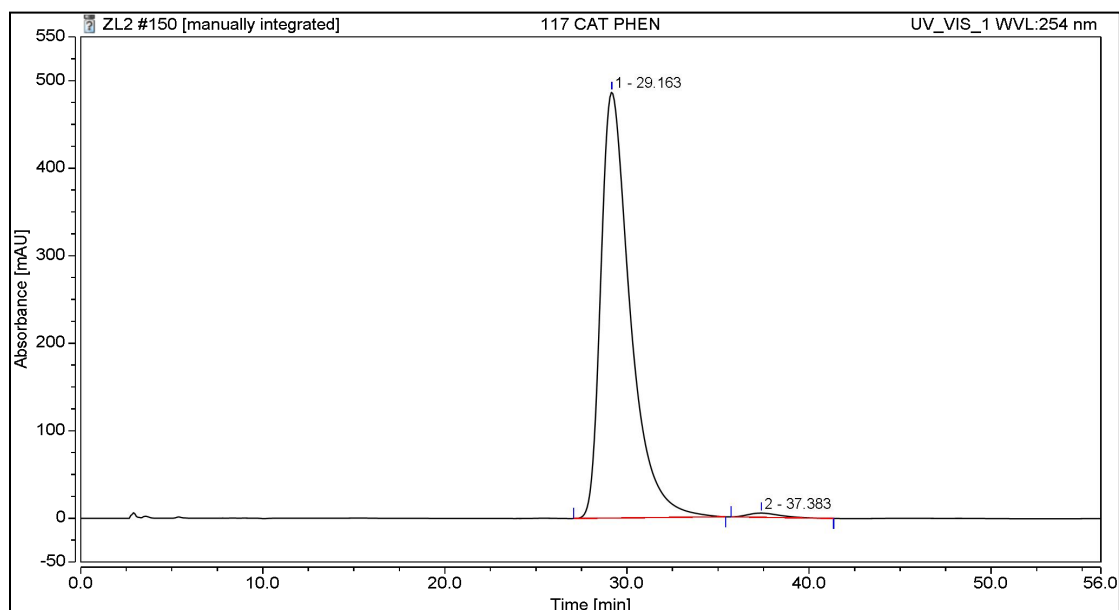
Integration Results						
No.	Peak Name	Retention Time min	Area mAU*min	Height mAU	Relative Area %	Relative Height %
1		11.125	579.613	214.700	95.45	98.45
2		27.050	27.658	3.380	4.55	1.55
Total:			607.271	218.080	100.00	100.00



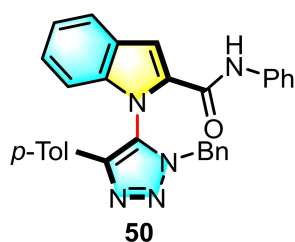
White solid, 18.6 mg, 43% yield, 99:1 er. [Chiral HPLC analysis of the product: Phenomenex 00G-4457-E0 250X4.6 mm 5u column; *n*-hexane/2-propanol = 90/10, flow rate = 1.0 mL/min, λ = 254 nm, *t* (major) = 29.16 min, *t* (minor) = 37.38 min]. $[\alpha]_D^{26} = -75.9^\circ$ (*c* = 0.5, CHCl₃). ¹H NMR (500 MHz, CDCl₃) δ 7.60 (d, *J* = 7.9 Hz, 1H), 7.16-7.10 (m, 4H), 7.06 (t, *J* = 7.6 Hz, 2H), 6.97 (d, *J* = 8.1 Hz, 2H), 6.94-6.86 (m, 3H), 6.63 (s, 1H), 6.38 (d, *J* = 8.2 Hz, 1H), 5.31 (d, *J* = 15.0 Hz, 1H), 5.27 (d, *J* = 15.0 Hz, 1H), 3.72 (s, 1H), 2.22 (s, 3H), 1.09-1.04 (m, 1H), 1.02-0.94 (m, 2H), 0.52-0.45 (m, 1H). ¹³C NMR (126 MHz, CDCl₃) δ 142.7, 142.2, 138.4, 133.9, 129.6, 128.8, 128.7, 128.6, 128.5, 127.8, 126.7, 125.6, 123.6, 121.5, 121.1, 110.1, 103.9, 52.4, 50.5, 21.3, 15.9, 14.0. HRMS (ESI, *m/z*) Calcd for C₂₇H₂₅N₄O (M+H)⁺: 421.2023; Found: 421.2033.



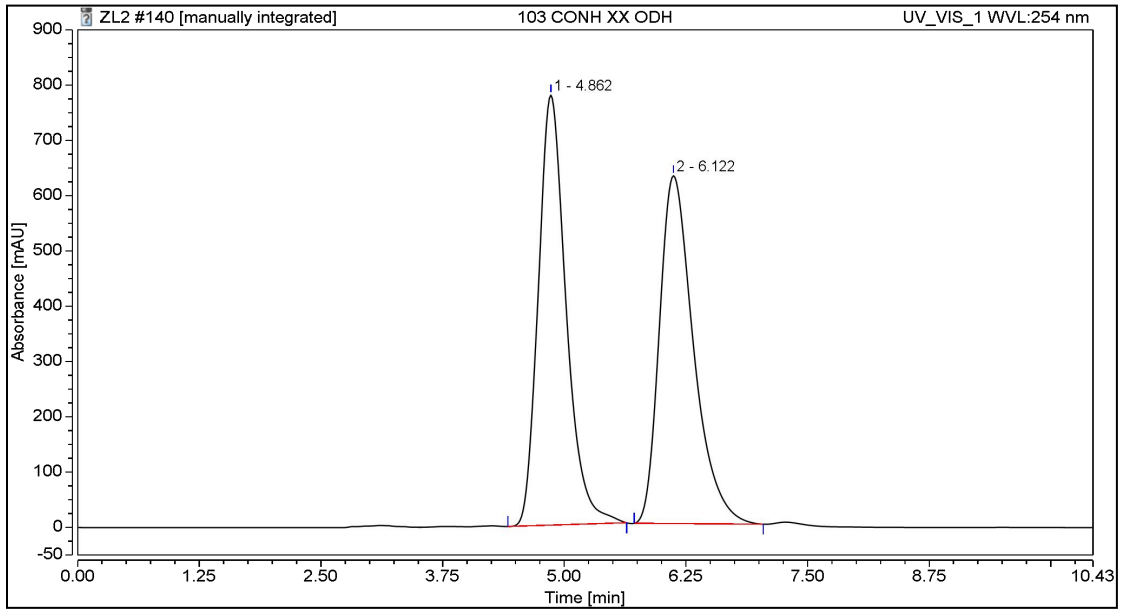
Integration Results						
No.	Peak Name	Retention Time min	Area mAU*min	Height mAU	Relative Area %	Relative Height %
1		28.990	169.456	65.153	49.87	56.22
2		36.513	170.320	50.746	50.13	43.78
Total:			339.777	115.899	100.00	100.00



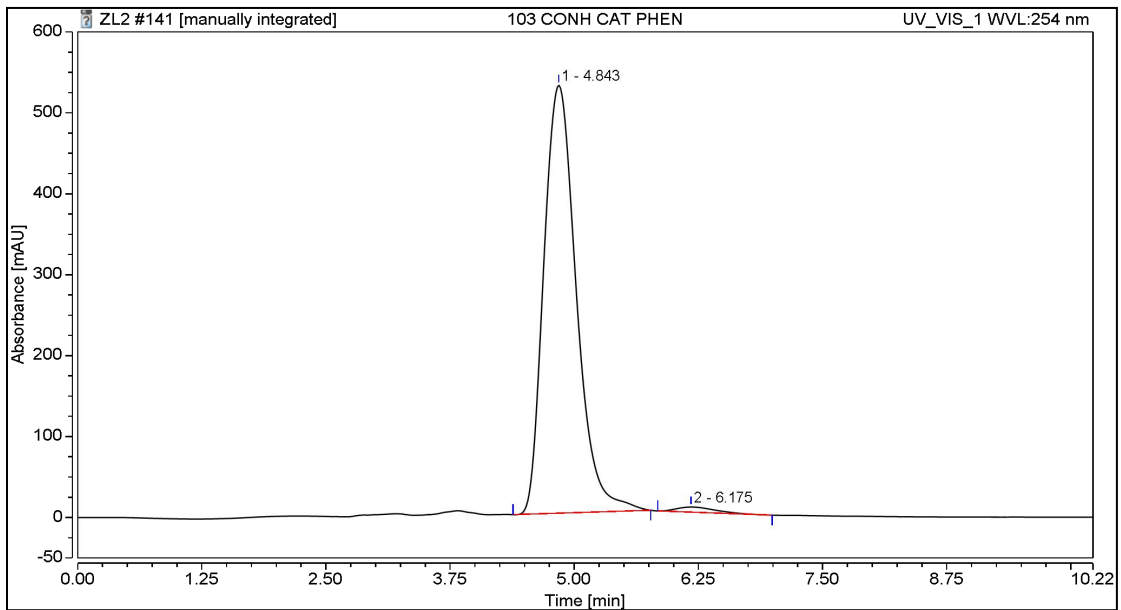
Integration Results						
No.	Peak Name	Retention Time min	Area mAU*min	Height mAU	Relative Area %	Relative Height %
1		29.163	911.088	486.701	98.90	99.01
2		37.383	10.175	4.891	1.10	0.99
Total:			921.263	491.592	100.00	100.00



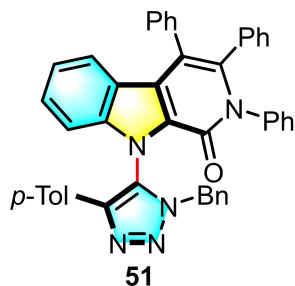
White solid, 37.6 mg, 78% yield, 98.5:1.5 er. [Chiral HPLC analysis of the product: Daicel Chiralcel OD-H 250X4.6 mm 5u column; *n*-hexane/2-propanol = 70/30, flow rate = 1.0 mL/min, $\lambda = 254$ nm, t (major) = 4.84 min, t (minor) = 6.18 min]. $[\alpha]_D^{26} = -20.4^\circ$ ($c = 1.0$, CHCl_3). **$^1\text{H NMR}$ (500 MHz, CDCl_3)** δ 7.95 (s, 1H), 7.66 (d, $J = 8.0$ Hz, 1H), 7.43 (d, $J = 7.9$ Hz, 2H), 7.37 (s, 1H), 7.26 (t, $J = 8.0$ Hz, 2H), 7.20 (d, $J = 8.2$ Hz, 2H), 7.15 (t, $J = 7.5$ Hz, 1H), 7.08 (t, $J = 7.4$ Hz, 1H), 7.05-6.99 (m, 2H), 6.97 (t, $J = 7.3$ Hz, 2H), 6.91 (t, $J = 9.0$ Hz, 4H), 6.46 (d, $J = 8.3$ Hz, 1H), 5.44 (d, $J = 15.0$ Hz, 1H), 5.27 (d, $J = 15.0$ Hz, 1H), 2.17 (s, 3H). **$^{13}\text{C NMR}$ (126 MHz, CDCl_3)** δ 158.3, 142.4, 139.1, 138.2, 137.4, 133.6, 132.3, 129.5, 129.1, 128.6, 128.5, 128.3, 128.3, 126.8, 126.6, 126.3, 125.5, 124.7, 122.6, 122.4, 120.3, 111.0, 108.9, 52.6, 21.3. **HRMS (ESI, m/z)** Calcd for $\text{C}_{31}\text{H}_{26}\text{N}_5\text{O}$ ($\text{M}+\text{H}$) $^+$: 484.2132; Found: 484.2130.



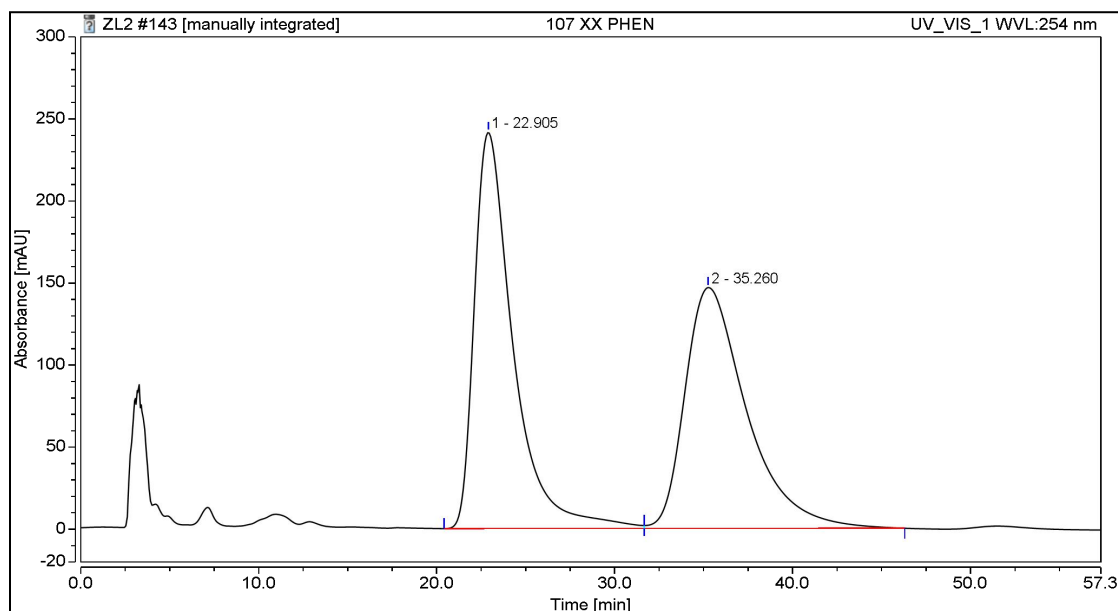
Integration Results						
No.	Peak Name	Retention Time min	Area mAU*min	Height mAU	Relative Area %	Relative Height %
1		4.862	257.629	778.075	50.19	55.29
2		6.122	255.629	629.303	49.81	44.71
Total:			513.258	1407.378	100.00	100.00



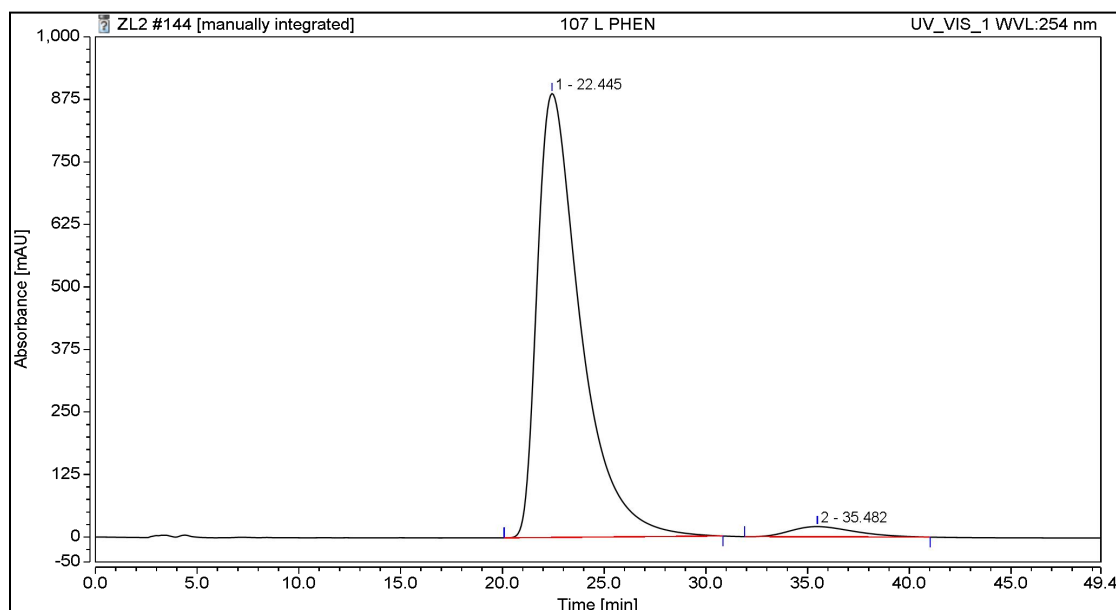
Integration Results						
No.	Peak Name	Retention Time min	Area mAU*min	Height mAU	Relative Area %	Relative Height %
1		4.843	200.646	528.855	98.58	98.82
2		6.175	2.886	6.341	1.42	1.18
Total:			203.532	535.196	100.00	100.00



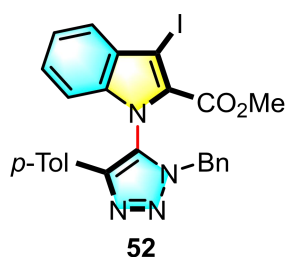
White solid, 43.5 mg, 67% yield, 96.5:3.5 er. [Chiral HPLC analysis of the product: Phenomenex 00G-4457-E0 250X4.6 mm 5u column; *n*-hexane/2-propanol = 90/10, flow rate = 1.0 mL/min, λ = 254 nm, *t* (major) = 22.45 min, *t* (minor) = 33.48 min]. $[\alpha]_D^{26} = -32.8^\circ$ (*c* = 0.9, CHCl₃). **¹H NMR (500 MHz, CDCl₃)** δ 7.39-7.28 (m, 7H), 7.24-7.16 (m, 2H), 7.15-7.06 (m, 5H), 7.05-6.98 (m, 5H), 6.97-6.88 (m, 7H), 6.74 (d, *J* = 8.1 Hz, 1H), 6.64 (d, *J* = 8.3 Hz, 1H), 5.53 (d, *J* = 15.0 Hz, 1H), 5.30 (d, *J* = 15.0 Hz, 1H), 2.25 (s, 3H). **¹³C NMR (126 MHz, CDCl₃)** δ 155.1, 142.4, 140.8, 140.2, 138.9, 137.9, 136.6, 134.3, 133.8, 131.5, 131.4, 131.2, 131.1, 129.8, 129.5, 129.3, 128.8, 128.7, 128.5, 128.4, 128.4, 128.3, 128.1, 128.0, 127.9, 127.6, 127.5, 127.4, 127.4, 127.3, 127.1, 126.0, 123.3, 123.1, 121.9, 116.7, 111.2, 52.9, 21.4. **HRMS (ESI, *m/z*)** Calcd for C₄₅H₃₄N₅O (*M*+H)⁺: 660.2758; Found: 660.2746.



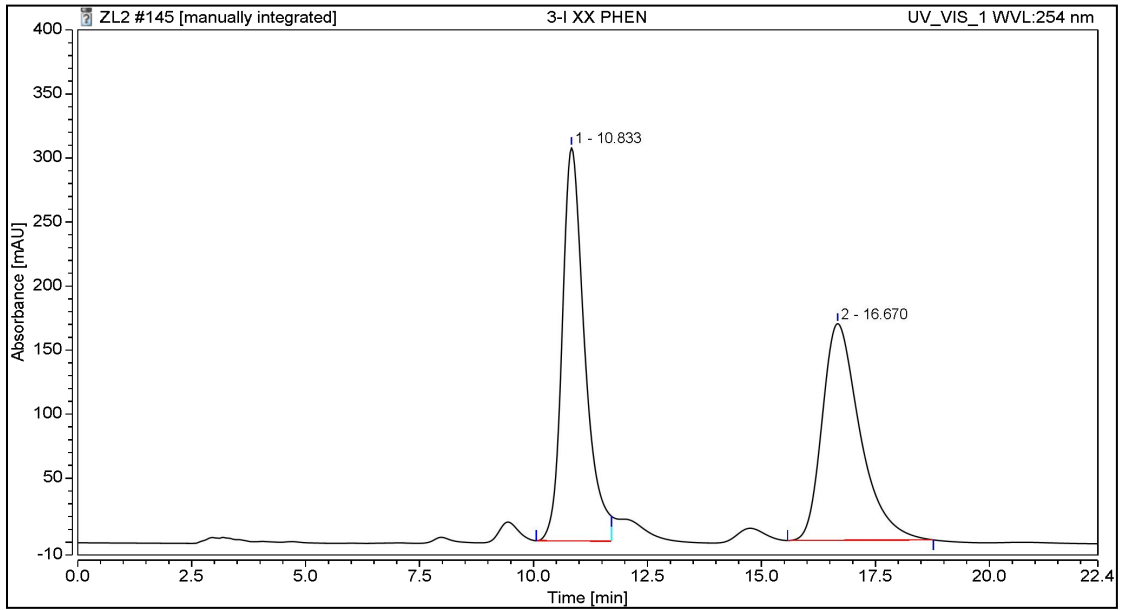
Integration Results						
No.	Peak Name	Retention Time min	Area mAU*min	Height mAU	Relative Area %	Relative Height %
1		22.905	608.485	241.396	50.84	62.19
2		35.260	588.436	146.788	49.16	37.81
Total:			1196.921	388.184	100.00	100.00



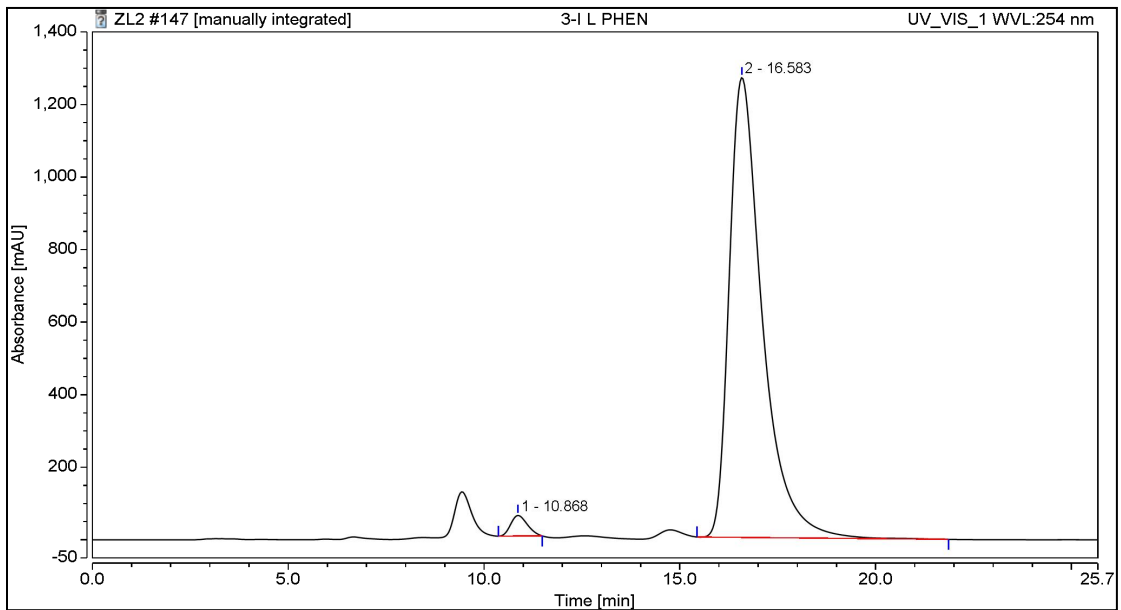
Integration Results						
No.	Peak Name	Retention Time min	Area mAU*min	Height mAU	Relative Area %	Relative Height %
1		22.445	2187.456	887.861	96.70	97.75
2		35.482	74.676	20.445	3.30	2.25
Total:			2262.133	908.306	100.00	100.00



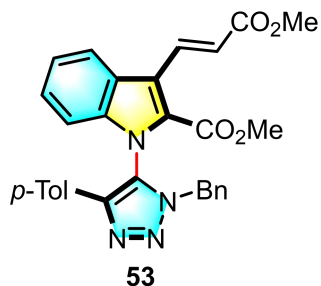
White solid, 53.7 mg, 98% yield, 98:2 er. [Chiral HPLC analysis of the product: Phenomenex 00G-4457-E0 250X4.6 mm 5u column; *n*-hexane/2-propanol = 70/30, flow rate = 1.0 mL/min, λ = 254 nm, *t* (major) = 16.58 min, *t* (minor) = 10.87 min]. $[\alpha]_D^{26} = -44.8^\circ$ (*c* = 0.6, CHCl₃). **¹H NMR (500 MHz, CDCl₃)** δ 7.63 (d, *J* = 8.1 Hz, 1H), 7.27 (t, *J* = 7.7 Hz, 1H), 7.19 (dd, *J* = 18.2, 7.8 Hz, 3H), 7.12 (t, *J* = 7.3 Hz, 1H), 7.06 (t, *J* = 7.4 Hz, 2H), 6.98 (d, *J* = 8.0 Hz, 2H), 6.86 (d, *J* = 7.4 Hz, 2H), 6.54 (d, *J* = 8.3 Hz, 1H), 5.23 (d, *J* = 15.0 Hz, 1H), 5.16 (d, *J* = 15.0 Hz, 1H), 3.54 (s, 3H), 2.22 (s, 3H). **¹³C NMR (126 MHz, CDCl₃)** δ 159.7, 142.5, 138.6, 138.4, 133.1, 131.1, 129.6, 128.6, 128.5, 128.3, 128.3, 128.2, 126.4, 125.4, 124.3, 123.4, 111.1, 73.3, 52.5, 52.0, 21.3. **HRMS (ESI, *m/z*)** Calcd for C₂₆H₂₂IN₄O₂ (M+H)⁺: 549.0782; Found: 549.0771.



Integration Results						
No.	Peak Name	Retention Time min	Area mAU*min	Height mAU	Relative Area %	Relative Height %
1		10.833	175.380	307.083	51.90	64.47
2		16.670	162.535	169.208	48.10	35.53
Total:			337.915	476.291	100.00	100.00

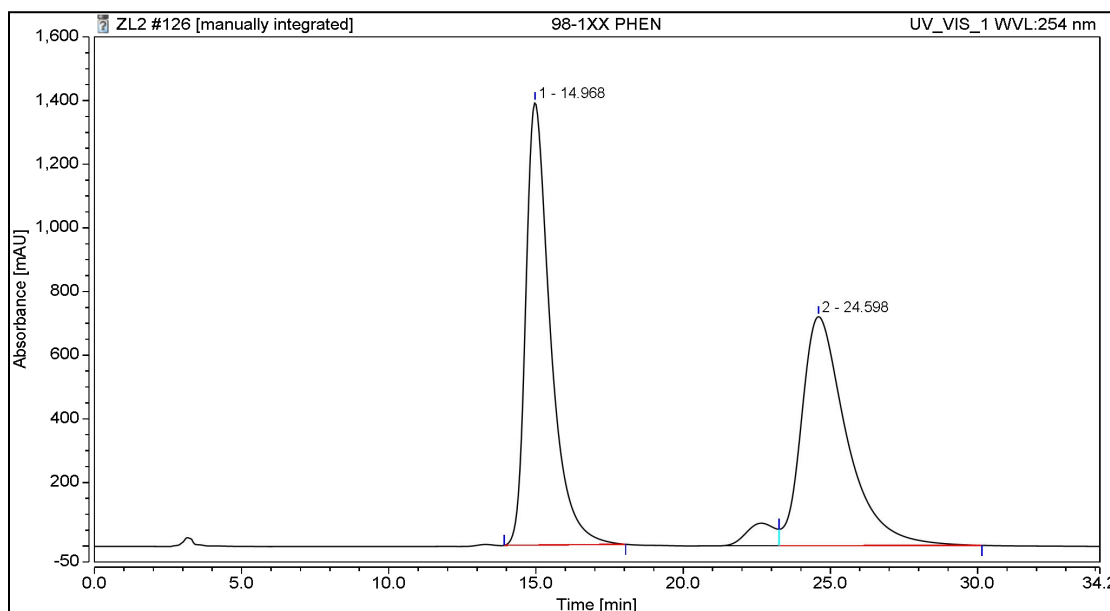


Integration Results						
No.	Peak Name	Retention Time min	Area mAU*min	Height mAU	Relative Area %	Relative Height %
1		10.868	28.028	56.777	2.21	4.29
2		16.583	1241.525	1268.031	97.79	95.71
Total:			1269.553	1324.808	100.00	100.00

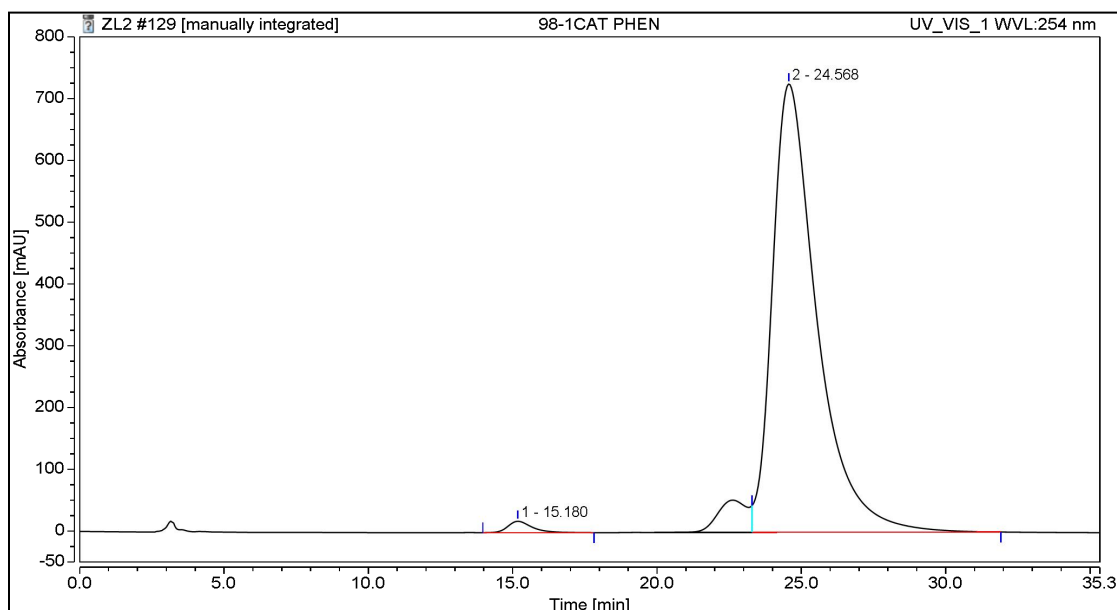


White solid, 46.5 mg, 92% yield, 98:2 er. [Chiral HPLC analysis of the product: Phenomenex 00G-4457-E0 250X4.6 mm 5u column; *n*-hexane/2-propanol = 70/30, flow rate = 1.0 mL/min, λ = 254 nm, t (major) = 24.57 min, t (minor) = 15.18 min]. $[\alpha]_D^{26} = -89.1^\circ$ ($c = 1.1$, CHCl_3). **$^1\text{H NMR}$ (500 MHz, CDCl_3)** δ 8.52 (d, $J = 16.4$ Hz, 1H), 8.03 (d, $J = 8.2$ Hz, 1H), 7.30 (t, $J = 7.3$ Hz, 1H), 7.19 (t, $J = 8.0$ Hz, 3H), 7.12 (t, $J = 7.4$ Hz, 1H), 7.06 (t, $J = 7.5$ Hz, 2H), 6.98 (d, $J = 8.1$ Hz, 2H), 6.88 (d, $J = 7.3$ Hz, 2H), 6.78 (d, $J = 16.4$ Hz, 1H), 6.60 (d, $J = 8.4$ Hz, 1H), 5.25 (d, $J = 15.0$ Hz, 1H), 5.18 (d, $J = 15.0$ Hz, 1H), 3.88 (s, 3H), 3.56 (s, 3H), 2.23 (s, 3H). **$^{13}\text{C NMR}$ (126 MHz, CDCl_3)** δ 167.5, 160.3, 142.6, 138.7, 138.5, 136.8, 133.2, 129.6, 128.6, 128.6, 128.3, 128.0, 127.7, 127.6, 126.4, 125.4, 125.2, 123.9, 122.3, 122.0, 121.7, 111.5, 52.6, 52.4, 51.9, 29.8, 21.3.

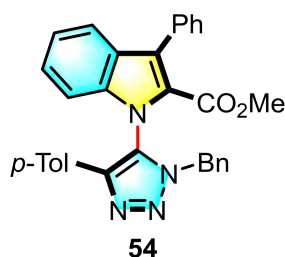
HRMS (ESI, m/z) Calcd for $\text{C}_{30}\text{H}_{27}\text{N}_4\text{O}_4$ ($\text{M}+\text{H}$) $^+$: 507.2027; Found: 507.2024.



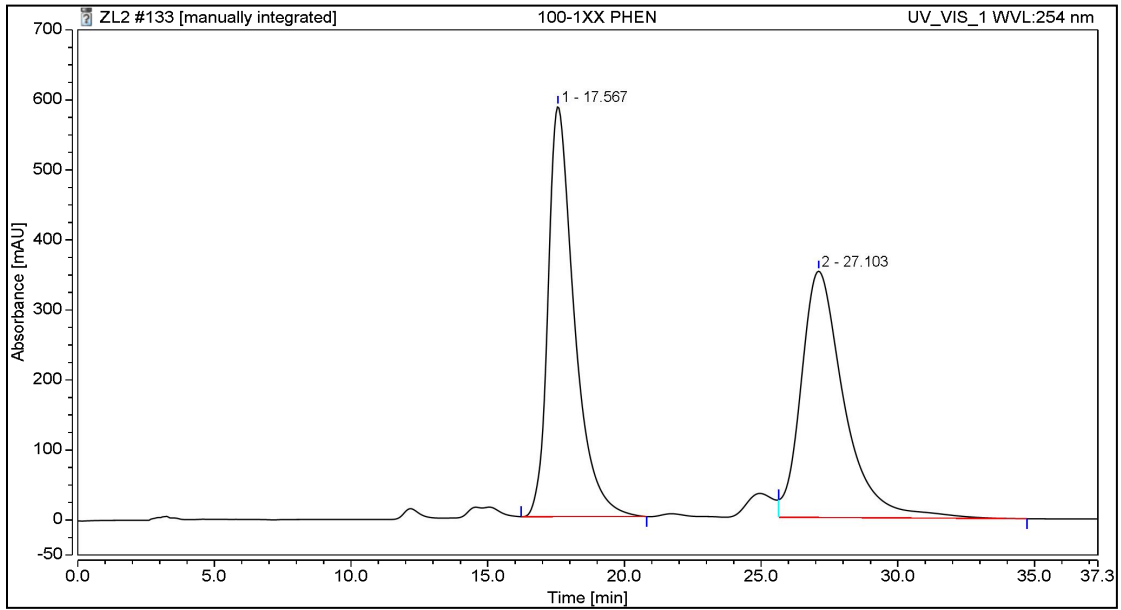
Integration Results						
No.	Peak Name	Retention Time min	Area mAU*min	Height mAU	Relative Area %	Relative Height %
1		14.968	1345.977	1391.257	51.38	65.90
2		24.598	1273.454	719.847	48.62	34.10
Total:			2619.430	2111.104	100.00	100.00



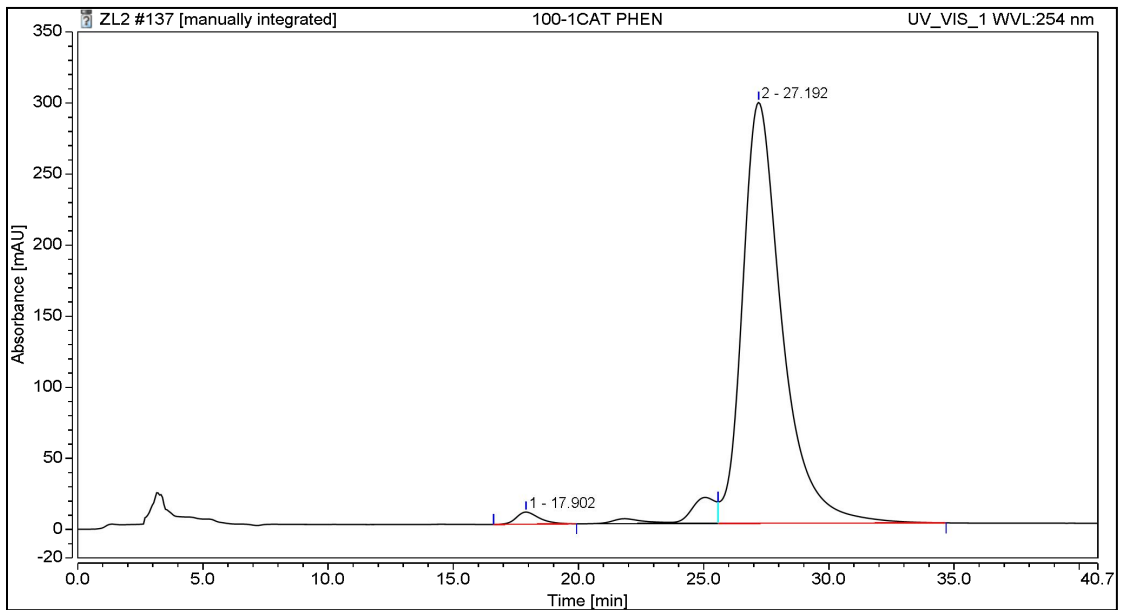
Integration Results						
No.	Peak Name	Retention Time min	Area mAU*min	Height mAU	Relative Area %	Relative Height %
1		15.180	18.049	18.456	1.37	2.48
2		24.568	1296.624	725.891	98.63	97.52
Total:			1314.673	744.347	100.00	100.00



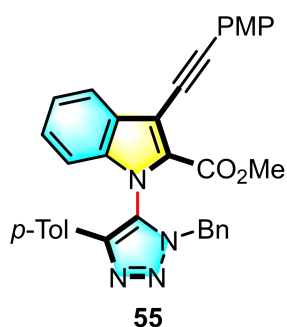
White solid, 46.3 mg, 93% yield, 98:2 er. [Chiral HPLC analysis of the product: Phenomenex 00G-4457-E0 250X4.6 mm 5u column; *n*-hexane/2-propanol = 80/20, flow rate = 1.0 mL/min, λ = 254 nm, t (major) = 27.19 min, t (minor) = 17.90 min]. $[\alpha]_D^{26} = -63.3^\circ$ ($c = 0.8$, CHCl_3). **$^1\text{H NMR}$ (500 MHz, CDCl_3)** δ 7.61 (dd, $J = 6.2, 2.4$ Hz, 1H), 7.58-7.49 (m, 4H), 7.46 (t, $J = 7.0$ Hz, 1H), 7.28 (d, $J = 8.1$ Hz, 2H), 7.21-7.06 (m, 5H), 7.00 (dd, $J = 18.2, 7.5$ Hz, 4H), 6.63 (dd, $J = 6.4, 2.2$ Hz, 1H), 5.34 (d, $J = 14.8$ Hz, 1H), 5.27 (d, $J = 14.9$ Hz, 1H), 3.35 (s, 3H), 2.25 (s, 3H). **$^{13}\text{C NMR}$ (126 MHz, CDCl_3)** δ 160.8, 142.6, 138.3, 138.3, 133.5, 132.9, 130.4, 129.6, 129.3, 128.8, 128.6, 128.5, 128.4, 128.2, 128.0, 127.7, 127.4, 126.7, 125.5, 124.2, 122.8, 122.1, 111.0, 52.6, 51.7, 21.3. **HRMS (ESI, m/z)** Calcd for $\text{C}_{32}\text{H}_{27}\text{N}_4\text{O}_2$ ($\text{M}+\text{H}$)⁺: 499.2129; Found: 499.2130.



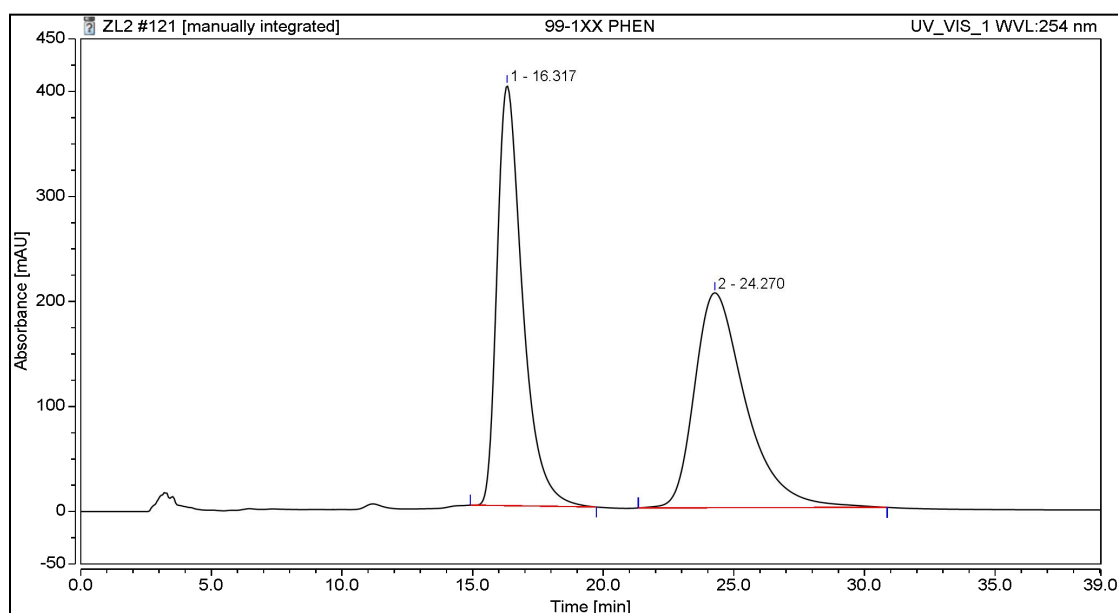
Integration Results						
No.	Peak Name	Retention Time min	Area mAU*min	Height mAU	Relative Area %	Relative Height %
1		17.567	653.096	586.009	50.51	62.49
2		27.103	640.030	351.809	49.49	37.51
Total:			1293.126	937.818	100.00	100.00



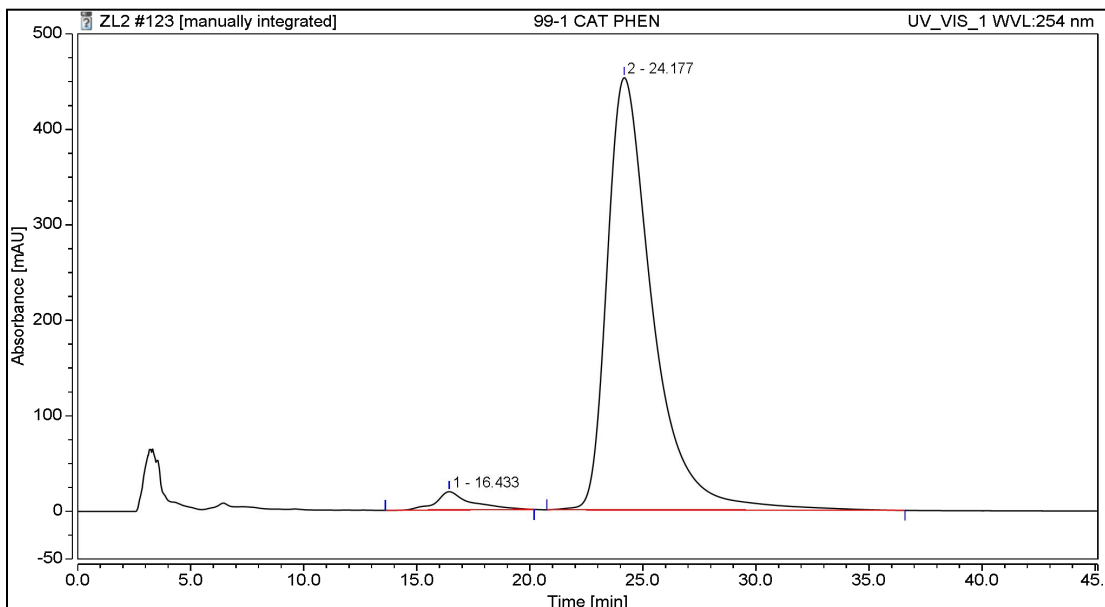
Integration Results						
No.	Peak Name	Retention Time min	Area mAU*min	Height mAU	Relative Area %	Relative Height %
1		17.902	9.161	8.575	1.67	2.81
2		27.192	540.702	296.135	98.33	97.19
Total:			549.863	304.709	100.00	100.00



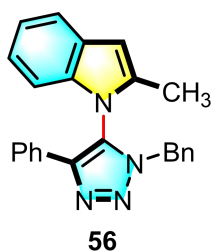
White solid, 43.6 mg, 79% yield, 97:2 er. [Chiral HPLC analysis of the product: Phenomenex 00G-4457-E0 250X4.6 mm 5u column; *n*-hexane/2-propanol = 70/30, flow rate = 1.0 mL/min, λ = 254 nm, *t* (major) = 24.18 min, *t* (minor) = 14.63 min]. $[\alpha]_D^{26} = -12.5^\circ$ (*c* = 0.7, CHCl₃). **¹H NMR (500 MHz, CDCl₃)** δ 7.92 (d, *J* = 8.0 Hz, 1H), 7.61 (d, *J* = 8.8 Hz, 2H), 7.26 (d, *J* = 15.0 Hz, 1H), 7.21 (d, *J* = 8.2 Hz, 2H), 7.15-7.08 (m, 2H), 7.06 (t, *J* = 7.3 Hz, 2H), 6.99-6.91 (m, 6H), 6.49 (d, *J* = 8.4 Hz, 1H), 5.34 (d, *J* = 14.8 Hz, 1H), 5.18 (d, *J* = 14.8 Hz, 1H), 3.87 (s, 3H), 3.69 (s, 3H), 2.23 (s, 3H). **¹³C NMR (126 MHz, CDCl₃)** δ 160.2, 142.6, 138.4, 138.1, 133.4, 129.6, 128.7, 128.5, 128.4, 128.3, 128.1, 127.8, 126.5, 125.5, 123.1, 122.0, 115.5, 114.4, 111.1, 110.3, 98.4, 80.2, 55.5, 52.6, 52.2, 21.3. **HRMS (ESI, *m/z*)** Calcd for C₃₅H₂₉N₄O₃ (M+H)⁺: 553.2234; Found: 553.2231.



Integration Results						
No.	Peak Name	Retention Time min	Area mAU*min	Height mAU	Relative Area %	Relative Height %
1		16.317	453.161	399.997	49.35	66.15
2		24.270	465.156	204.693	50.65	33.85
Total:			918.317	604.690	100.00	100.00



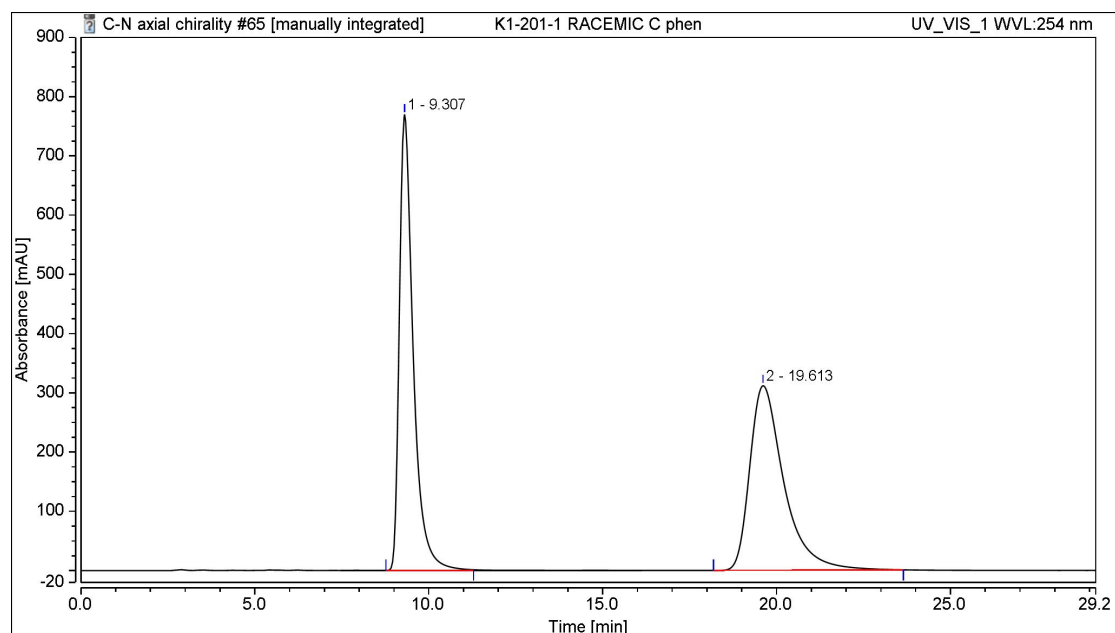
Integration Results						
No.	Peak Name	Retention Time min	Area mAU*min	Height mAU	Relative Area %	Relative Height %
1		16.433	34.778	19.156	3.19	4.06
2		24.177	1054.594	452.821	96.81	95.94
Total:			1089.372	471.977	100.00	100.00



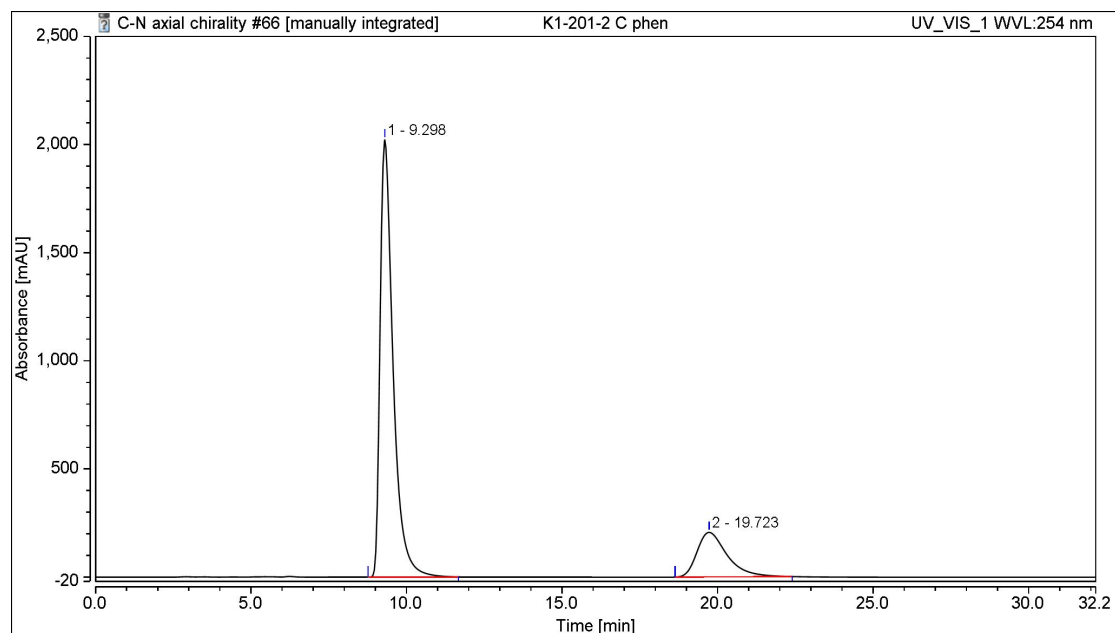
White solid, 35.0 mg, 96% yield, 81:19 er. [Chiral HPLC analysis of the product: Phenomenex 00G-4457-E0 250X4.6 mm 5u column; *n*-hexane/2-propanol = 70/30, flow rate = 1.0 mL/min, λ = 254 nm, *t* (major) = 9.30 min, *t* (minor) = 19.72 min]. $[\alpha]_D^{26} = +22.1^\circ$ (*c* = 1.4, CHCl₃). **¹H NMR (500 MHz, CDCl₃)** δ 7.63 (d, *J* = 7.9 Hz, 1H), 7.39-7.33 (m, 2H), 7.25-7.15 (m, 7H), 7.11 (t, *J* = 7.6 Hz, 1H), 6.91 (d, *J* = 7.3 Hz, 2H), 6.82 (d, *J* = 8.1 Hz, 1H), 6.44 (s, 1H), 5.50 (d, *J* = 14.5 Hz, 1H), 5.00 (d, *J* = 14.5 Hz, 1H), 1.55 (s, 3H). **¹³C NMR (126 MHz, CDCl₃)** δ 141.6, 135.9, 132.5, 128.3, 128.2, 127.8,

127.7, 127.7, 127.5, 127.3, 127.0, 124.2, 121.5, 120.5, 119.4, 108.5, 102.9, 51.2, 10.8.

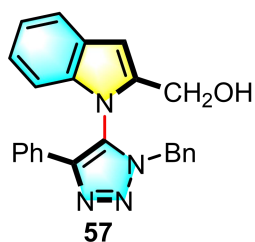
HRMS (ESI, m/z) Calcd for C₂₄H₂₁N₄ (M+H)⁺: 365.1761; Found: 365.1764.



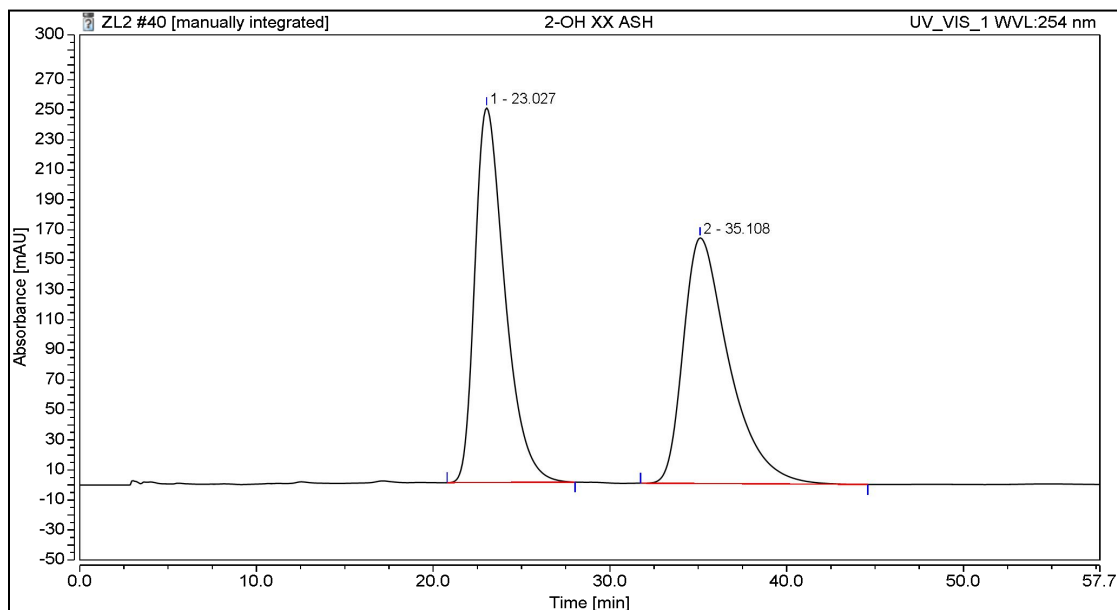
Integration Results						
No.	Peak Name	Retention Time min	Area mAU*min	Height mAU	Relative Area %	Relative Height %
1		9.307	355.917	769.392	50.17	71.17
2		19.613	353.491	311.665	49.83	28.83
Total:			709.408	1081.057	100.00	100.00



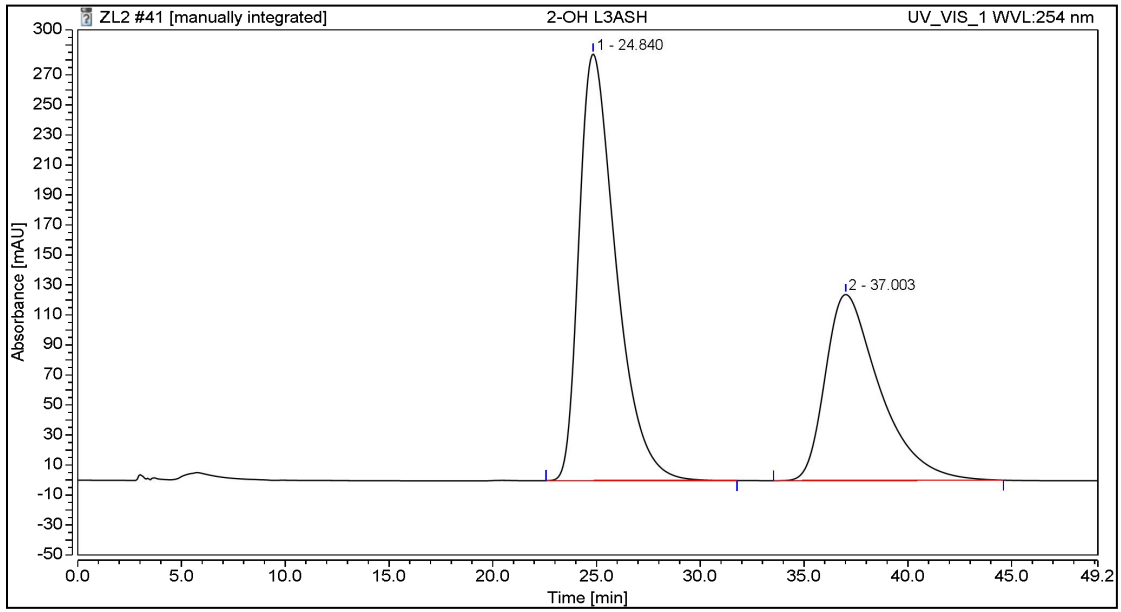
Integration Results						
No.	Peak Name	Retention Time min	Area mAU*min	Height mAU	Relative Area %	Relative Height %
1		9.298	982.056	2021.871	80.97	90.74
2		19.723	230.760	206.261	19.03	9.26
Total:			1212.816	2228.132	100.00	100.00



White solid, 35.7 mg, 94% yield, 61:39 er. [Chiral HPLC analysis of the product: Daicel Chiralpak AS-H 250X4.6 mm 5u column; *n*-hexane/2-propanol = 90/10, flow rate = 1.0 mL/min, $\lambda = 254$ nm, t (major) = 24.84 min, t (minor) = 37.00 min]. $[\alpha]_D^{26} = -46.9^\circ$ ($c = 1.1$, CHCl_3). $^1\text{H NMR}$ (500 MHz, CDCl_3) δ 7.67 (d, $J = 7.5$ Hz, 1H), 7.28 (s, 2H), 7.24-6.97 (m, 8H), 6.87 (s, 2H), 6.76 (s, 1H), 6.56 (t, $J = 6.8$ Hz, 1H), 5.36 (d, $J = 14.5$ Hz, 1H), 5.15 (d, $J = 14.5$ Hz, 1H), 4.40-4.17 (m, 2H), 2.67-2.42 (m, 1H). $^{13}\text{C NMR}$ (126 MHz, CDCl_3) δ 142.7, 139.4, 137.9, 133.7, 129.1, 129.0, 128.8, 128.7, 128.7, 128.5, 128.0, 125.5, 123.8, 121.8, 121.4, 110.1, 105.8, 56.7, 52.5. HRMS (ESI, m/z) Calcd for $\text{C}_{24}\text{H}_{21}\text{N}_4\text{O}$ ($\text{M}+\text{H}$) $^+$: 381.1710; Found: 381.1708.

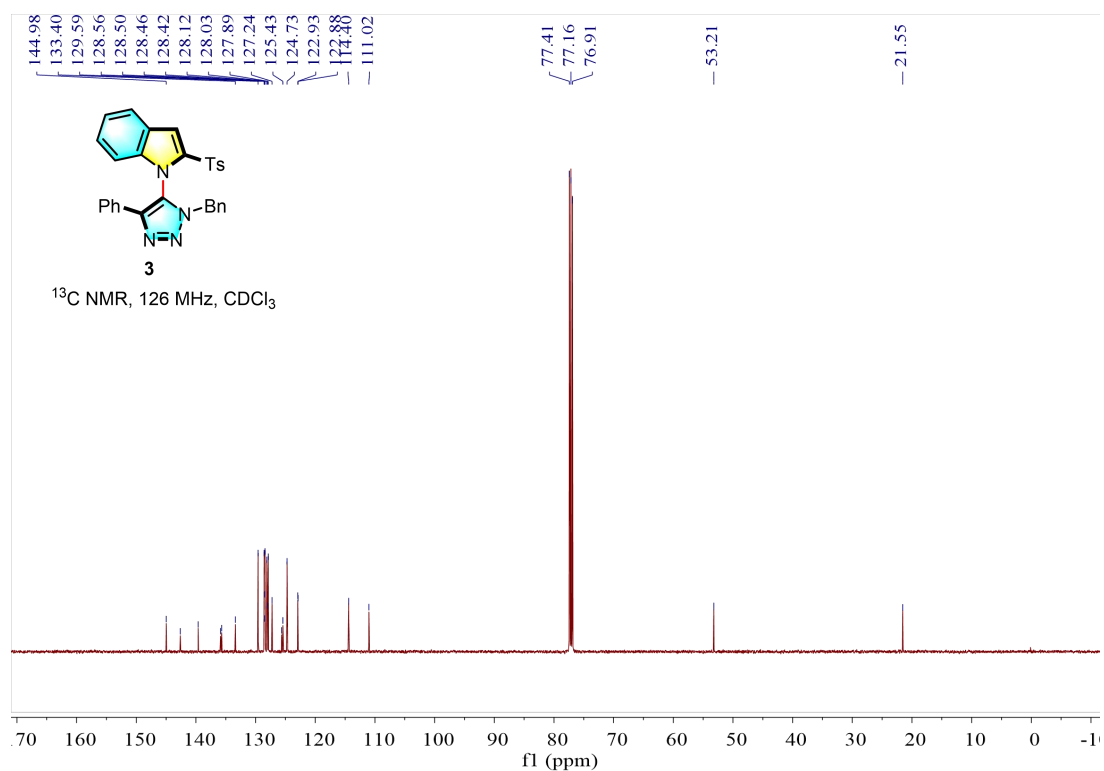
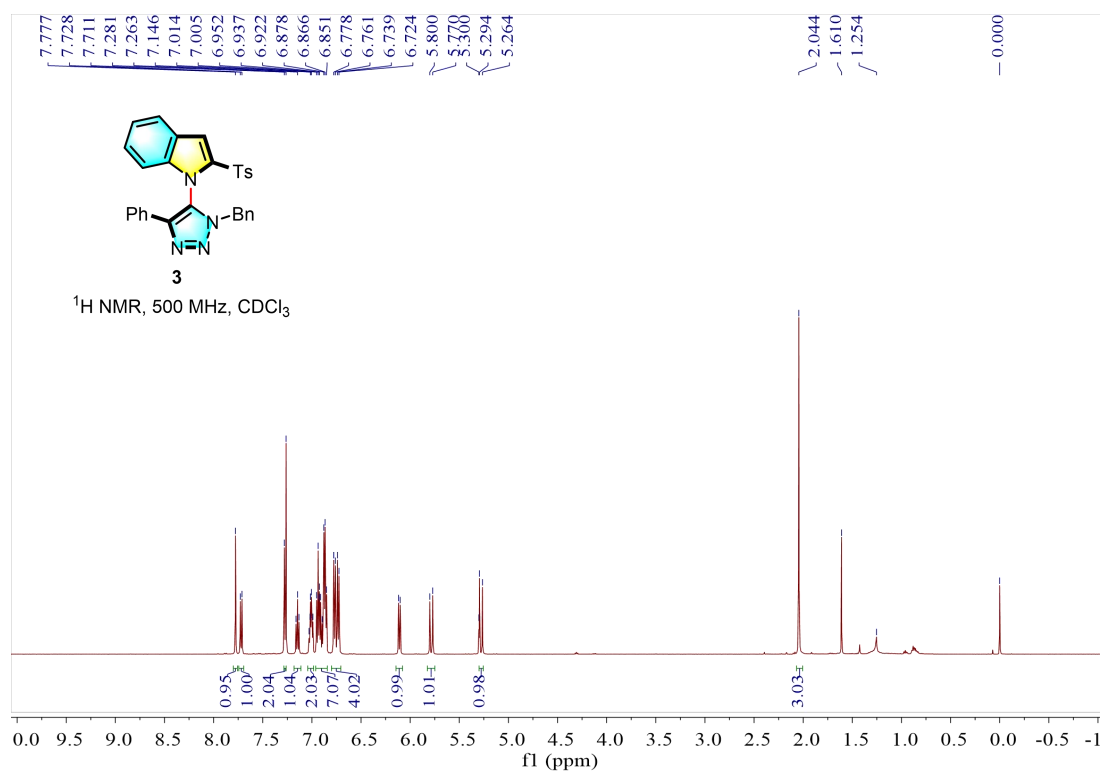


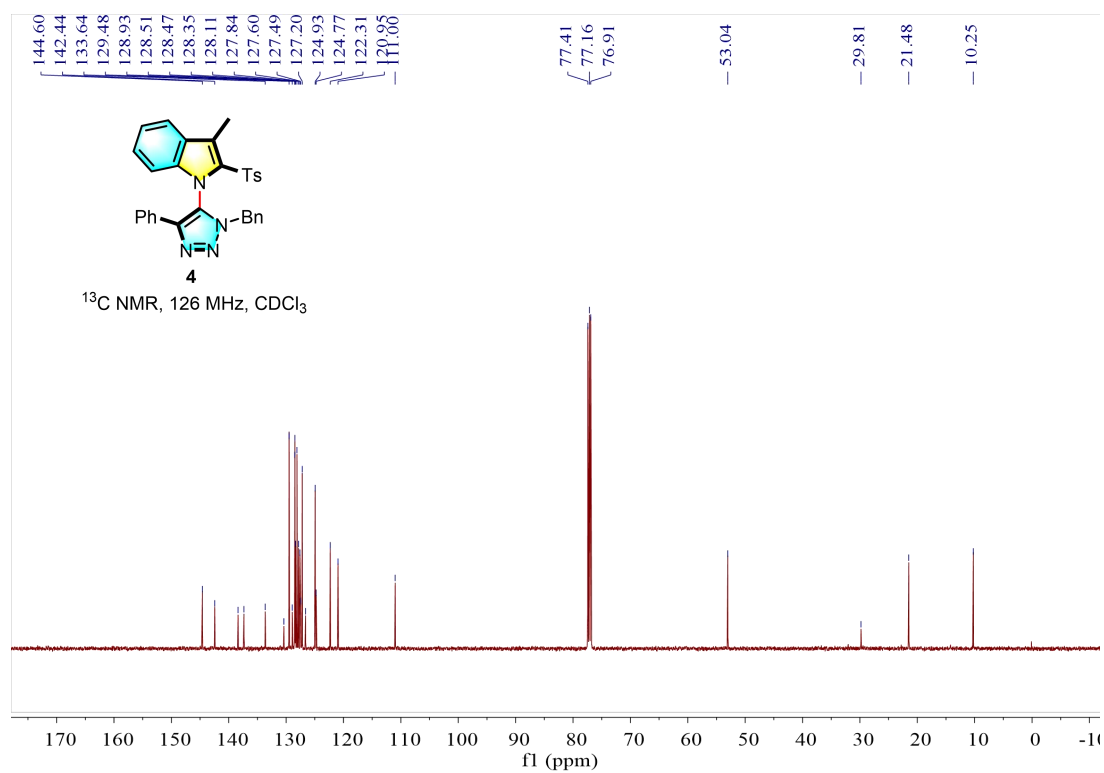
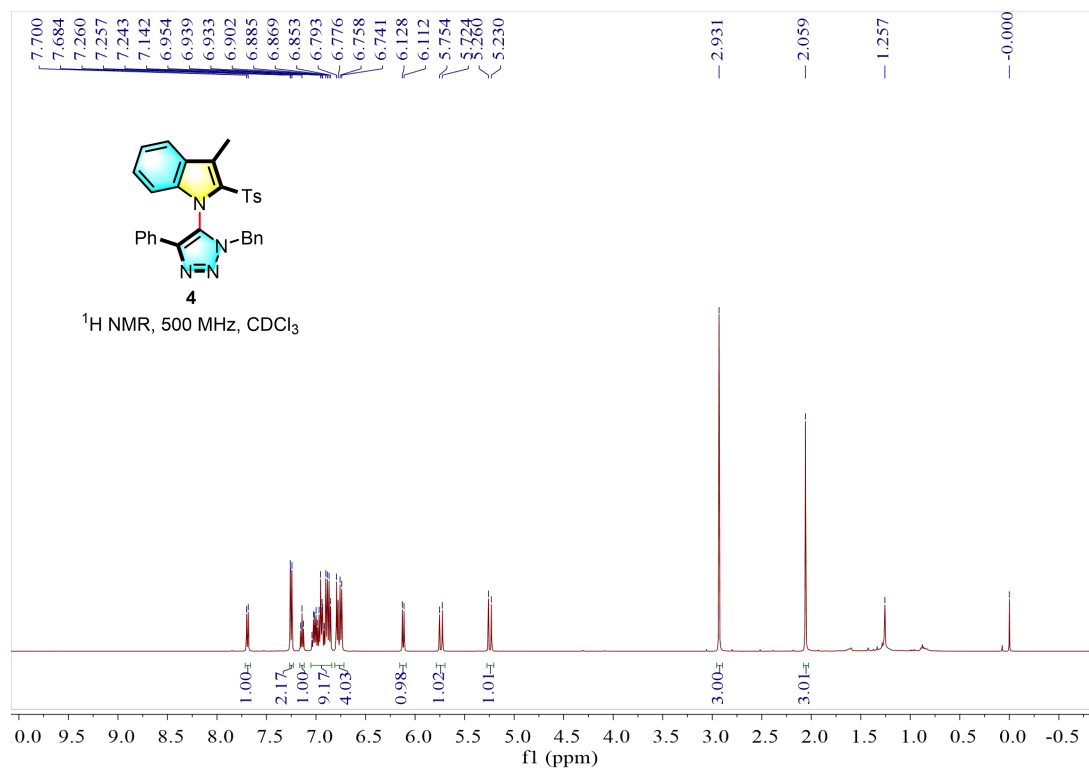
Integration Results						
No.	Peak Name	Retention Time min	Area mAU*min	Height mAU	Relative Area %	Relative Height %
1		23.027	491.458	249.733	50.05	60.40
2		35.108	490.428	163.719	49.95	39.60
Total:			981.886	413.452	100.00	100.00

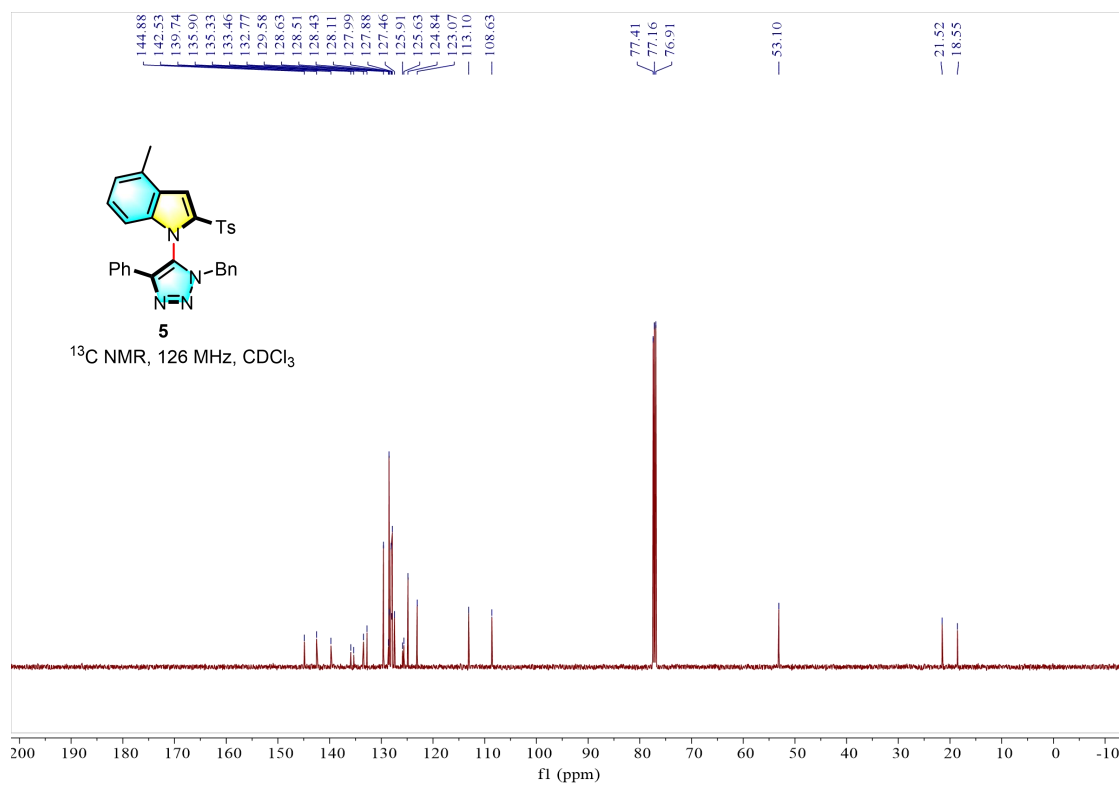
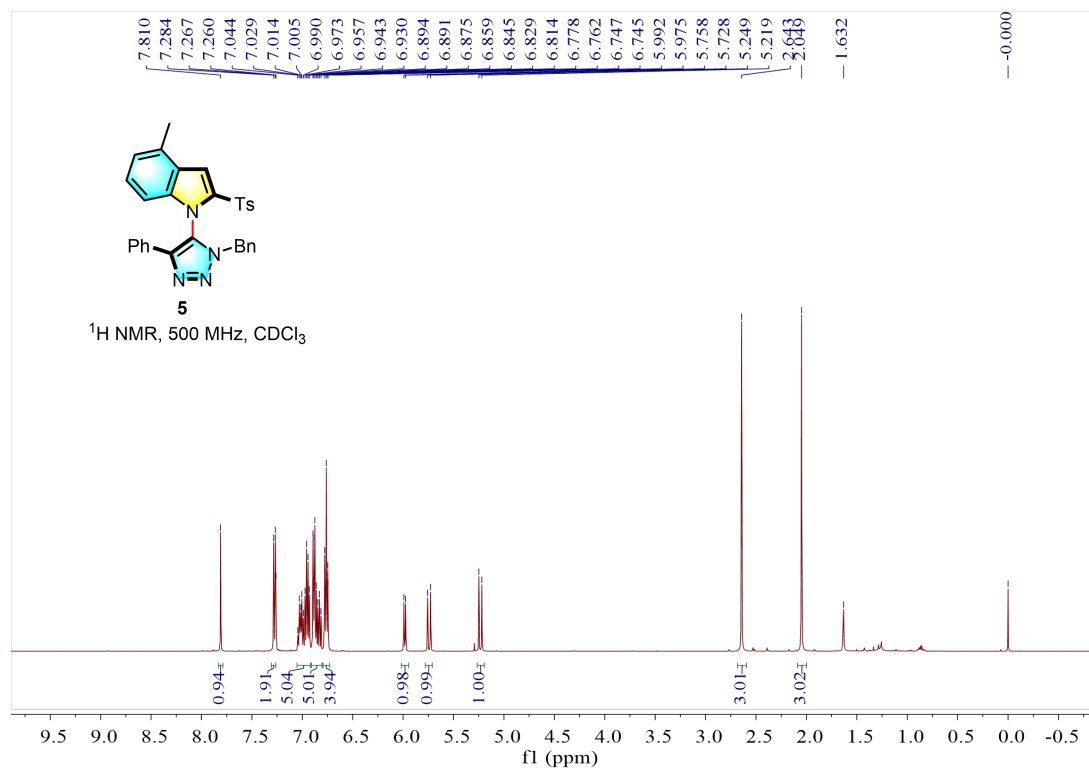


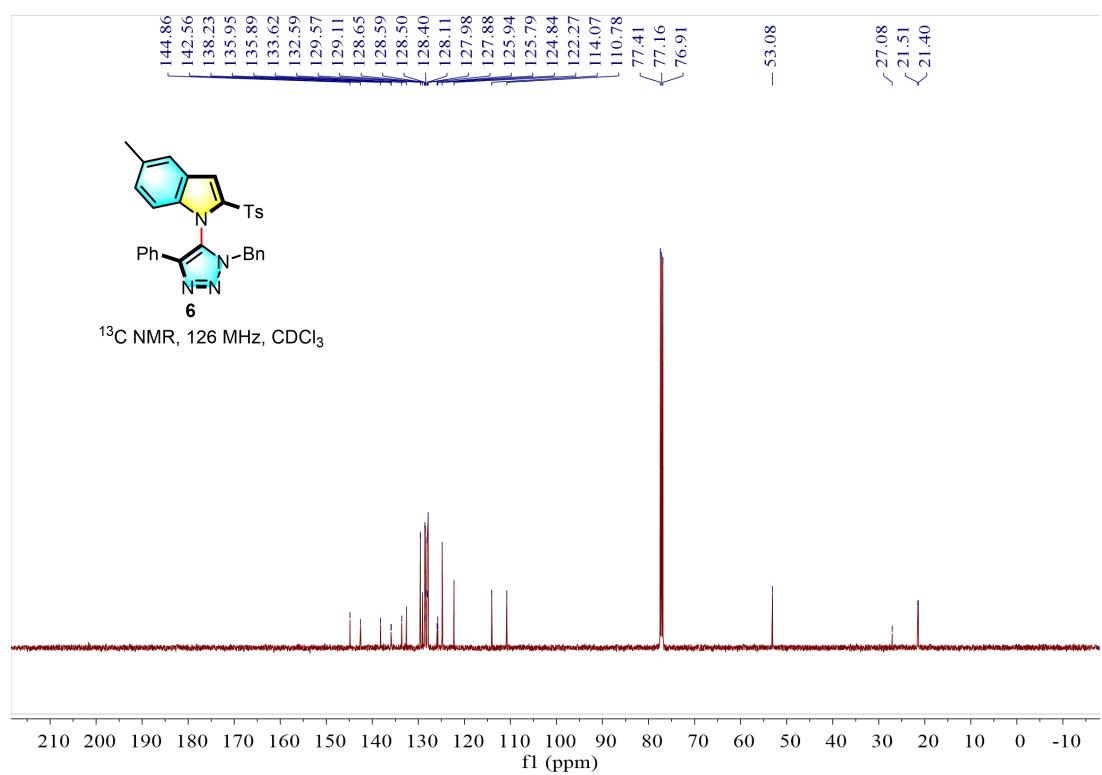
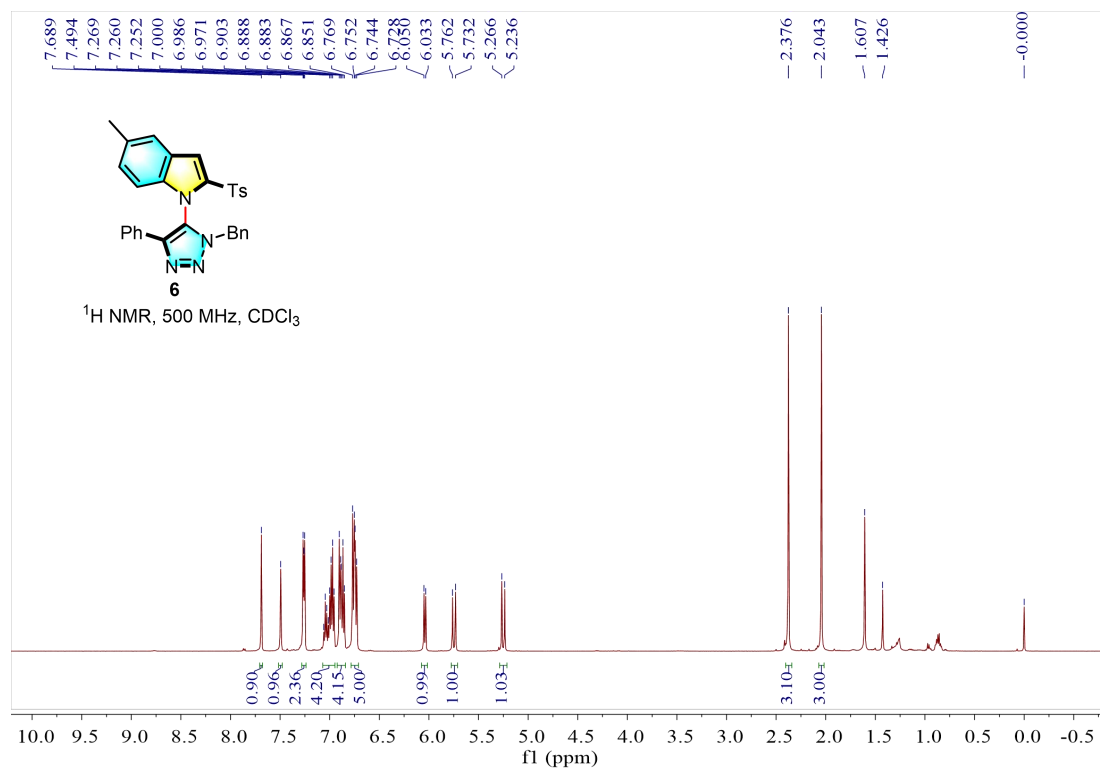
Integration Results						
No.	Peak Name	Retention Time min	Area mAU*min	Height mAU	Relative Area %	Relative Height %
1		24.840	587.316	284.366	60.94	69.64
2		37.003	376.511	123.988	39.06	30.36
Total:			963.827	408.354	100.00	100.00

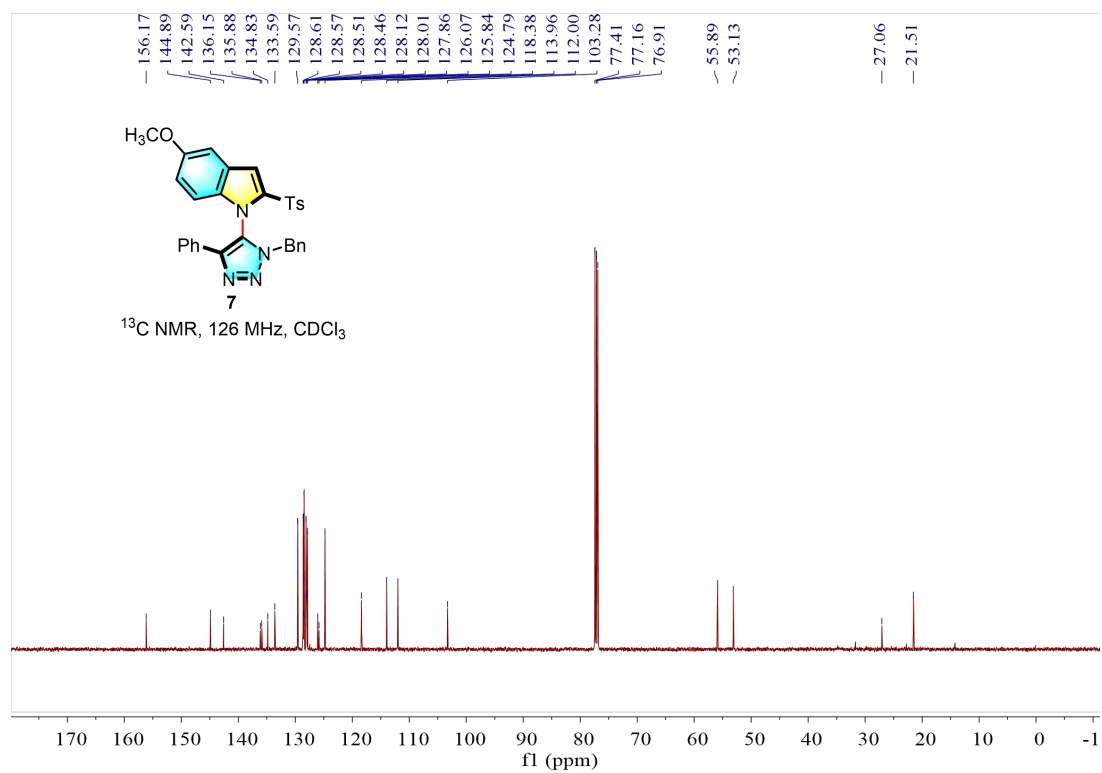
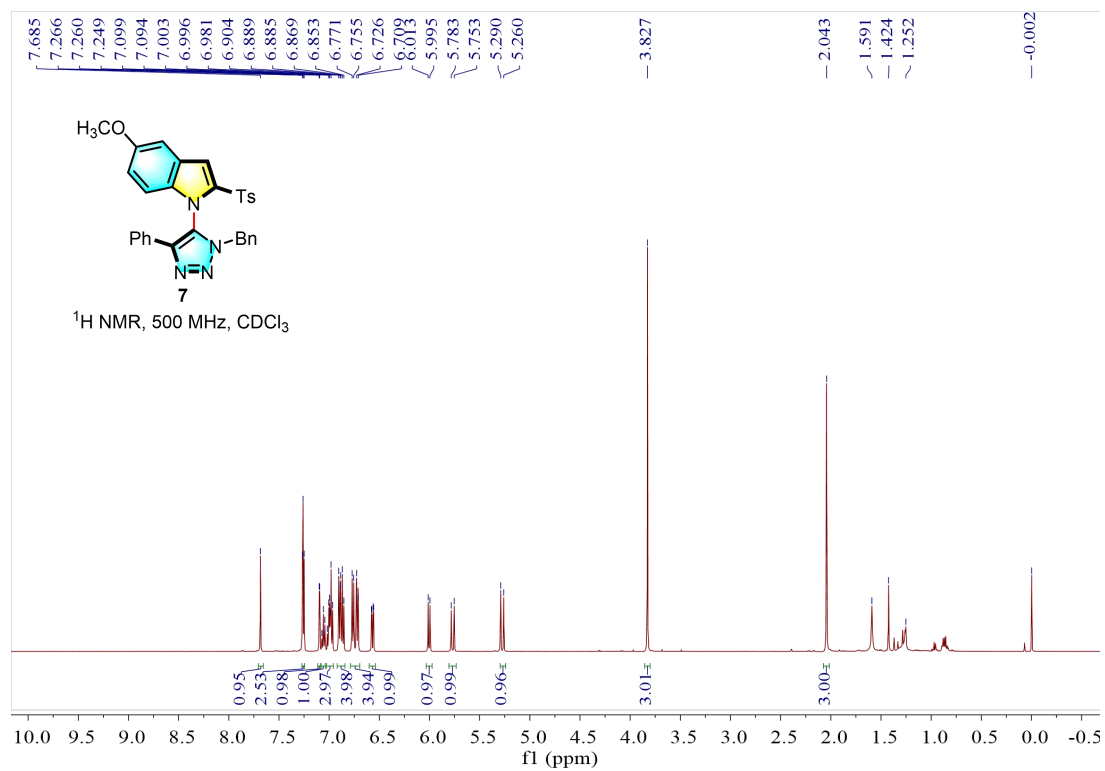
9. NMR spectra

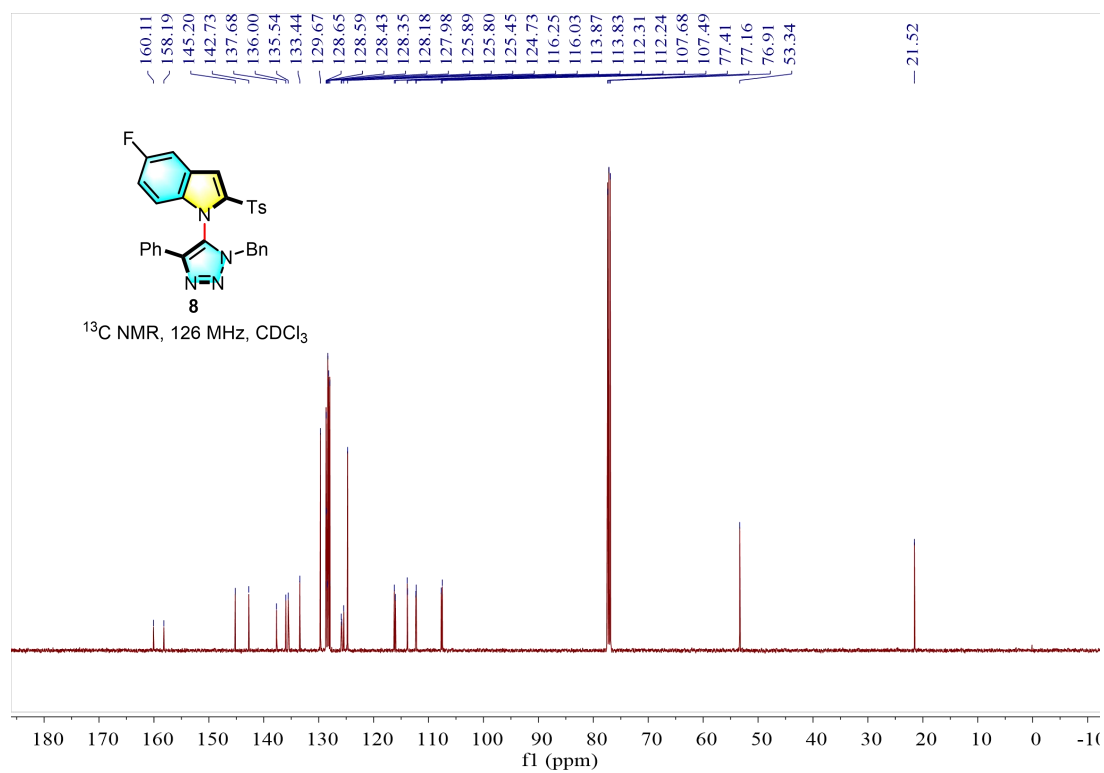
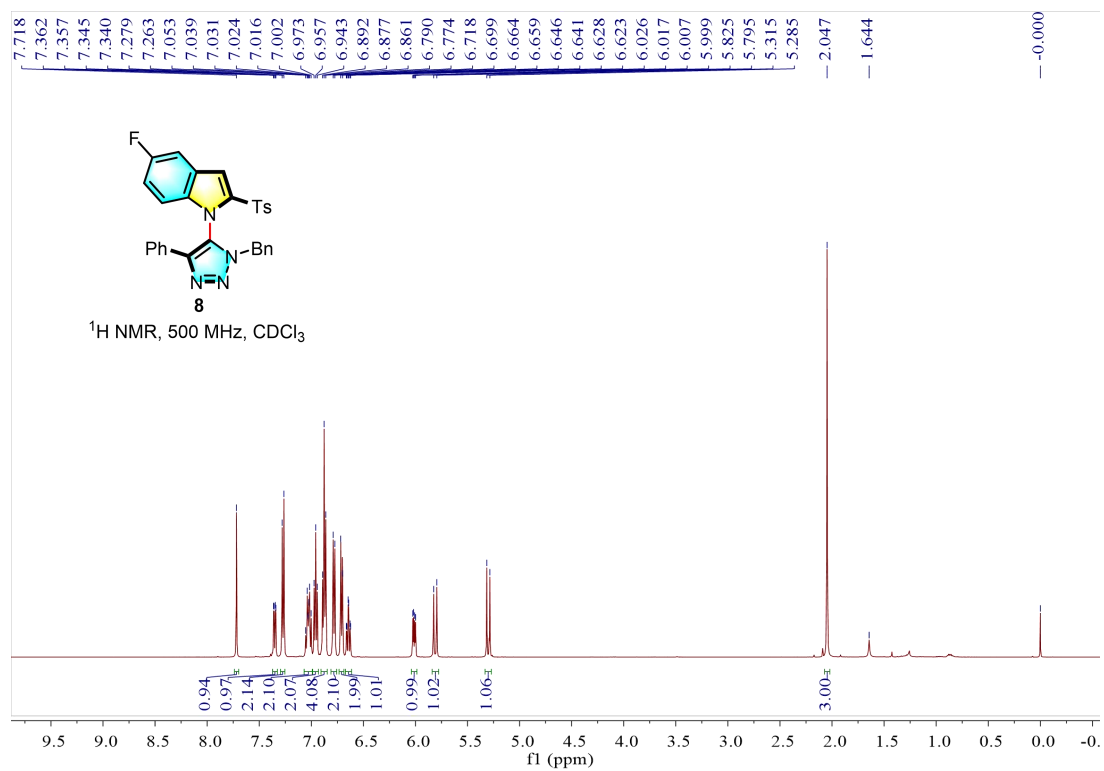


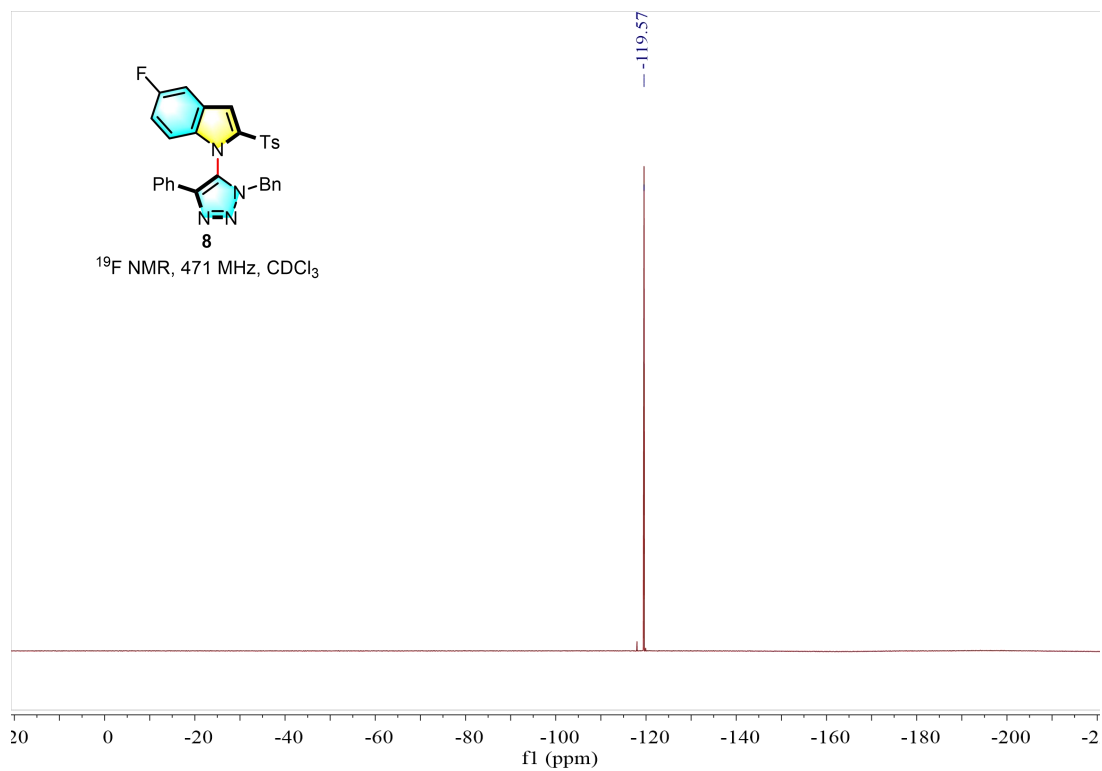


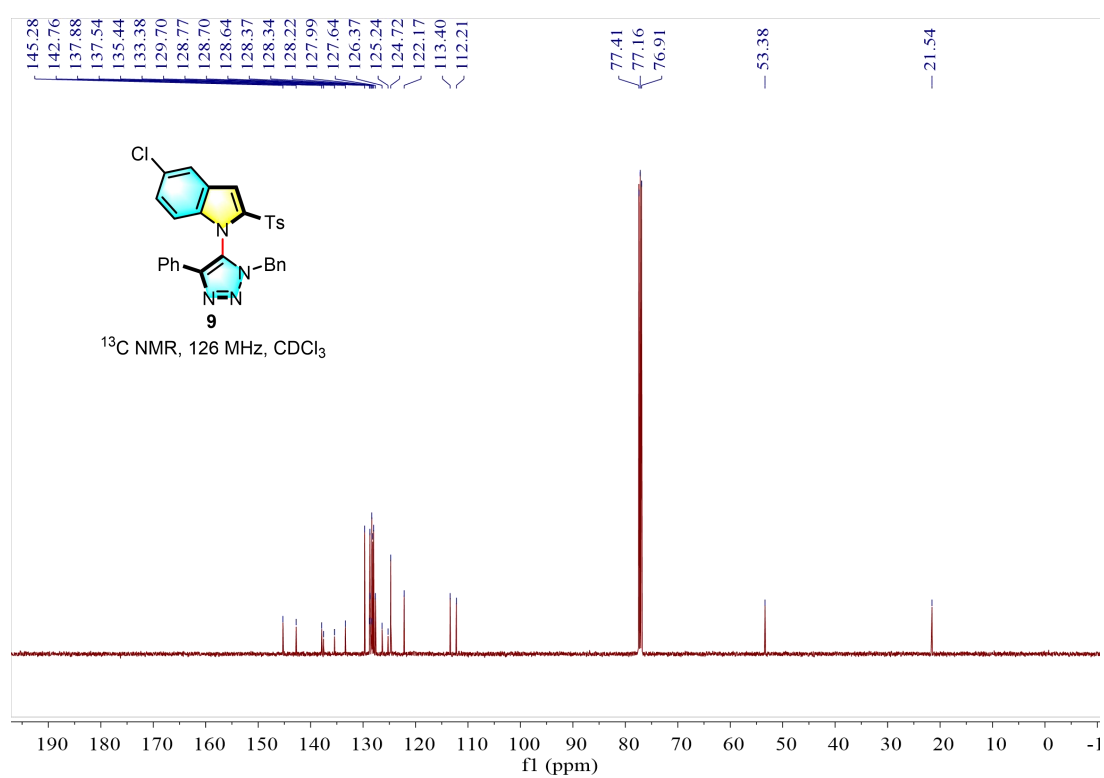
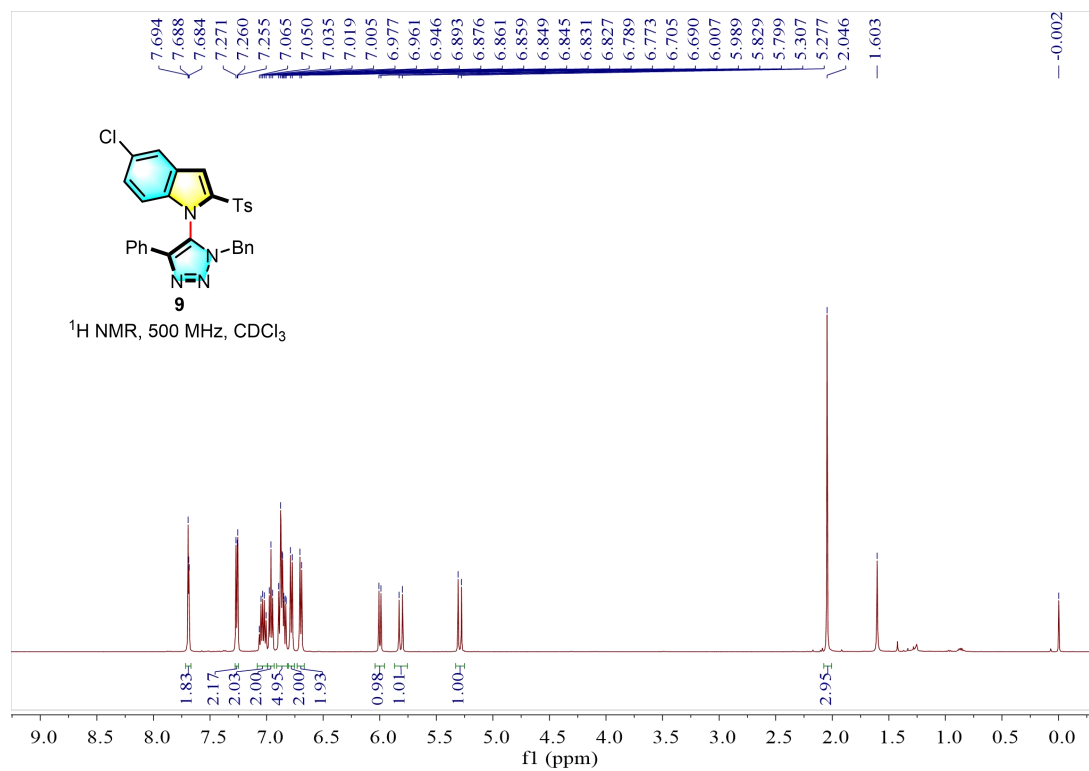


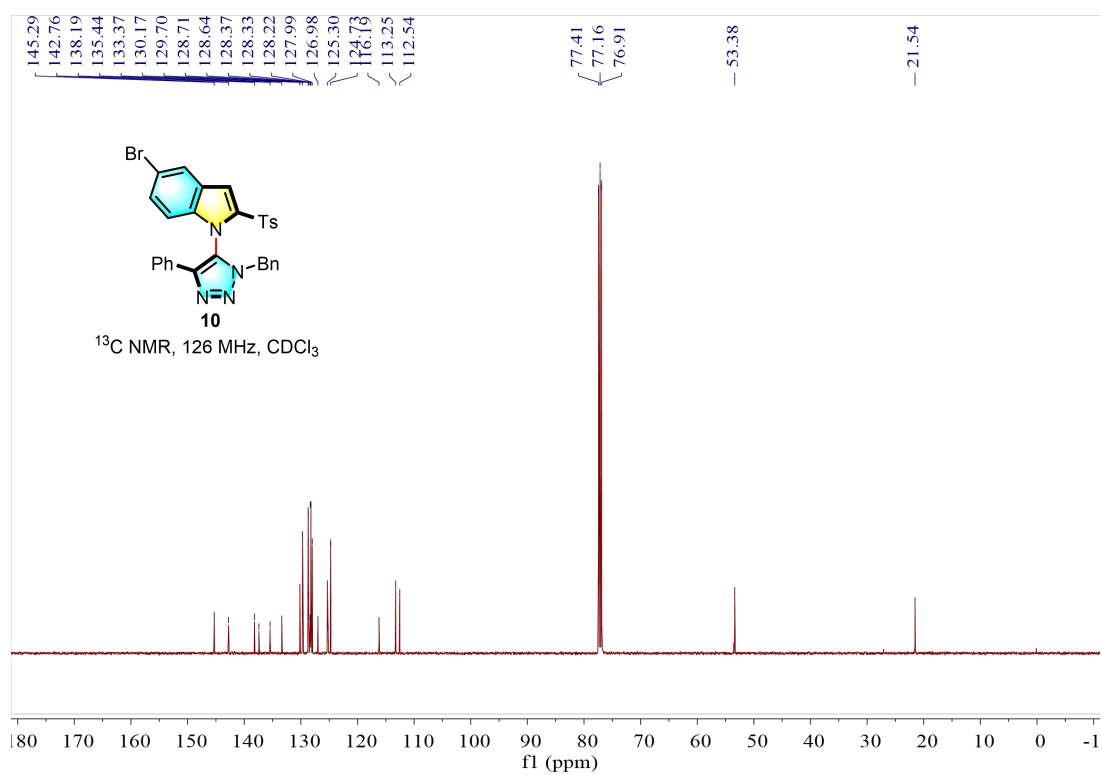
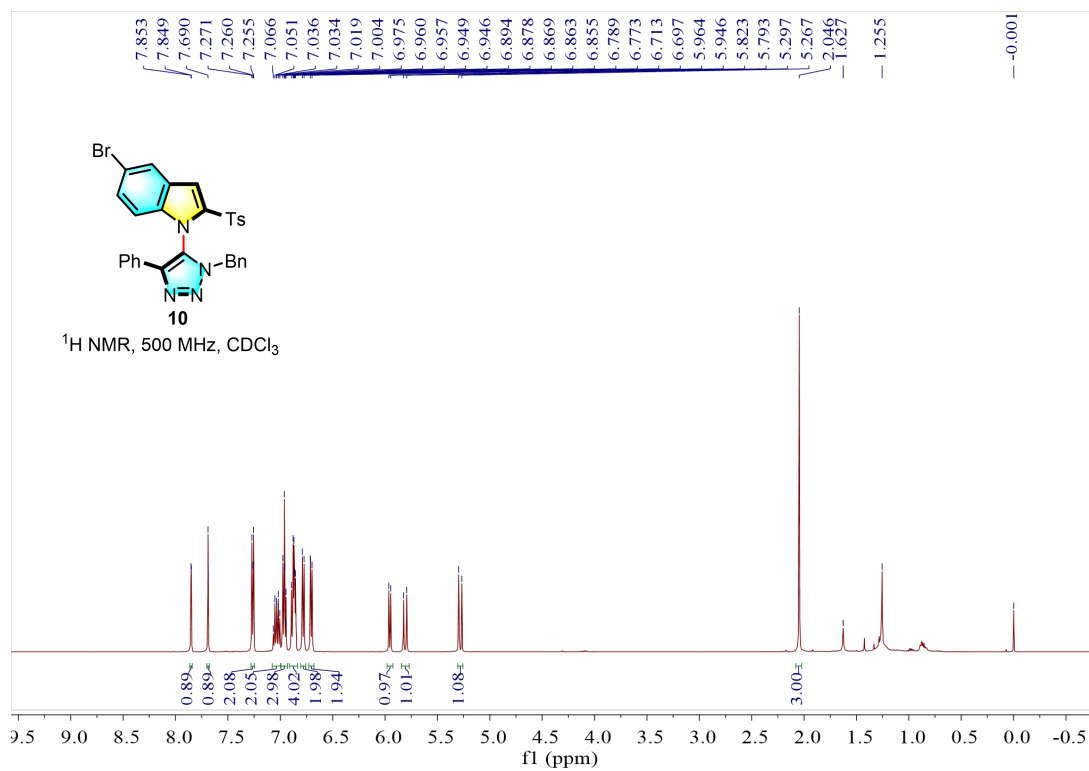


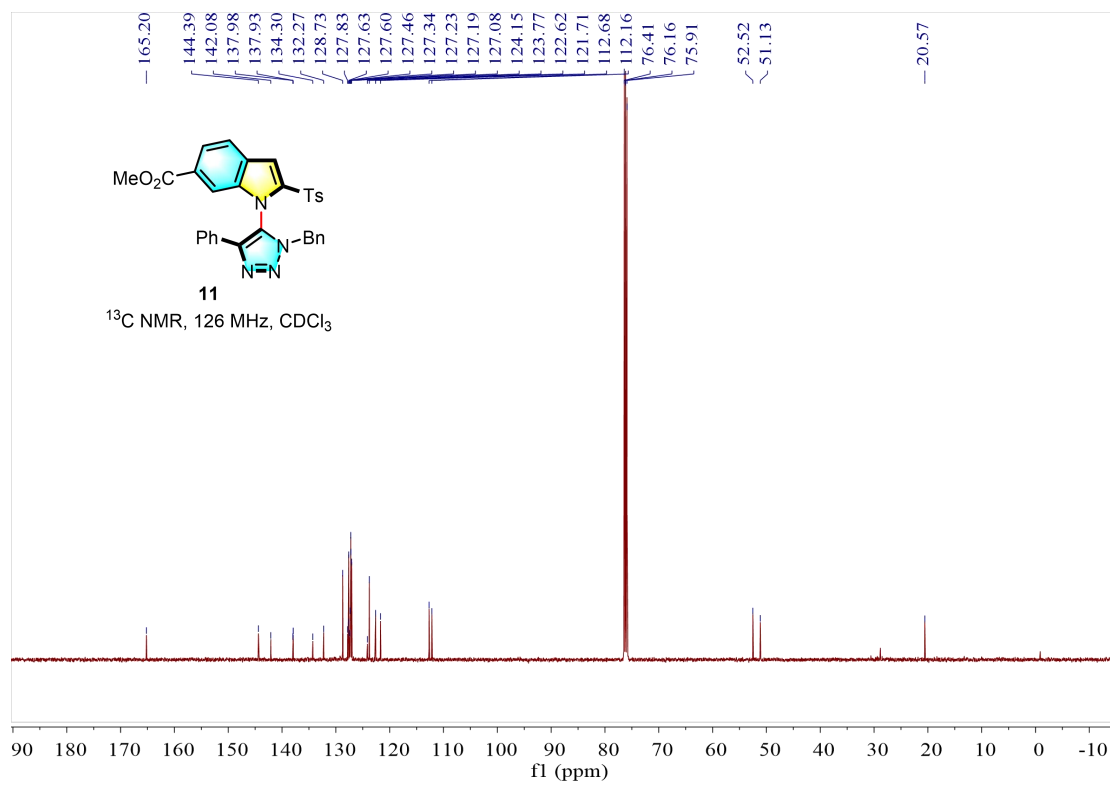
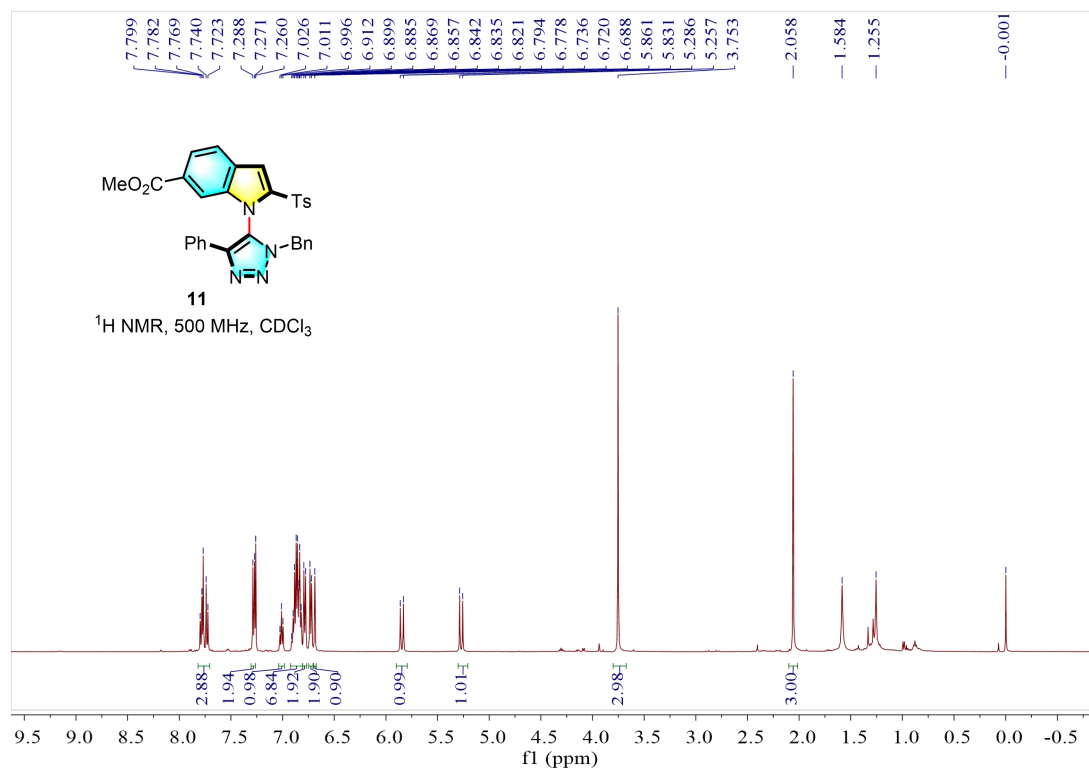


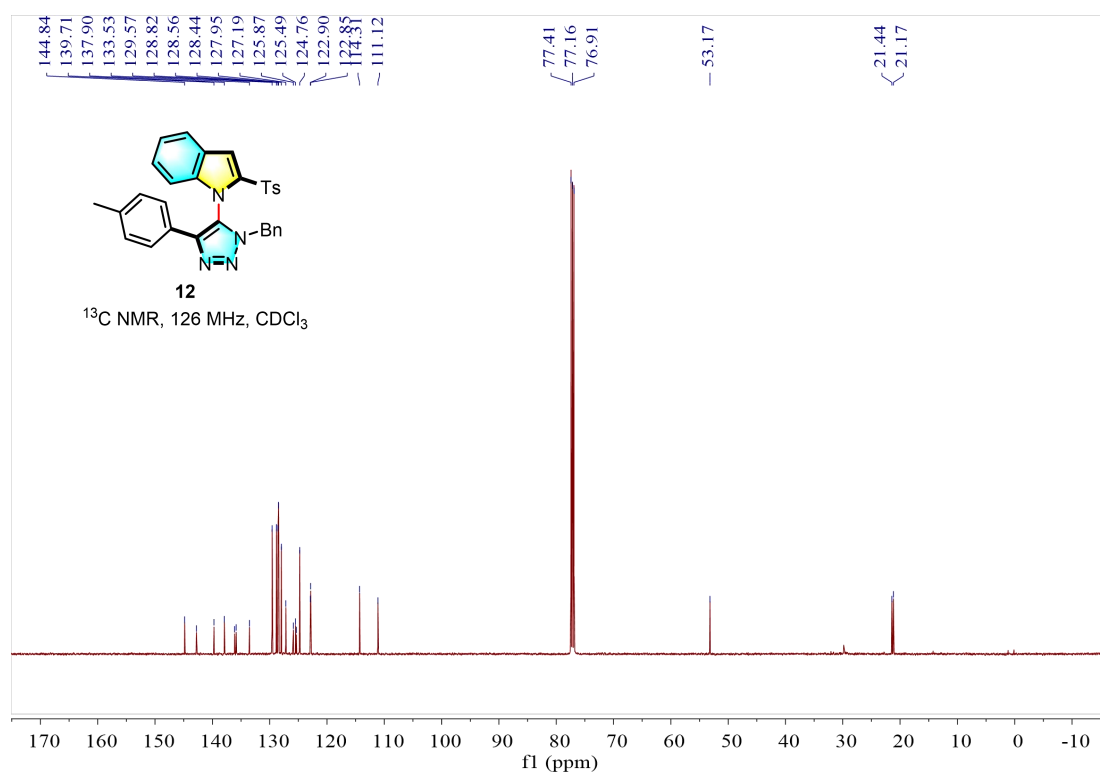
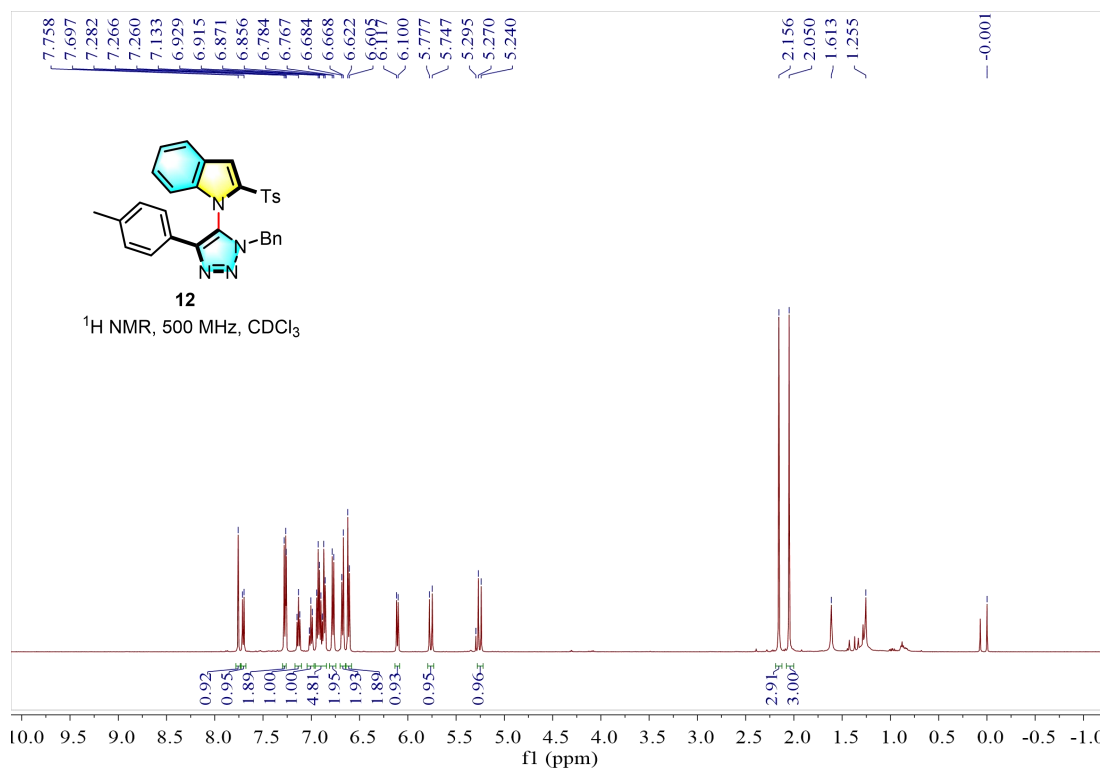


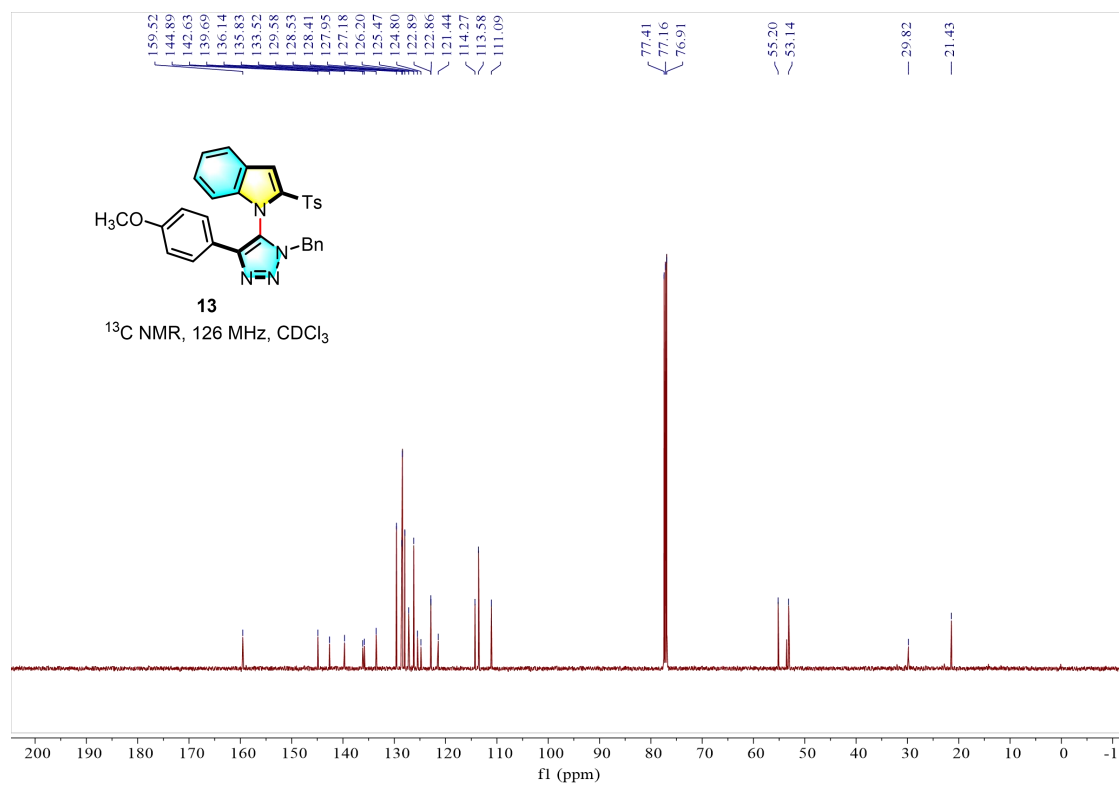
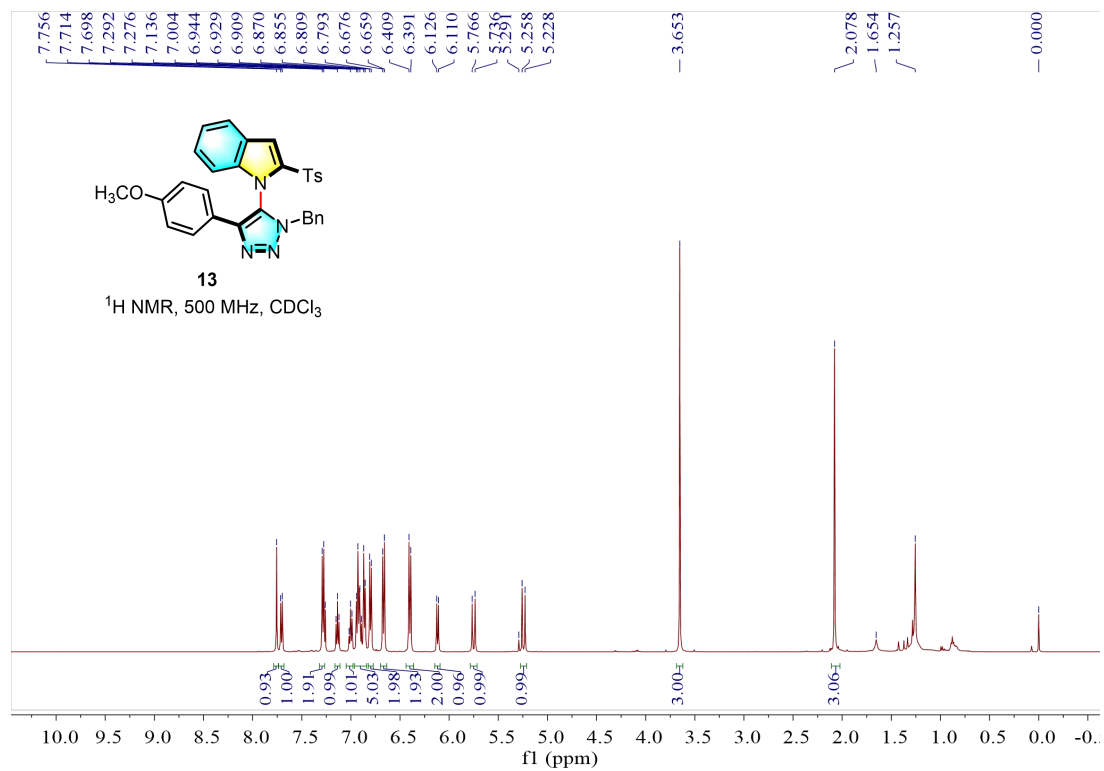


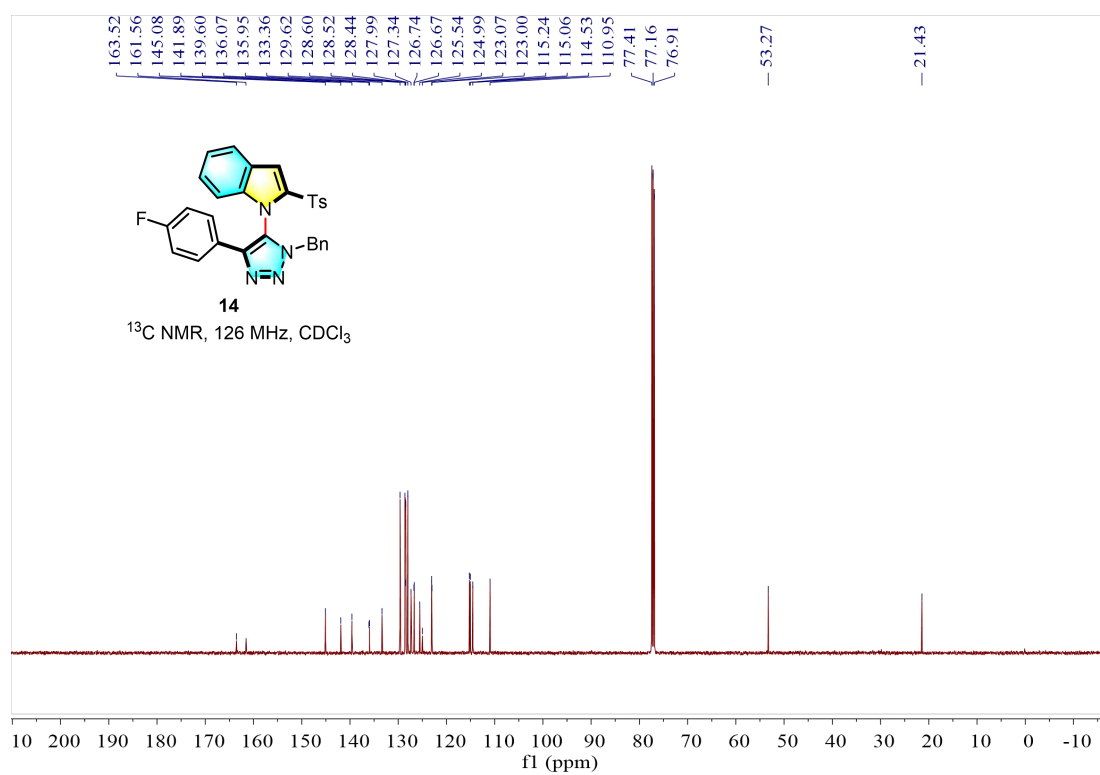
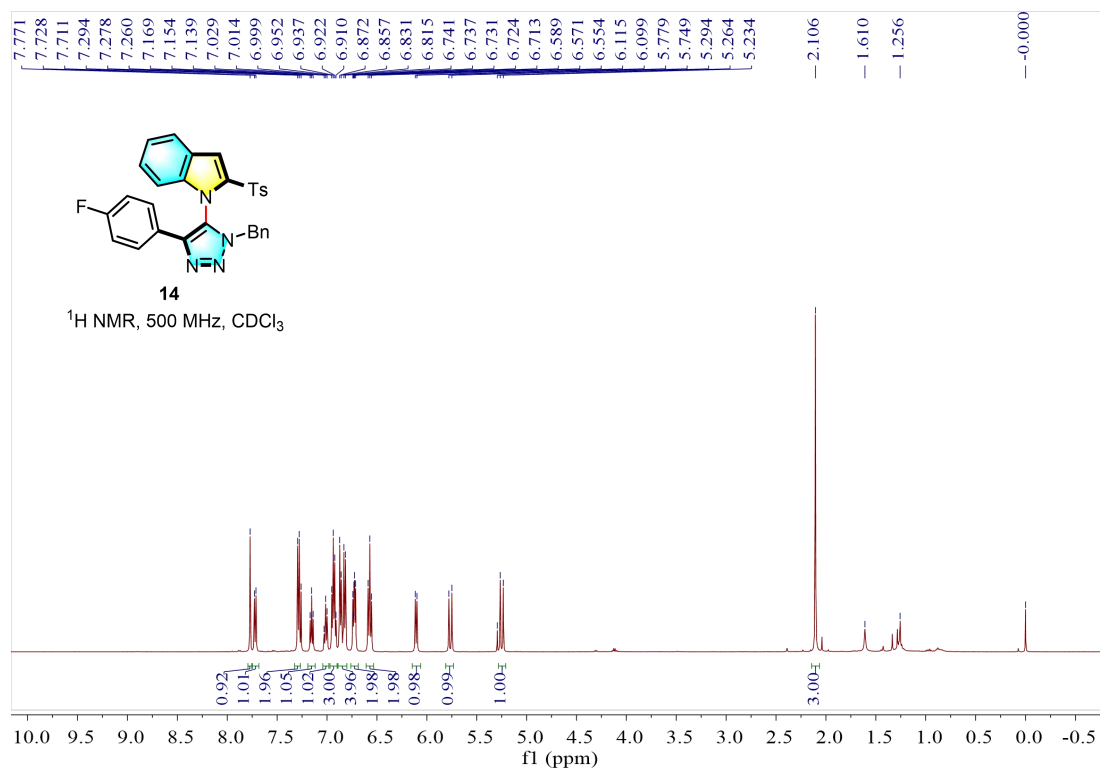


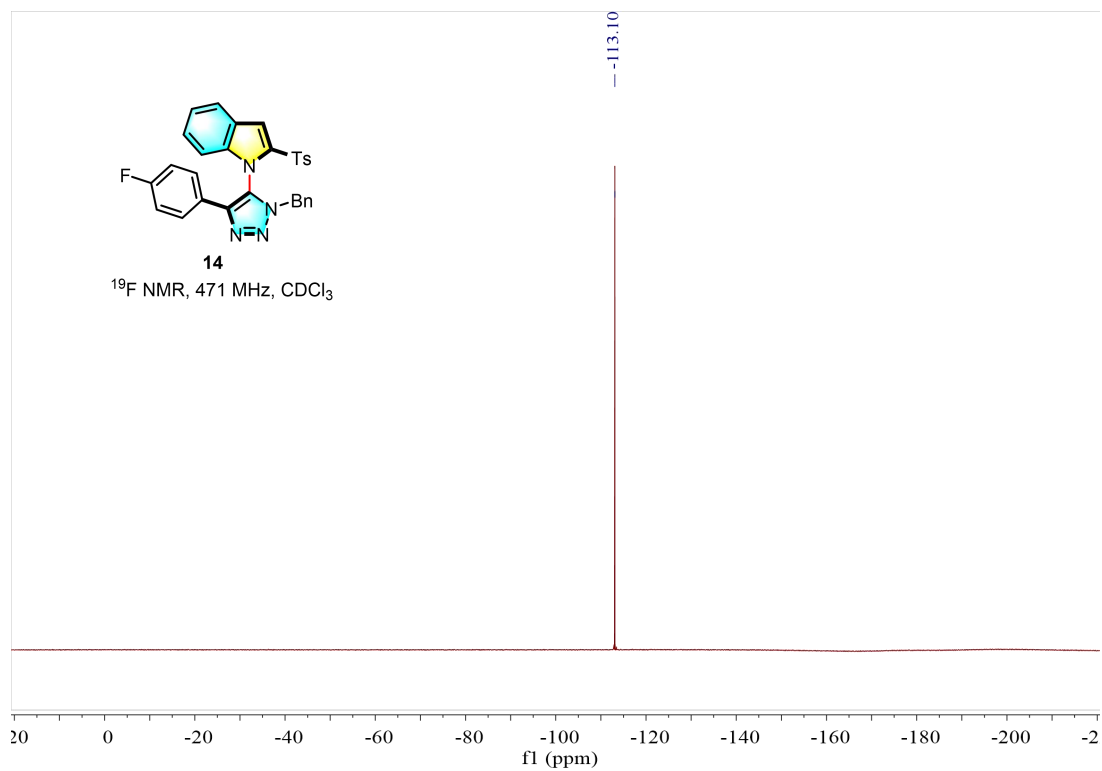


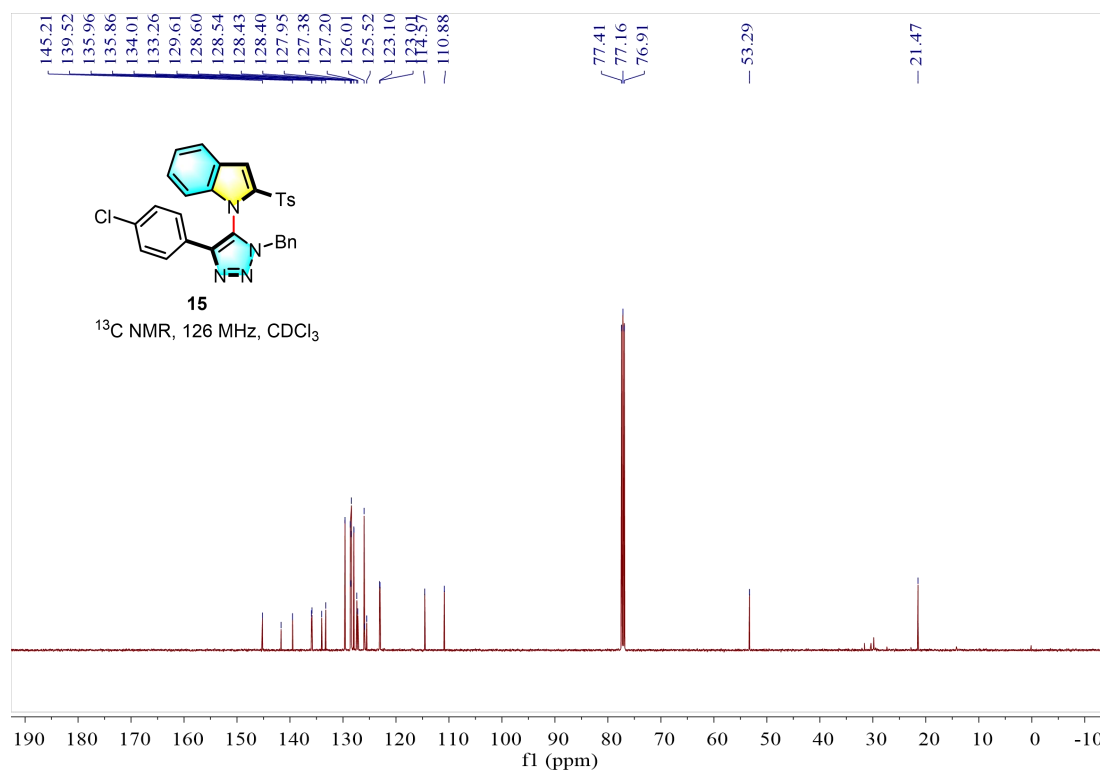
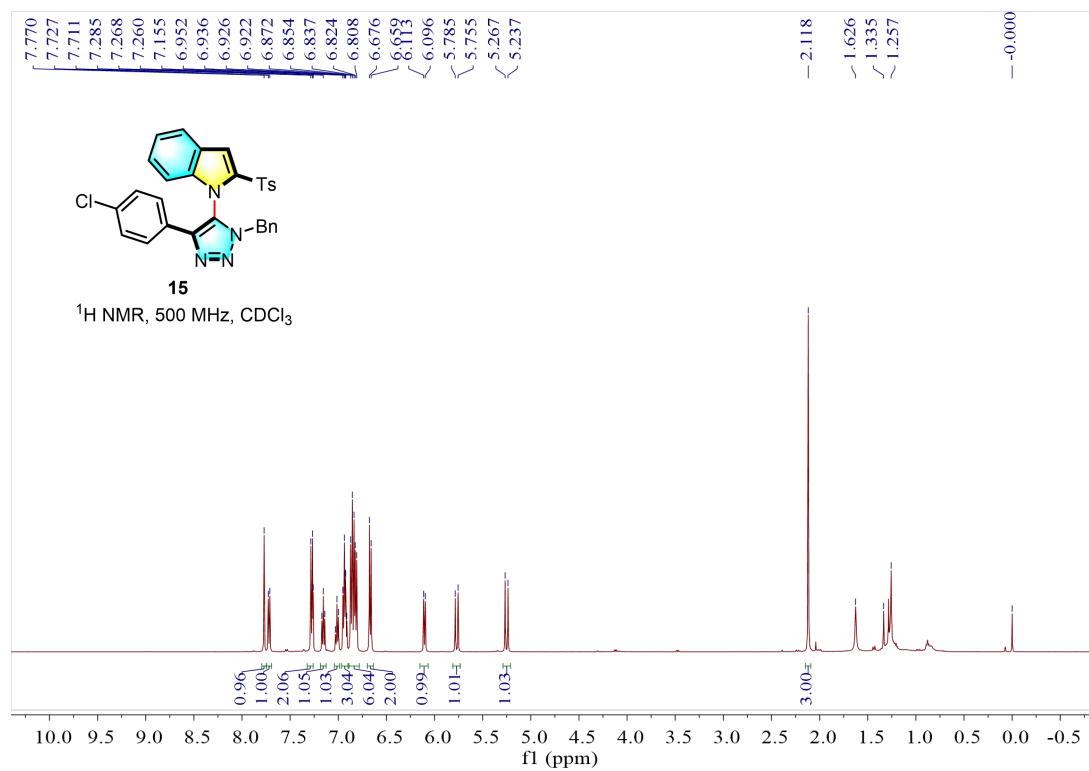


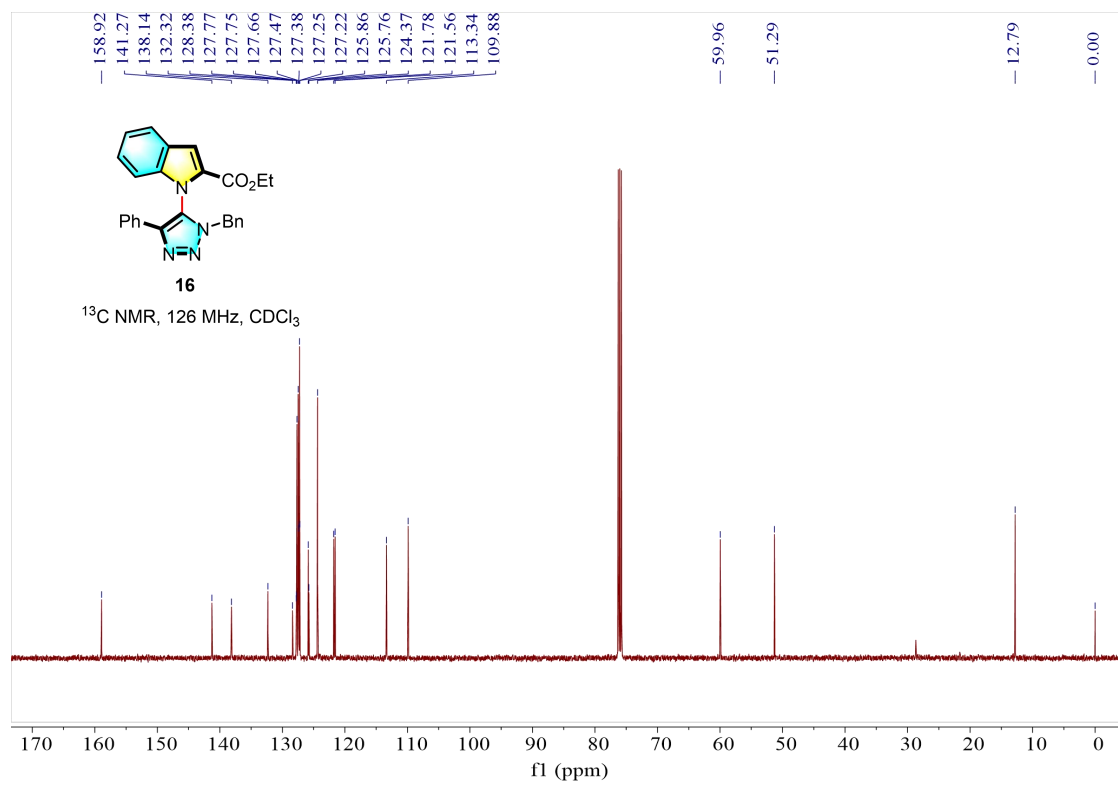
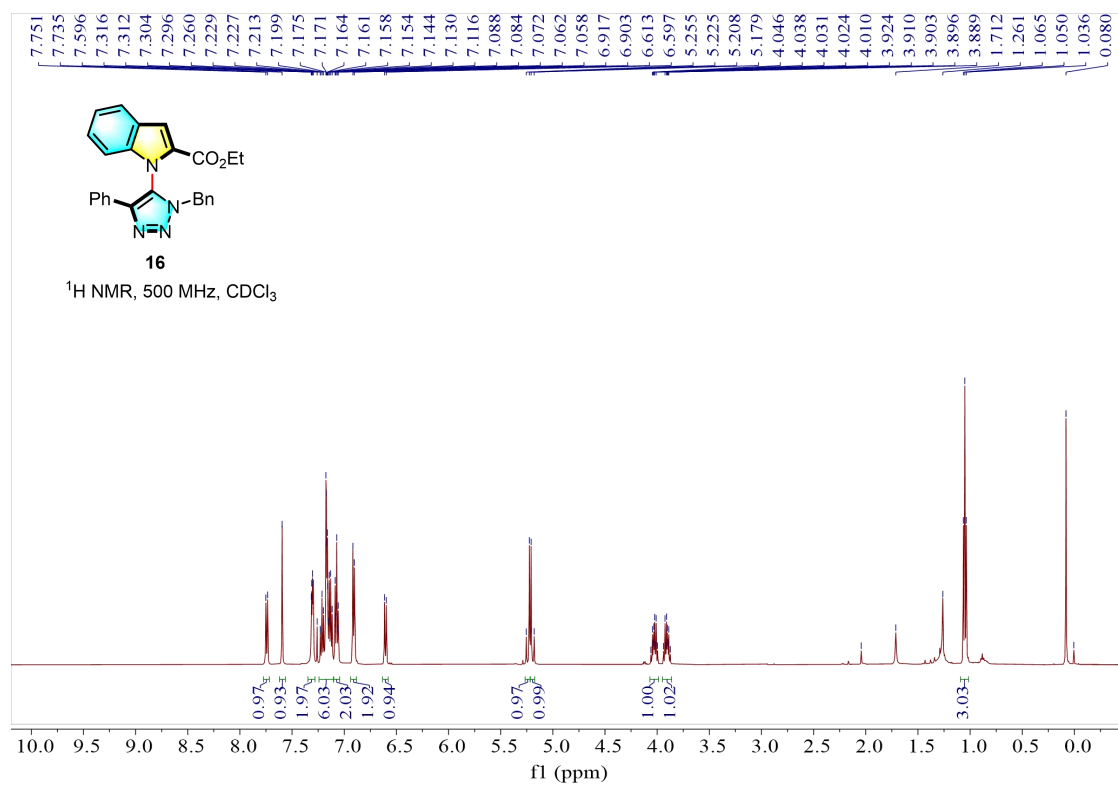


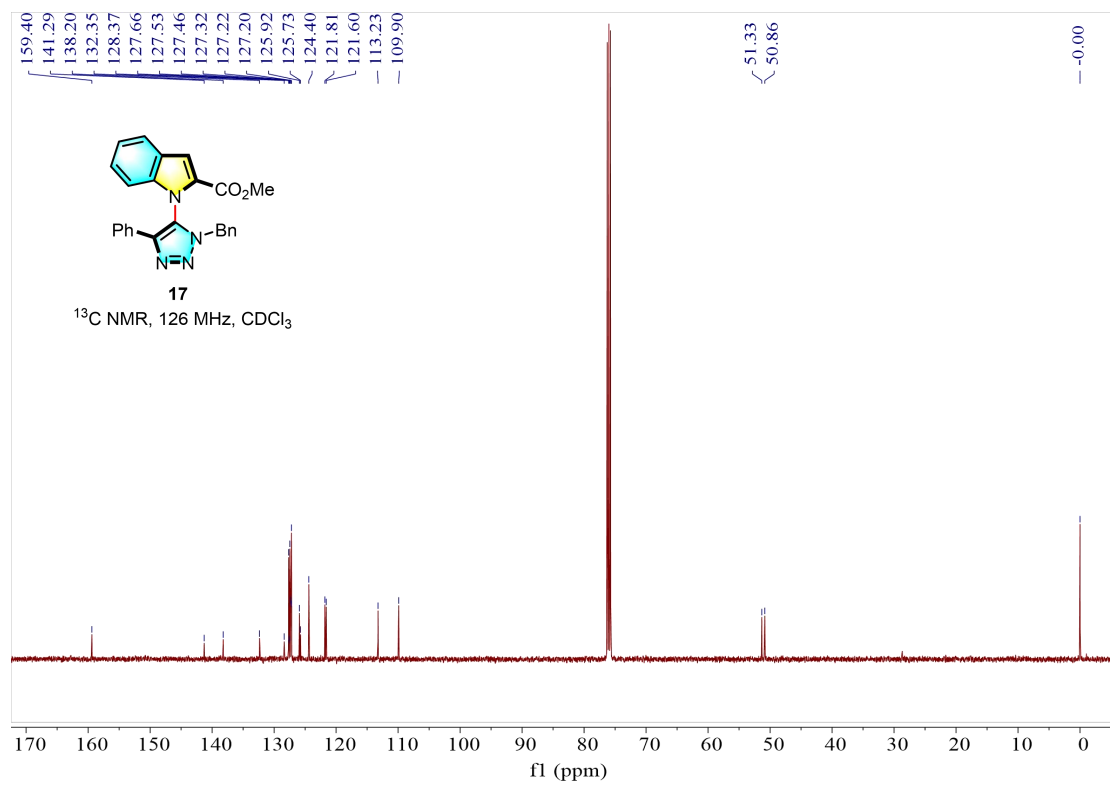
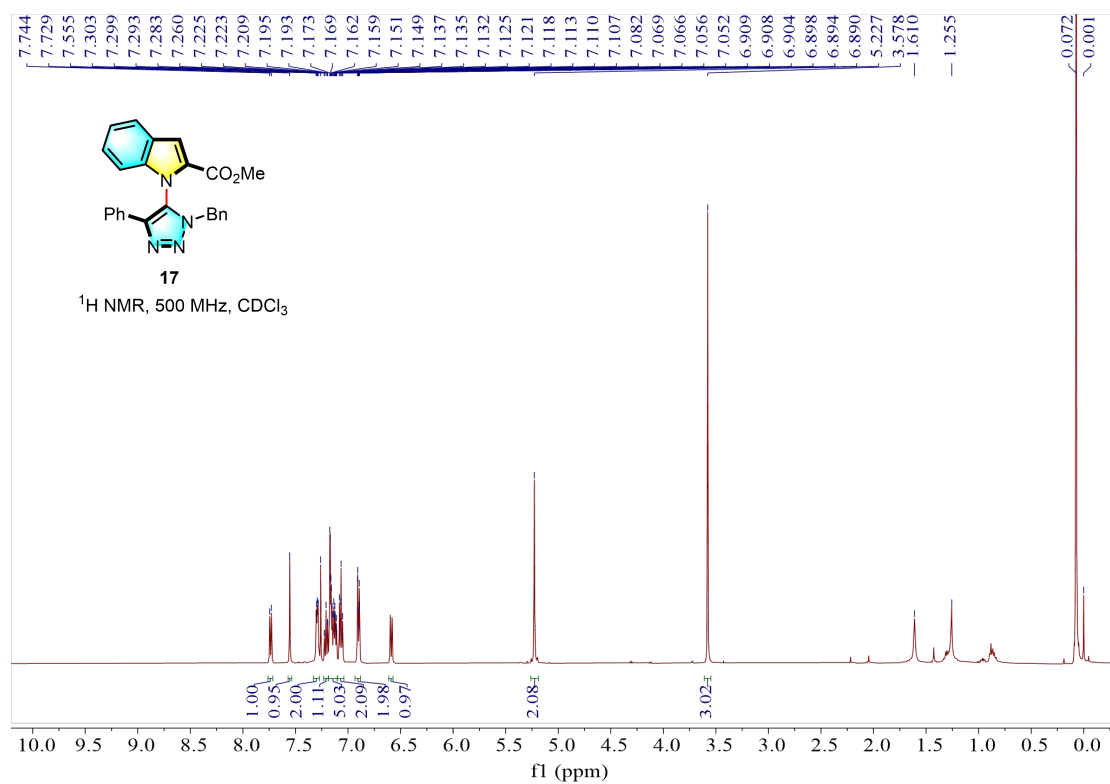


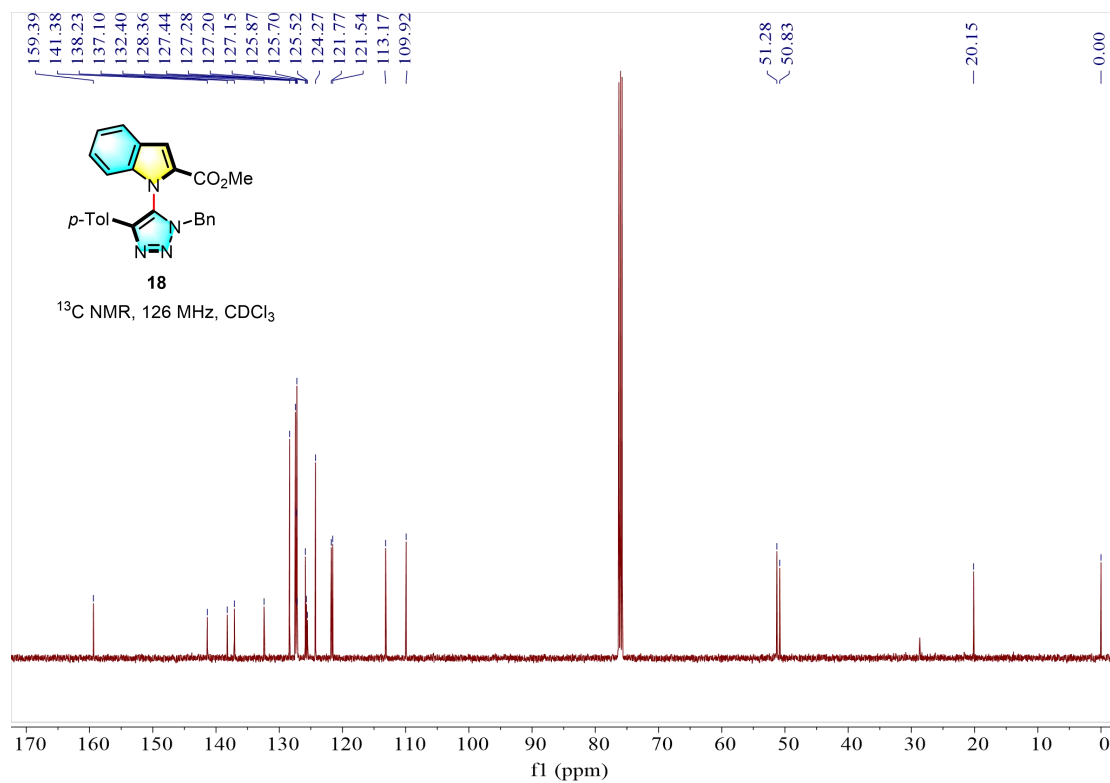
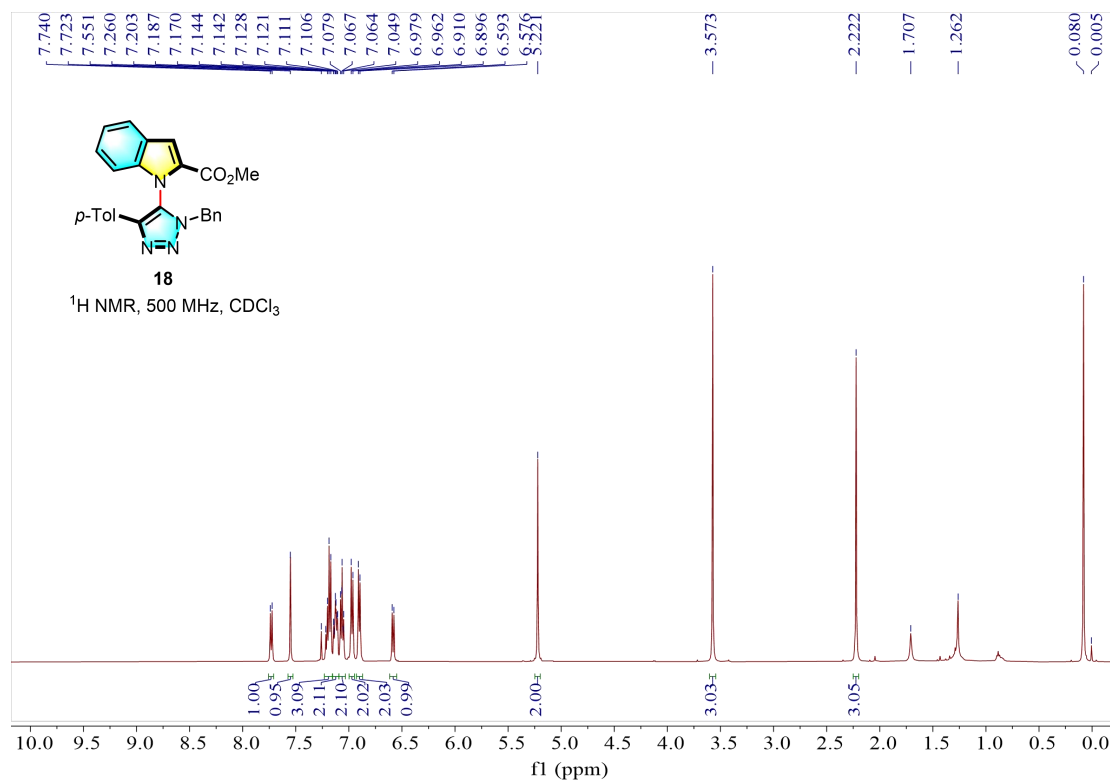


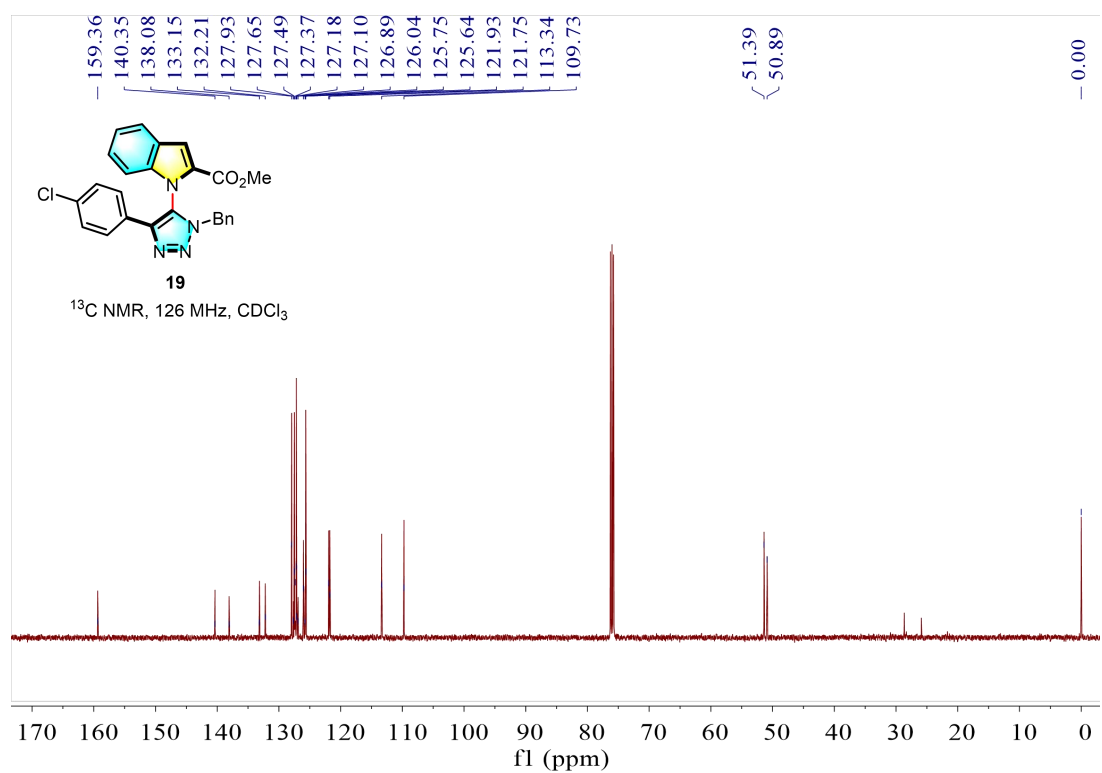
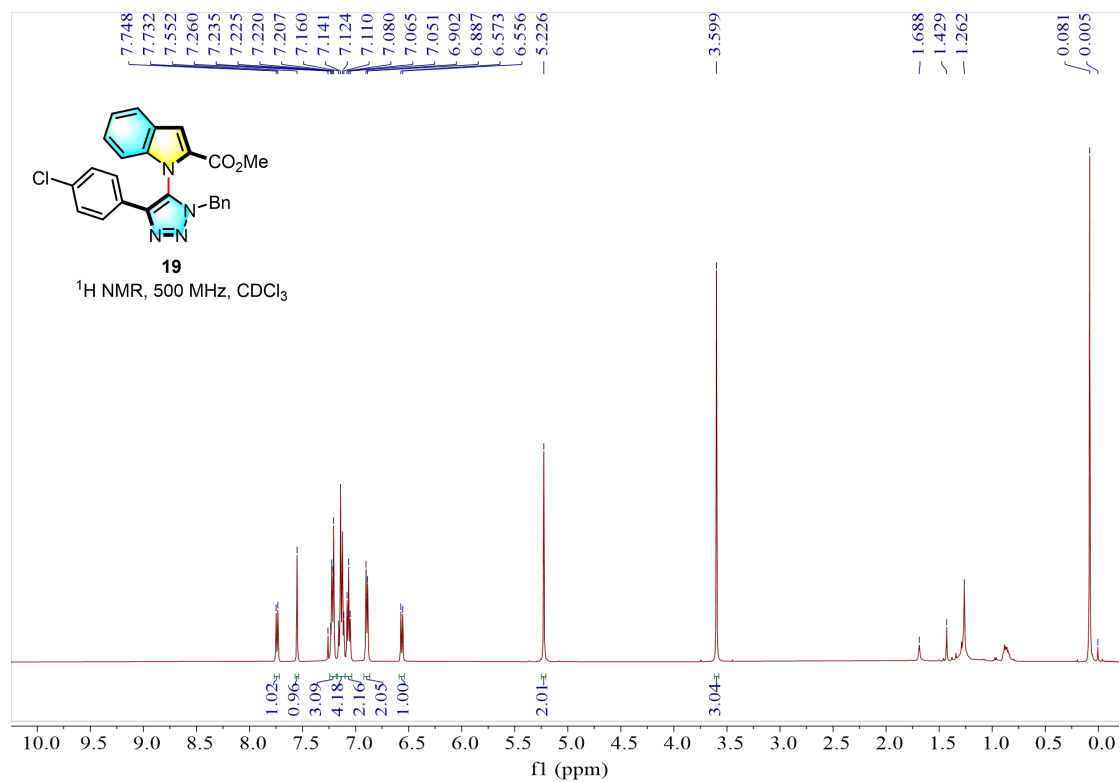


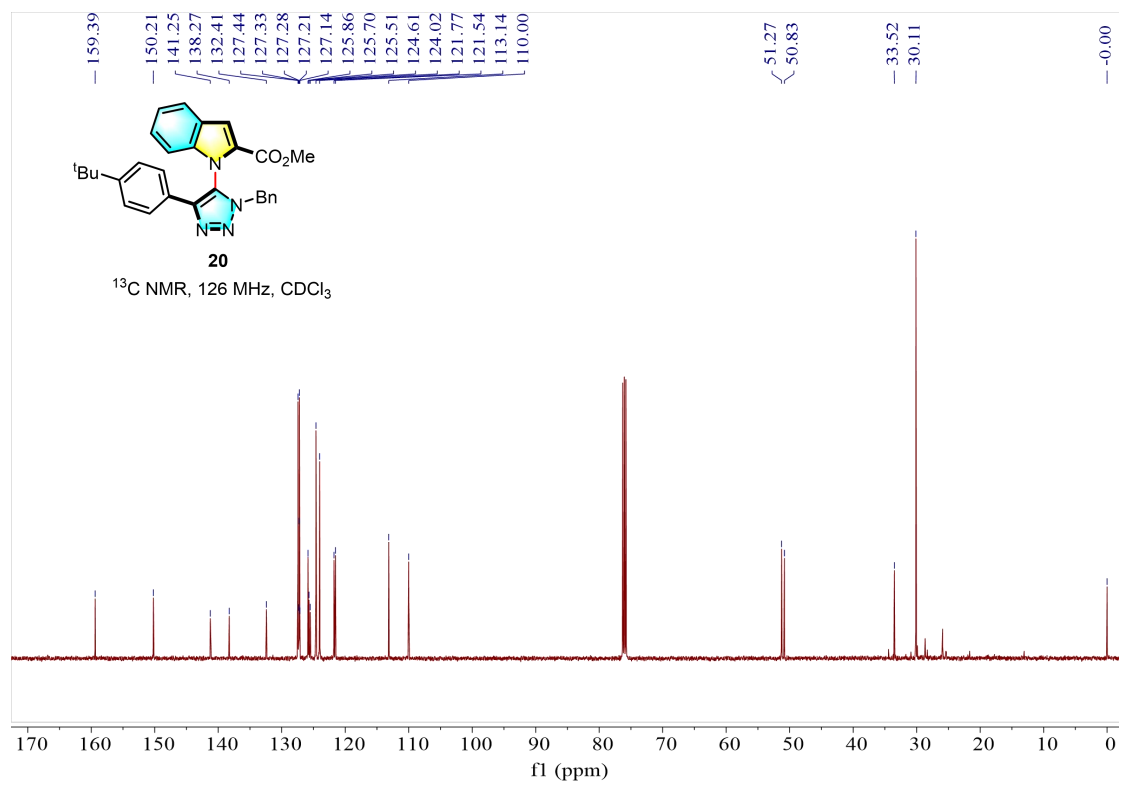
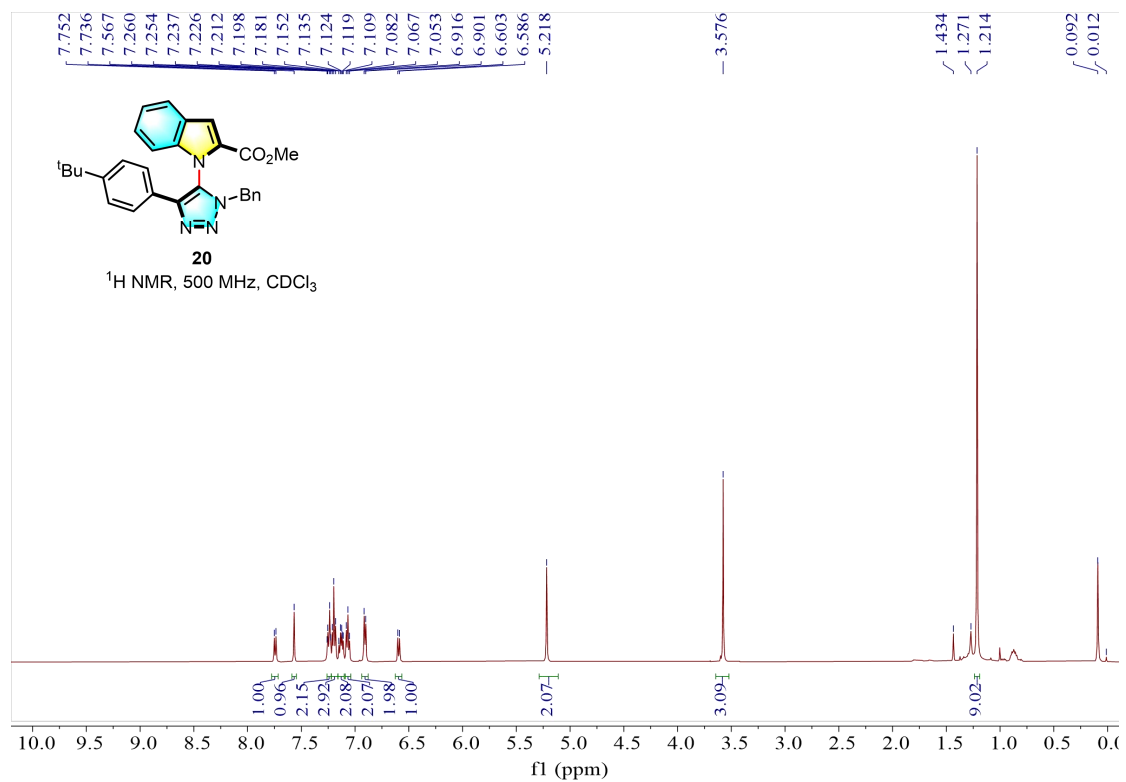


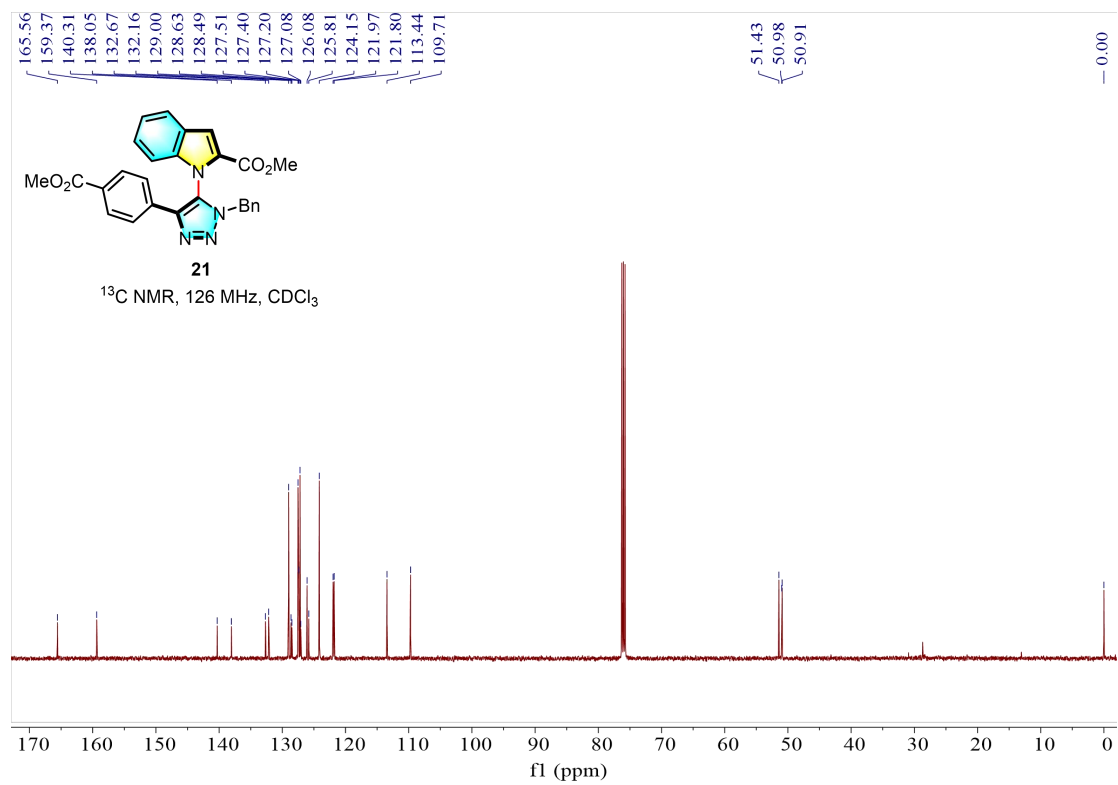
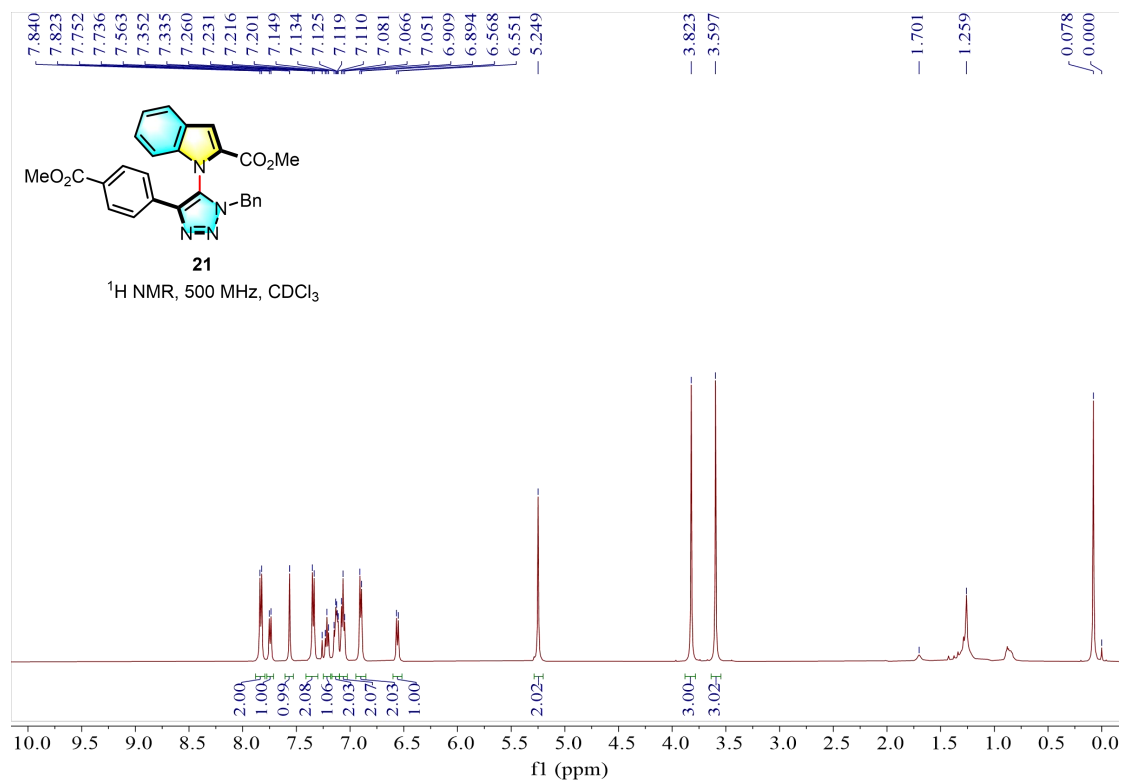


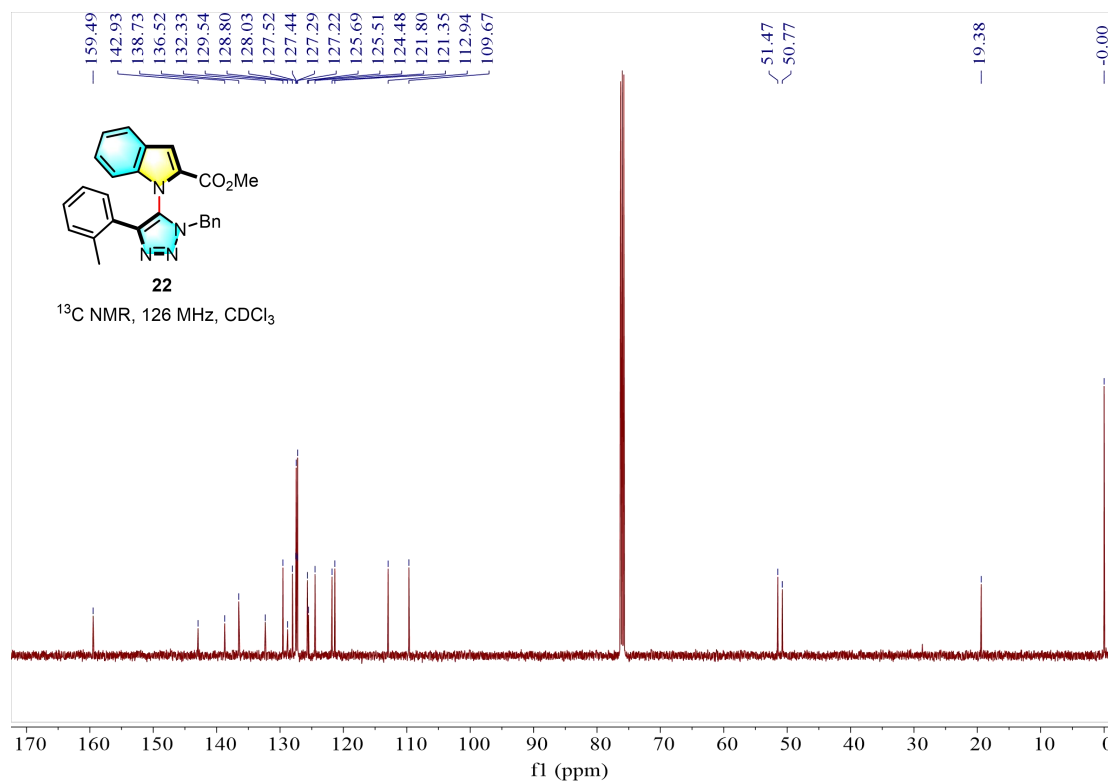
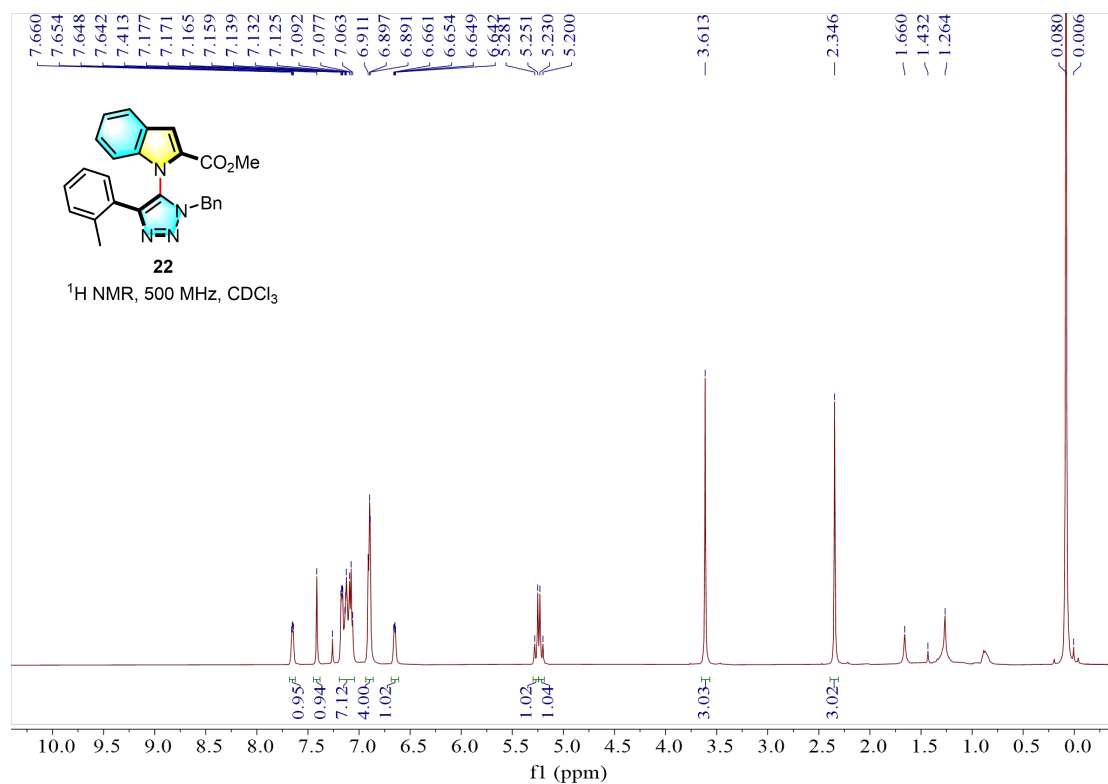


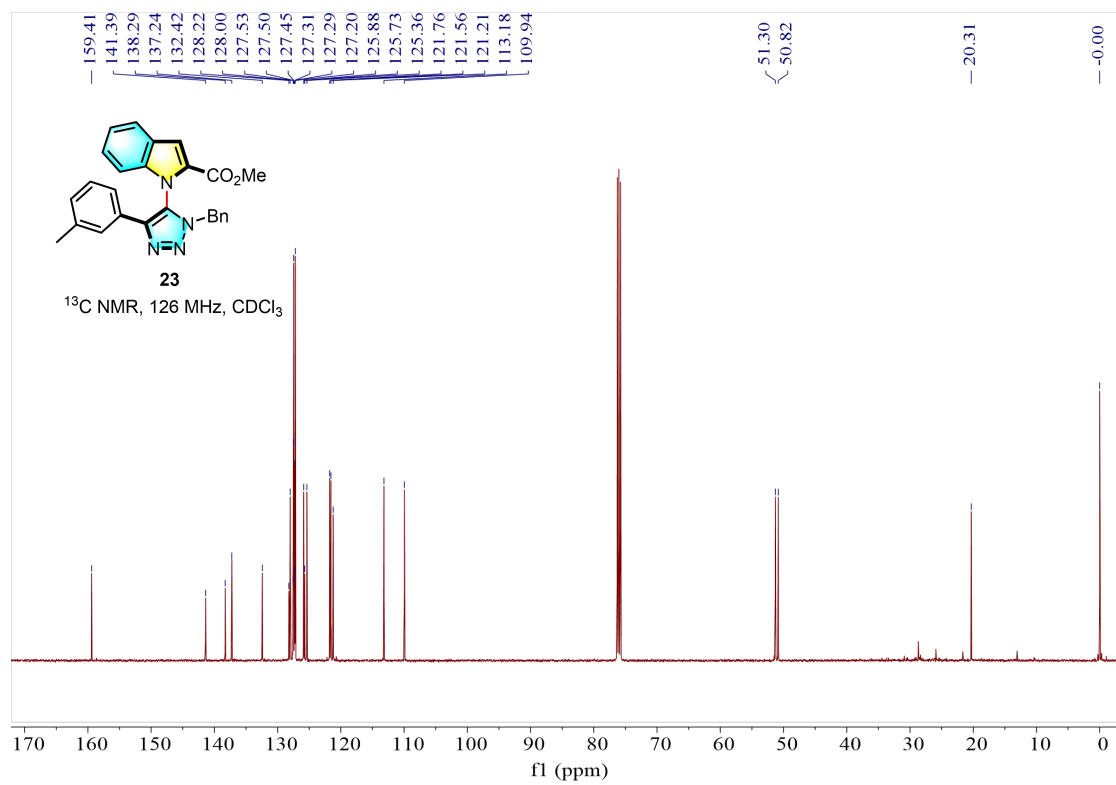
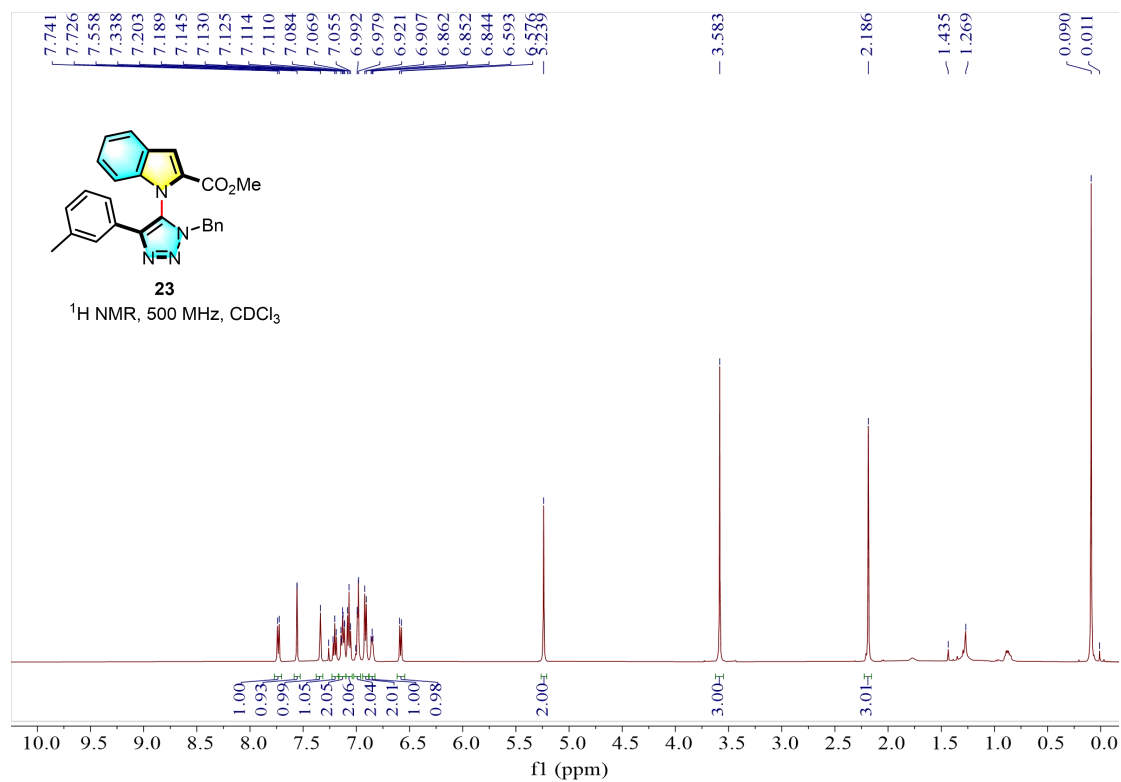


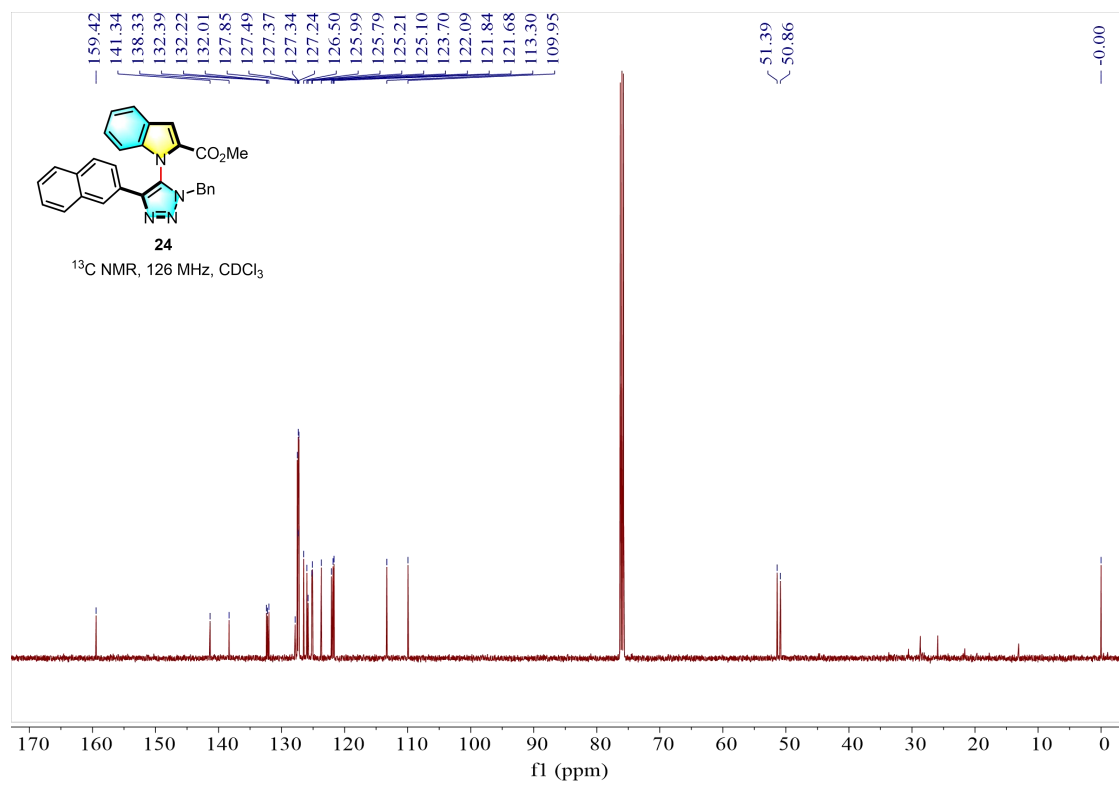
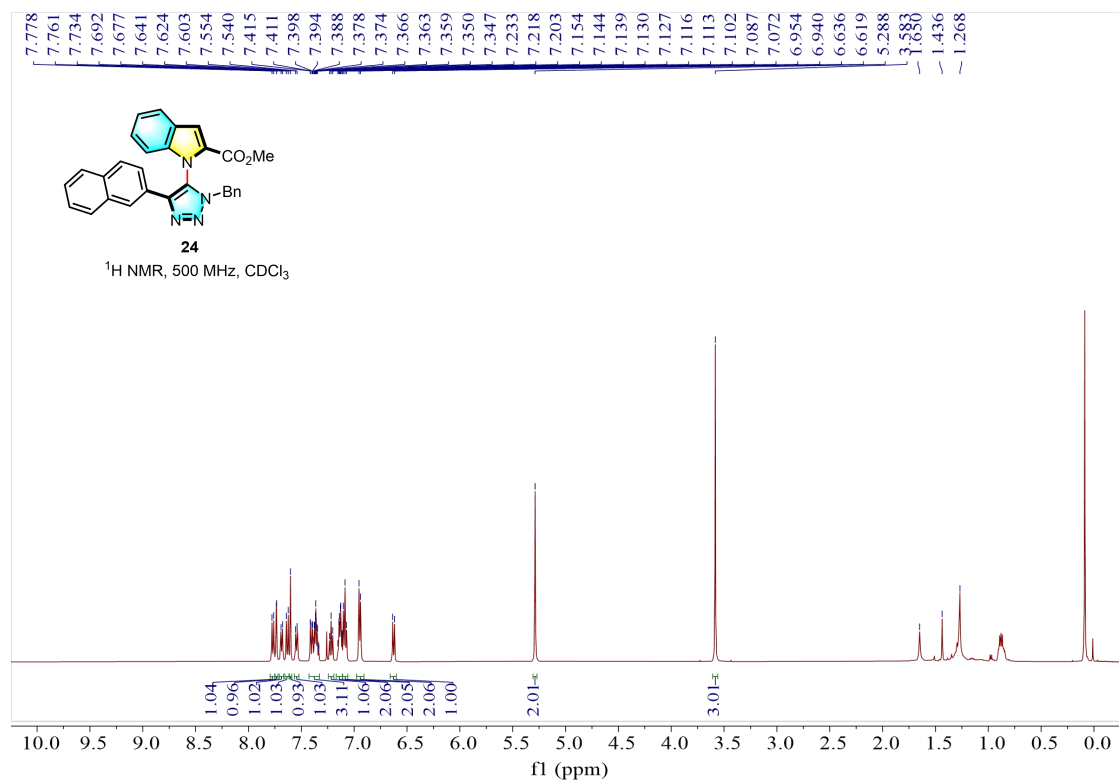


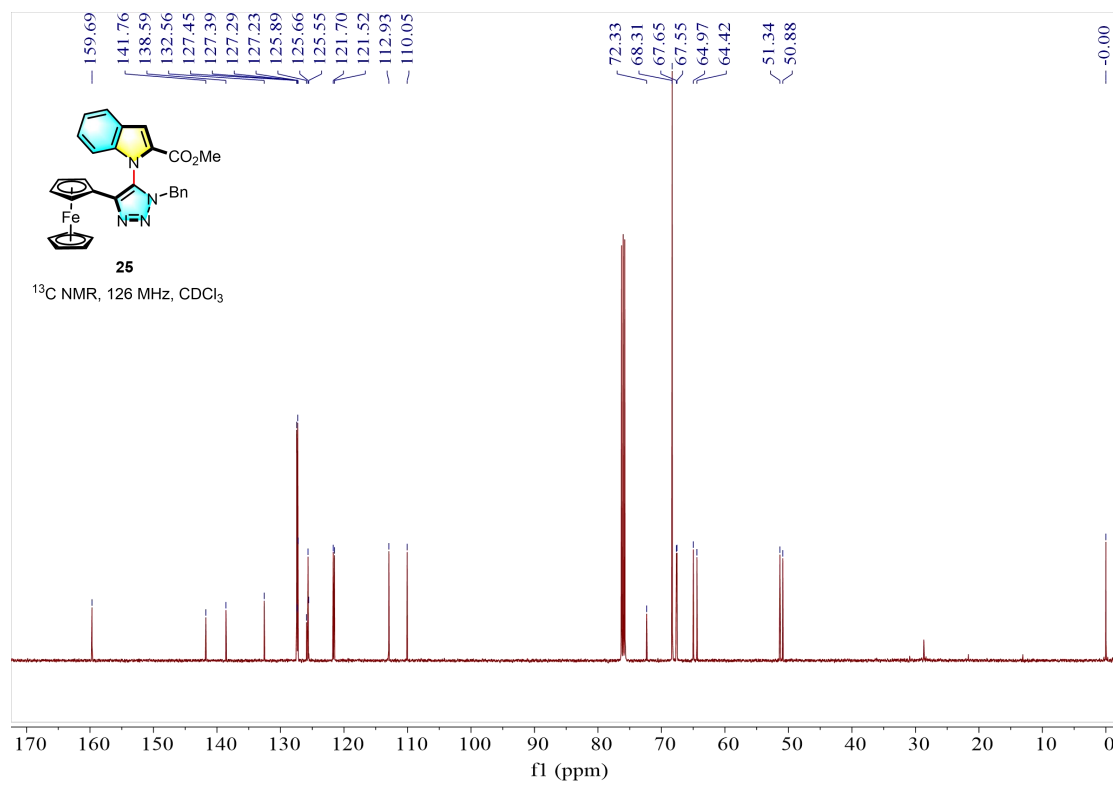
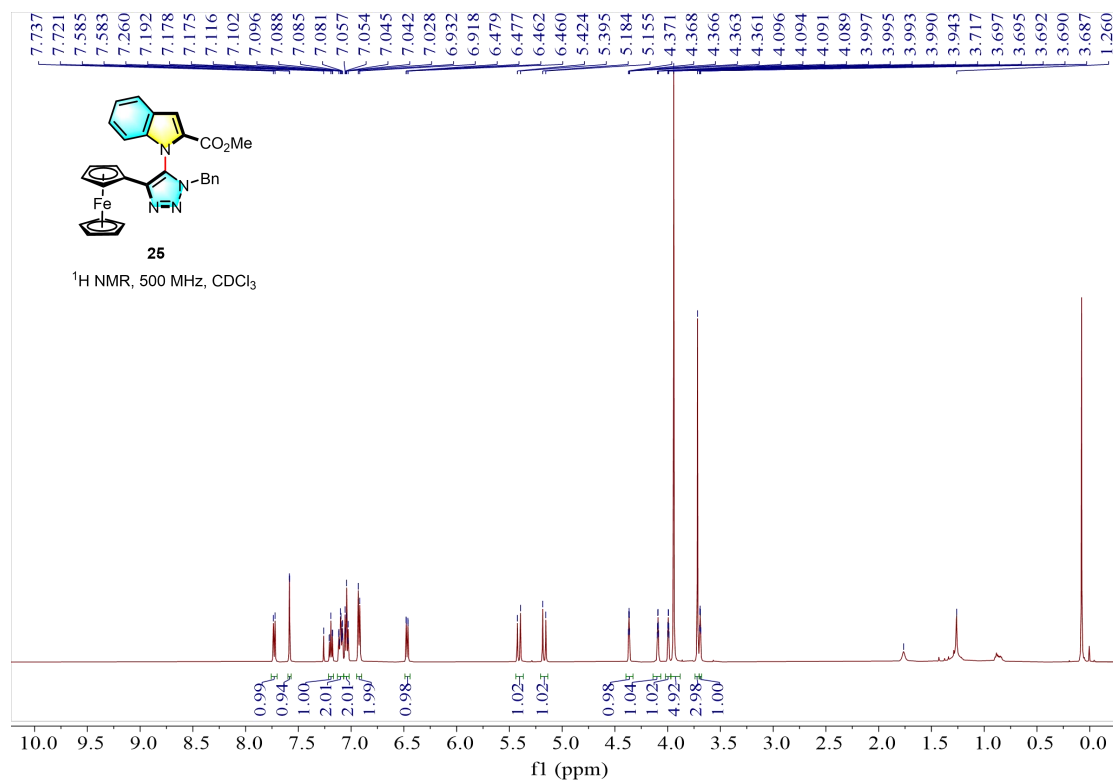


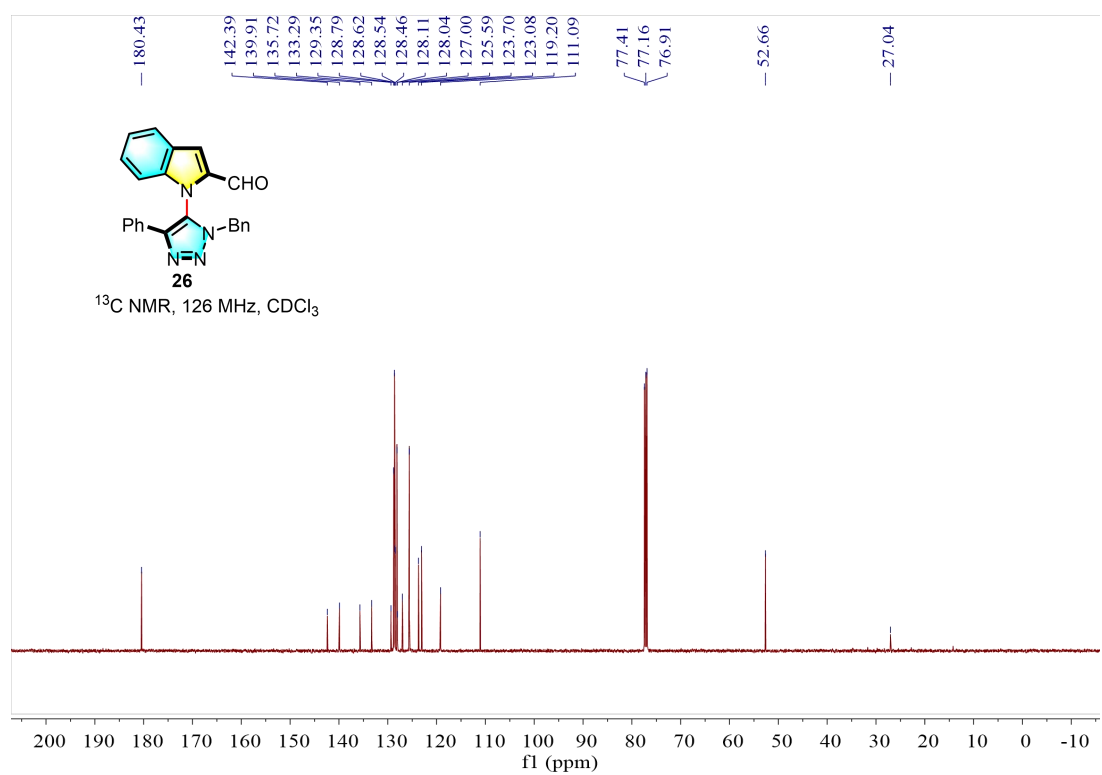
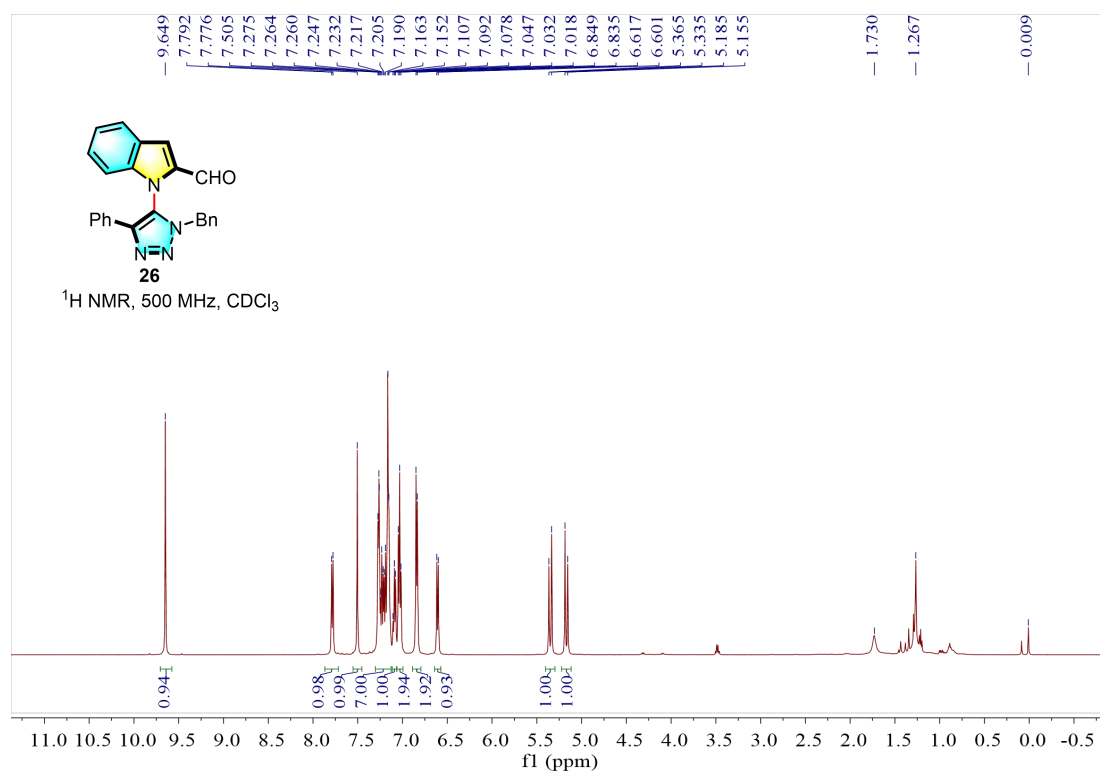


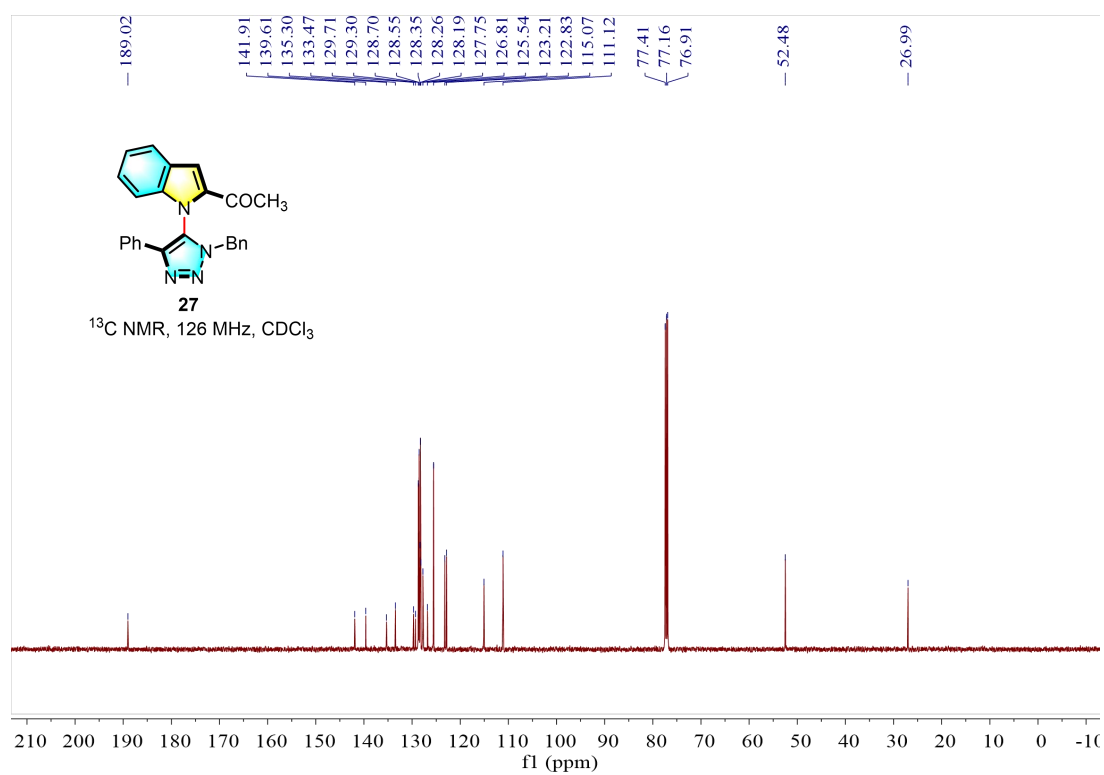
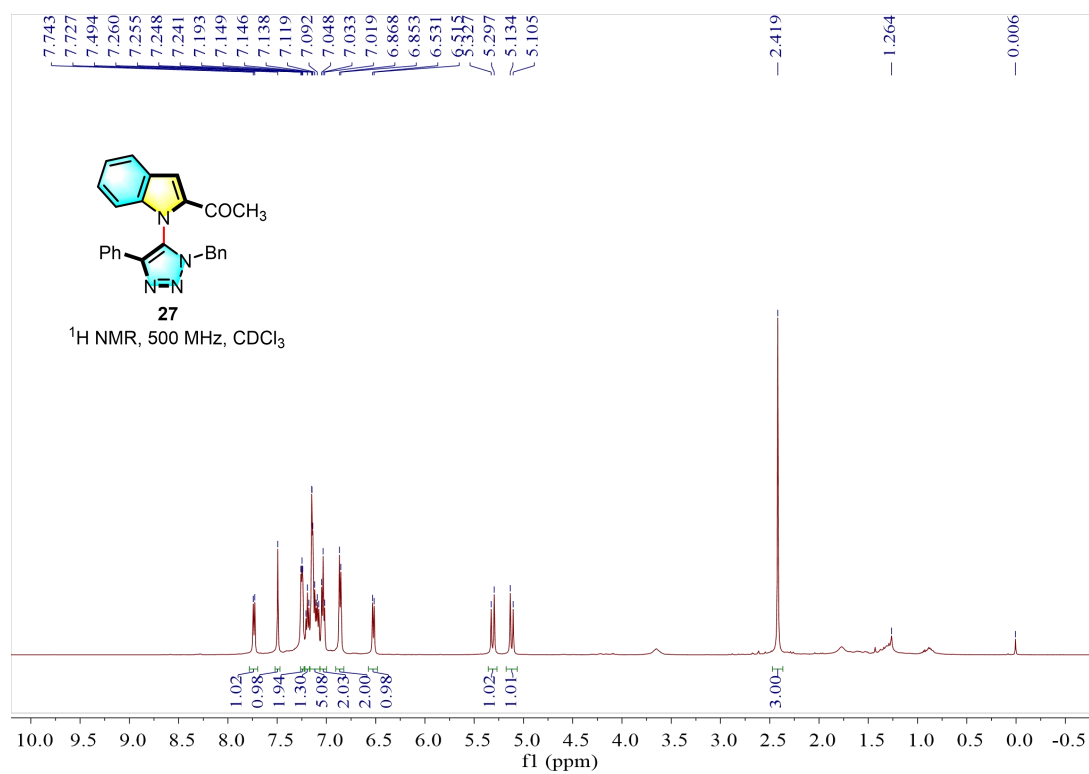


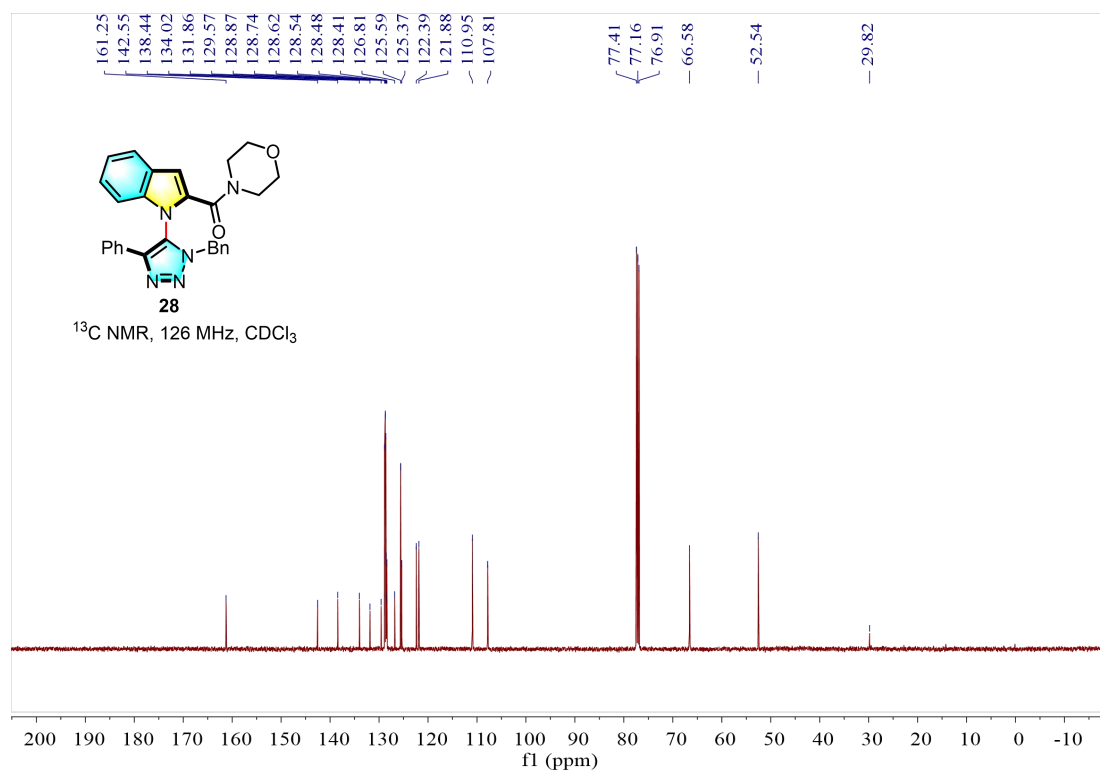
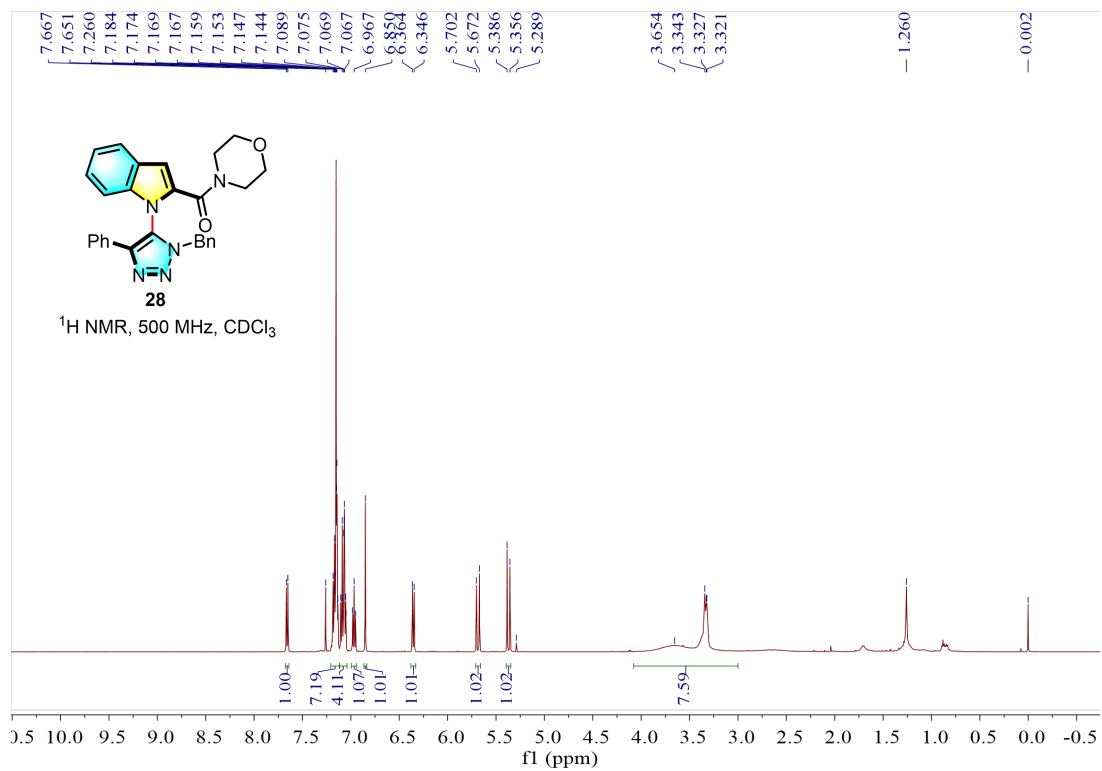


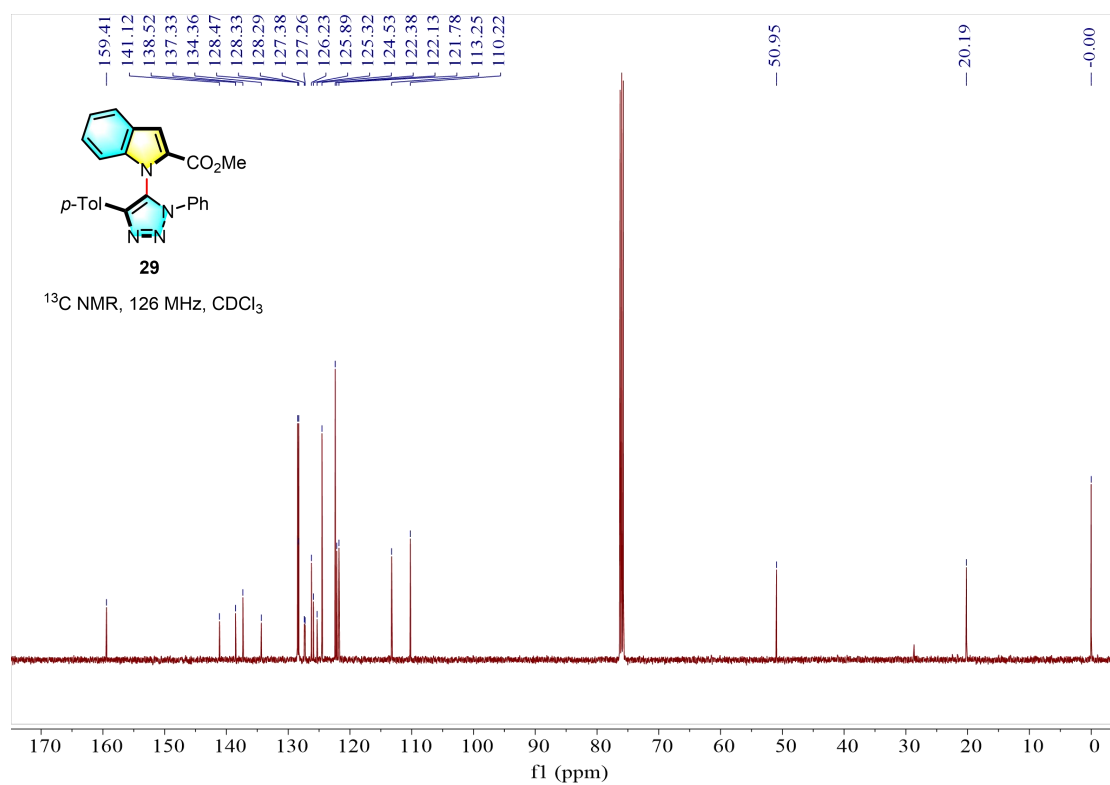
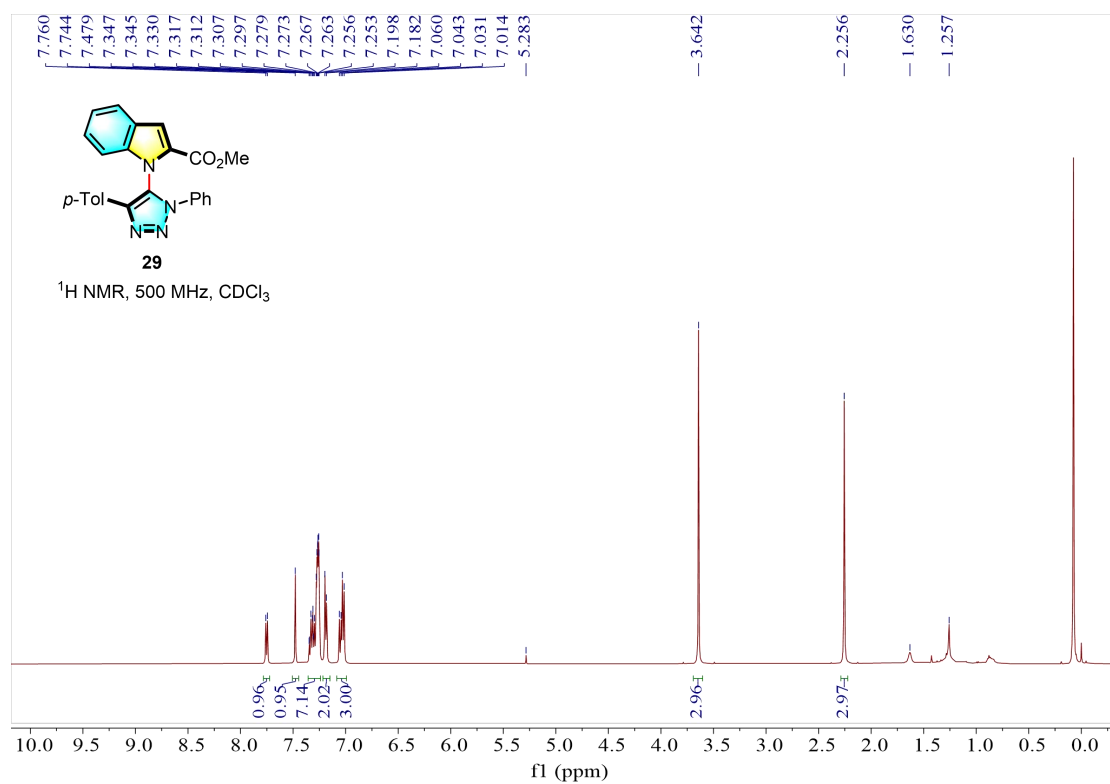


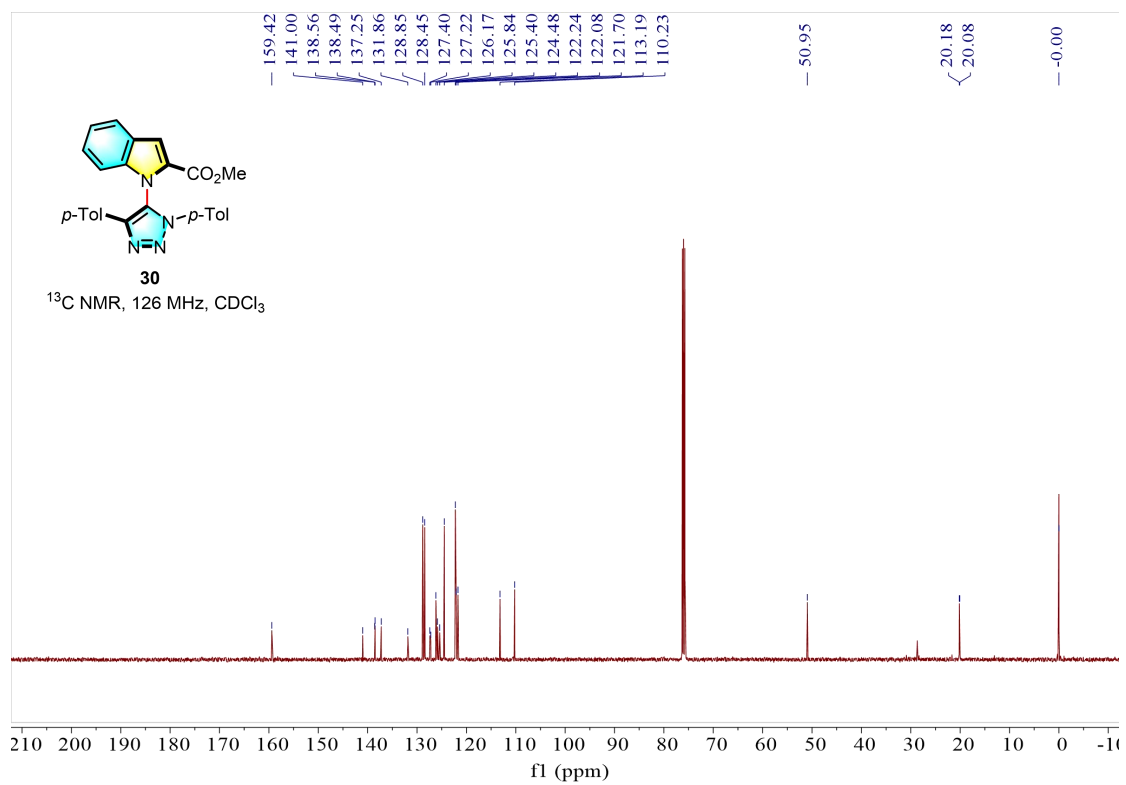
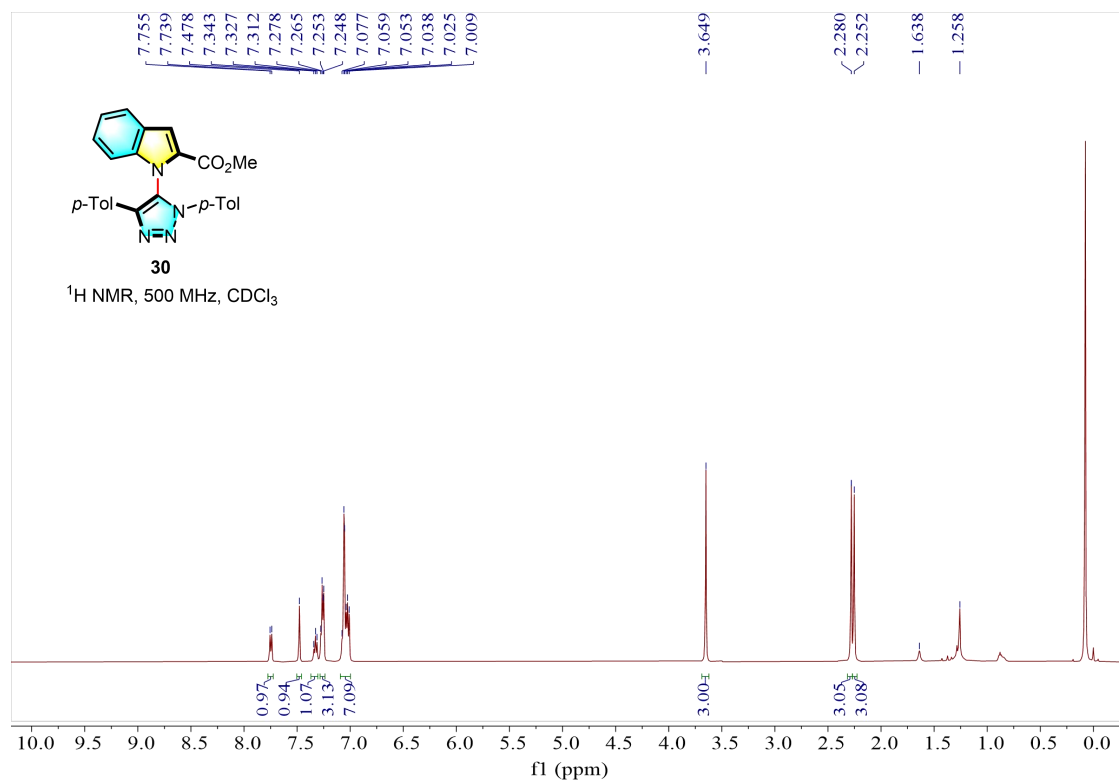


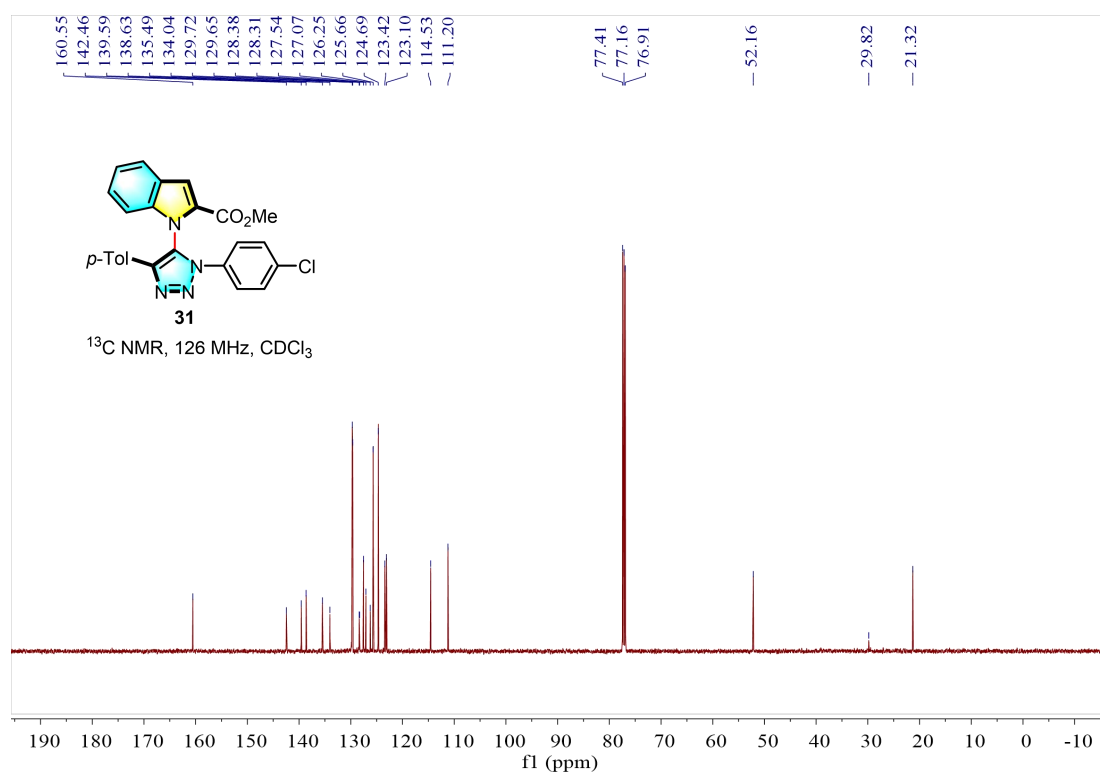
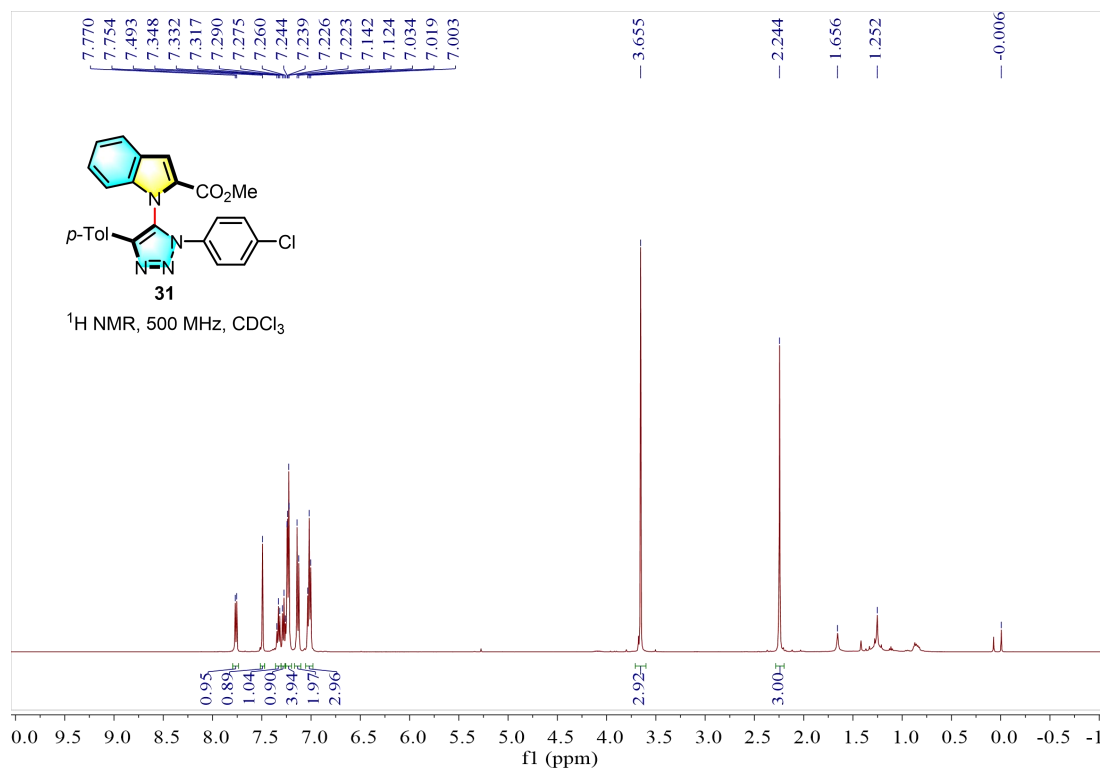


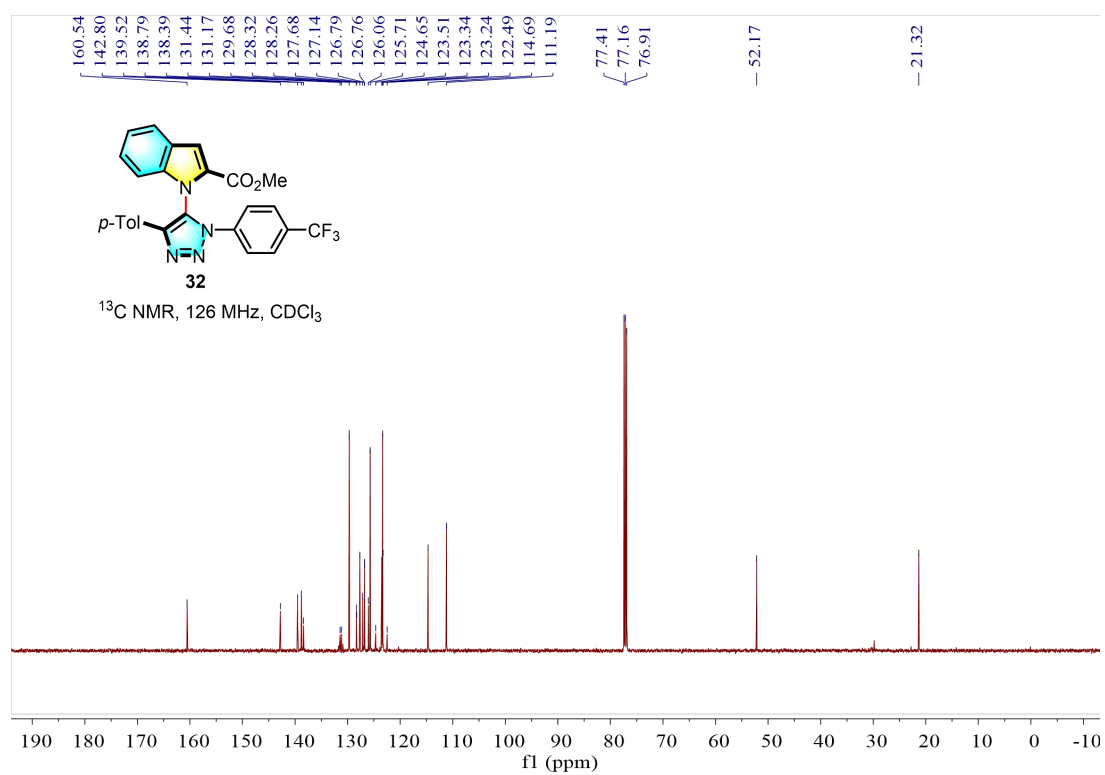
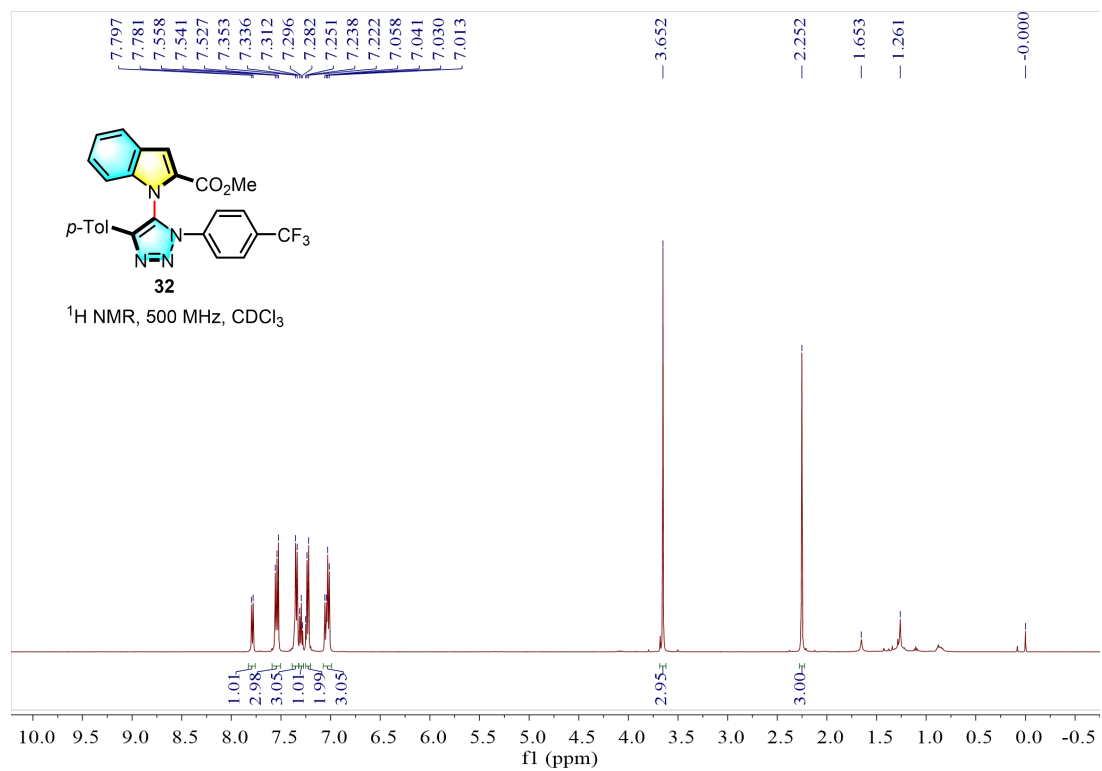


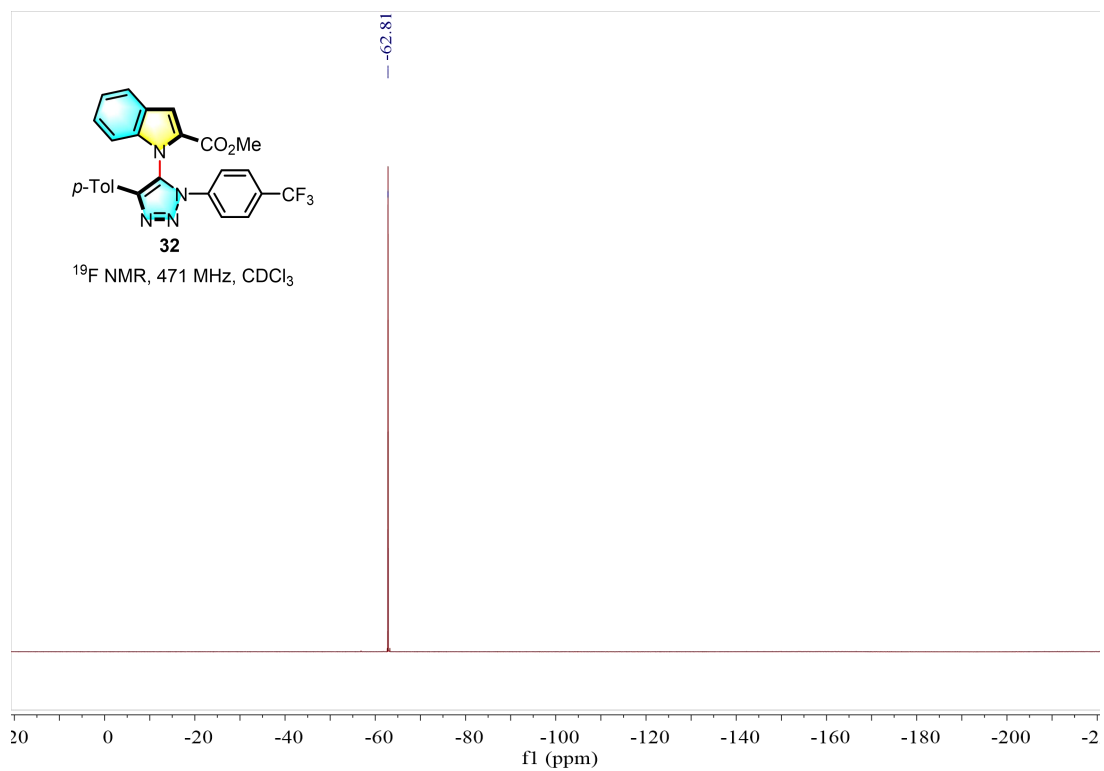


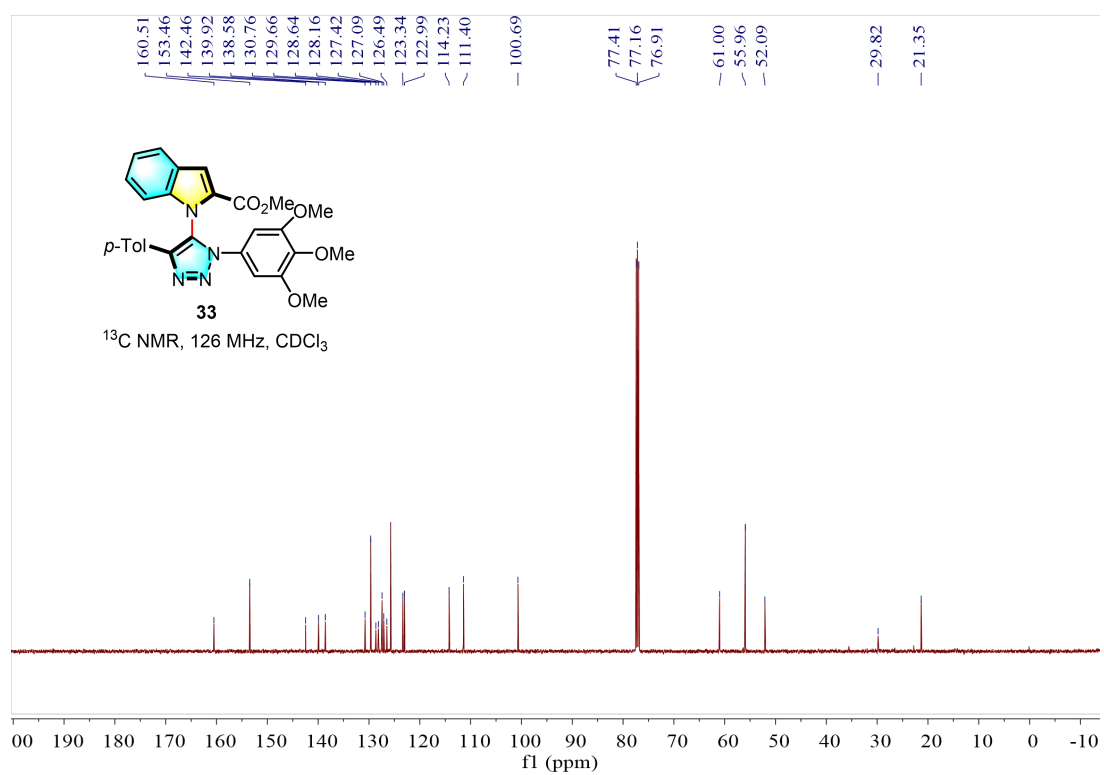
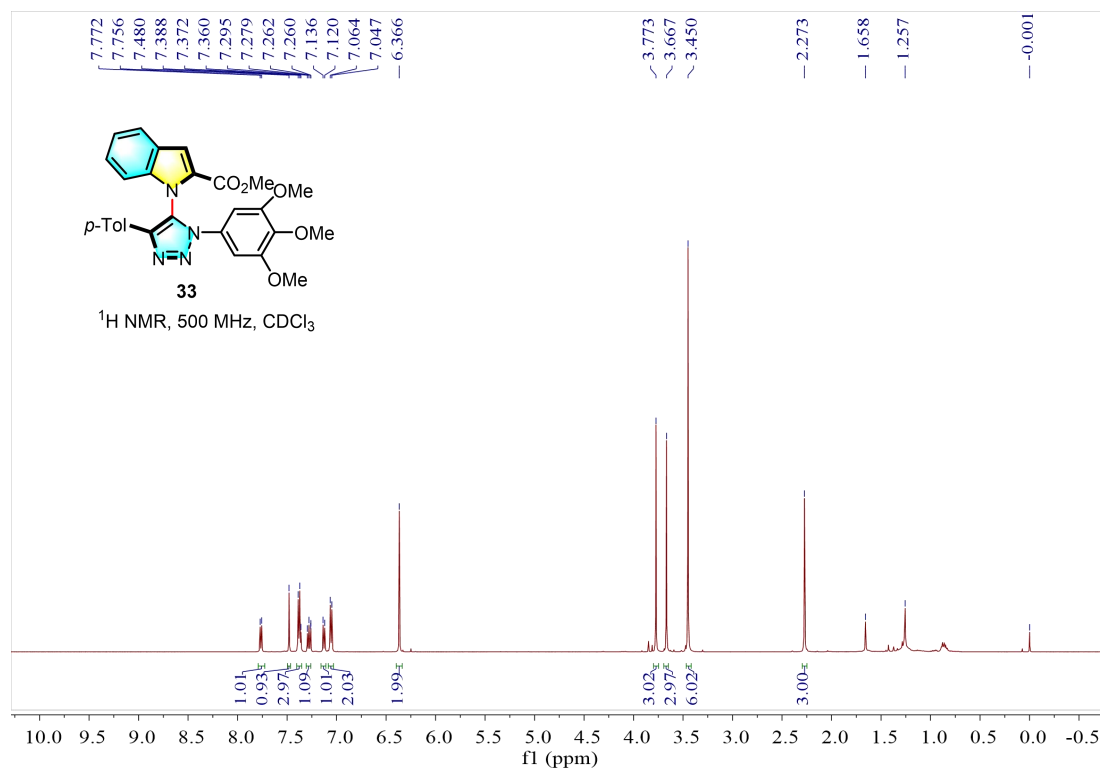


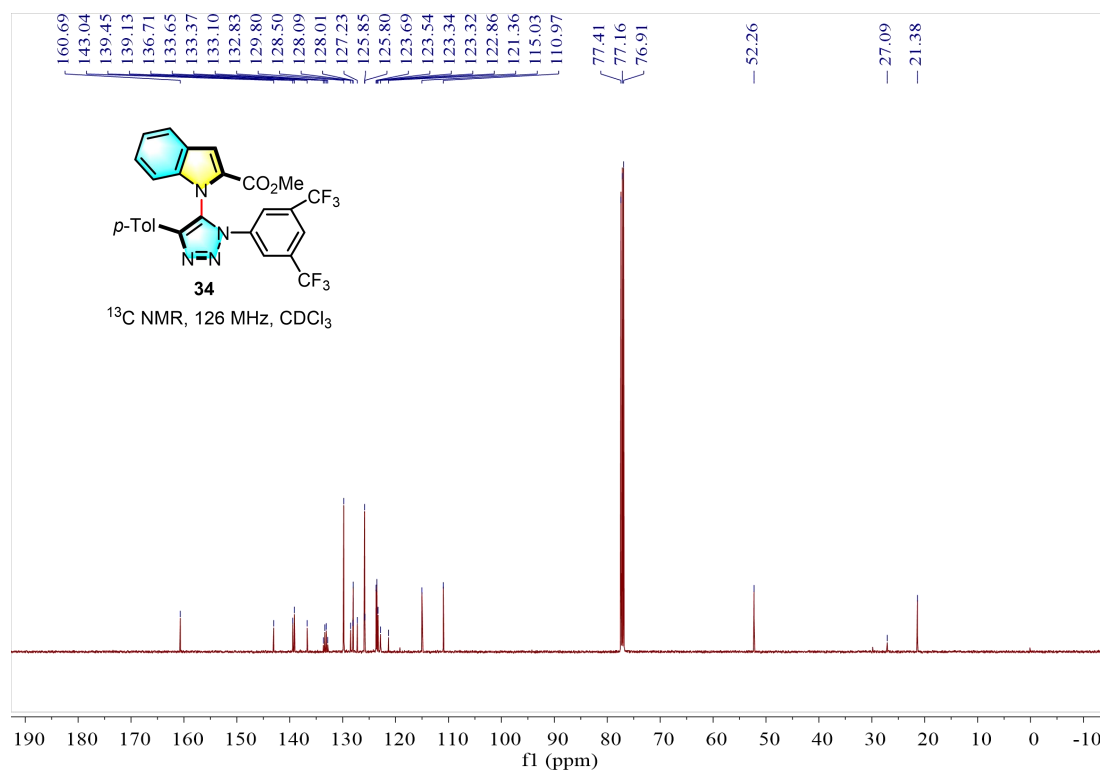
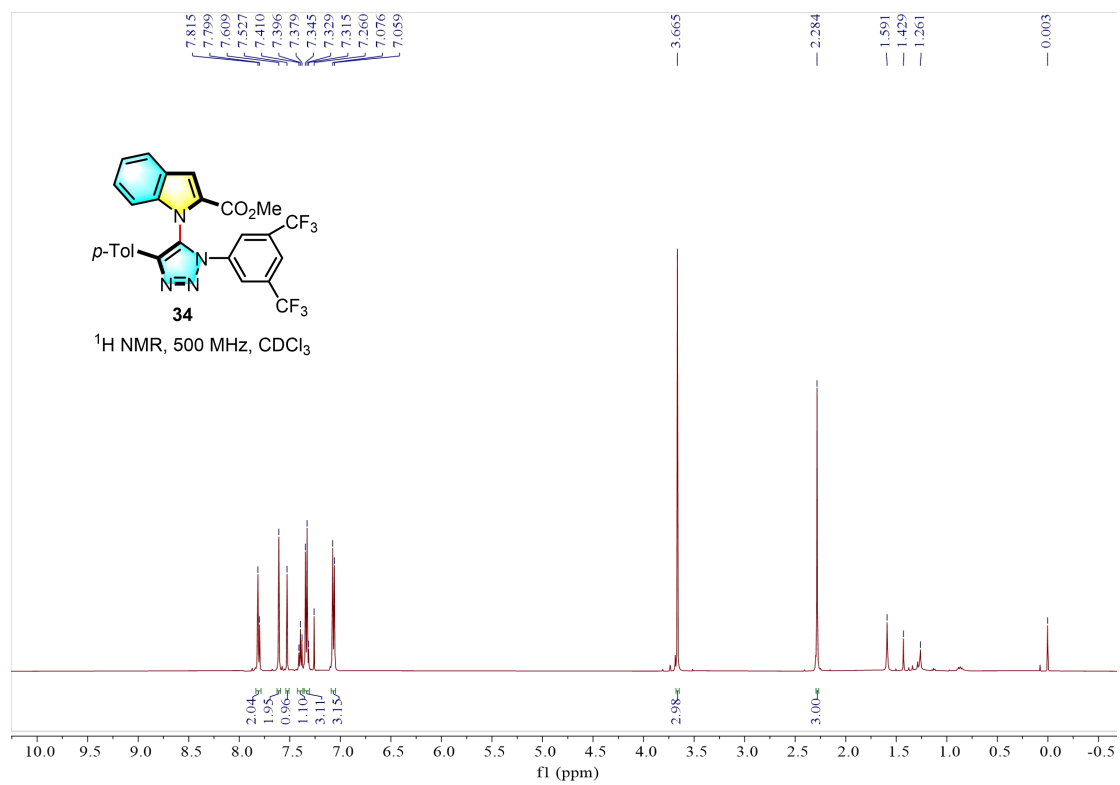


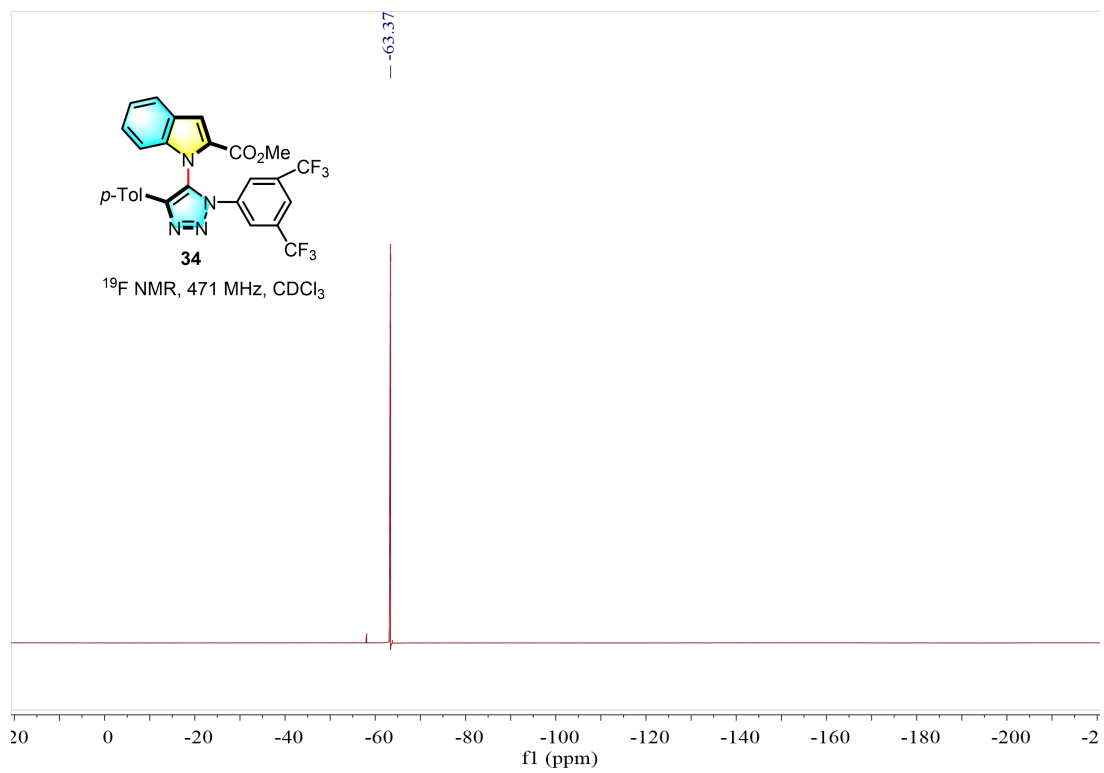


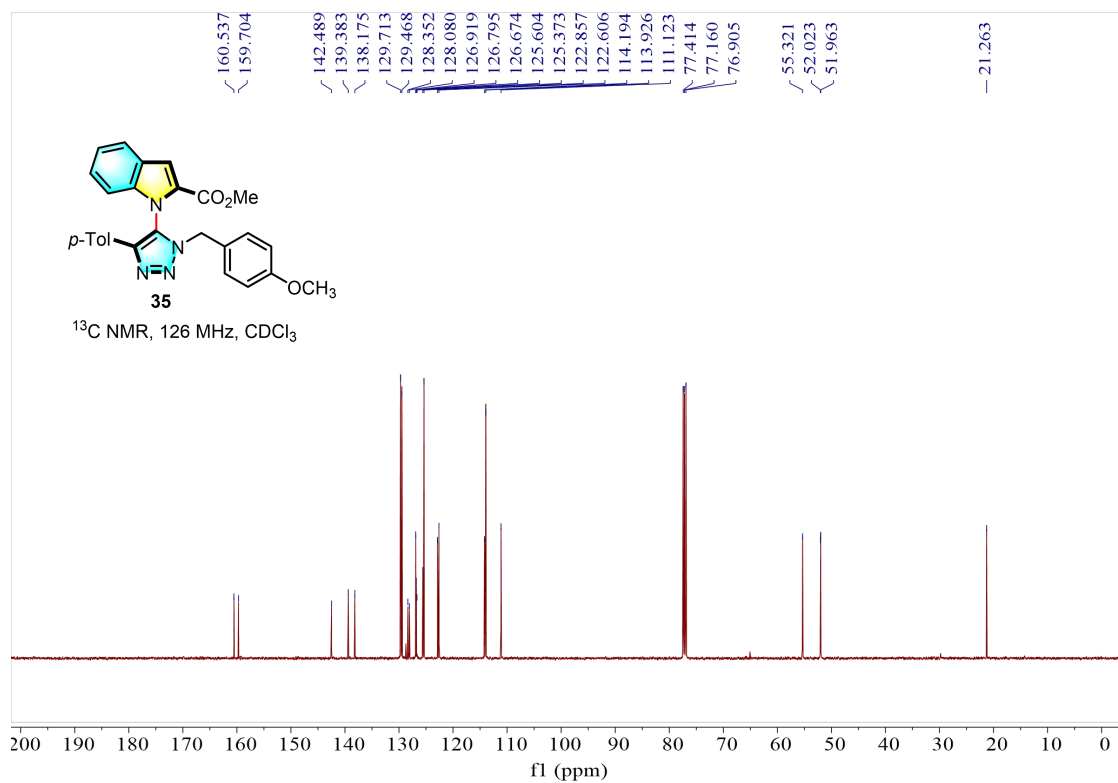
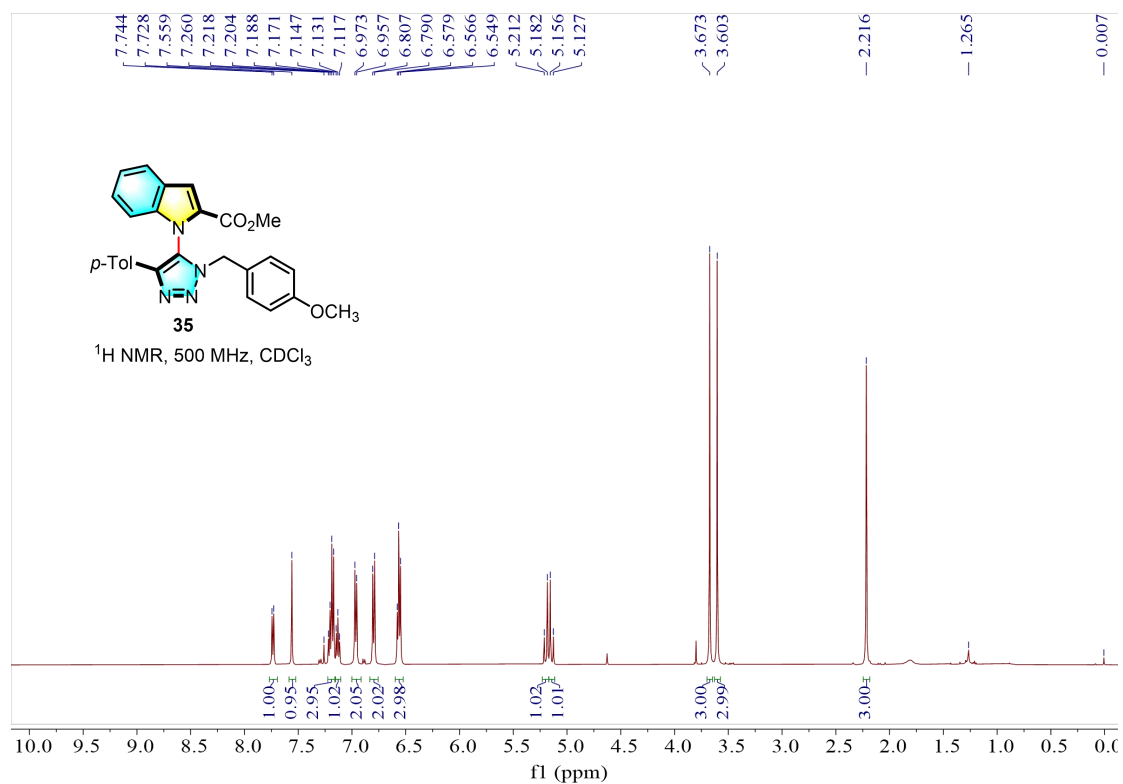


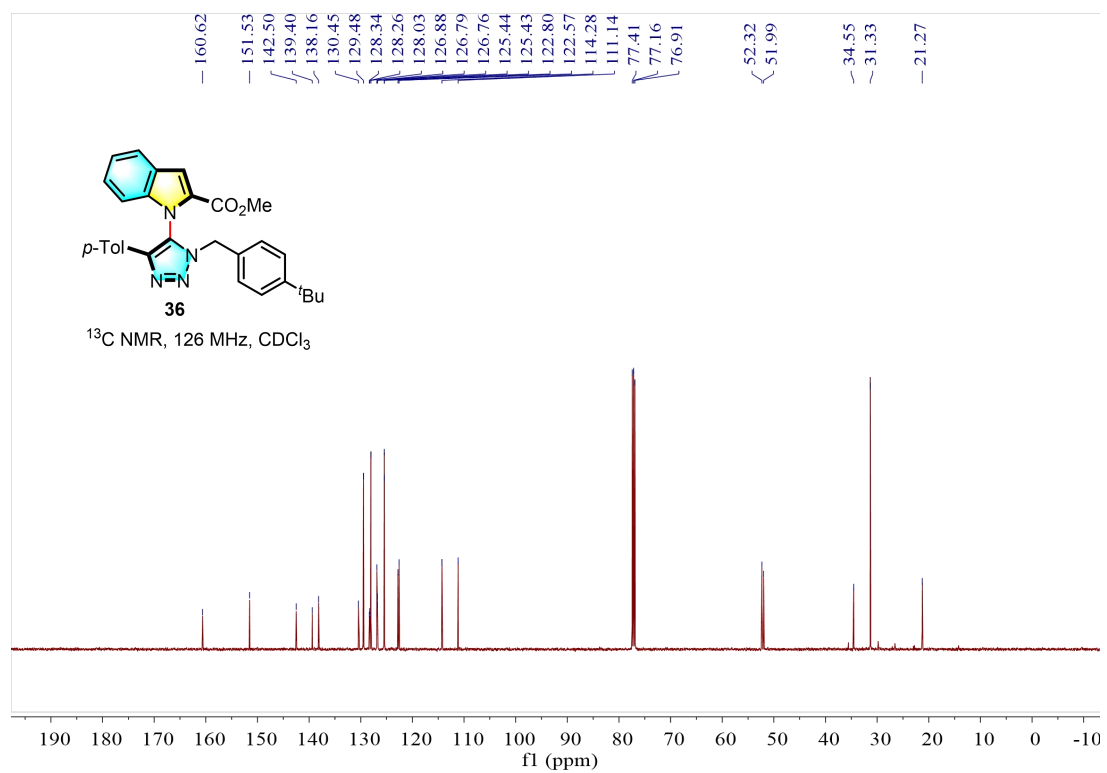
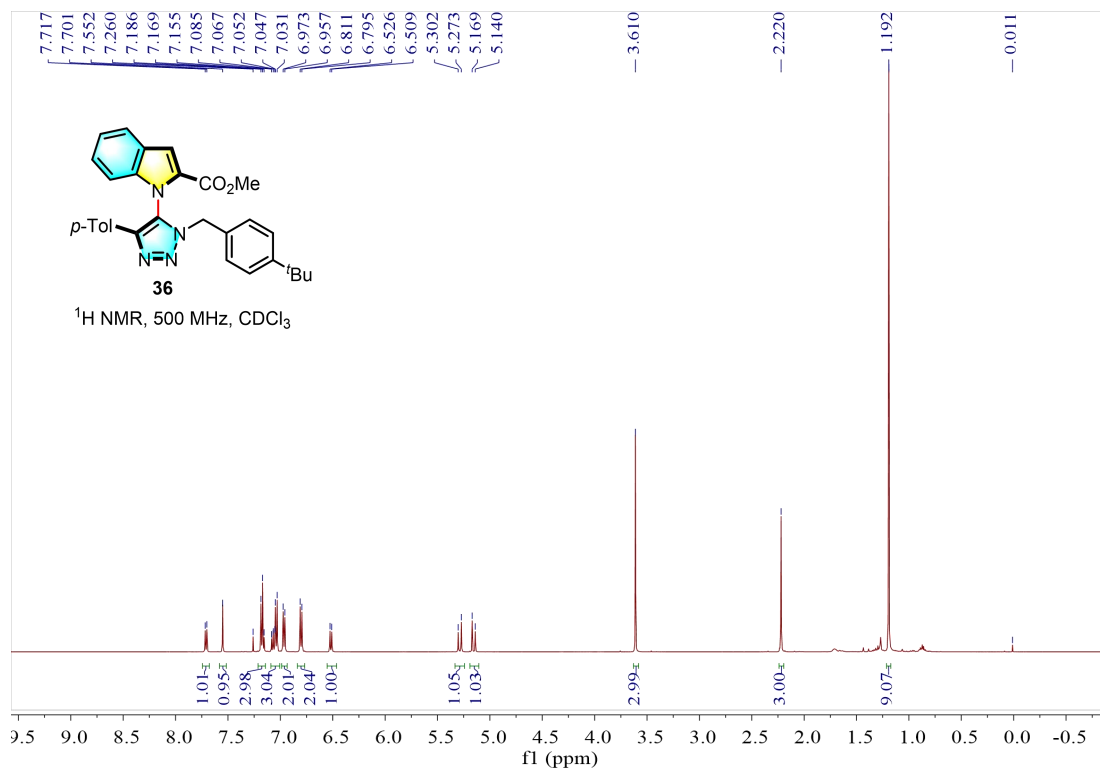


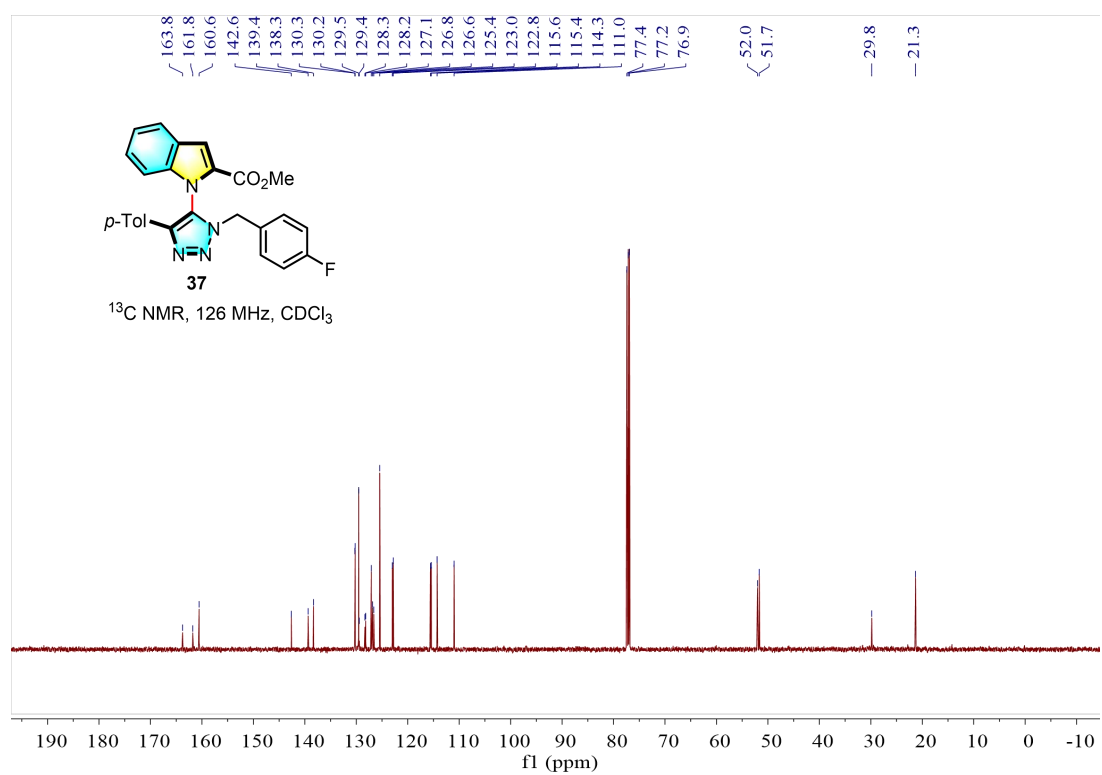
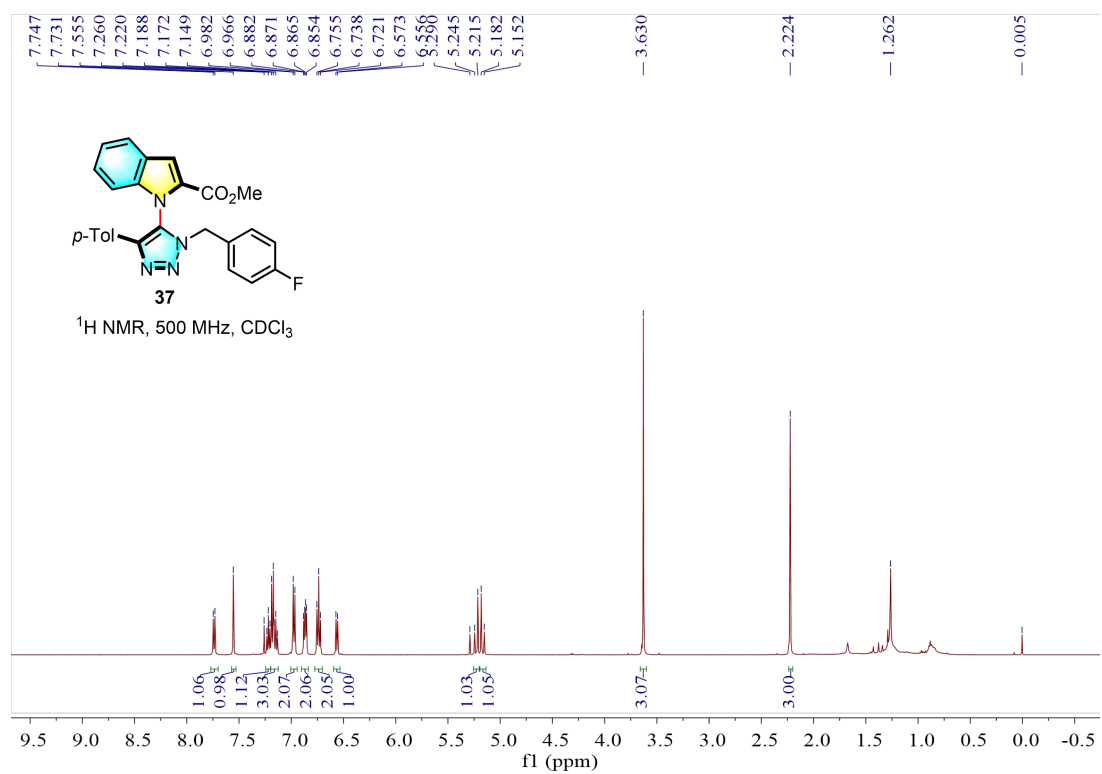


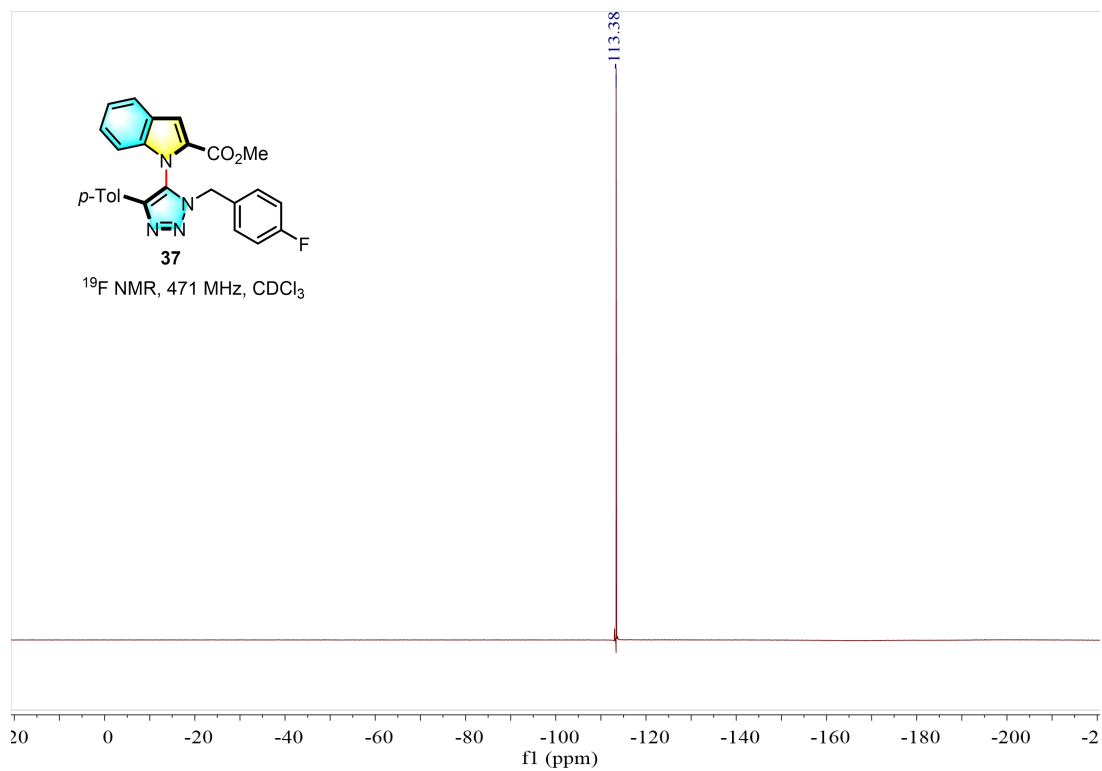


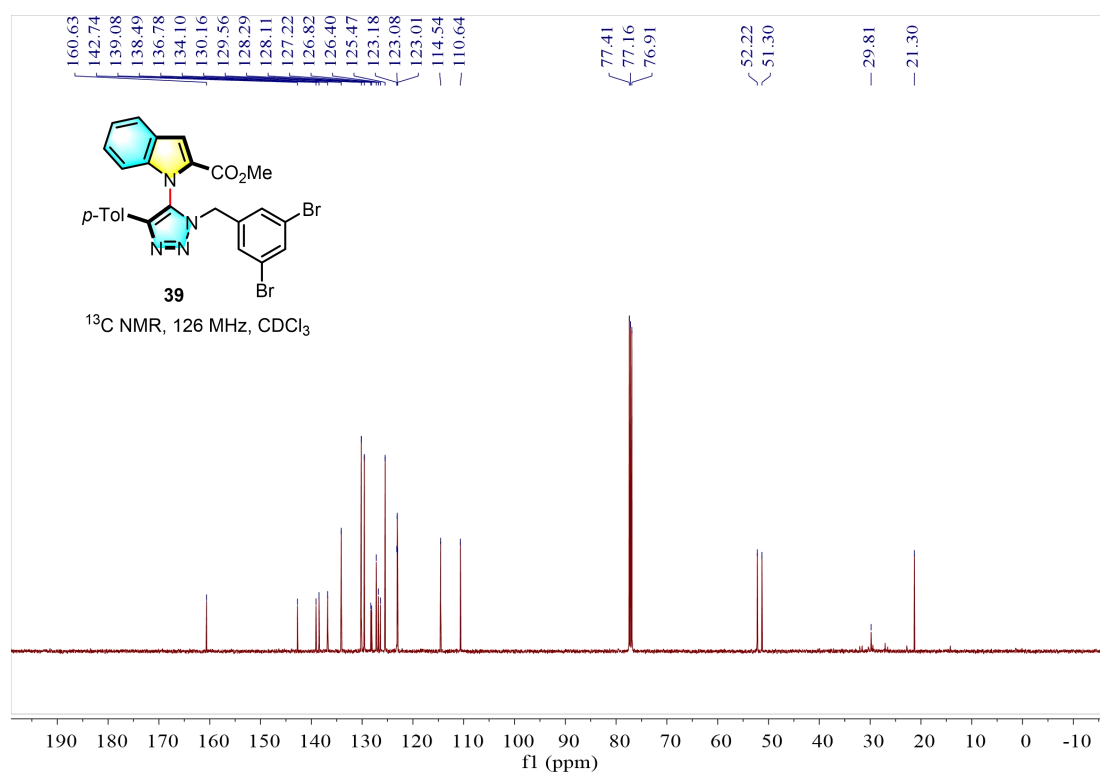
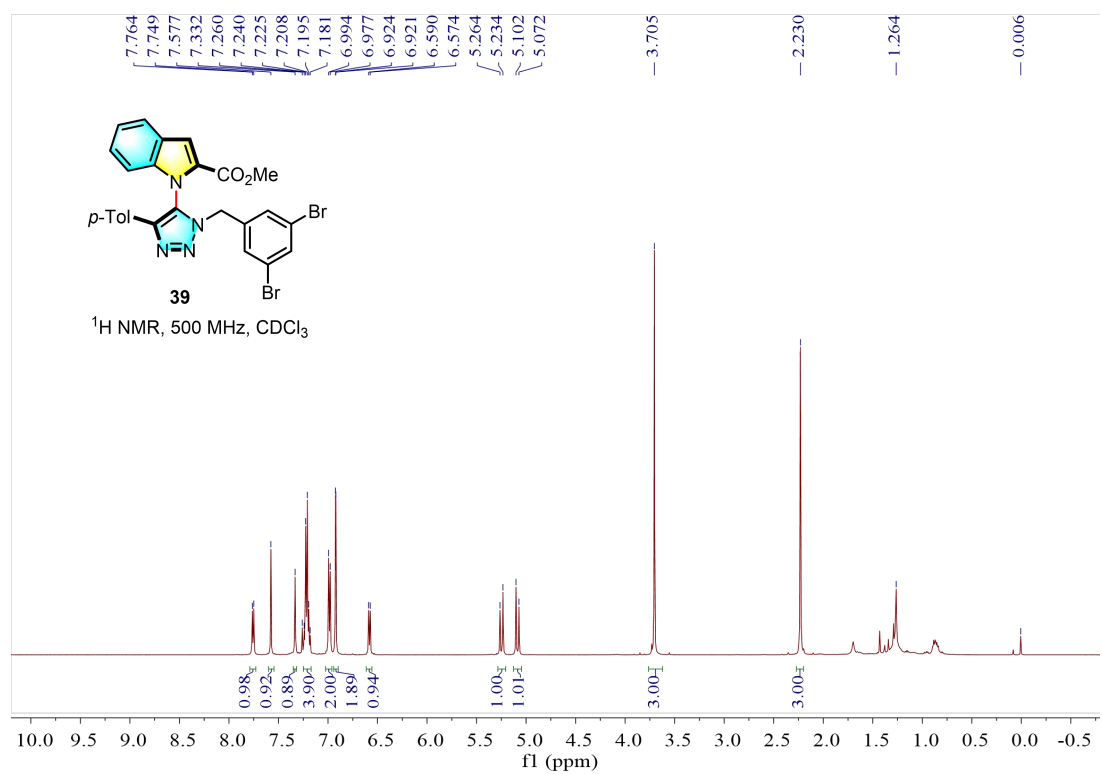


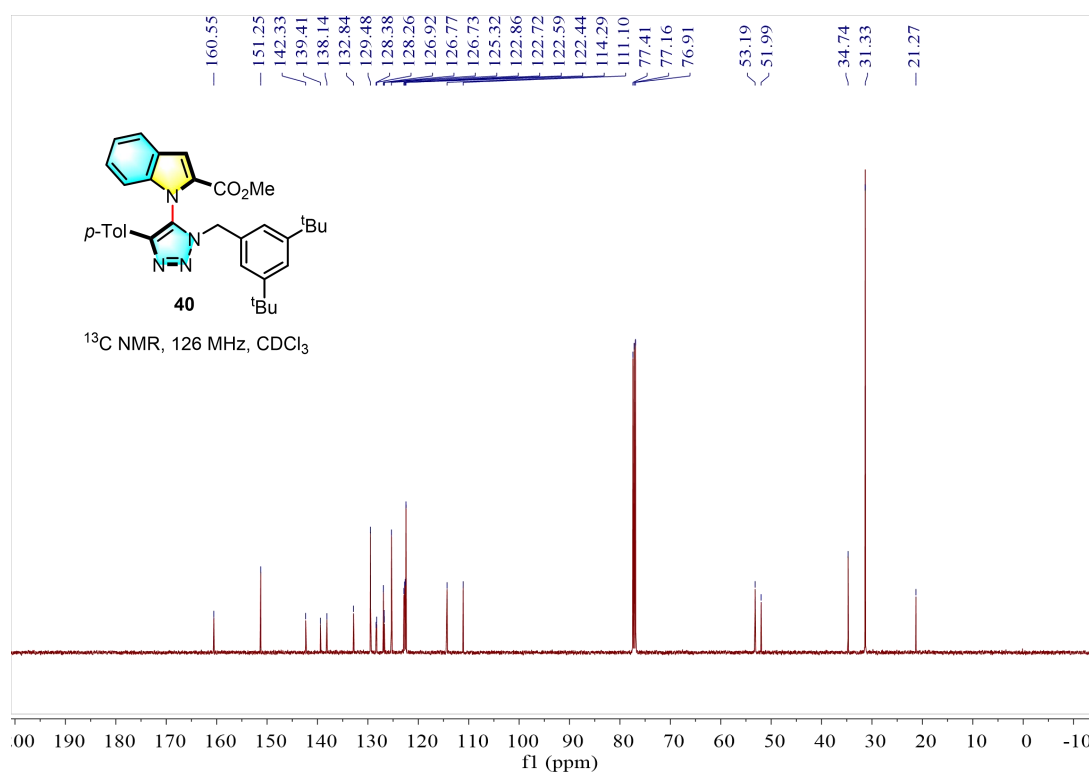
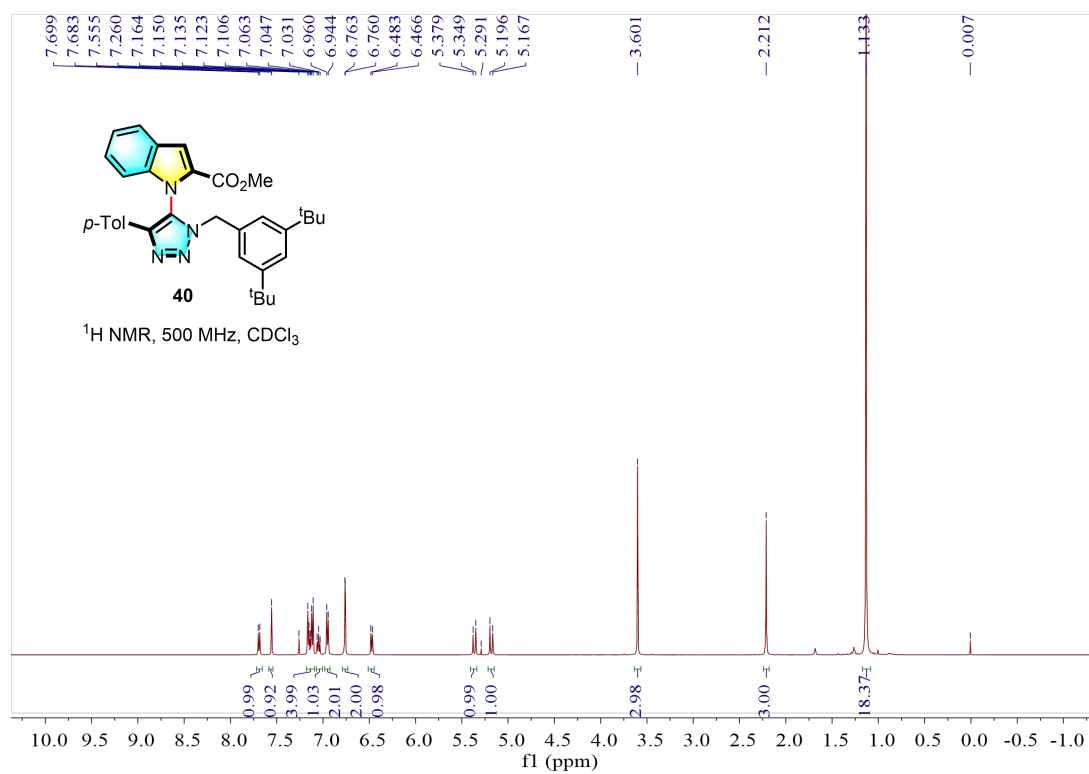


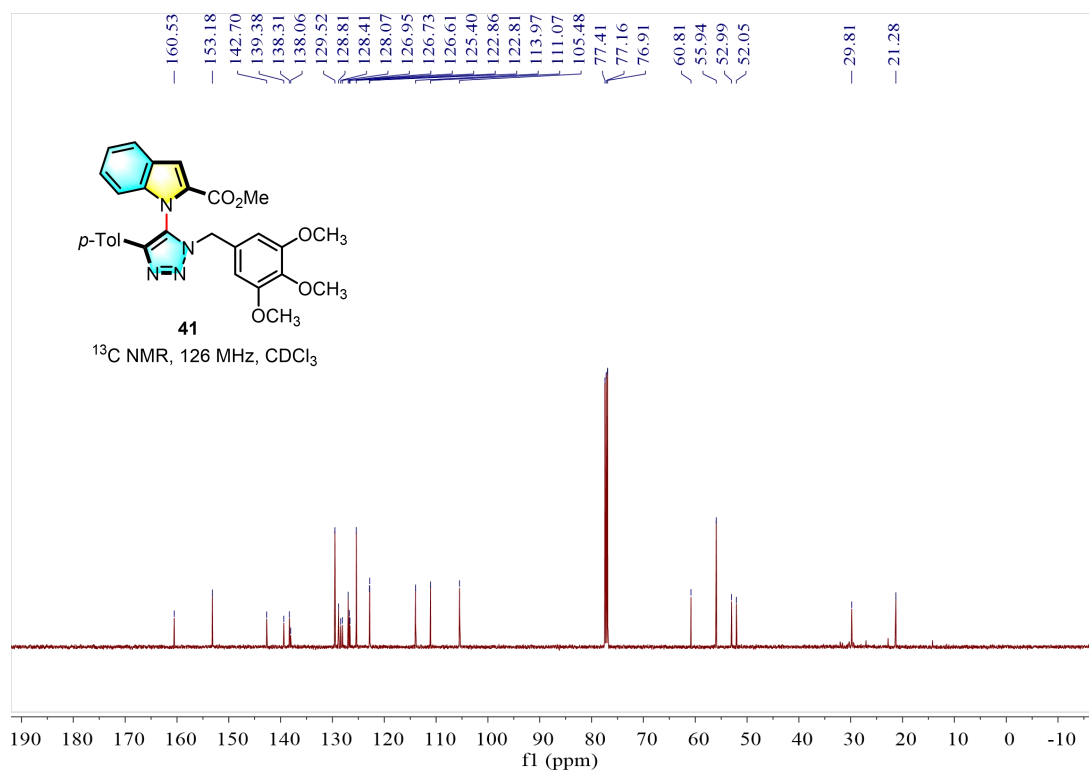
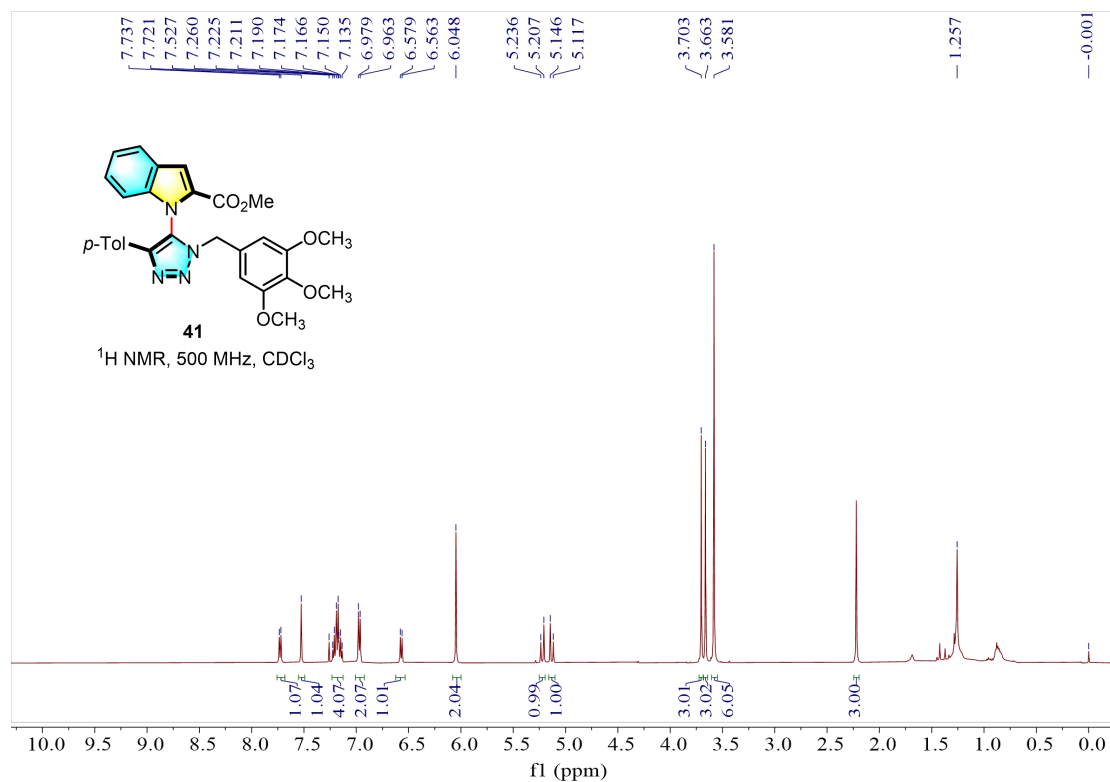


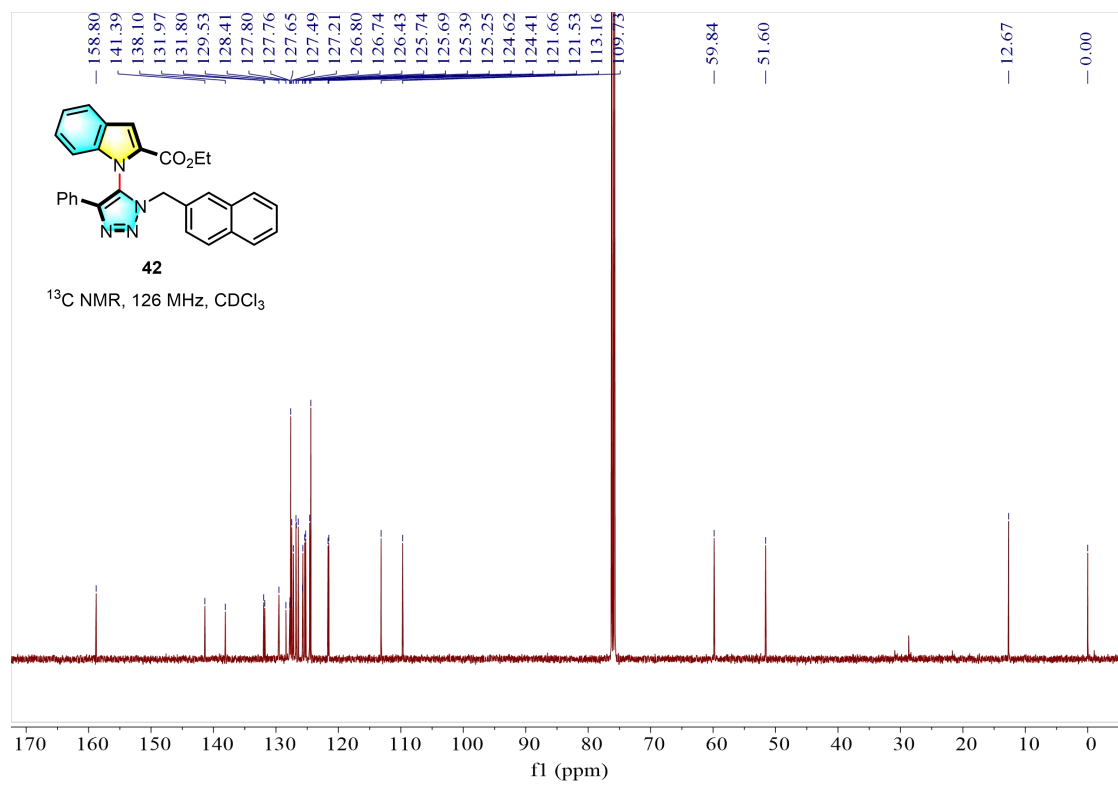
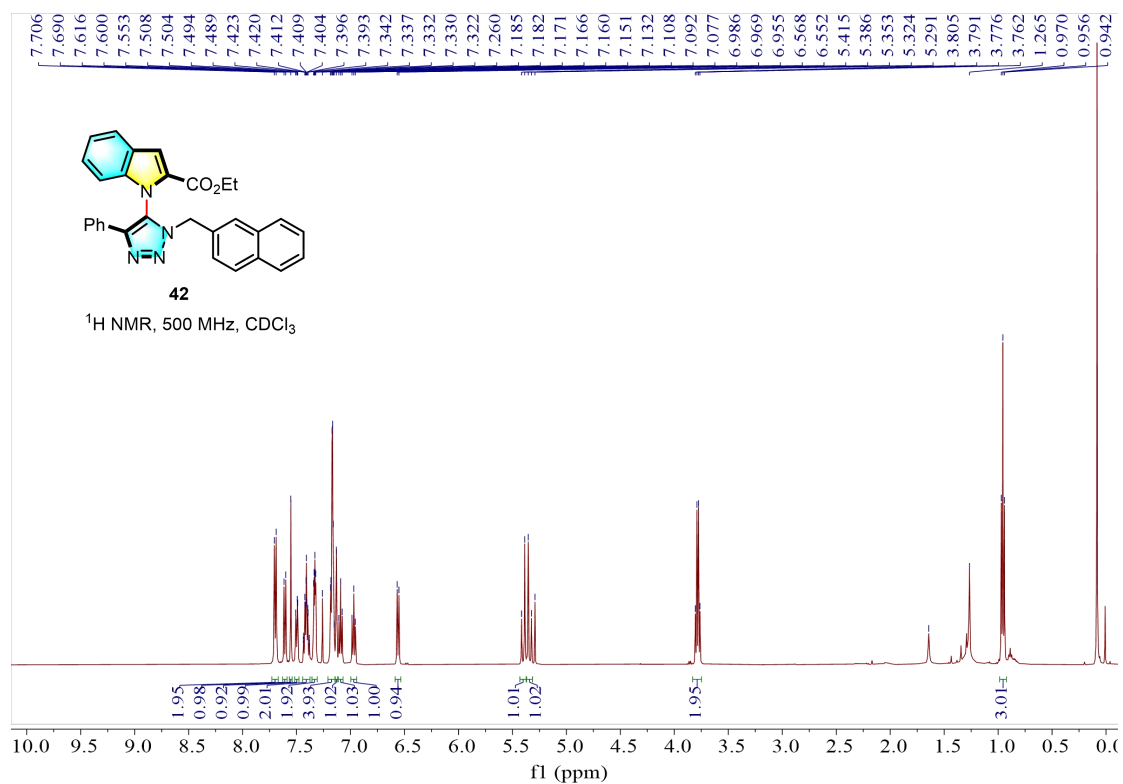


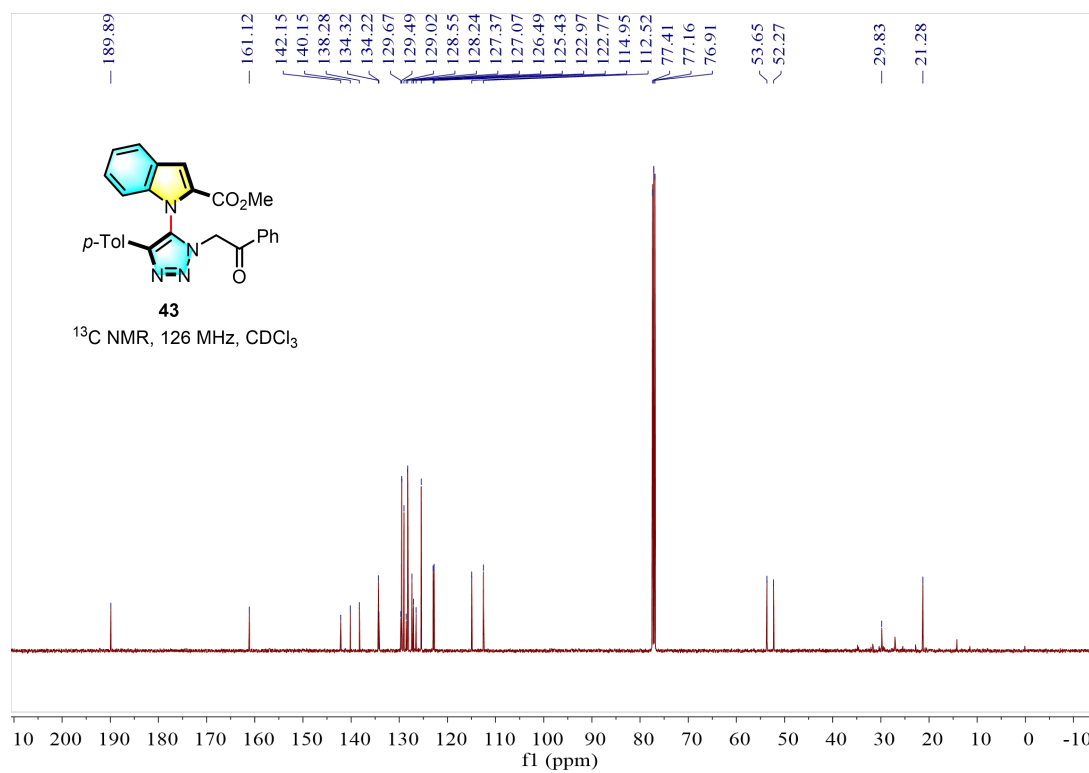
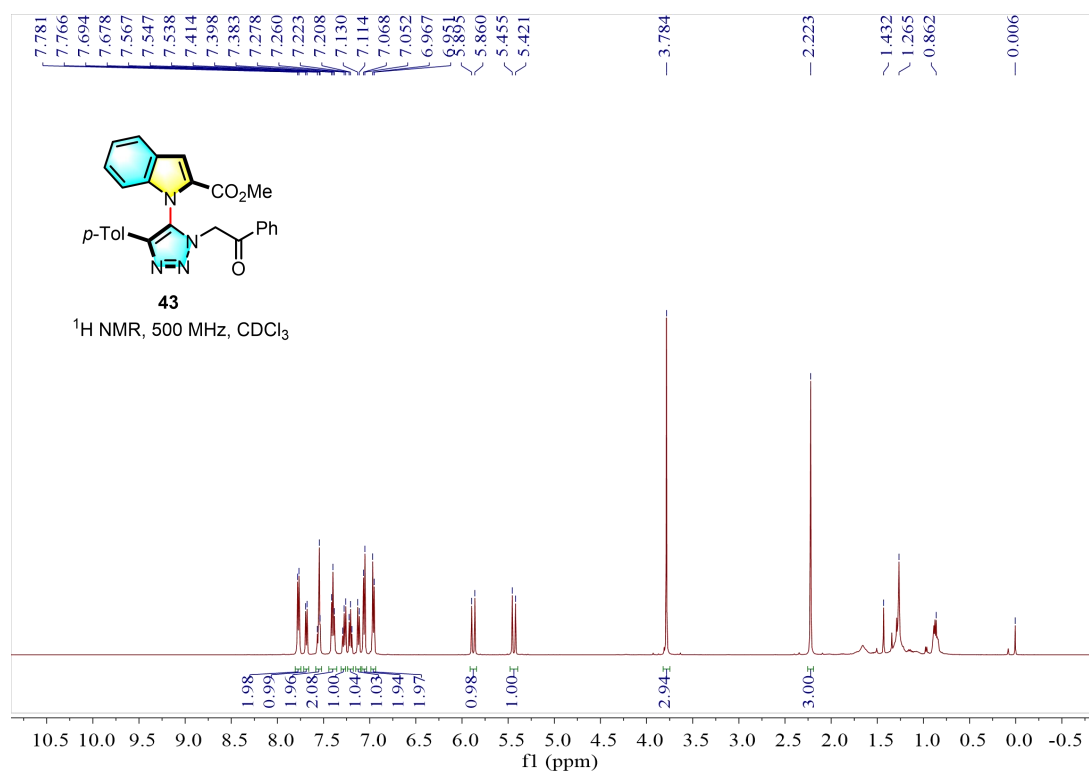


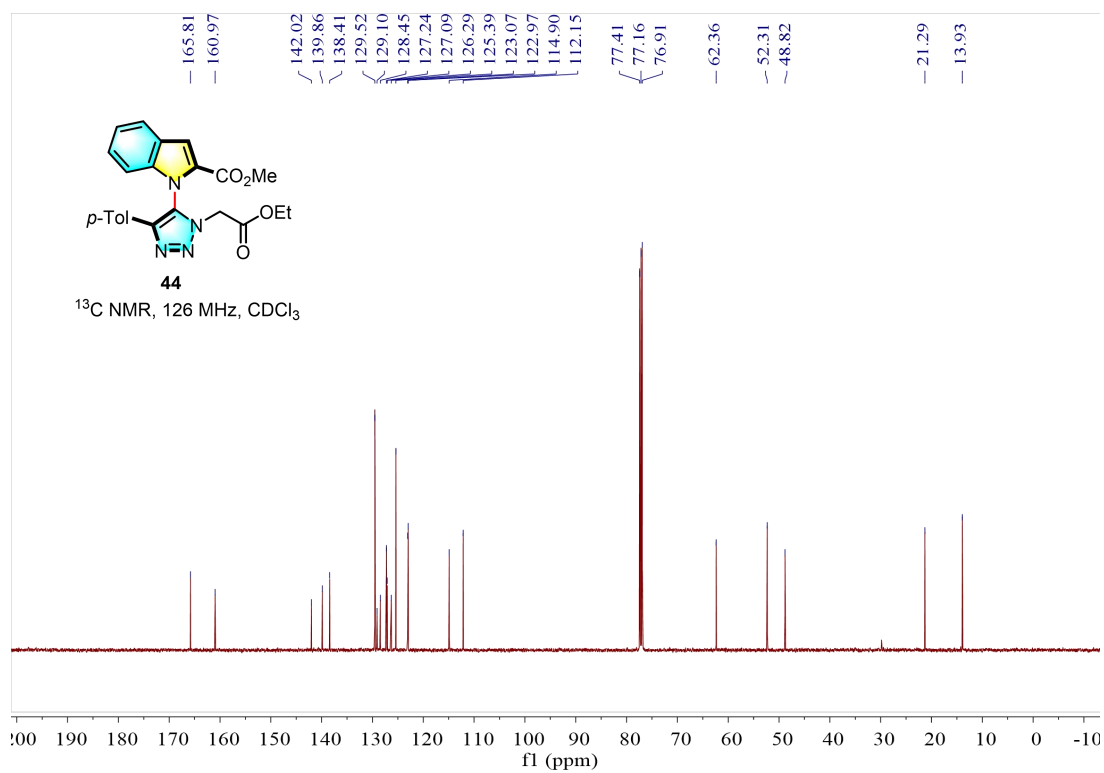
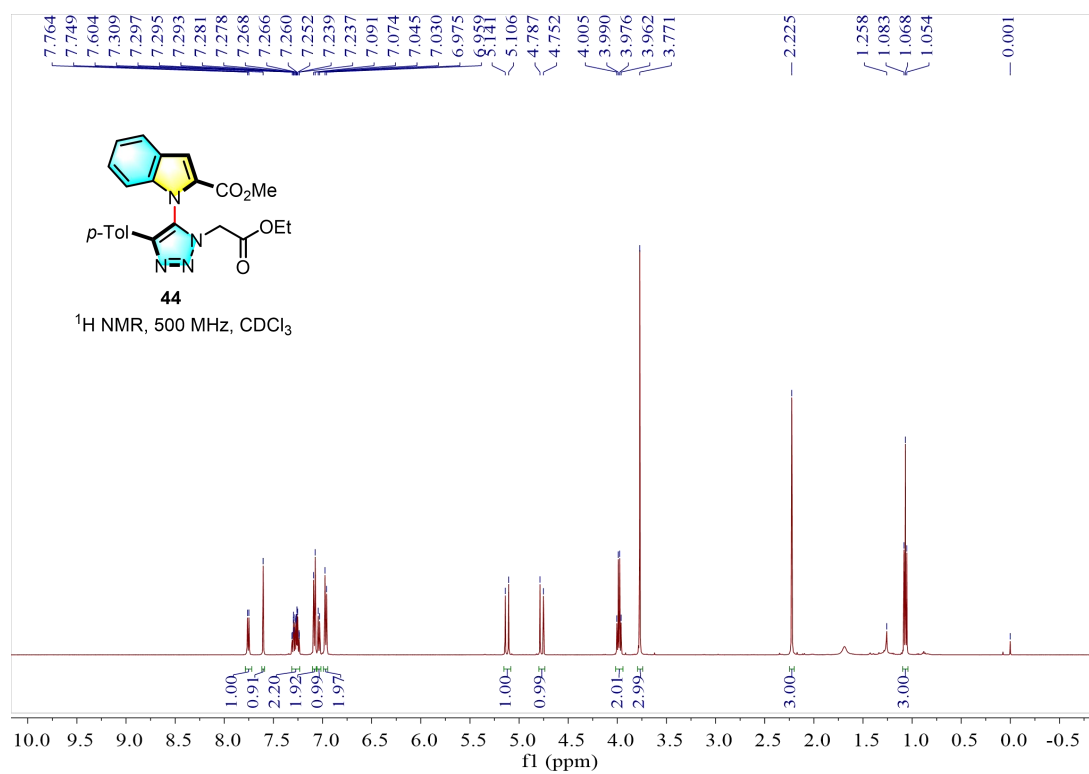


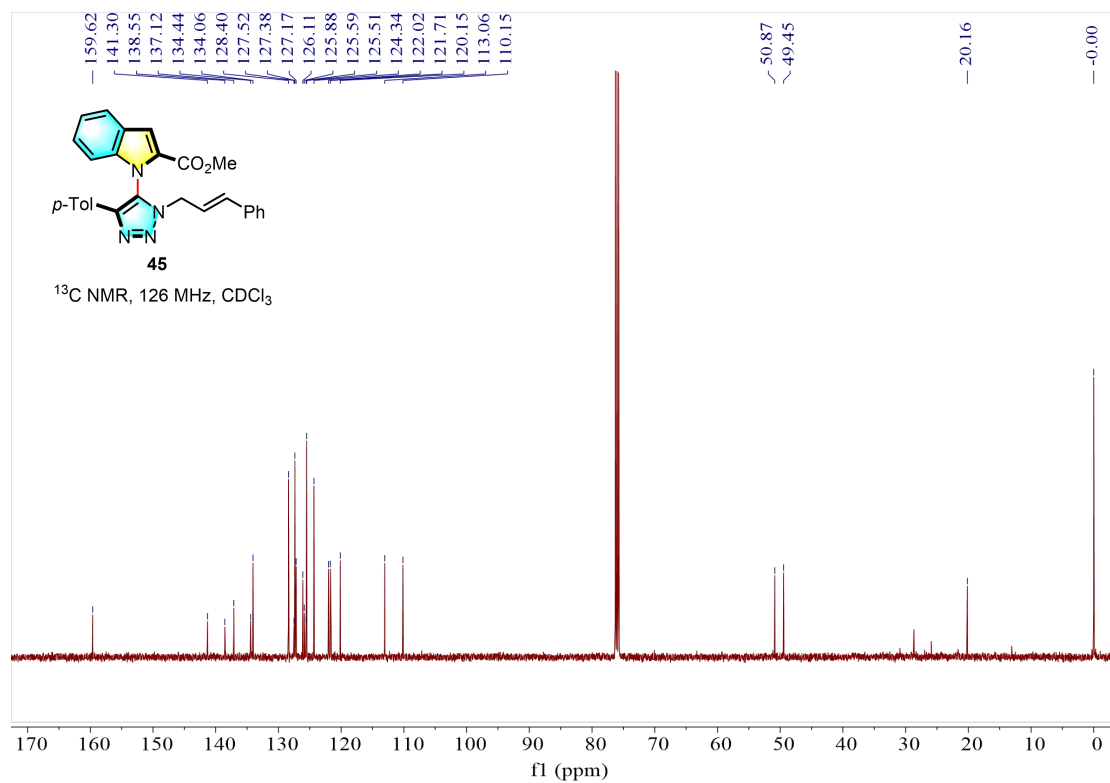
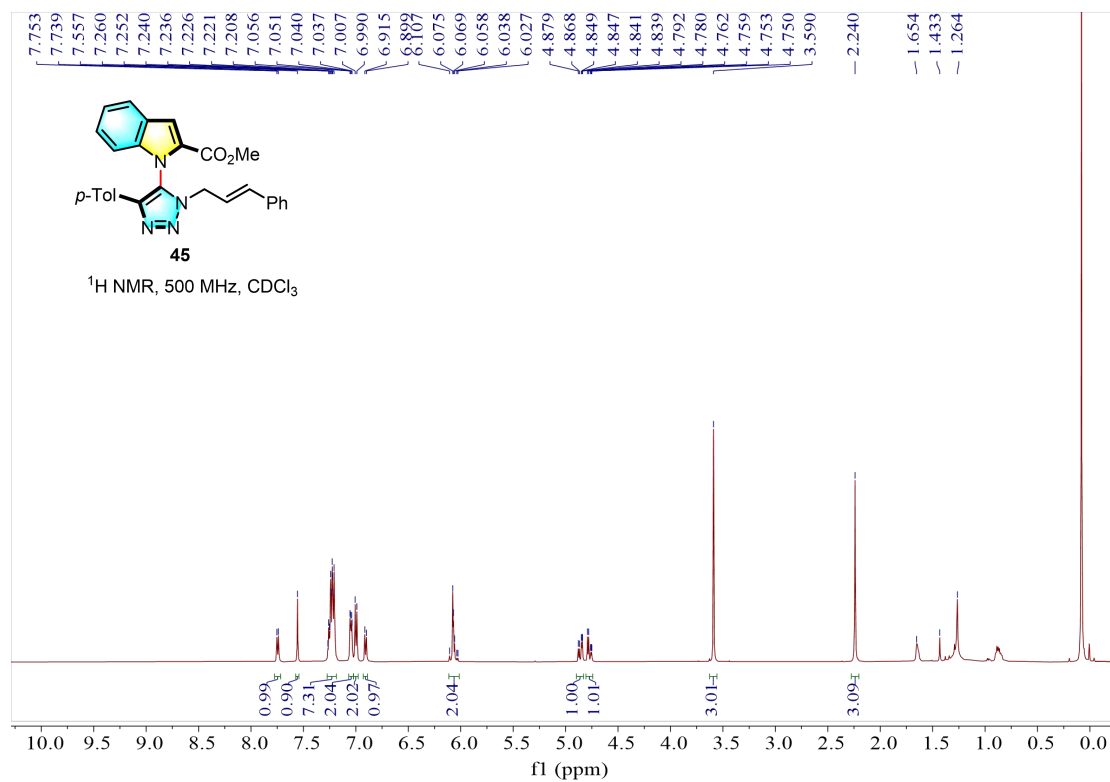


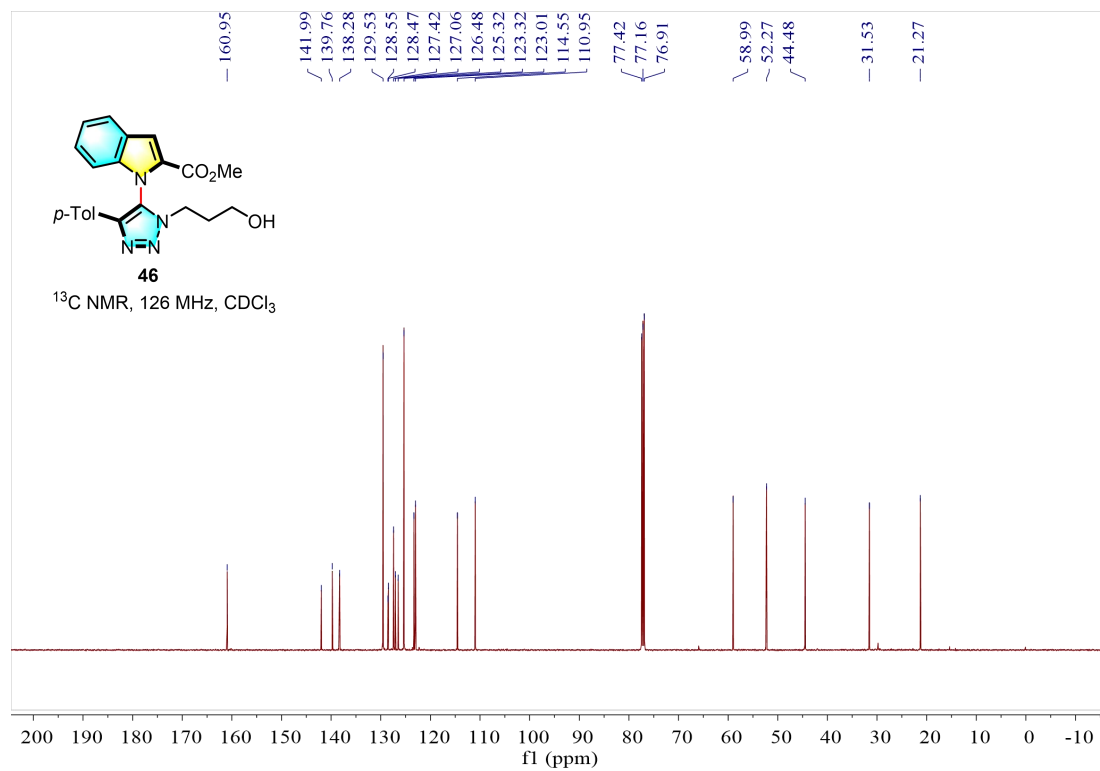
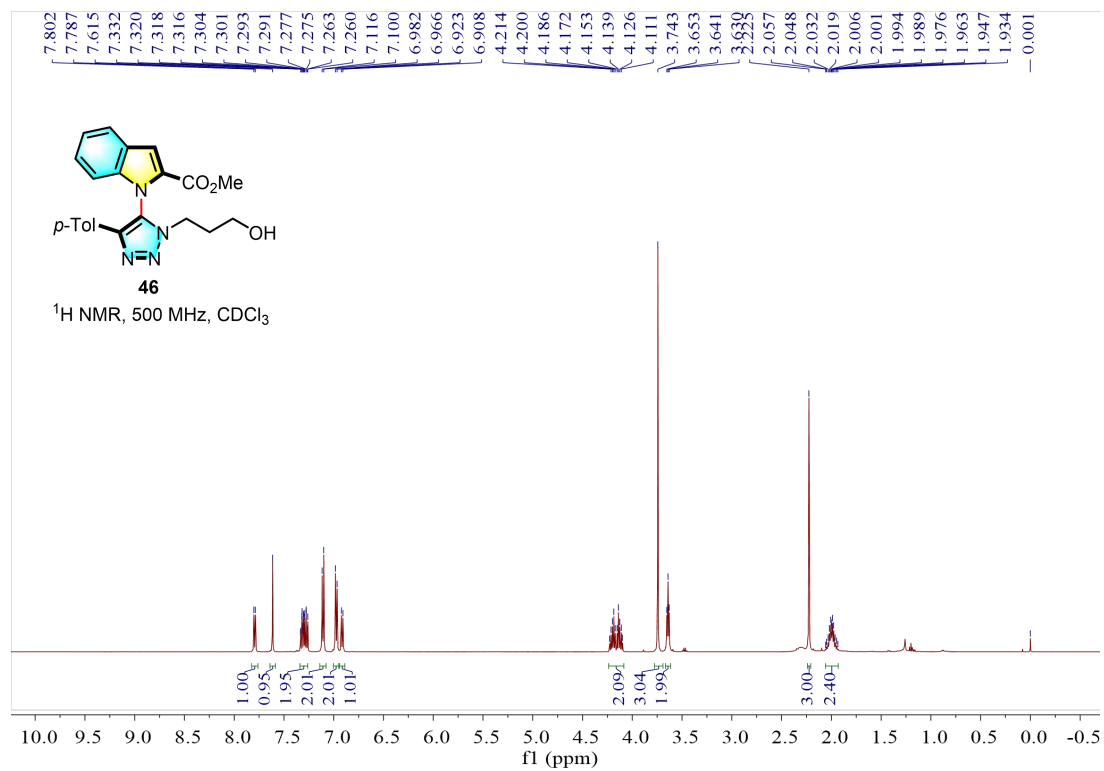


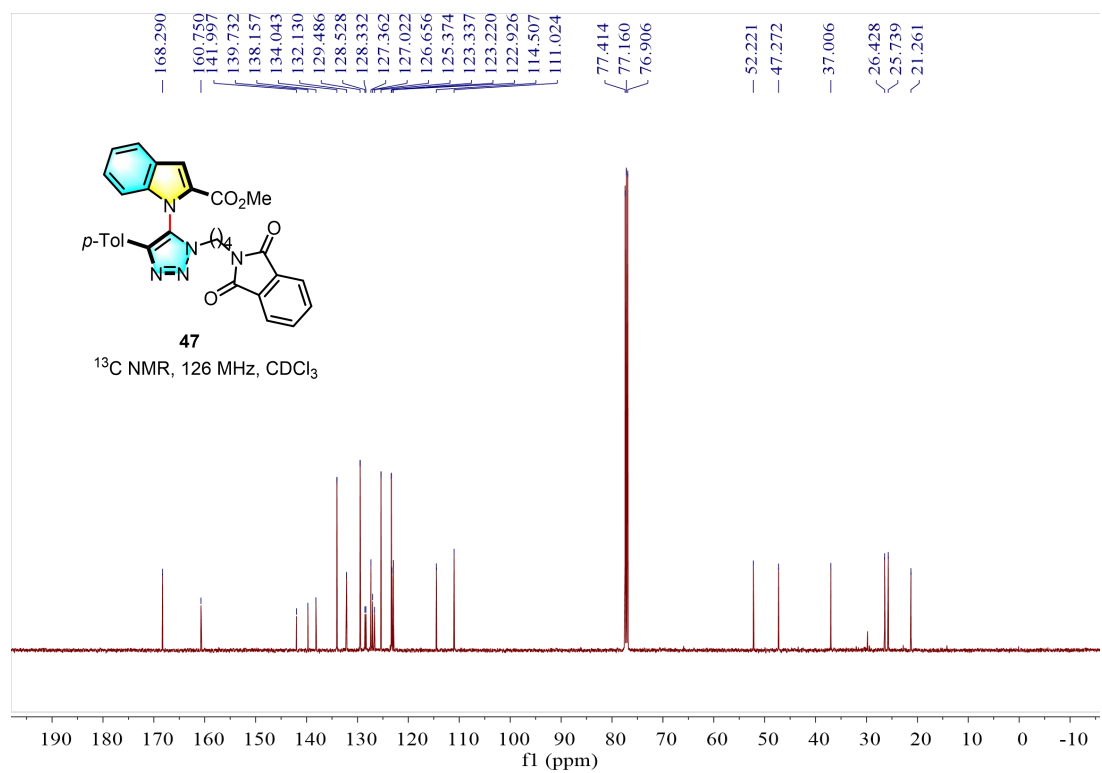
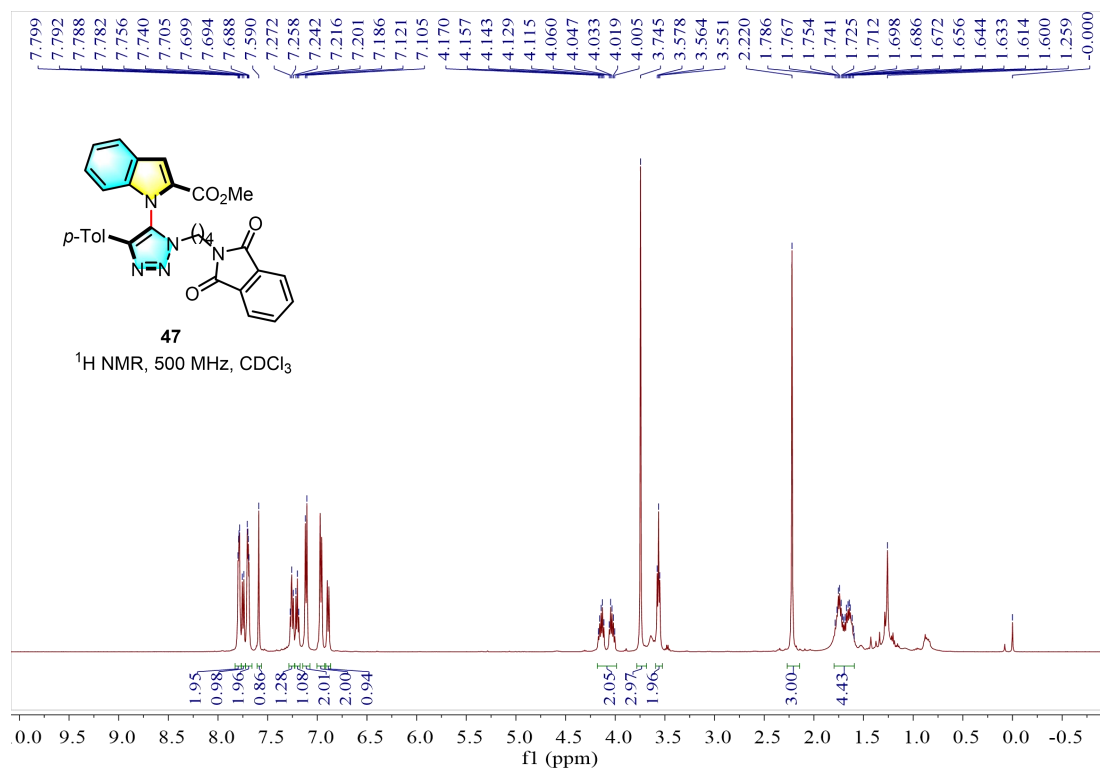


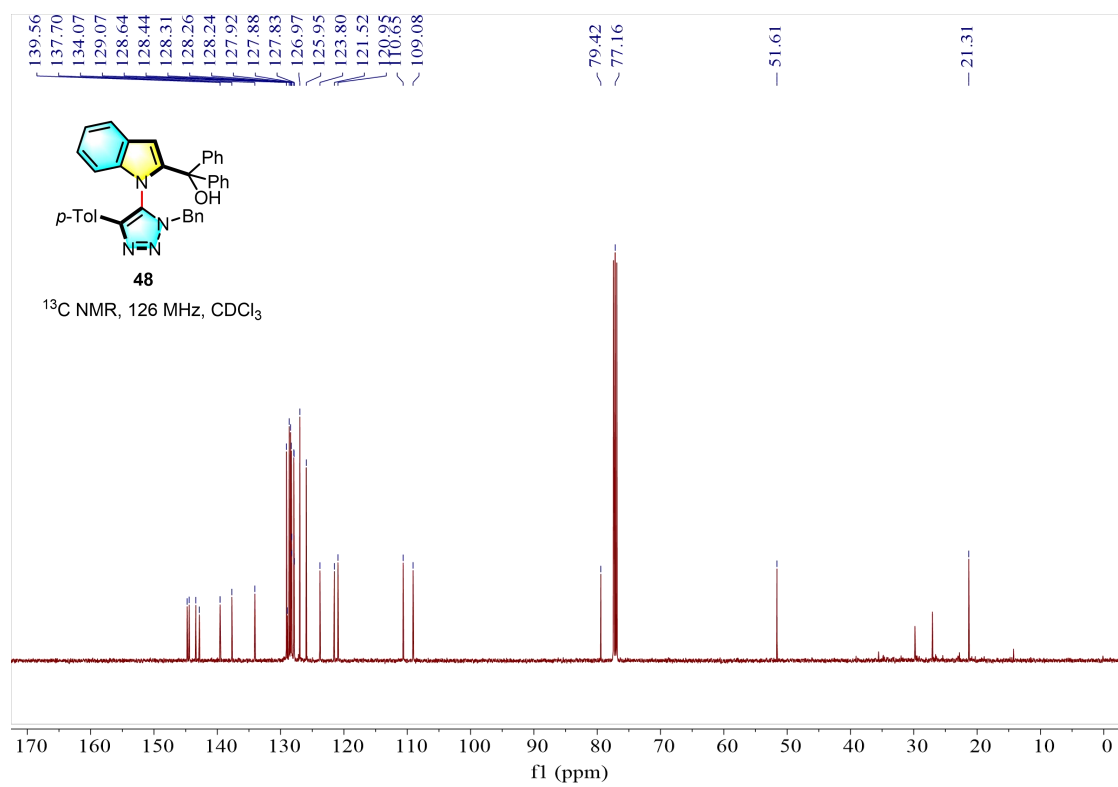
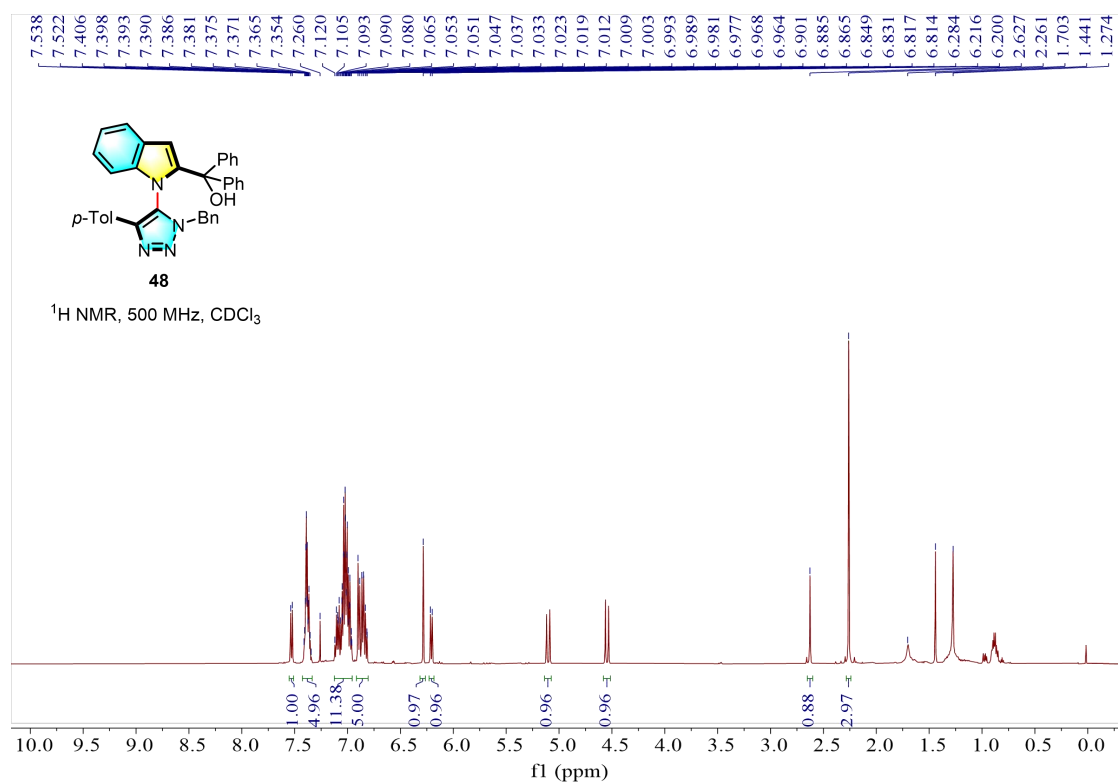


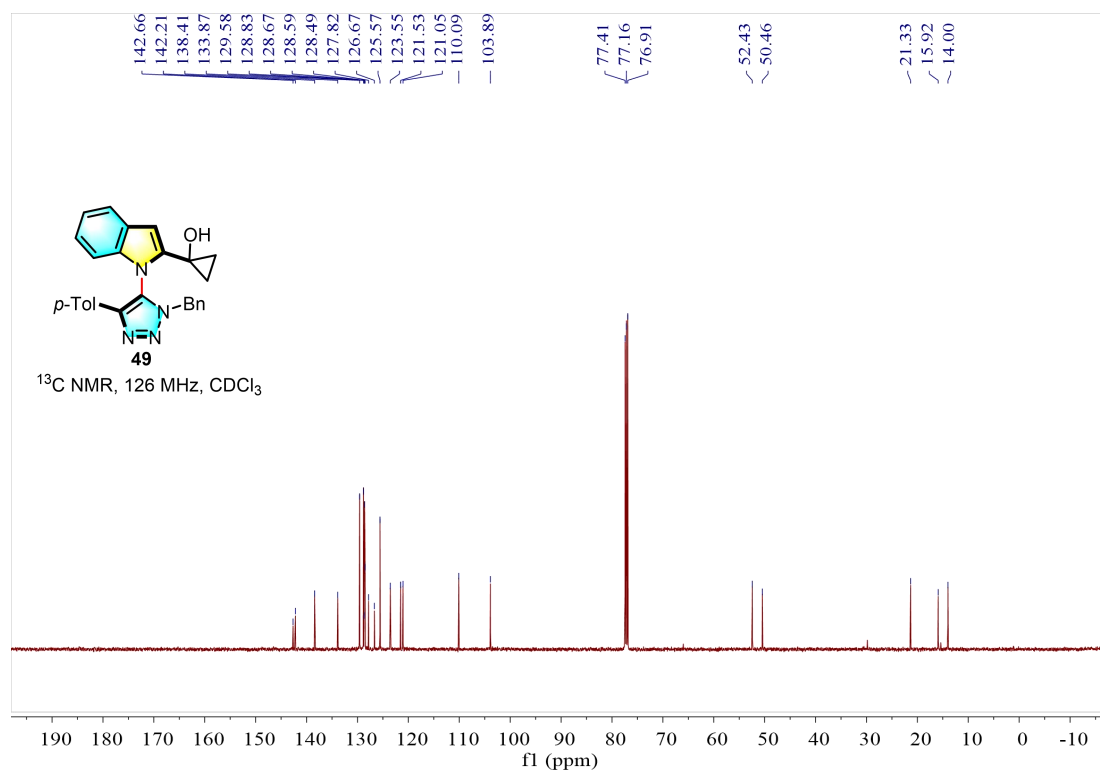
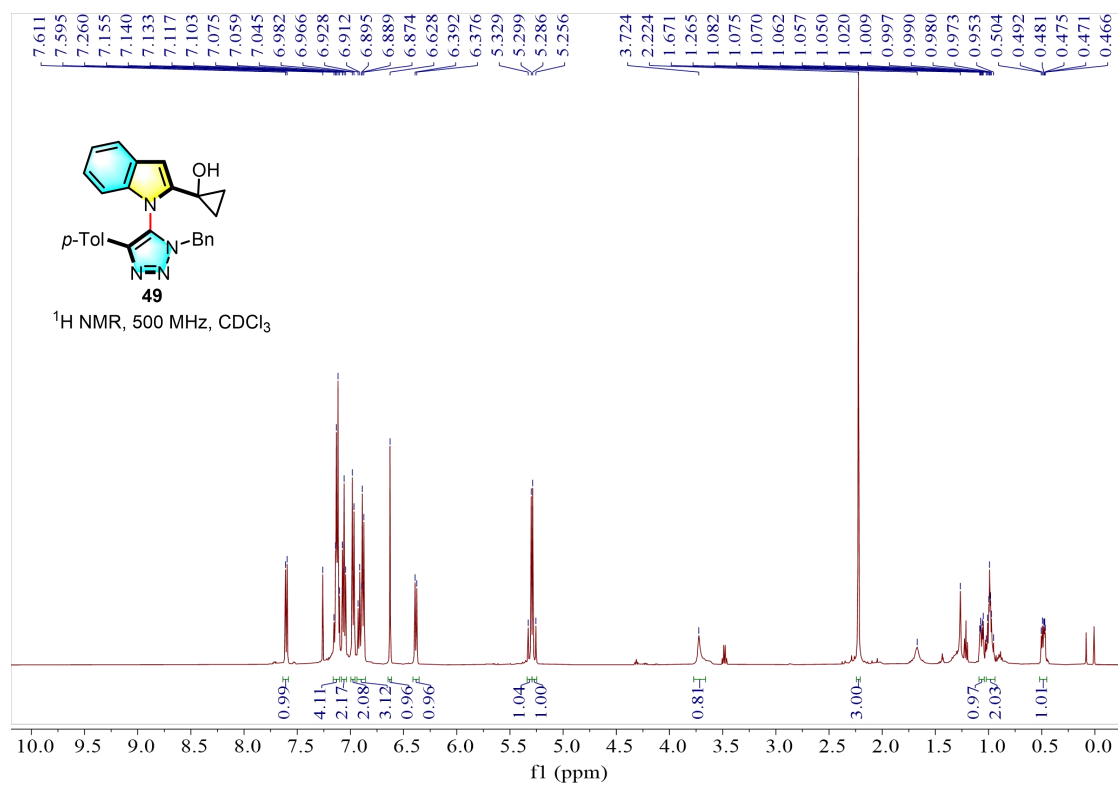


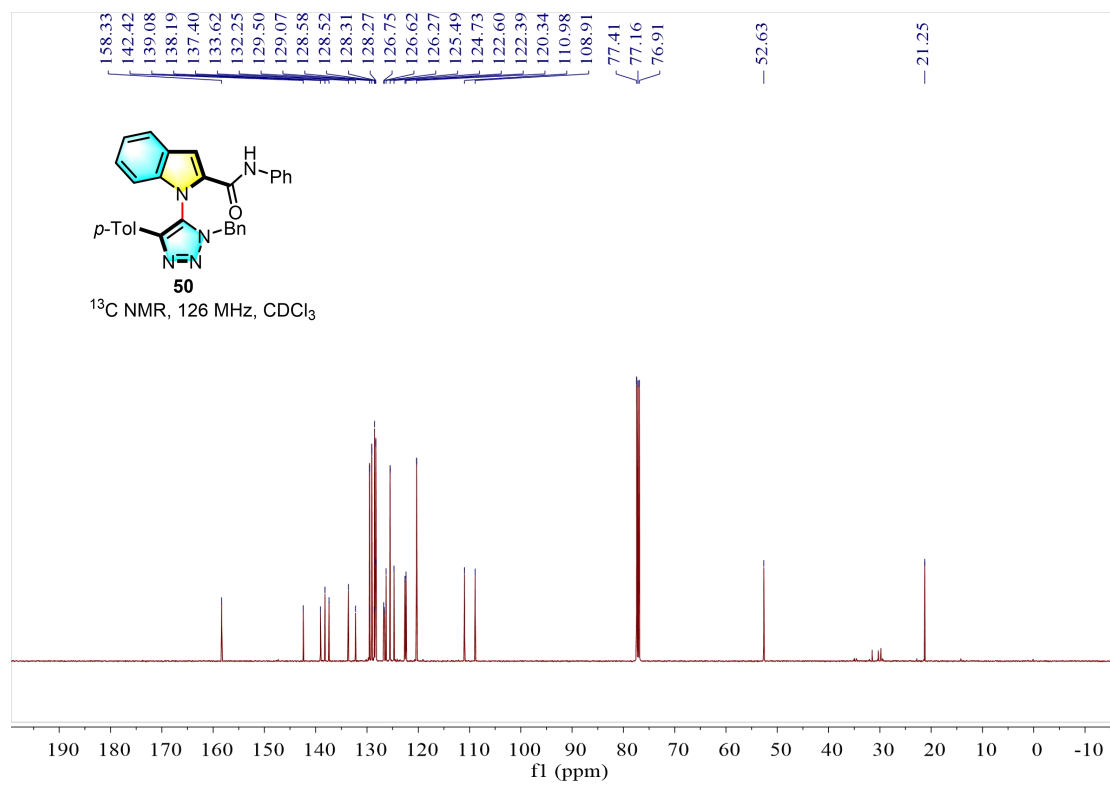
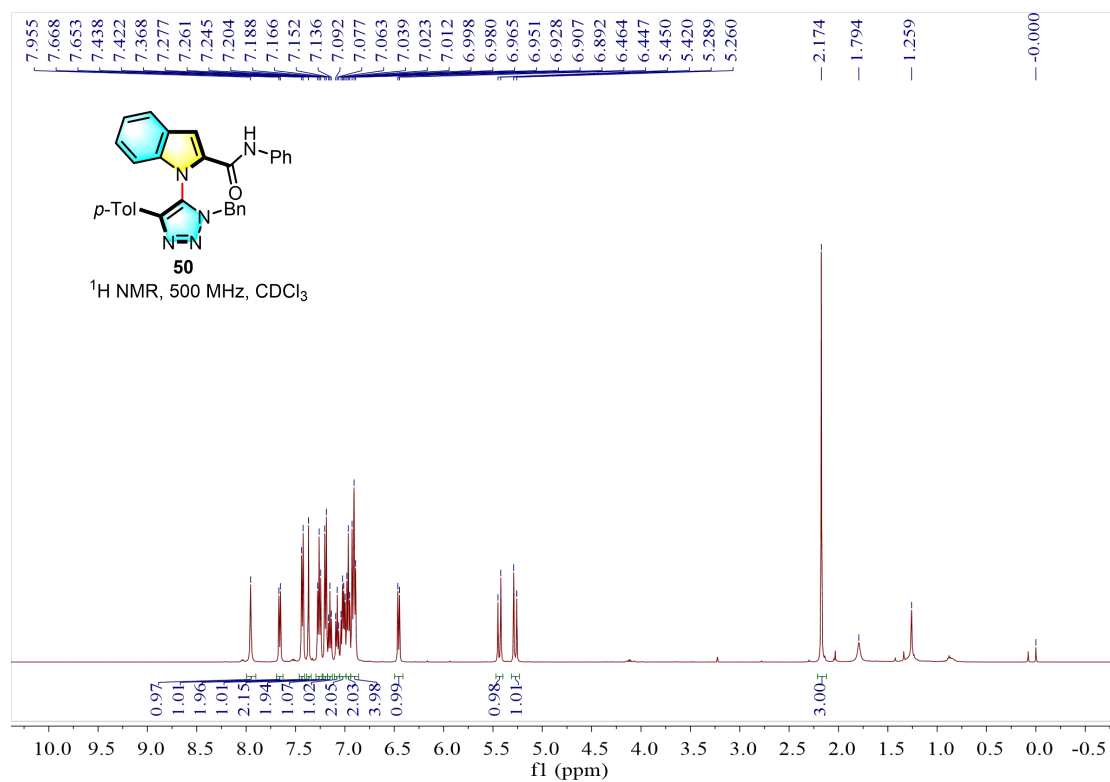


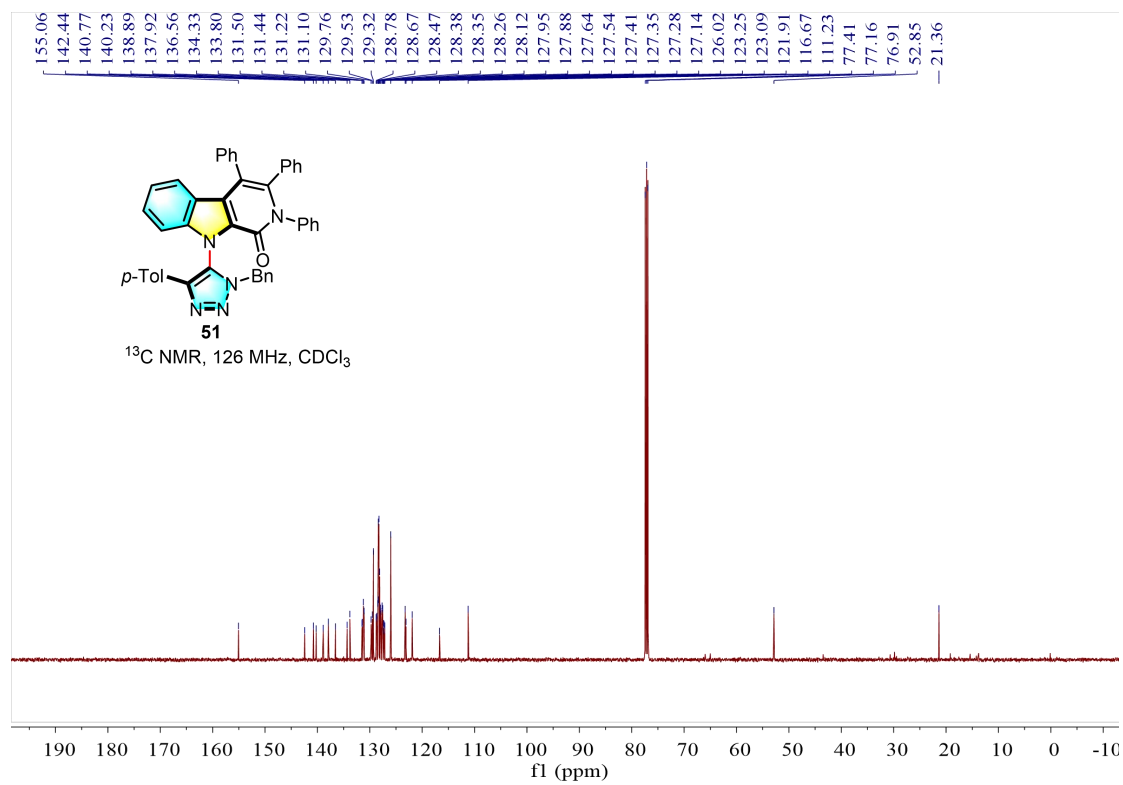
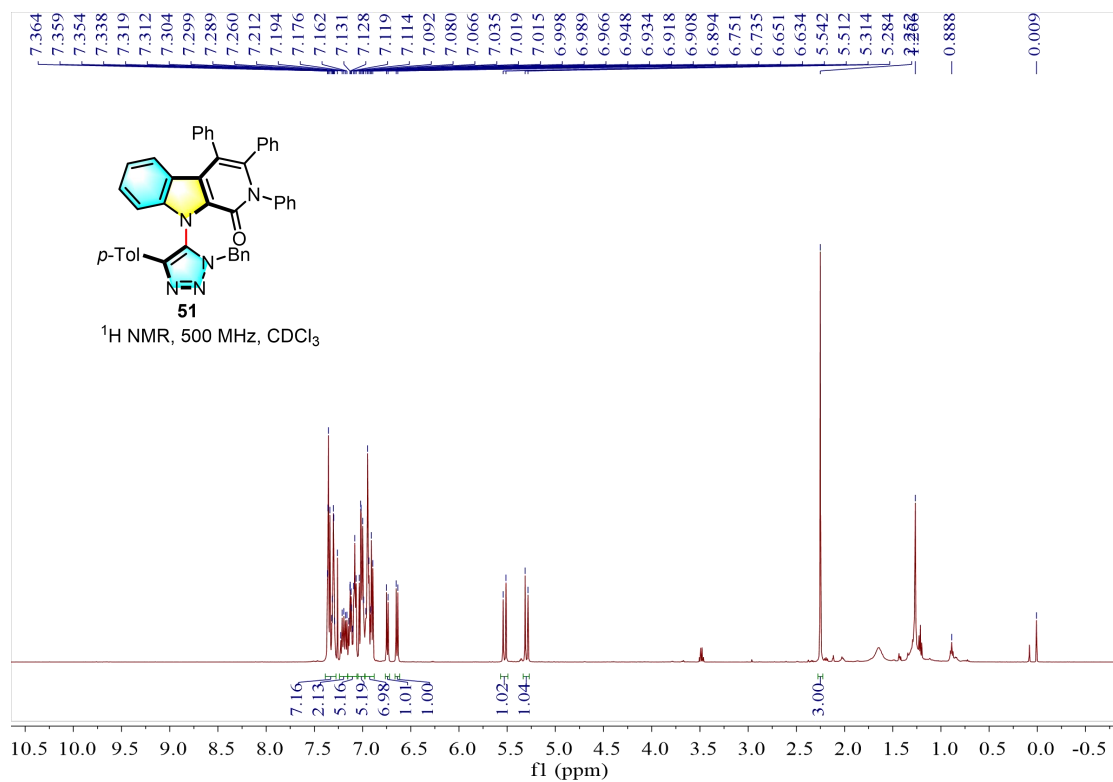


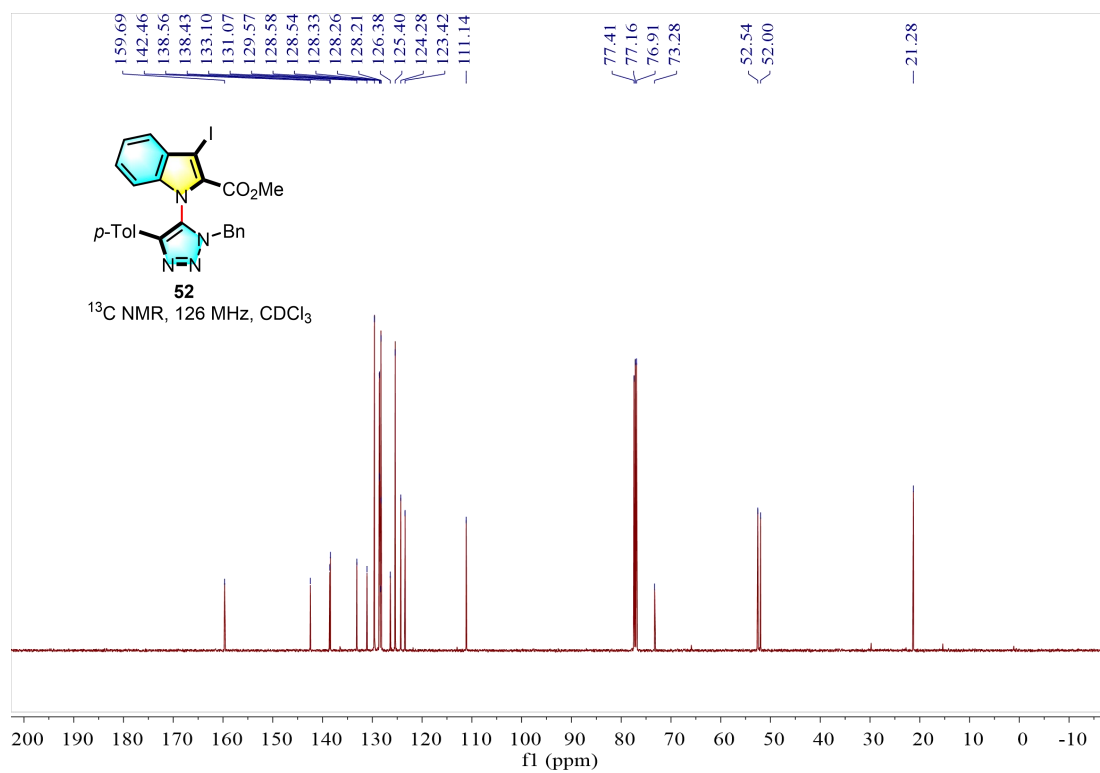
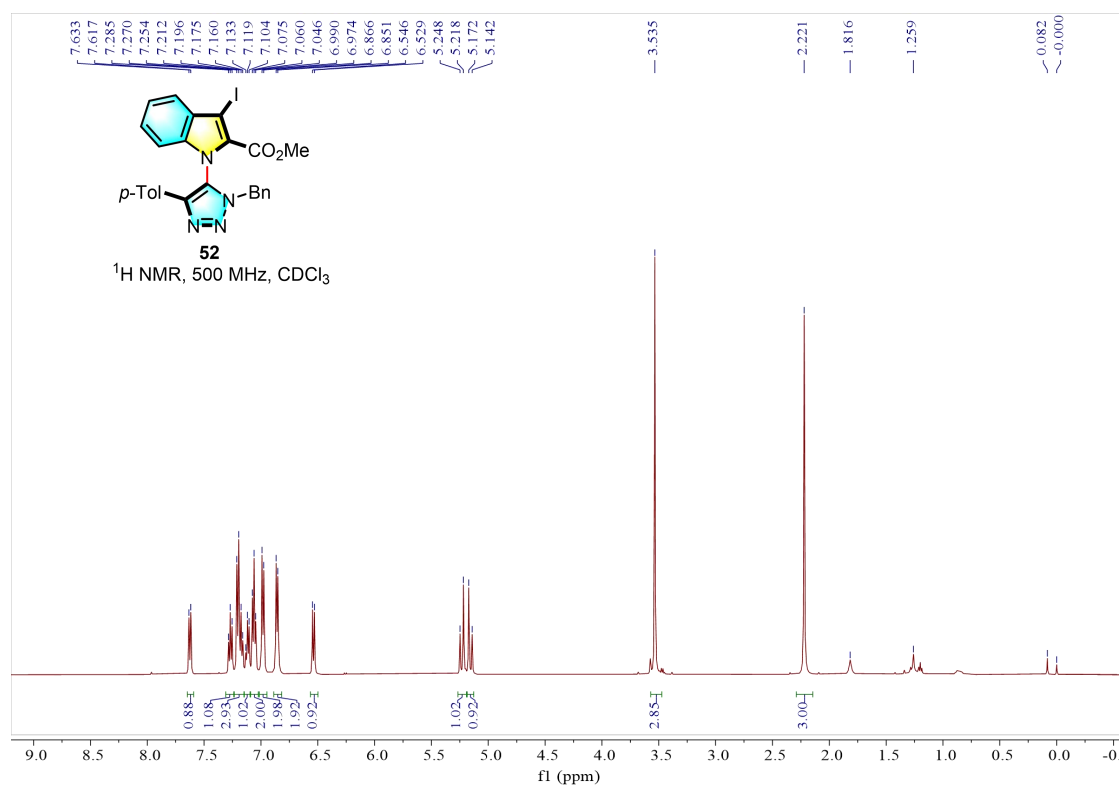


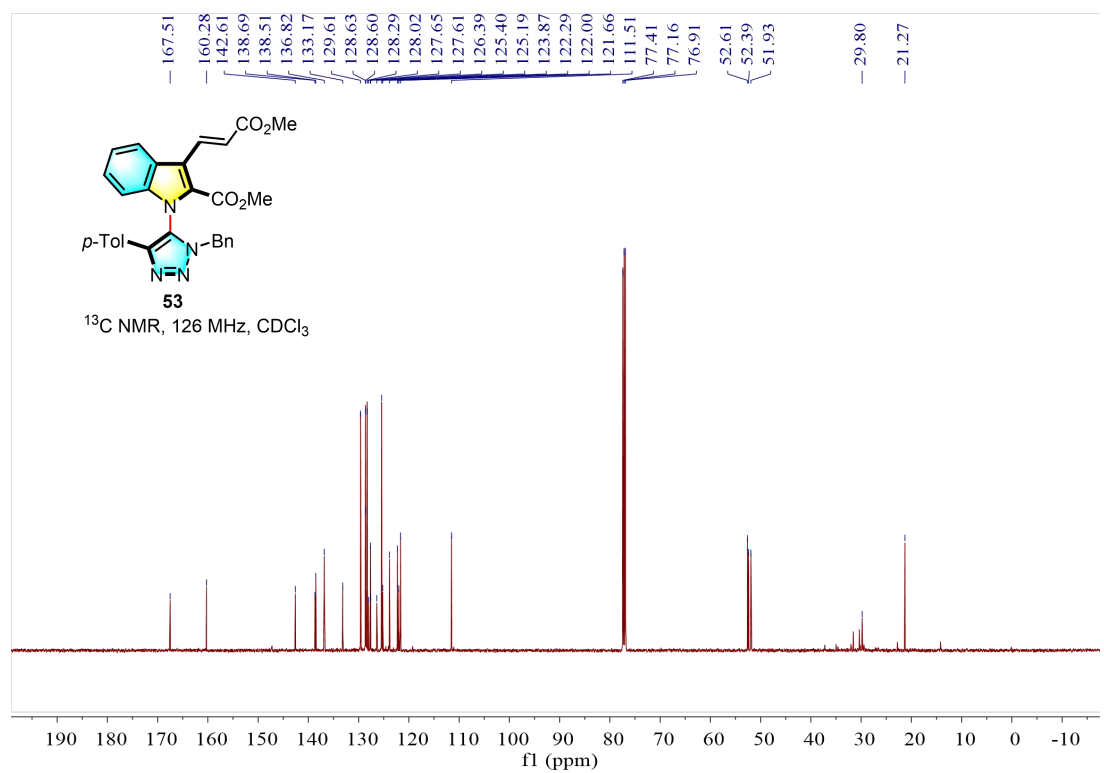
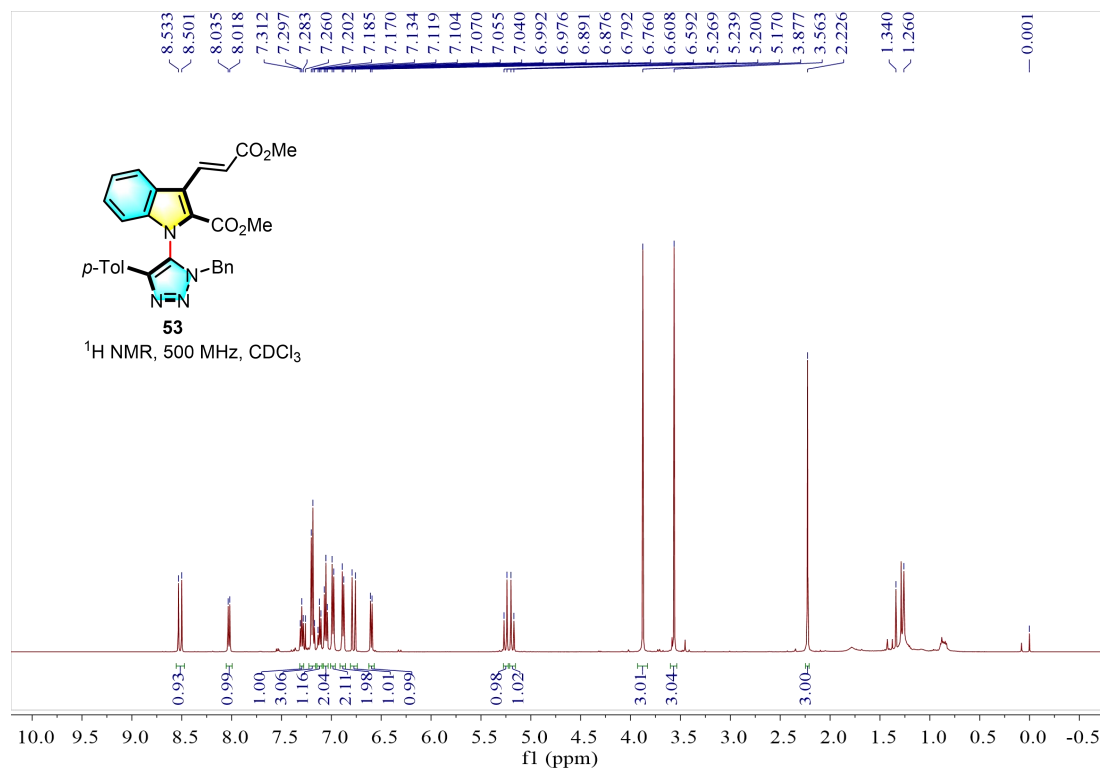


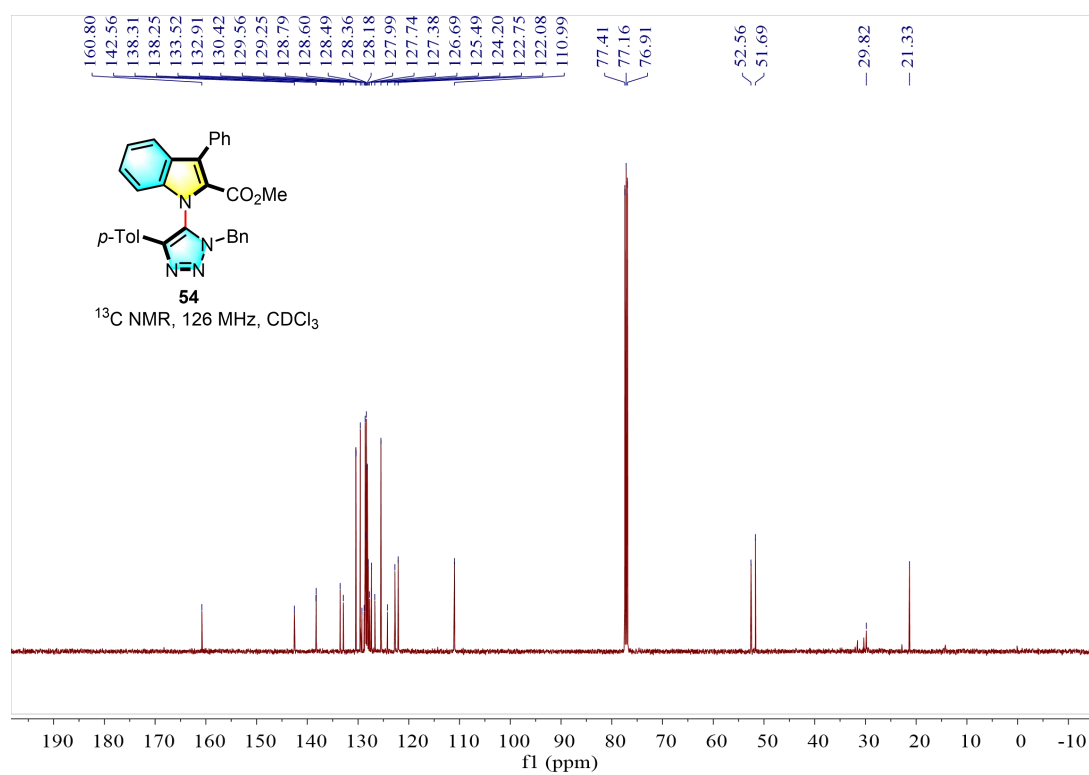
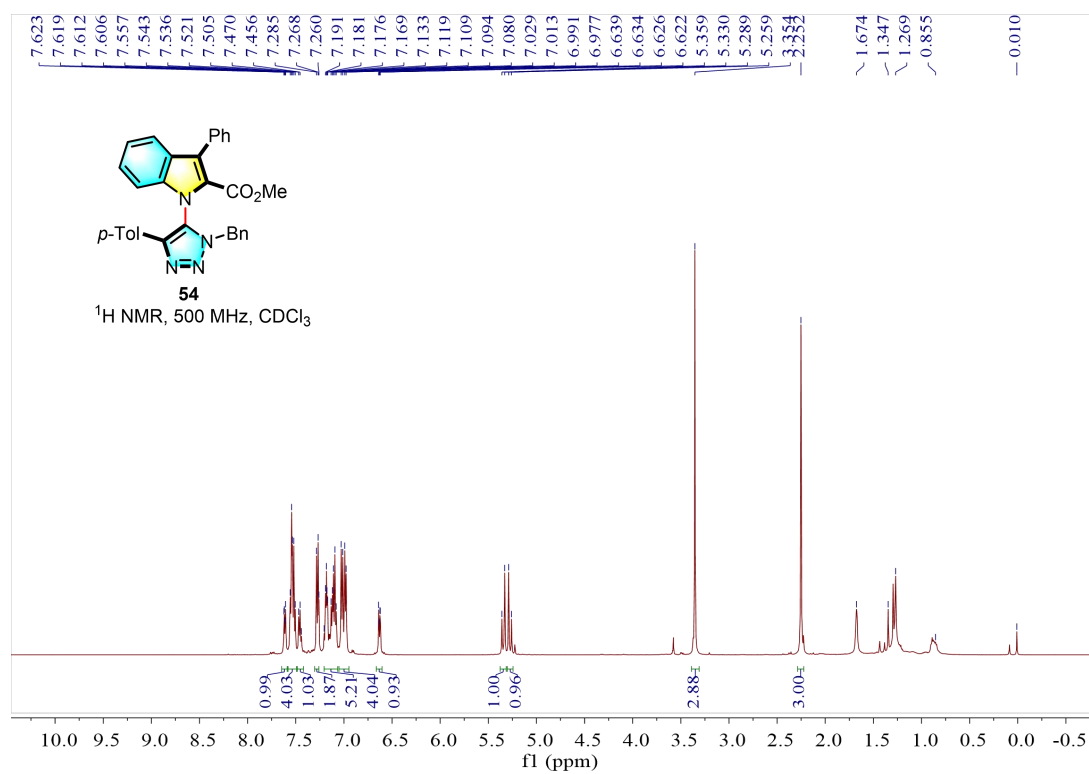


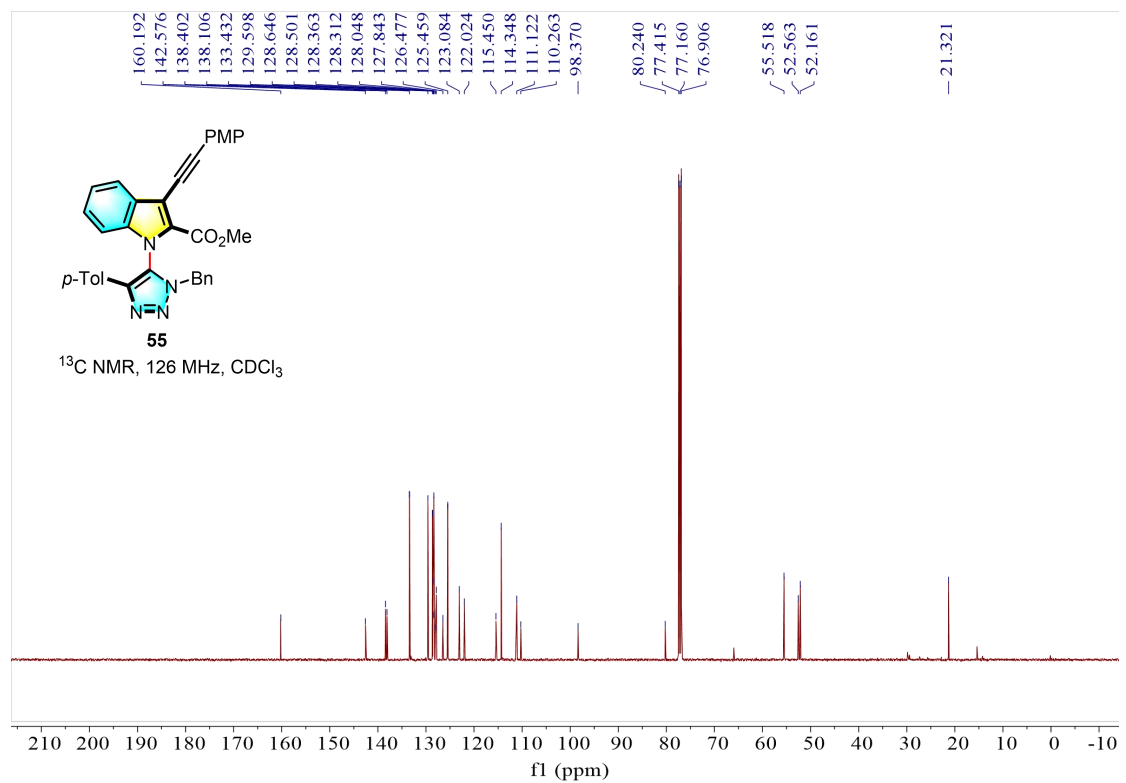
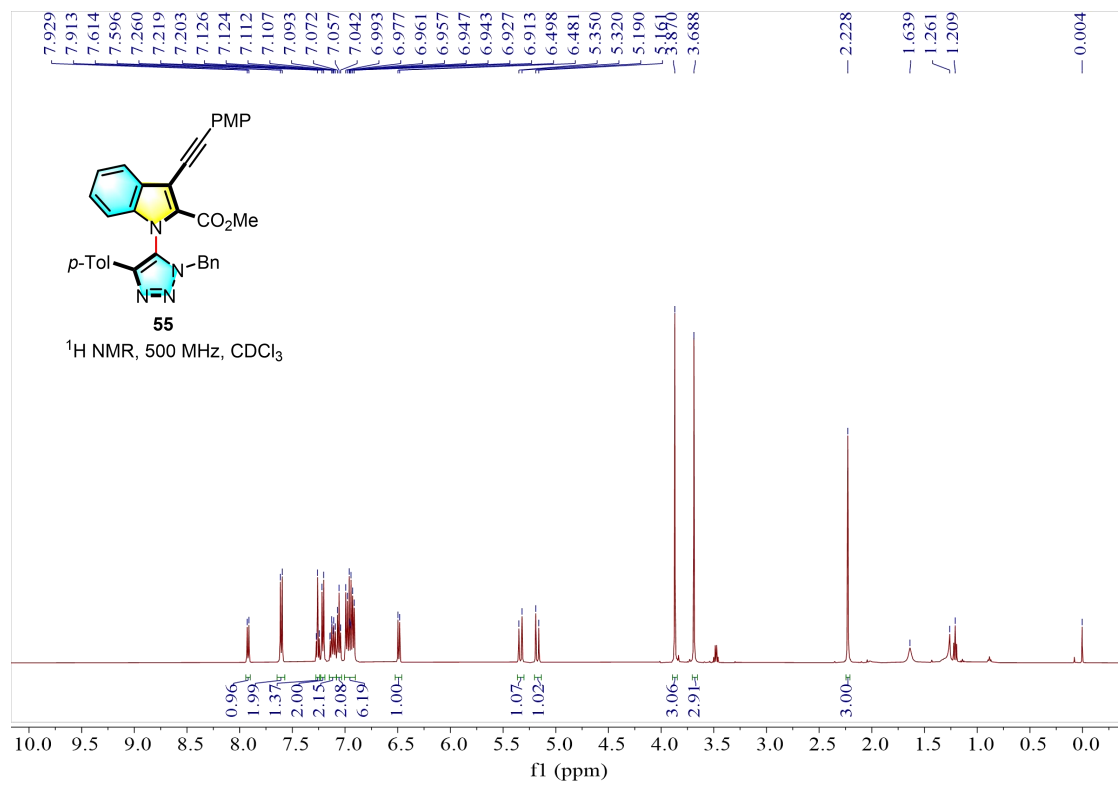


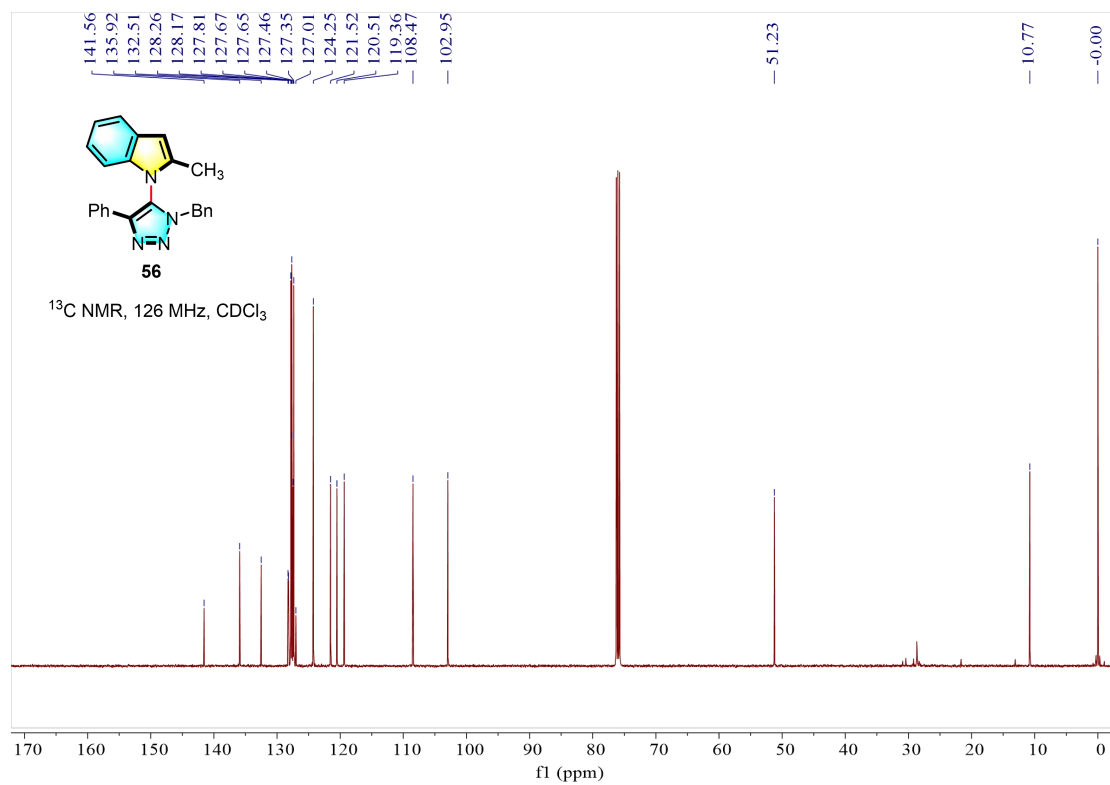
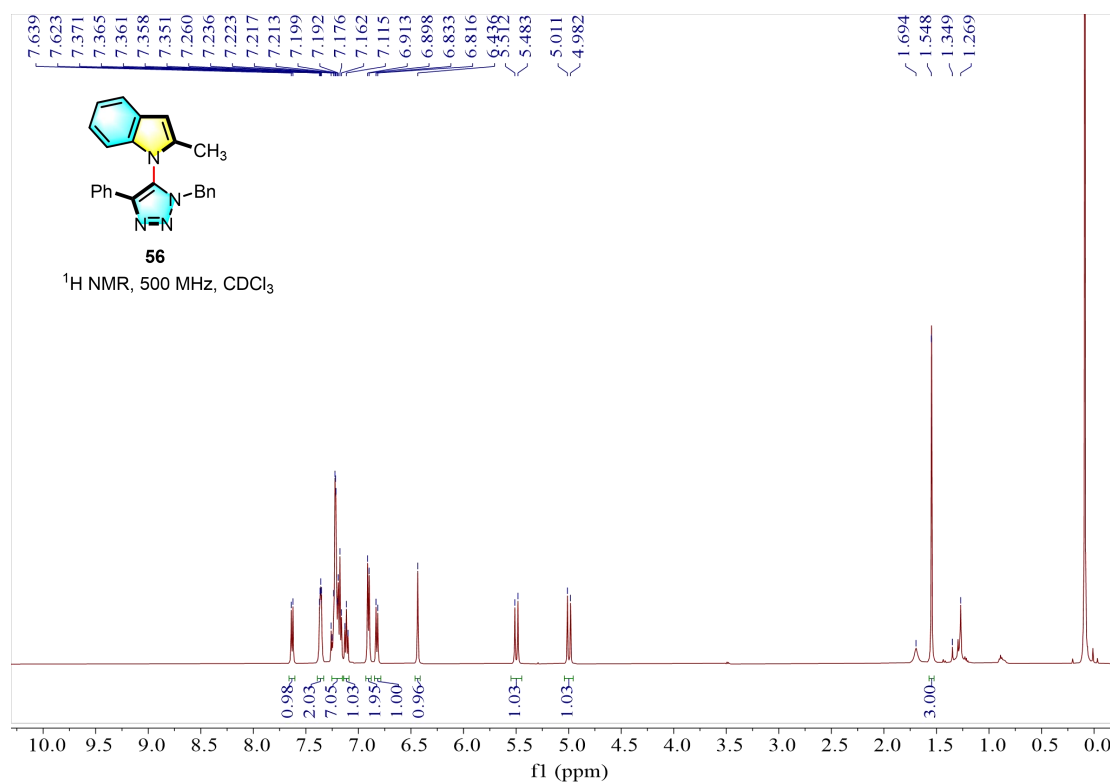


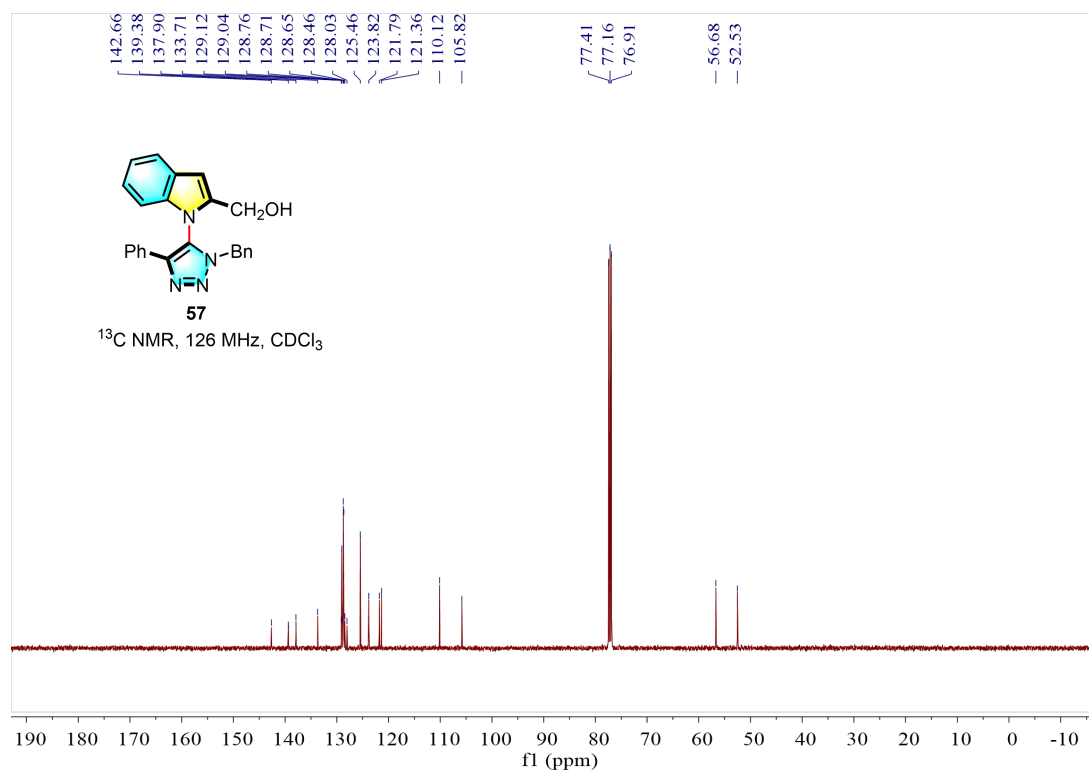
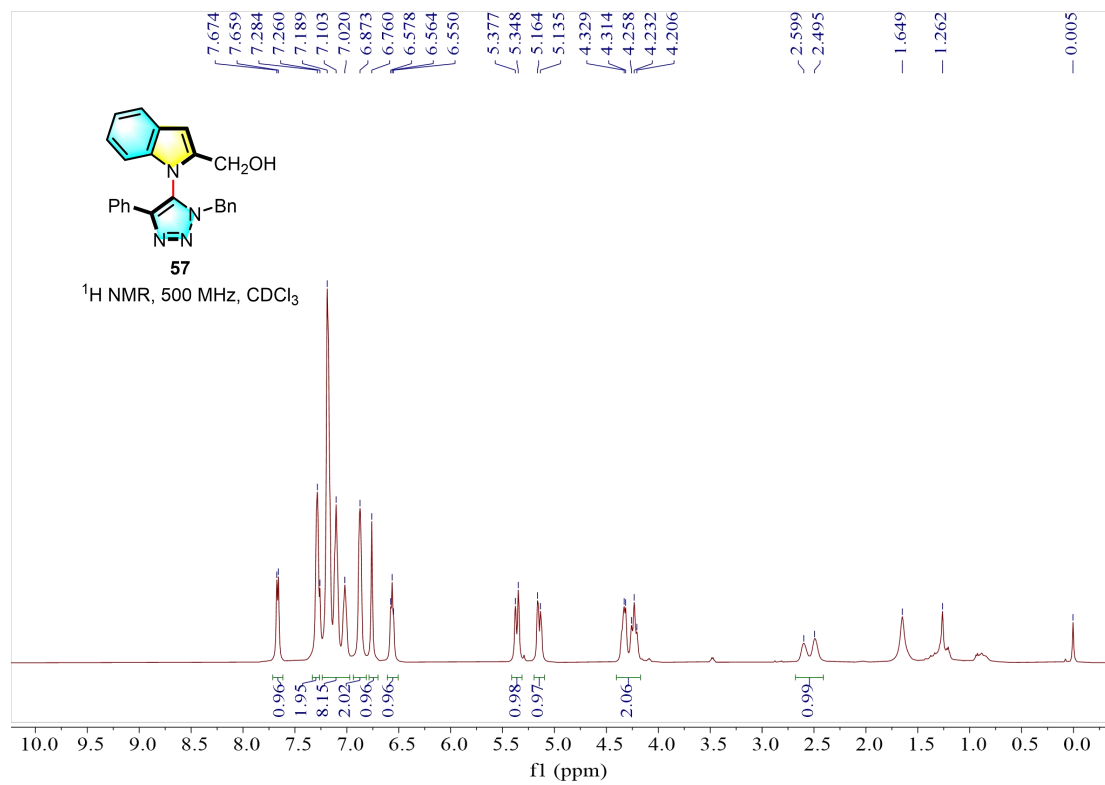












10. References

- [1] F. Wang, J. Jing, Y. Zhao, X. Zhu, X.-P. Zhang, L. Zhao, P. Hu, W.-Q. Deng, X. Li, *Angew. Chem. Int. Ed.*, **2021**, *60*, 16628-16633.
- [2] Y. Zhang, R. P. Hsung, M. R. Tracey, K. C. M. Kurtz, E. L. Vera, *Org. Lett.*, **2004**, *6*, 1151-1154.
- [3] X. Zeng, Y. Tu, Z. Zhang, C. You, J. Wu, Z. Ye, J. Zhao, *J. Org. Chem.*, **2019**, *84*, 4458-4466.
- [4] L. Zeng, J. Li, S. Cui, *Angew. Chem. Int. Ed.*, **2022**, *61*, e202205037.