Supporting Information

Stereoselective Synthesis of Functionalized Azepines *via* Gold and Palladium Relay Catalysis

Wu-Lin Yang,*[,1] Jia-Huan Shen,[1] Zeng-Hui Zhao,[1] Zhongao Wang,[1] and Wei-Ping Deng*[,2,1]

[1]*Shanghai Key Laboratory of Chemical Biology & School of Pharmacy, East China University of Science and Technology, 130 Meilong Road, Shanghai 200237, China*

[2]*Key Laboratory of the Ministry of Education for Advanced Catalysis Materials, Department of Chemistry, Zhejiang Normal University, Jinhua 321004, China*

E-mail: yangwl@ecust.edu.cn, weiping_deng@ecust.edu.cn

Contents

1. General information

^{1}H NMR spectra were recorded on a Bruker DPX 400 MHz spectrometer in $CDCl_3$ or $(CD_3)_2SO$. Chemical shifts were reported in ppm with the internal TMS signal at 0.0 ppm as a standard. The spectra are interpreted as: s = singlet, d = doublet, t = triplet, q = quartet, m = multiplet, dd = doublet of doublets, dt = doublet of triplets, ddd = doublet of doublet of doublets, coupling constant (s) *J* are reported in Hz and relative integrations are reported. ^{13}C NMR (100 MHz) spectra were recorded on a Bruker DPX 400 MHz spectrometer in $CDCl_3$ or $(CD_3)_2SO$. ^{13}C NMR (150 MHz) spectrum were recorded on Bruker Ascend 600 MHz spectrometer in $CDCl_3$ or $(CD_3)_2SO$. Chemical shifts were reported in ppm with the internal signal at 77.16 ppm ($CDCl_3$) or 39.70 ppm ($(CD_3)_2SO$) as a standard. ^{19}F NMR (376 MHz) spectra were recorded on a Bruker DPX 400 MHz spectrometer in $CDCl_3$ and referenced relative to $CFCl_3$. Optical rotations were measured on an AUTOPOL V. Enantiomeric excesses were determined by analysis of HPLC traces, obtained by using Chiralpak AD-H, AS-H, IF, IA, IB, and Chiralcel OD-H columns with *n*-hexane and ethanol or *i*-propanol as solvents. (Chiralpak AD-H, AS-H, IF, IA, IB, and chiralcel OD-H columns were purchased from Daicel Chiral Technologies (China) Co., LTD.) Melting points were obtained in open capillary tubes using MPA 100 automatic melting point apparatus which were made in Stanford Research System. High-resolution mass spectra (HRMS) were recorded on a Waters GCT Premier mass spectrometer using EI-TOF (electron ionization-time of flight). Commercially available materials purchased from Adamas-beta and Bidepharm, which were used as received. Anhydrous CH_2Cl_2 was distilled from calcium hydride, anhydrous THF was distilled from sodium/benzophenone. Ph_3PAuCl, $AgPF_6$ and $Pd_2(dba)_3$ purchased from Bidepharm. Enynamides **1** were prepared according to the literature procedures.[1] Cyano-TMM donor **2**,[2] benzoyl-TMM donor **4**,[3] and amino-TMM donor **6**[4] were prepared according to the literature procedures.

2. References

[1] L. Zhou, X. Wu, X. Yang, C. Mou, R. Song, S. Yu, H. Chai, L. Pan, Z. Jin and Y. R. Chi, Gold and Carbene Relay Catalytic Enantioselective Cycloisomerization/Cyclization Reactions of Ynamides and Enals, *Angew. Chem. Int. Ed.*, 2020, **59**, 1557-1561

[2] B. M. Trost and G. Mata, Enantioselective Palladium-Catalyzed [3+2] Cycloaddition of Trimethylenemethane and Fluorinated Ketones, *Angew. Chem. Int. Ed.*, 2018, **57**, 12333-12337.

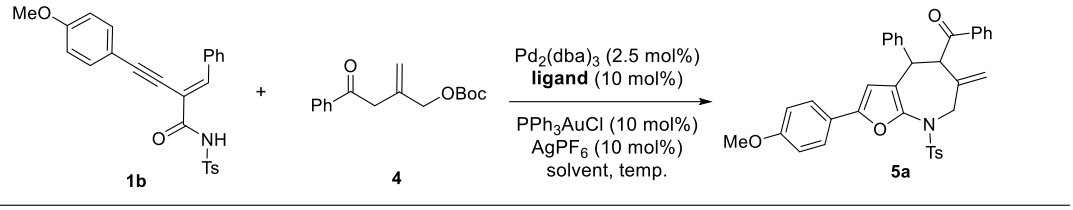
[3] B. M. Trost, Z. Zuo and Y. Wang, Pd(0)-Catalyzed Diastereo- and Enantioselective Intermolecular Cycloaddition for Rapid Assembly of 2-Acyl-methylenecyclopentanes, *Org.*

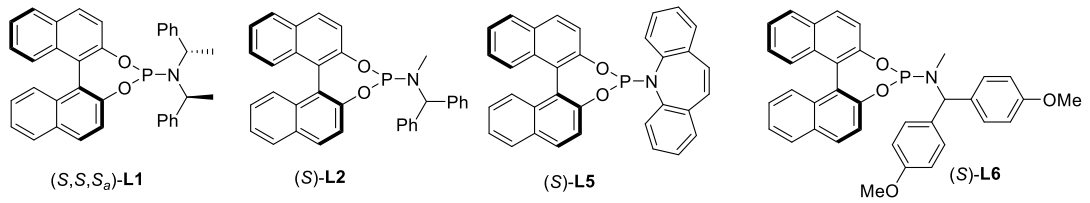
Lett., 2021, **23**, 979-983.

[4] B. M. Trost and Y. Wang, A Deprotonation Approach to the Unprecedented Amino-Trimethylenemethane Chemistry: Regio-, Diastereo-, and Enantioselective Synthesis of Complex Amino Cycles, *Angew. Chem. Int. Ed.*, 2018, **57**, 11025-11029.

3. Optimization studies

Table S1 Optimization for the asymmetric cascade reaction of benzoyl-TMM donor 4 with ynamide 1b[a]

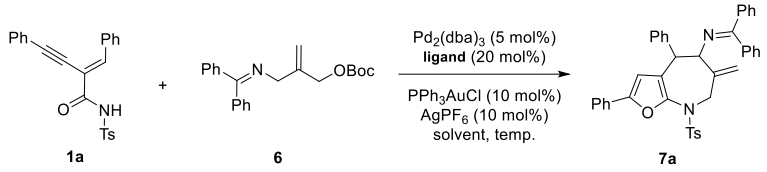


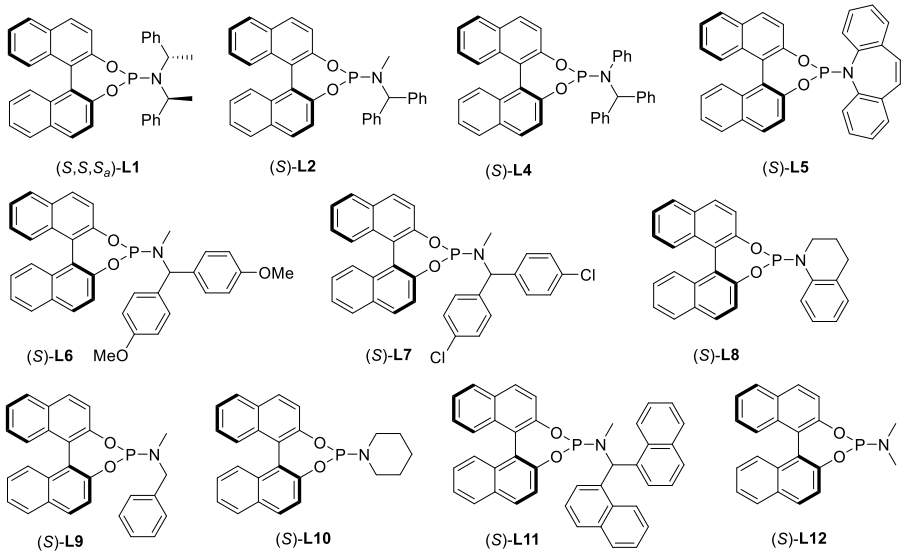


entry	ligand	solvent	temp. (°C)	yield (%)[b]	dr[c]	ee (%)[d]
1	**L2**	toluene	rt	81	8:1	75/51
2	**L2**	$PhCF_3$	rt	79	7:1	84/63
3	**L2**	CH_2Cl_2	rt	72	4:1	50/37
4	**L2**	THF	rt	67	10:1	68/50
5	**L1**	$PhCF_3$	rt	79	1.5:1	55/54
6	**L5**	$PhCF_3$	rt	86	1:1.5	38/17
7	**L6**	$PhCF_3$	rt	89	12:1	92/67
8	**L6**	$PhCF_3$	0	93	12:1	94/77
9	**L6**	$PhCF_3$	-10	92	12:1	94/74

[a]The reactions were performed with **1b** (0.10 mmol), **4** (0.12 mmol), $Pd_2(dba)_3$ (2.5 mol%), ligand (10 mol%), Ph_3PAuCl (10 mol%) and $AgPF_6$ (10 mol%) in solvent (0.05 M) at the indicated temperature. [b]Isolated yield of product **5a**. [c]dr was determined by ^1H NMR spectroscopic analysis. [d]ee value was determined by chiral HPLC analysis.

Table S2 Optimization for the asymmetric cascade reaction of amino-TMM donor 6 with ynamide 1a[a]

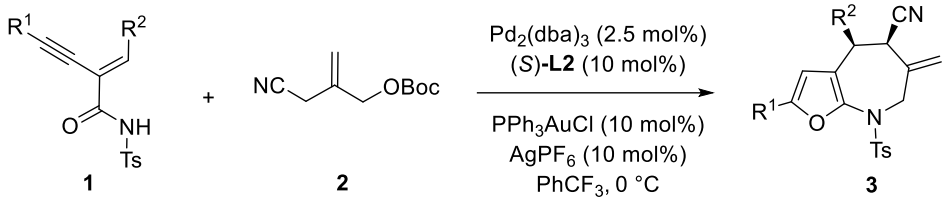




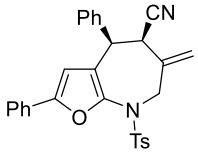
entry	ligand	solvent	temp. (°C)	yield (%)[b]	dr[c]	ee (%)[d]
1[e]	**L2**	toluene	rt	trace	-	-
2	**L1**	toluene	rt	58	3:1	81/61
3	**L2**	toluene	rt	74	4:1	95/81
4	**L4**	toluene	rt	33	3:1	61/60
5	**L5**	toluene	rt	85	4:1	60/50
6	**L6**	toluene	rt	65	3:1	60/66
7	**L7**	toluene	rt	72	3:1	90/86
8	**L8**	toluene	rt	67	2:1	55/40
9	**L9**	toluene	rt	65	1:2	90/80
10	**L10**	toluene	rt	65	1:1	75/50
11	**L11**	toluene	rt	64	3:1	60/50
12	**L12**	toluene	rt	72	1:1	80/84
13	**L2**	$PhCF_3$	rt	58	4:1	90/70
14	**L2**	THF	rt	-	-	-
15	**L2**	CH_2Cl_2	rt	80	3.5:1	90/68
16	**L2**	CH_3CN	rt	-	-	-
17	**L2**	toluene	0	70	4:1	93/80

[a]The reactions were performed with **1a** (0.10 mmol), **6** (0.12 mmol), $Pd_2(dba)_3$ (5 mol%), ligand (20 mol%), Ph_3PAuCl (10 mol%) and $AgPF_6$ (10 mol%) in solvent (0.05 M) at the indicated temperature. [b]Isolated yield of product **7a**. [c]dr was determined by ^1H NMR spectroscopic analysis. [d]ee value was determined by chiral HPLC analysis. [e]$Pd_2(dba)_3$ (2.5 mol%) and (*S*)-**L2** (10 mol%) were used.

4. Preparation and characterization data of cyano-substituted furo[2,3-*b*]azepines 3



General procedure A: Under a nitrogen atmosphere, two flame dried 10 mL Schlenk tube A and B, the tube A was charged with Ph_3PAuCl (4.9 mg, 0.01 mmol, 10 mol%) and $AgPF_6$ (2.5 mg, 0.01 mmol, 10 mol%), the tube B was charged with ligand (*S*)-**L2** (5.1 mg, 0.01 mmol, 10 mol%), and $Pd_2(dba)_3$ (2.3 mg, 0.0025 mmol, 2.5 mol%). After the tube A and B were evacuated and backfilled with nitrogen, freshly distilled $PhCF_3$ (1.0 mL) was added respectively, then stirred at room temperature for 15-20 minutes while the solution of tube A turned white turbid and the solution of tube B turned light green. Then, enynamides **1** (0.1 mmol, 1.0 equiv) were added to tube A, and the reaction mixture immediately turned golden yellow. After 5 minutes, cyano-TMM donor **2** (24 mg, 0.12 mmol, 1.2 equiv) was added to tube A sequentially. The solution of tube B was then transferred to tube A at 0 °C. The reaction mixture was stirred at 0 °C for the indicated time, which was evaporated under reduced pressure at 30 °C. The crude residue was purified by flash chromatography (petroleum ether/EtOAc = 10/1) to give the desired products **3**.



(4*R*,5*R*)-6-Methylene-2,4-diphenyl-8-tosyl-5,6,7,8-tetrahydro-4*H*-furo[2,3-*b*]azepine-5-carbonitrile (3a): Following the general procedure **A**, compound **3a** was obtained as a white solid in 98% yield (47.1 mg), 13:1 dr and 97% ee, purified by flash chromatography (petroleum ether/EtOAc = 10/1) ; R_f = 0.5 (petroleum ether/EtOAc = 4/1); mp = 150-152 °C; $[\alpha]_D^{25}$ = +114.1 (*c* = 0.20, CH_2Cl_2); **^{1}H NMR** (400 MHz, $CDCl_3$) δ 7.78 (d, *J* = 8.2 Hz, 2H), 7.46 (d, *J* = 7.4 Hz, 2H), 7.40 – 7.29 (m, 7H), 7.30 – 7.20 (m, 3H), 6.16 (s, 1H), 5.39 (brs, 1H), 5.12 (brs, 1H), 4.78 (d, *J* = 15.8 Hz, 1H), 4.22 (d, *J* = 15.8 Hz, 1H), 3.83 (d, *J* = 3.0 Hz, 1H), 3.74 (d, *J* = 2.7 Hz, 1H), 2.50 (s, 3H); **^{13}C NMR** (100 MHz, $CDCl_3$) δ 150.7, 144.7, 142.6, 138.0, 137.3, 136.5, 129.8(4) (2C), 129.8(1), 128.9 (2C), 128.8 (2C), 128.7(6) (2C), 128.4, 128.2 (2C), 128.1, 123.8 (2C), 120.8, 119.2, 118.3, 107.4, 53.3, 44.4, 41.6, 21.8; **HRMS** (EI-TOF) m/z: $[M]^+$ calcd for $[C_{29}H_{24}N_2O_3S]^+$: 480.1502; found: 480.1510. **HPLC** (Chiralpak AS-H, *n*-hexane/ethanol = 90/10, flow rate = 1.0 mL/min, λ = 220 nm) t_R= 12.83 min (*trans*-major), 19.10 (*trans*-minor),

22.20 min (*cis*-minor), 26.06 min (*cis*-major).

The preparation and X-ray analysis of the single crystal 3a

Compound **3a** (10.0 mg) was charged in a screw-top vial. Drops of isopropyl ether were added with shaking until all the compound has dissolved. The lid was then loosely screwed on the vial, and a single crystal was obtained by natural volatilization at room temperature. The data set was collected by a Bruker APEX-II CCD at 293(2) K equipped with Mo radiation source (Kα = 0.71073 Å). Applied with multi-scan absorption correction, the structure solution was solved and refinement was processed by SHELXTL and OLEX2 program package. CCDC 2124706 contains the supplementary crystallographic data, and can be obtained free of charge via www.ccdc.cam.ac.uk/conts/retrieving.html.

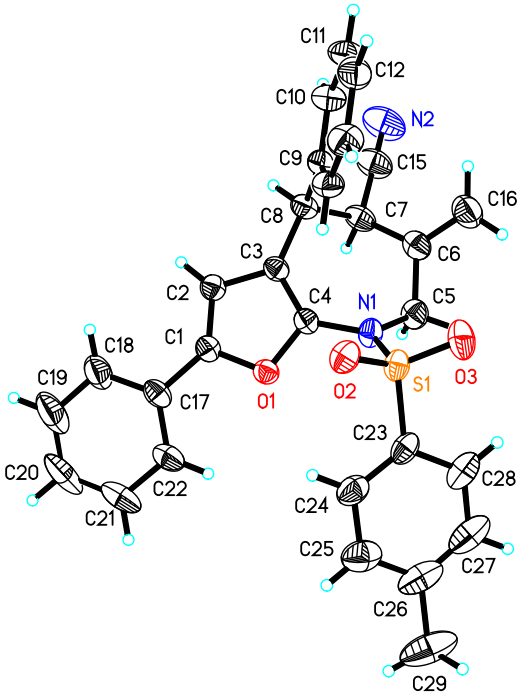
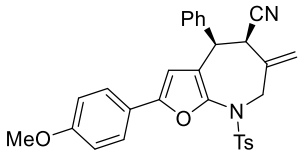


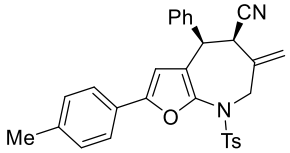
Fig S1. The thermal ellipsoid plot for X-ray structure of (4*R*,5*R*)-**3a** with the ellipsoid contour at 30% probability level

Identification code	mo_d8v20438_0m	
Empirical formula	C29 H24 N2 O3 S	
Formula weight	480.56	
Temperature	293(2) K	
Wavelength	0.71073 Å	
Crystal system	Monoclinic	
Space group	P 21	
Unit cell dimensions	a = 9.3577(3) Å	α= 90 °.
	b = 11.4290(3) Å	β= 108.2730(10) °.

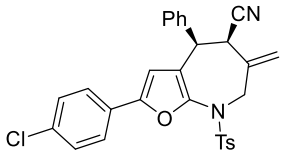
	c = 12.3964(3) Å γ = 90 °.
Volume	1258.93(6) $Å^3$
Z	2
Density (calculated)	1.268 Mg/m^3
Absorption coefficient	0.162 mm^{-1}
F(000)	504
Crystal size	0.190 x 0.150 x 0.110 mm^3
Theta range for data collection	2.292 to 26.000 °.
Index ranges	-10<=h<=11, -14<=k<=14, -15<=l<=15
Reflections collected	18025
Independent reflections	4916 [R(int) = 0.0552]
Completeness to theta = 25.242 °	99.5 %
Absorption correction	Semi-empirical from equivalents
Max. and min. transmission	0.7456 and 0.5267
Refinement method	Full-matrix least-squares on F^2
Data / restraints / parameters	4916 / 1 / 326
Goodness-of-fit on F^2	1.025
Final R indices [I>2sigma(I)]	R1 = 0.0417, wR2 = 0.1048
R indices (all data)	R1 = 0.0504, wR2 = 0.1137
Absolute structure parameter	0.00(5)
Extinction coefficient	0.065(12)
Largest diff. peak and hole	0.264 and -0.243 $e.Å^{-3}$



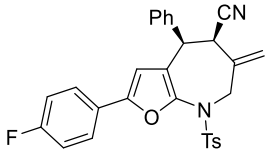
(4*R*,5*R*)-2-(4-Methoxyphenyl)-6-methylene-4-phenyl-8-tosyl-5,6,7,8-tetrahydro-4*H*-furo[2,3-*b*]azepine-5-carbonitrile (3b): Following the general procedure **A**, compound **3b** was obtained as a white solid in 94% yield (48.3 mg), 8:1 dr and 97% ee, purified by flash chromatography (petroleum ether/EtOAc = 10/1); R_f = 0.45 (petroleum ether/EtOAc = 4/1); mp = 192-194 °C; $[\alpha]_D^{25}$ = +118.5 (*c* = 0.20, CH_2Cl_2); **^{1}H NMR** (400 MHz, $CDCl_3$) δ 7.77 (d, *J* = 8.3 Hz, 2H), 7.43 – 7.32 (m, 7H), 7.29 – 7.22 (m, 2H), 6.90 – 6.81 (m, 2H), 6.02 (s, 1H), 5.38 (brs, 1H), 5.10 (brs, 1H), 4.78 (d, *J* = 15.8 Hz, 1H), 4.21 (d, *J* = 15.7 Hz, 1H), 3.81 (s, 3H), 3.80 (d, *J* = 3.2 Hz, 1H), 3.69 (d, *J* = 3.2 Hz, 1H), 2.50 (s, 3H). **^{13}C NMR** (100 MHz, $CDCl_3$) δ 159.6, 150.8, 144.7, 141.8, 138.1, 137.4, 136.5, 129.8 (2C), 128.8(2) (2C), 128.7(9) (2C), 128.3, 128.2 (2C), 125.4 (2C), 122.9, 120.8, 119.2, 118.3, 114.2 (2C), 105.8, 55.5, 53.3, 44.4, 41.7, 21.8; **HRMS** (EI-TOF) m/z: [M]+ calcd for $[C_{30}H_{26}N_2O_4S]^+$: 510.1608; found: 510.1615. **HPLC** (Chiralpak AS-H, *n*-hexane/ethanol = 90/10, flow rate = 1.0 mL/min, λ = 220 nm) t_R= 11.92 min (*trans*-major), 15.86 min (*trans*-minor), 19.97 min (*cis*-minor), 23.95 min (*cis*-major).



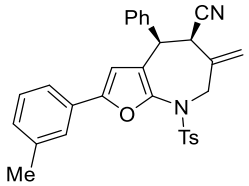
(4*R*,5*R*)-6-Methylene-4-phenyl-2-(*p*-tolyl)-8-tosyl-5,6,7,8-tetrahydro-4*H*-furo[2,3-*b*]azepine-5-carbonitrile (3c): Following the general procedure **A**, compound **3c** was obtained as a white solid in 97% yield (48.2 mg), 11:1 dr and 96% ee, purified by flash chromatography (petroleum ether/EtOAc = 10/1); R_f = 0.4 (petroleum ether/EtOAc = 10/1); mp = 153-155 °C; $[\alpha]_D^{25}$ = +101.0 (*c* = 0.20, CH_2Cl_2); **^{1}H NMR** (400 MHz, $CDCl_3$) δ 7.77 (d, *J* = 8.2 Hz, 2H), 7.36 (m, 7H), 7.30 – 7.22 (m, 2H), 7.12 (d, *J* = 7.9 Hz, 2H), 6.10 (s, 1H), 5.38 (brs, 1H), 5.11 (brs, 1H), 4.78 (d, *J* = 15.8 Hz, 1H), 4.21 (d, *J* = 15.8 Hz, 1H), 3.82 (d, *J* = 3.3 Hz, 1H), 3.72 (d, *J* = 3.3 Hz, 1H), 2.49 (s, 3H), 2.33 (s, 3H). **^{13}C NMR** (100 MHz, $CDCl_3$) δ 150.9, 144.7, 142.1, 138.0, 137.9 (8), 137.4, 136.5, 129.8 (2C), 129.4 (2C), 128.8 (1) (2C), 128.7 (9) (2C), 128.3, 128.2 (2C), 127.1, 123.8 (2C), 120.7, 119.1, 118.3, 106.6, 53.3, 44.4, 41.6, 21.8, 21.4; **HRMS** (EI-TOF) m/z: $[M]^+$ calcd for $[C_{30}H_{26}N_2O_3S]^+$: 494.1659; found: 494.1667. **HPLC** (Chiralpak AS-H, *n*-hexane/ethanol = 90/10, flow rate = 1.0 mL/min, λ = 220 nm) t_R= 11.86 min (*trans*-major), 15.22 min (*trans*-minor), 20.02 min (*cis*-minor), 27.27 min (*cis*-major).



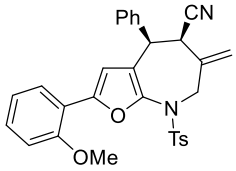
(4*R*,5*R*)-2-(4-Chlorophenyl)-6-methylene-4-phenyl-8-tosyl-5,6,7,8-tetrahydro-4*H*-furo[2,3-*b*]azepine-5-carbonitrile (3d): Following the general procedure **A**, compound **3d** was obtained as a white solid in 96% yield (49.2 mg), 8:1 dr and 96% ee, purified by flash chromatography (petroleum ether/EtOAc = 10/1); R_f = 0.4 (petroleum ether/EtOAc = 4/1); mp = 177–179 °C; $[\alpha]_D^{25}$ = +122.3 (*c* = 0.20, CH_2Cl_2); **^{1}H NMR** (400 MHz,$CDCl_3$) δ 7.76 (d, *J* = 8.1 Hz, 2H), 7.41 – 7.33 (m, 7H), 7.32 – 7.22 (m, 4H), 6.15 (s, 1H), 5.40 (brs, 1H), 5.13 (brs, 1H), 4.78 (d, *J* = 15.8 Hz, 1H), 4.21 (d, *J* = 15.8 Hz, 1H), 3.80 (d, *J* = 3.2 Hz, 1H), 3.70 (d, *J* = 3.2 Hz, 1H), 2.50 (s, 3H); **^{13}C NMR** (100 MHz, $CDCl_3$) δ 149.6, 144.8, 142.8, 137.9, 137.3, 136.5, 133.7, 129.9 (2C), 129.1 (2C), 128.9 (2C), 128.7 (2C), 128.5, 128.3, 128.2 (2C), 125.1 (2C), 121.1, 119.5, 118.2, 107.8, 53.2, 44.4, 41.7, 21.8; **HRMS** (EI-TOF) m/z: $[M]^+$ calcd for $[C_{29}H_{23}ClN_2O_3S]^+$: 514.1112; found: 514.1116. **HPLC** (Chiralpak AS-H, *n*-hexane/ethanol = 90/10, flow rate = 1.0 mL/min, λ = 220 nm) t_R= 15.44 min (*trans*-major), 19.01 min (*trans*-minor), 25.02 min (*cis*-minor), 35.22 min (*cis*-major).



(4*R*,5*R*)-2-(4-Fluorophenyl)-6-methylene-4-phenyl-8-tosyl-5,6,7,8-tetrahydro-4*H*-furo[2,3-*b*]azepine-5-carbonitrile (3e): Following the general procedure **A**, compound **3e** was obtained as a white solid in 94% yield (47.2 mg), 6:1 dr and 96% ee, purified by flash chromatography (petroleum ether/EtOAc = 10/1); R_f = 0.4 (petroleum ether/EtOAc = 4/1); mp = 91-93 °C; $[\alpha]_D^{25}$ = +122.5 (*c* = 0.20, CH_2Cl_2); **^{1}H NMR** (400 MHz, $CDCl_3$) δ 7.76 (d, *J* = 8.3 Hz, 2H), 7.46 – 7.41 (m, 2H), 7.41 – 7.33 (m, 5H), 7.29 – 7.23 (m, 2H), 7.05 – 6.98 (m, 2H), 6.09 (s, 1H), 5.40 (brs, 1H), 5.12 (brs, 1H), 4.78 (d, *J* = 15.8 Hz, 1H), 4.21 (d, *J* = 15.8 Hz, 1H), 3.79 (d, *J* = 3.2 Hz, 1H), 3.68 (d, *J* = 3.2 Hz, 1H), 2.50 (s, 3H). **^{13}C NMR** (100 MHz, $CDCl_3$) δ 162.5 (d, C-F, $^1J_{C\text{-}F}$ = 248.2 Hz), 149.9, 144.8, 142.5, 137.9, 137.3, 136.5, 129.8 (2C), 128.9 (2C), 128.7 (2C), 128.4, 128.2 (2C), 126.2 (d, C-F, $^4J_{C\text{-}F}$ = 3.3 Hz), 125.7 (d, C-F, $^3J_{C\text{-}F}$ = 8.1 Hz, 2C), 121.0, 119.4, 118.2, 115.84 (d, C-F, $^2J_{C\text{-}F}$ = 22.0 Hz, 2C), 107.0, 53.2, 44.3, 41.7, 21.8. **^{19}F NMR** (376 MHz, $CDCl_3$) δ -113.05 – -113.12 (m). **HRMS** (EI-TOF) m/z: $[M]^+$ calcd for $[C_{29}H_{23}FN_2O_3S]^+$: 498.1408; found: 498.1415. **HPLC** (Chiralpak AS-H, *n*-hexane/ethanol = 90/10, flow rate = 1.0 mL/min, λ = 220 nm) t_R= 14.24 min (*trans*-major), 20.22 min (*trans*-minor), 23.93 min (*cis*-minor), 33.06 min (*cis*-major).

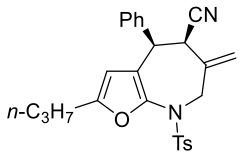


(4*R*,5*R*)-6-Methylene-4-phenyl-2-(*m*-tolyl)-8-tosyl-5,6,7,8-tetrahydro-4*H*-furo[2,3-*b*]azepine-5-carbonitrile (3f): Following the general procedure **A**, compound **3f** was obtained as a white solid in 97% yield (48.2 mg), 12:1 dr and 96% ee, purified by flash chromatography (petroleum ether/EtOAc = 10/1); R_f = 0.5 (petroleum ether/EtOAc = 4/1); mp = 133-135 °C; $[\alpha]_D^{25}$ = +69.6 (*c* = 0.20, CH_2Cl_2); **^{1}H NMR** (400 MHz, $CDCl_3$) δ 7.78 (d, *J* = 8.3 Hz, 2H), 7.40 – 7.33 (m, 5H), 7.30 – 7.24 (m, 4H), 7.23 – 7.18 (m, 1H), 7.06 (d, *J* = 7.4 Hz, 1H), 6.14 (s, 1H), 5.39 (brs, 1H), 5.11 (brs, 1H), 4.79 (d, *J* = 15.8 Hz, 1H), 4.22 (d, *J* = 15.8 Hz, 1H), 3.83 (d, *J* = 3.3 Hz, 1H), 3.73 (d, *J* = 3.3 Hz, 1H), 2.49 (s, 3H), 2.33 (s, 3H). **^{13}C NMR** (100 MHz, $CDCl_3$) δ 150.8, 144.7, 142.4, 138.4, 138.0, 137.3, 136.6, 129.8 (2C), 129.7, 128.8, 128.8 (2C), 128.7 (8) (2C), 128.7, 128.4, 128.2 (2C), 124.4, 121.0, 120.8, 119.1, 118.2, 107.2, 53.3, 44.4, 41.6, 21.8, 21.5. **HRMS** (EI-TOF) m/z: $[M]^+$ calcd for $[C_{30}H_{26}N_2O_3S]^+$: 494.1659; found: 494.1662. **HPLC** (Chiralpak IA, *n*-hexane/ethanol = 90/10, flow rate = 1.0 mL/min, λ = 220 nm) t_R= 11.76 min (*trans*-minor), 12.91 min (*cis*-major), 18.83 min (*cis*-major), 22.33 min (*trans*-minor).

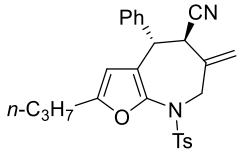


(4*R*,5*R*)-2-(2-Methoxyphenyl)-6-methylene-4-phenyl-8-tosyl-5,6,7,8-tetrahydro-4*H*-furo[2,3-*b*]azepine-5-carbonitrile (3g): Following the general procedure **A**, compound **3g** was obtained as a white solid in 97% yield (49.3 mg), 10:1 dr and 96% ee, purified by flash chromatography (petroleum ether/EtOAc = 10/1); R_f = 0.5 (petroleum ether/EtOAc = 4/1); mp = 188-190 °C; $[\alpha]_D^{25}$ = +86.5 (*c* = 0.20, CH_2Cl_2); **^{1}H NMR** (400 MHz, $CDCl_3$) δ 7.79 (d, *J* = 8.0 Hz, 2H), 7.62 – 7.53 (m, 1H), 7.41 – 7.30 (m, 5H), 7.30 – 7.16 (m, 3H), 7.02 – 6.93 (m, 1H), 6.88 (d, *J* = 8.3 Hz, 1H), 6.48 (s, 1H), 5.34 (brs, 1H), 5.08 (brs, 1H), 4.76 (d, *J* = 16.0 Hz, 1H), 4.27 (d, *J* = 15.9 Hz, 1H), 3.89 (d, *J* = 3.3 Hz, 1H), 3.85 (d, *J* = 3.3 Hz, 1H), 3.79 (s, 3H), 2.49 (s, 3H). **^{13}C NMR** (100 MHz, $CDCl_3$) δ 155.7, 147.2, 144.7, 141.9, 137.9, 137.1, 136.7, 129.8 (2C), 129.0 (2C), 128.7, 128.6 (2C), 128.2, 128.1 (2C), 125.9, 120.8, 120.2, 118.7, 118.4, 118.1, 112.3, 111.0, 55.4, 53.8, 44.4, 41.4, 21.8; **HRMS** (EI-TOF) m/z: $[M]^+$ calcd for $[C_{30}H_{26}ClN_2O_4S]^+$: 510.1608; found: 510.1619. **HPLC** (Chiralpak AS-H, *n*-hexane/ethanol =

90/10, flow rate = 1.0 mL/min, λ = 220 nm) t_R= 14.21 min (*trans*-major), 20.82 min (*trans*-minor), 25.75 min (*cis*-minor), 31.11 min (*cis*-major).

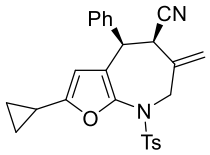


(4*R*,5*R*)-6-Methylene-4-phenyl-2-propyl-8-tosyl-5,6,7,8-tetrahydro-4*H*-furo[2,3-*b*]azepine-5-carbonitrile (*cis*-3h) (major): Following the general procedure **A**, compound **3h** was obtained as a white solid in 53% yield (24.2 mg), 93% ee, purified by flash chromatography (petroleum ether/EtOAc = 10/1); R_f = 0.45 (petroleum ether/EtOAc = 4/1); mp = 110-112 °C; $[\alpha]_D^{25}$ = +106.3 (*c* = 0.20, CH_2Cl_2); **^{1}H NMR** (400 MHz, $CDCl_3$) δ 7.69 (d, *J* = 8.1 Hz, 2H), 7.40 – 7.28 (m, 5H), 7.22 – 7.13 (m, 2H), 5.53 (s, 1H), 5.35 (s, 1H), 5.07 (s, 1H), 4.72 (d, *J* = 15.8 Hz, 1H), 4.13 (d, *J* = 15.8 Hz, 1H), 3.71 (d, *J* = 3.1 Hz, 1H), 3.52 (d, *J* = 3.2 Hz, 1H), 2.51 – 2.45 (m, 5H), 1.57 (q, *J* = 7.4 Hz, 2H), 0.91 (t, *J* = 7.4 Hz, 3H). **^{13}C NMR** (100 MHz, $CDCl_3$) δ 153.8, 144.5, 141.1, 138.3, 137.6, 136.3, 129.7 (2C), 128.7 (2C), 128.7 (2C), 128.1 (9), 128.1 (5) (2C), 120.7, 118.3 118.0, 107.9, 53.1, 44.3, 41.8, 30.2, 21.8, 21.1, 13.7. **HRMS** (EI-TOF) m/z: $[M]^+$ calcd for $[C_{26}H_{26}N_2O_3S]^+$: 446.1659; found: 446.1663. **HPLC** (Chiralpak AS-H, *n*-hexane/ethanol = 90/10, flow rate = 1.0 mL/min, λ = 220 nm) t_R=12.65 min (major), 13.67 min (minor).

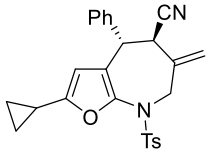


(4*S*,5*R*)-6-Methylene-4-phenyl-2-propyl-8-tosyl-5,6,7,8-tetrahydro-4*H*-furo[2,3-*b*]azepine-5-carbonitrile (*trans*-3h) (minor): Following the general procedure **A**, compound **3h** was obtained as a white solid in 42% yield (19.1 mg), 95% ee, purified by flash chromatography (petroleum ether/EtOAc = 10/1); R_f = 0.4 (petroleum ether/EtOAc = 4/1); mp = 154-156 °C; $[\alpha]_D^{25}$ = +60.2 (*c* = 0.20, CH_2Cl_2); **^{1}H NMR** (400 MHz, $CDCl_3$) δ 7.87 (d, *J* = 8.1 Hz, 2H), 7.41 – 7.28 (m, 7H), 5.58 (d, *J* = 2.0 Hz, 1H), 5.56 (s, 1H), 5.24 (d, *J* = 1.9 Hz, 1H), 4.66 (d, *J* = 15.3 Hz, 1H), 4.14 (d, *J* = 15.3 Hz, 1H), 3.95 (d, *J* = 11.0 Hz, 1H), 3.76 (d, *J* = 11.0 Hz, 1H), 2.48 (s, 3H), 2.44 (t, *J* = 7.6 Hz, 2H), 1.64 – 1.45 (m, 2H), 0.90 (t, *J* = 7.4 Hz, 3H). **^{13}C NMR** (100 MHz, $CDCl_3$) δ 154.3, 144.5, 139.9, 139.4, 138.5, 136.8, 130.0 (2C), 129.0 (2C), 128.6 (2C), 128.2, 127.9 (2C), 119.5, 117.5, 117.3, 107.6, 55.5, 49.5, 40.3, 30.2, 21.8, 20.9, 13.8. **HRMS** (EI-TOF) m/z: $[M]^+$ calcd for $[C_{26}H_{26}N_2O_3S]^+$: 446.1659; found: 446.1666. **HPLC** (Chiralpak AS-H, *n*-hexane/ethanol = 90/10, flow rate = 1.0 mL/min, λ = 220 nm)

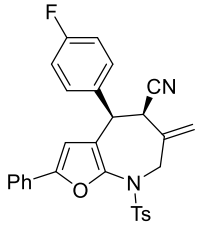
t_R=8.37 min (major), 11.10 min (minor).



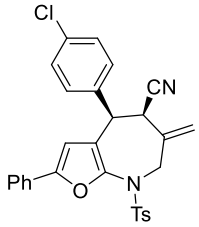
(4*R*,5*R*)-2-Cyclopropyl-6-methylene-4-phenyl-8-tosyl-5,6,7,8-tetrahydro-4*H*-furo[2,3-*b*]azepine-5-carbonitrile (*cis*-3i) (major): Following the general procedure **A**, compound **3i** was obtained as a white solid in 60% yield (27.4 mg), 93% ee, purified by flash chromatography (petroleum ether/EtOAc = 10/1); R_f = 0.45 (petroleum ether/EtOAc = 4/1); mp = 66-68 °C; $[\alpha]_D^{25}$ = +121.2 (*c* = 0.20, CH_2Cl_2); **^{1}H NMR** (400 MHz, $CDCl_3$) δ 7.69 (d, *J* = 8.0 Hz, 2H), 7.38 – 7.28 (m, 5H), 7.19 (m, 2H), 5.49 (s, 1H), 5.34 (s, 1H), 5.06 (s, 1H), 4.71 (d, *J* = 15.8 Hz, 1H), 4.12 (d, *J* = 15.8 Hz, 1H), 3.72 (d, *J* = 3.2 Hz, 1H), 3.54 (d, *J* = 3.2 Hz, 1H), 2.48 (s, 3H), 1.75 (tt, *J* = 8.4, 5.1 Hz, 1H), 0.87 – 0.77 (m, 2H), 0.73 – 0.62 (m, 2H). **^{13}C NMR** (100 MHz, $CDCl_3$) δ 154.6, 144.6, 140.5, 138.2, 137.6, 136.4, 129.7 (2C), 128.7 (2C), 128.7 (2C), 128.2, 128.1 (2C), 120.7, 118.3, 118.1, 106.3, 53.1, 44.3, 41.7, 21.8, 9.1, 7.1, 7.0. **HRMS** (EI-TOF) m/z: $[M]^+$ calcd for $[C_{26}H_{24}N_2O_3S]^+$: 444.1502; found: 444.1510. **HPLC** (Chiralpak AS-H, *n*-hexane/ethanol = 90/10, flow rate = 1.0 mL/min, λ = 220 nm) t_R= 16.09 min (major), 18.61 min (minor).



(4*S*,5*R*)-2-Cyclopropyl-6-methylene-4-phenyl-8-tosyl-5,6,7,8-tetrahydro-4*H*-furo[2,3-*b*]azepine-5-carbonitrile (*trans*-3i) (minor): Following the general procedure **A**, compound **3i** was obtained as a white solid in 39% yield (17.1 mg), 96% ee, purified by flash chromatography (petroleum ether/EtOAc = 10/1); R_f = 0.4 (petroleum ether/EtOAc = 4/1); mp = 136-138 °C; $[\alpha]_D^{25}$ = +76.5 (*c* = 0.20, CH_2Cl_2); **^{1}H NMR** (400 MHz, $CDCl_3$) δ 7.86 (d, *J* = 8.1 Hz, 2H), 7.42 – 7.28 (m, 7H), 5.57 (d, *J* = 2.0 Hz, 1H), 5.53 (s, 1H), 5.24 (d, *J* = 1.9 Hz, 1H), 4.67 (d, *J* = 15.3, 1H), 4.13 (d, *J* = 15.3 Hz, 1H), 3.95 (d, *J* = 11.0 Hz, 1H), 3.74 (d, *J* = 11.0 Hz, 1H), 2.48 (s, 3H), 1.71 (tt, *J* = 8.4, 5.1 Hz, 1H), 0.85 – 0.75 (m, 2H), 0.69 – 0.59 (m, 2H). **^{13}C NMR** (100 MHz, $CDCl_3$) δ 155.1, 144.6, 139.8, 138.8, 138.5, 136.8, 130.0 (2C), 129.1 (2C), 128.6 (2C), 128.2, 127.9 (2C), 119.5, 117.7, 117.3, 106.1, 55.5, 49.6, 40.2, 21.8, 9.0, 7.1, 6.8. **HRMS** (EI-TOF) m/z: $[M]^+$ calcd for $[C_{26}H_{24}N_2O_3S]^+$: 444.1502; found: 444.1503. **HPLC** (Chiralpak AS-H, *n*-hexane/ethanol = 90/10, flow rate = 1.0 mL/min, λ = 220 nm) t_R=10.90 min (major), 14.84 min (minor).

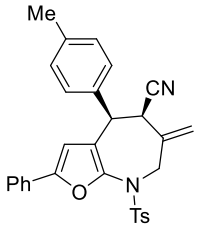


(4*R*,5*R*)-4-(4-Fluorophenyl)-6-methylene-2-phenyl-8-tosyl-5,6,7,8-tetrahydro-4*H*-furo[2,3-*b*]azepine-5-carbonitrile (3j): Following the general procedure **A**, compound **3j** was obtained as a white solid in 92% yield (46.3 mg), 12:1 dr and 98% ee, purified by flash chromatography (petroleum ether/EtOAc = 10/1); R_f = 0.4 (petroleum ether/EtOAc = 4/1); mp = 77-79 °C; $[\alpha]_D^{25}$ = +59.5 (*c* = 0.20, CH_2Cl_2); **^{1}H NMR** (400 MHz, $CDCl_3$) δ 7.81 (d, *J* = 8.3 Hz, 2H), 7.49 – 7.42 (m, 2H), 7.41 – 7.30 (m, 4H), 7.29 – 7.22 (m, 3H), 7.10 – 7.02 (m, 2H), 6.15 (s, 1H), 5.38 (brs, 1H), 5.10 (brs, 1H), 4.75 (d, *J* = 15.9 Hz, 1H), 4.24 (d, *J* = 15.9 Hz, 1H), 3.92 – 3.87 (m, 2H), 2.50 (s, 3H). **^{13}C NMR** (100 MHz, $CDCl_3$) δ 162.6 (d, C-F, $^1J_{C\text{-}F}$ = 247.4 Hz), 150.8, 144.8, 142.5, 136.83, 136.6, 133.6 (d, C-F, $^4J_{C\text{-}F}$ = 3.3 Hz), 130.7 (d, C-F, $^3J_{C\text{-}F}$ = 8.1 Hz, 2C), 129.9 (2C), 129.7, 128.8 (2C), 128.1 (4), 128.1(0) (2C), 123.8 (2C), 120.7, 118.6, 118.2, 115.71 (d, C-F, $^2J_{C\text{-}F}$ = 21.5 Hz, 2C), 107.1, 53.6, 43.8, 41.2, 21.8. **^{19}F NMR** (376 MHz, $CDCl_3$) δ -113.55 – -113.62 (m). **HRMS** (EI-TOF) m/z: $[M]^+$ calcd for $[C_{29}H_{23}FN_2O_3S]^+$: 498.1408; found: 498.1415. **HPLC** (Chiralpak AS-H, *n*-hexane/ethanol = 90/10, flow rate = 1.0 mL/min, λ = 220 nm) t_R= 12.41 min (*trans*-major), 14.11 min (*trans*- minor), 20.59 min (*cis*-minor), 23.21 min (*cis*-major).

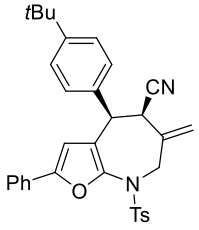


(4*R*,5*R*)-4-(4-Chlorophenyl)-6-methylene-2-phenyl-8-tosyl-5,6,7,8-tetrahydro-4*H*-furo[2,3-*b*]azepine-5-carbonitrile (3k): Following the general procedure **A**, compound **3k** was obtained as a white solid in 98% yield (49.8 mg), 11:1 dr and 97% ee, purified by flash chromatography (petroleum ether/EtOAc = 10/1); R_f = 0.5 (petroleum ether/EtOAc = 4/1); mp =94-96 °C; $[\alpha]_D^{25}$ = +66.7 (*c* = 0.20, CH_2Cl_2); **^{1}H NMR** (400 MHz, $CDCl_3$) δ 7.80 (d, *J* = 8.3 Hz, 2H), 7.47 – 7.42 (m, 2H), 7.35 (m, 6H), 7.29 – 7.16 (m, 3H), 6.14 (s, 1H), 5.38 (brs, 1H), 5.10 (brs, 1H), 4.74 (d, *J* = 15.9 Hz, 1H), 4.24 (d, *J* = 15.9 Hz, 1H), 4.02-3.78 (m, 2H), 2.49 (s, 3H). **^{13}C NMR** (100 MHz, $CDCl_3$) δ 150.8, 144.8, 142.6, 136.7, 136.6, 136.3, 134.3, 130.3 (2C), 129.9 (2C), 129.6, 128.9 (2C), 128.8 (2C), 128.2, 128.1 (2C), 123.8 (2C), 120.7, 118.3, 118.1,

107.1, 53.6, 43.9, 41.0, 21.8. **HRMS** (EI-TOF) m/z: $[M]^+$ calcd for $[C_{29}H_{23}ClN_2O_3S]^+$: 514.1112; found: 514.1121. **HPLC** (Chiralpak AS-H, *n*-hexane/ethanol = 90/10, flow rate = 1.0 mL/min, λ = 220 nm) t_R= 11.98 min (*trans*-major), 13.37 min (*trans*-minor), 19.78 min (*cis*-minor), 22.45 min (*cis*-major).

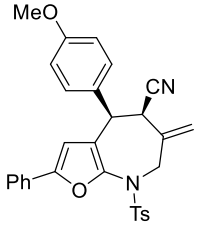


(4*R*,5*R*)-6-Methylene-2-phenyl-4-(*p*-tolyl)-8-tosyl-5,6,7,8-tetrahydro-4*H*-furo[2,3-*b*]azepine-5-carbonitrile (3l): Following the general procedure **A**, compound **3l** was obtained as a white solid in 94% yield (45.8 mg), 14:1 dr and 96% ee, purified by flash chromatography (petroleum ether/EtOAc = 10/1); R_f = 0.4 (petroleum ether/EtOAc = 4/1); mp = 90-92 °C; $[\alpha]_D^{25}$ = +107.5 (*c* = 0.20, CH_2Cl_2); **^{1}H NMR** (400 MHz, $CDCl_3$) δ 7.77 (d, *J* = 8.1 Hz, 2H), 7.51 – 7.44 (m, 2H), 7.40 – 7.29 (m, 4H), 7.28 – 7.21 (m, 1H), 7.20 – 7.11 (m, 4H), 6.17 (s, 1H), 5.38 (brs, 1H), 5.11 (brs, 1H), 4.78 (d, *J* = 15.8 Hz, 1H), 4.21 (d, *J* = 15.7 Hz, 1H), 3.79 (d, *J* = 3.3 Hz, 1H), 3.69 (d, *J* = 3.3 Hz, 1H), 2.49 (s, 3H), 2.36 (s, 3H). **^{13}C NMR** (100 MHz, $CDCl_3$) δ 150.6, 144.7, 142.5, 138.1, 137.3, 136.5, 135.0, 129.8 (2), 129.8 (2C), 129.5 (2C), 128.7 (2C), 128.7 (2C), 128.2 (2C), 128.0, 123.8 (2C), 120.7, 119.4, 118.3, 107.4, 53.3, 44.0, 41.7, 21.8, 21.2. **HRMS** (EI-TOF) m/z: $[M]^+$ calcd for $[C_{30}H_{26}N_2O_3S]^+$: 494.1659; found: 494.1666. **HPLC** (Chiralpak IA, *n*-hexane/ethanol = 90/10, flow rate = 1.0 mL/min, λ = 220 nm) t_R=13.47 min (*trans*-major), 15.74 min (*cis*-minor), 20.06 min (*cis*-major), 22.45 min (*trans*-minor).

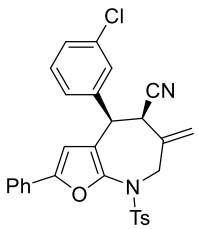


(4*R*,5*R*)-4-(4-(*tert*-Butyl)phenyl)-6-methylene-2-phenyl-8-tosyl-5,6,7,8-tetrahydro-4*H*-furo[2,3-*b*]azepine-5-carbonitrile (3m): Following the general procedure **A**, compound **3m** was obtained as a white solid in 95% yield (51.1 mg), 14:1 dr and 99% ee, purified by flash chromatography (petroleum ether/EtOAc = 10/1); R_f = 0.5 (petroleum ether/EtOAc = 4/1); m.p = 98-100 °C; $[\alpha]_D^{25}$ = +122.6 (*c* = 0.20, CH_2Cl_2); **^{1}H NMR** (400 MHz, $CDCl_3$) δ 7.75 (d, *J* = 8.1 Hz, 2H), 7.51 – 7.46 (m, 2H), 7.41 – 7.29 (m, 6H), 7.28 – 7.21 (m, 1H), 7.18 (d, *J* = 8.1 Hz, 2H), 6.20 (s, 1H), 5.41 (brs, 1H), 5.12 (brs, 1H), 4.78 (d, *J* = 15.7 Hz, 1H), 4.20 (d, *J* = 15.6 Hz,

1H), 3.74 (d, *J* = 3.0 Hz, 1H), 3.58 (d, *J* = 3.1 Hz, 1H), 2.50 (s, 3H), 1.33 (s, 9H). **^{13}C NMR** (100 MHz, $CDCl_3$) δ 151.3, 150.6, 144.7, 142.5, 137.6, 136.5, 135.0, 129.9, 129.8 (2C), 128.7 (2C), 128.3 (2C), 128.2 (2C), 128.0, 125.8 (2C), 123.9 (2C), 121.1, 119.7, 118.3, 107.5, 53.0, 43.9, 42.2, 34.7, 31.4 (3C), 21.8. **HRMS** (EI-TOF) m/z: $[M]^+$ calcd for $[C_{33}H_{32}N_2O_3S]^+$: 536.2128; found: 536.2131. **HPLC** (Chiralpak IB, *n*-hexane/ethanol = 90/10, flow rate = 1.0 mL/min, λ = 220 nm) t_R= 9.96 min (*trans*-minor), 10.87 min (*trans*-major), 11.61 min (*cis*-major), 12.28 min (*cis*-minor).

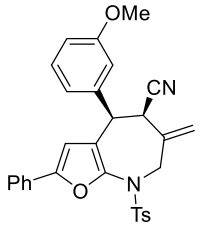


(4*R*,5*R*)-4-(4-Methoxyphenyl)-6-methylene-2-phenyl-8-tosyl-5,6,7,8-tetrahydro-4*H*-furo[2,3-*b*]azepine-5-carbonitrile (3n): Following the general procedure **A**, compound **3n** was obtained as a white solid in 98% yield (49.7 mg), 16:1 dr and 96% ee, purified by flash chromatography (petroleum ether/EtOAc = 10/1); R_f = 0.4 (petroleum ether/EtOAc = 4/1); mp = 100-102 °C; $[\alpha]_D^{25}$ = +107.3 (*c* = 0.20, CH_2Cl_2); **^{1}H NMR** (400 MHz, $CDCl_3$) δ 7.78 (d, *J* = 8.3 Hz, 2H), 7.50 – 7.43 (m, 2H), 7.40 – 7.29 (m, 4H), 7.28 – 7.21 (m, 1H), 7.21 – 7.15 (m, 2H), 6.92 – 6.86 (m, 2H), 6.18 (s, 1H), 5.37 (brs, 1H), 5.10 (brs, 1H), 4.76 (d, *J* = 15.9 Hz, 1H), 4.22 (d, *J* = 15.8 Hz, 1H), 3.81 (m, 4H), 3.74 (d, *J* = 3.3 Hz, 1H), 2.49 (s, 3H). **^{13}C NMR** (100 MHz, $CDCl_3$) δ 159.5, 150.6, 144.7, 142.4, 137.2, 136.5, 129.9 (2C), 129.8(1) (2C), 129.8(0), 128.7 (2C), 128.1 (2C), 128.0, 123.8 (2C), 120.7, 119.4, 118.4, 114.1 (2C), 107.4, 55.4, 53.4, 43.7, 41.7, 21.8. **HRMS** (EI-TOF) m/z: $[M]^+$ calcd for $[C_{30}H_{26}N_2O_4S]^+$: 510.1608; found: 510.1611. **HPLC** (Chiralpak IF, *n*-hexane/ethanol = 90/10, flow rate = 1.0 mL/min, λ = 220 nm) t_R=30.80 min (minor), 36.59 min (major).

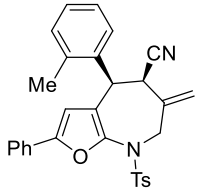


(4*R*,5*R*)-4-(3-Chlorophenyl)-6-methylene-2-phenyl-8-tosyl-5,6,7,8-tetrahydro-4*H*-furo[2,3-*b*]azepine-5-carbonitrile (3o): Following the general procedure **A**, compound **3o** was obtained as a white solid in 94% yield (49.3 mg), 12:1 dr and 95% ee; purified by flash chromatography (petroleum ether/EtOAc = 10/1), R_f = 0.4 (petroleum ether/EtOAc = 4/1); m.p

= 87-89 °C; $[\alpha]_D^{25}$ = +123.3 (*c* = 0.20, CH_2Cl_2); **^{1}H NMR** (400 MHz, $CDCl_3$) δ 7.78 (d, *J* = 8.2 Hz, 2H), 7.50 – 7.44 (m, 2H), 7.40 – 7.30 (m, 6H), 7.30 – 7.22 (m, 2H), 7.12 (d, *J* = 2.1 Hz, 1H), 6.14 (s, 1H), 5.42 (brs, 1H), 5.13 (brs, 1H), 4.78 (d, *J* = 15.8 Hz, 1H), 4.22 (d, *J* = 15.8 Hz, 1H), 3.86 (d, *J* = 3.3 Hz, 1H), 3.69 (d, *J* = 3.4 Hz, 1H), 2.51 (s, 3H). **^{13}C NMR** (100 MHz, $CDCl_3$) δ 150.9, 144.9, 142.6, 139.8, 136.9, 136.4, 134.6, 130.2, 129.9 (2C), 129.6, 129.1, 128.8 (2C), 128.6, 128.1 (9), 128.1 (7) (2C), 126.9, 123.9 (2C), 121.0, 118.5, 117.9, 107.0, 53.4, 44.0, 41.1, 21.8. **HRMS** (EI-TOF) m/z: $[M]^+$ calcd for $[C_{29}H_{23}ClN_2O_3S]^+$: 514.1112; found: 514.1115. **HPLC** (Chiralpak AS-H, *n*-hexane/ethanol = 90/10, flow rate = 1.0 mL/min, λ = 220 nm) t_R= 12.58 min (*trans*-major), 16.52 min (*trans*-minor), 19.34 min (*cis*-minor), 29.48 min (*cis*-major).

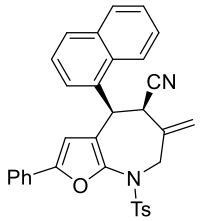


(4*R*,5*R*)-4-(3-methoxyphenyl)-6-methylene-2-phenyl-8-tosyl-5,6,7,8-tetrahydro-4*H*-furo[2,3-*b*]azepine-5-carbonitrile (3p): Following the general procedure **A**, compound **3p** was obtained as a white solid in 98% yield (50.2 mg), 17:1 dr and 97% ee, purified by flash chromatography (petroleum ether/EtOAc = 10/1); R_f = 0.5 (petroleum ether/EtOAc = 4/1); mp = 88-90 °C; $[\alpha]_D^{25}$ = +109.4 (*c* = 0.20, CH_2Cl_2); **^{1}H NMR** (400 MHz, $CDCl_3$) δ 7.77 (d, *J* = 8.3 Hz, 2H), 7.51 – 7.44 (m, 2H), 7.42 – 7.19 (m, 6H), 6.93 – 6.83 (m, 2H), 6.83 – 6.76 (m, 1H), 6.20 (s, 1H), 5.41 (brs, 1H), 5.16 (brs, 1H), 4.76 (d, *J* = 15.8 Hz, 1H), 4.22 (d, *J* = 15.3 Hz, 1H), 3.83 – 3.77 (m, 4H), 3.65 (d, *J* = 3.1 Hz, 1H), 2.49 (s, 3H). **^{13}C NMR** (100 MHz, $CDCl_3$) δ 159.8, 150.7, 144.7, 142.5, 139.5, 137.4, 136.5, 129.9, 129.8, 129.8 (2C), 128.74 (2C), 128.2 (2C), 128.0, 123.8 (2C), 121.0, 120.9, 119.2, 118.3, 114.6, 113.7, 107.4, 55.4, 53.2, 44.4, 41.8, 21.8; **HRMS** (EI-TOF) m/z: $[M]^+$ calcd for $[C_{30}H_{26}N_2O_4S]^+$: 510.1608; found: 510.1612. **HPLC** (Chiralpak AS-H, *n*-hexane/ethanol = 90/10, flow rate = 1.0 mL/min, λ = 220 nm) t_R= 13.80 min (*trans*-major), 15.85 min (*trans*-minor), 27.91 min (*cis*-minor), 33.18 min (*cis*-major).

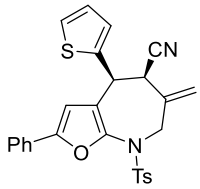


(4*R*,5*R*)-6-Methylene-2-phenyl-4-(o-tolyl)-8-tosyl-5,6,7,8-tetrahydro-4*H*-furo[2,3-

***b*]azepine-5-carbonitrile (3q)**: Following the general procedure **A**, compound **3q** was obtained as a white solid in 97% yield (48.1 mg), >20:1 dr and 96% ee, purified by flash chromatography (petroleum ether/EtOAc = 10/1); R_f = 0.4 (petroleum ether/EtOAc = 4/1); mp = 194-196 °C; $[\alpha]_D^{25}$ = +150.8 (*c* = 0.20, CH_2Cl_2); **^{1}H NMR** (400 MHz, $CDCl_3$) δ 7.78 (d, *J* = 8.3 Hz, 2H), 7.60 – 7.51 (m, 1H), 7.47 – 7.38 (m, 2H), 7.36 – 7.16 (m, 8H), 6.05 (s, 1H), 5.49 (brs, 1H), 5.23 (brs, 1H), 4.84 (d, *J* = 15.4 Hz, 1H), 4.19 (d, *J* = 15.4 Hz, 1H), 4.12 (d, *J* = 3.0 Hz, 1H), 3.79 (d, *J* = 3.0 Hz, 1H), 2.45 (s, 3H), 2.15 (s, 3H). **^{13}C NMR** (100 MHz, $CDCl_3$) δ 150.7, 144.6, 142.6, 138.6, 136.9, 136.7, 136.1, 131.1, 129.9, 129.8 (2C), 128.7 (2C), 128.1 (2) (2C), 128.0 (7), 128.0, 127.5, 126.6, 123.8 (2C), 121.5, 120.2, 118.2, 107.3, 52.2, 41.9, 39.9, 21.7, 19.9; **HRMS** (EI-TOF) m/z: $[M]^+$ calcd for $[C_{30}H_{26}N_2O_3S]^+$: 494.1659; found: 494.1667. **HPLC** (Chiralpak AS-H, *n*-hexane/ethanol = 90/10, flow rate = 1.0 mL/min, 220 nm) t_R= 11.20 min (*trans*-major), 15.34 min (*trans*-minor), 18.43 min (*cis*-minor), 22.58 min (*cis*-major).

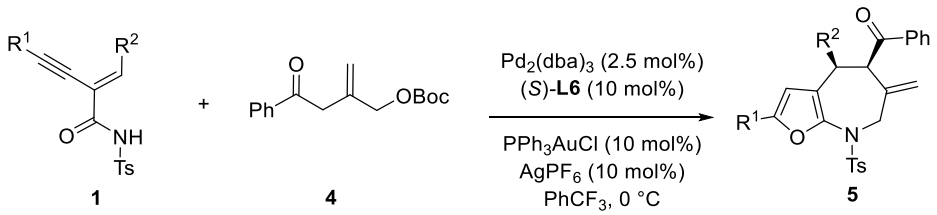


(4*R*,5*R*)-6-Methylene-4-(naphthalen-1-yl)-2-phenyl-8-tosyl-5,6,7,8-tetrahydro-4*H*-furo[2,3-*b*]azepine-5-carbonitrile (3r): Following the general procedure **A**, compound **3r** was obtained as a white solid in 98% yield (51.9 mg),13:1 dr and 97% ee, purified by flash chromatography (petroleum ether/EtOAc = 10/1); R_f = 0.5 (petroleum ether/EtOAc = 4/1); mp = 111-113 °C; $[\alpha]_D^{25}$ = +151.5 (*c* = 0.20, CH_2Cl_2); **^{1}H NMR** (400 MHz, $CDCl_3$) δ 7.95 – 7.77 (m, 5H), 7.59 – 7.49 (m, 3H), 7.49 – 7.42 (m, 1H), 7.40-7.34 (m, 4H), 7.31 – 7.23 (m, 2H), 7.22 – 7.17 (m, 1H), 5.93 (brs, 1H), 5.55 (brs, 1H), 5.28 (s, 1H), 4.90 (d, *J* = 15.3 Hz, 1H), 4.63 (d, *J* = 2.7 Hz, 1H), 4.25 (d, *J* = 15.2 Hz, 1H), 3.93 (d, *J* = 2.7 Hz, 1H), 2.45 (s, 3H); **^{13}C NMR** (100 MHz, $CDCl_3$) δ 150.8, 144.7, 142.5, 139.0, 137.0, 134.2, 134.1, 131.1, 129.9 (2C), 129.8, 129.3, 128.9, 128.7 (2C), 128.3 (2C), 128.0, 126.8, 126.2, 125.5, 125.1, 123.8 (2C), 122.8, 122.0, 120.9, 118.2, 107.5, 52.0, 42.4, 39.4, 21.9; **HRMS** (EI-TOF) m/z: $[M]^+$ calcd for $[C_{33}H_{26}N_2O_3S]^+$: 530.1659; found: 530.1660. **HPLC** (Chiralpak AS-H, *n*-hexane/ethanol = 90/10, flow rate = 1.0 mL/min, λ = 220 nm) t_R= 14.56 min (*trans*-major), 19.72 min (*trans*-minor), 30.50 min (*cis*-minor), 37.00 min (*cis*-major).

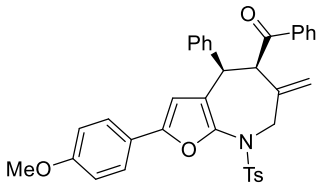


(4*S*,5*R*)-6-Methylene-2-phenyl-4-(thiophen-2-yl)-8-tosyl-5,6,7,8-tetrahydro-4*H*-furo[2,3-*b*]azepine-5-carbonitrile (3s): Following the general procedure **A**, compound **3s** was obtained as a white solid in 98% yield (48.2 mg), 13:1 dr and 97% ee, purified by flash chromatography (petroleum ether/EtOAc = 10/1); R_f = 0.5 (petroleum ether/EtOAc = 4/1); mp = 115-117 °C; $[\alpha]_D^{25}$ = +96.5 (*c* = 0.20, CH_2Cl_2); **^{1}H NMR** (400 MHz, $CDCl_3$) δ 7.74 (d, *J* = 8.2 Hz, 2H), 7.53 – 7.47 (m, 2H), 7.37 – 7.30 (m, 4H), 7.29 – 7.22 (m, 2H), 7.12 (d, *J* = 3.5 Hz, 1H), 7.07 – 6.99 (m, 1H), 6.30 (s, 1H), 5.43 (brs, 1H), 5.26 (brs, 1H), 4.77 (d, *J* = 15.9 Hz, 1H), 4.19 (d, *J* = 15.8 Hz, 1H), 3.90 (d, *J* = 2.9 Hz, 1H), 3.81 (d, *J* = 2.8 Hz, 1H), 2.49 (s, 3H). **^{13}C NMR** (100 MHz, $CDCl_3$) δ 150.8, 144.9, 142.3, 140.3, 137.0, 136.1, 129.9 (2C), 129.7, 128.8 (2C), 128.2 (2C), 128.1, 127.4, 126.6, 125.1, 123.9 (2C), 121.4, 119.3, 118.0, 107.2, 53.4, 42.5, 39.6, 21.8. **HRMS** (EI-TOF) m/z: $[M]^+$ calcd for $[C_{27}H_{22}N_2O_3S_2]^+$: 486.1066; found: 486.1069. **HPLC** (Chiralpak IC, *n*-hexane/ethanol = 90/10, flow rate = 1.0 mL/min, λ = 220 nm) t_R=22.93 min (*trans*-minor), 25.42 min (*cis*-major), 28.75 min (*trans*-major), 33.11 min (*cis*-minor).

5. Preparation and characterization data of benzoyl-substituted furo[2,3-*b*]azepines 5

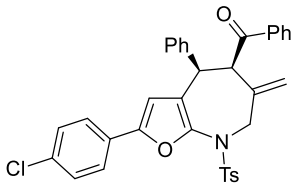


General procedure B: Under a nitrogen atmosphere, two flame dried 10 mL Schlenk tube A and B, the tube A was charged with Ph_3PAuCl (4.9 mg, 0.01 mmol, 10 mol%) and $AgPF_6$ (2.5 mg, 0.01 mmol, 10 mol%), the tube B was charged with ligand (*S*)-**L6** (5.7 mg, 0.01 mmol, 10 mol%), and $Pd_2(dba)_3$ (2.3 mg, 0.0025 mmol, 2.5 mol%). After the tube A and B were evacuated and backfilled with nitrogen, freshly distilled $PhCF_3$ (1.0 mL) was added respectively, then stirred at room temperature for 15-20 minutes while the solution of A tube turned white turbid and the solution of B tube turned light green. Then, enynamides **1** (0.1 mmol, 1.0 equiv) were added to tube A, and the reaction mixture immediately turned golden yellow. After 5 minutes, TMM donor **4** (33.2 mg, 0.12 mmol, 1.2 equiv) was added to tube A sequentially. The solution of tube B was then transferred to tube A at 0 °C. The reaction mixture was stirred at 0 °C for the indicated time, which was evaporated under reduced pressure at 30 °C. The crude residue was purified by flash chromatography (petroleum ether/EtOAc = 10/1) to give the desired products **5**.

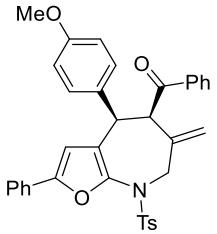


(4*R*,5*R*)-2-(4-Methoxyphenyl)-6-methylene-4-phenyl-8-tosyl-5,6,7,8-tetrahydro-4*H*-furo[2,3-*b*]azepin-5-yl)(phenyl)methanone (5a): Following the general procedure **B**, compound **5a** was obtained as a white solid in 93% yield (55.1 mg), 12:1 dr and 94% ee, purified by flash chromatography (petroleum ether/EtOAc = 10/1); R_f = 0.6 (petroleum ether/EtOAc = 4/1); m.p = 109-111 °C; $[\alpha]_D^{25}$ = +45.2 (*c* = 0.20, CH_2Cl_2); **^{1}H NMR** (400 MHz, $CDCl_3$) δ 7.81 (d, *J* = 8.0 Hz, 2H), 7.79 – 7.72 (m, 2H), 7.51 – 7.45 (m, 1H), 7.42 (d, *J* = 8.8 Hz, 2H), 7.38 – 7.32 (m, 4H), 7.23 – 7.18 (m, 3H), 7.07 – 7.01 (m, 2H), 6.84 (d, *J* = 8.8 Hz, 2H), 6.03 (s, 1H), 5.36 (brs, 1H), 5.03 (brs, 1H), 4.85 – 4.77 (m, 2H), 4.15 (d, *J* = 15.4 Hz, 1H), 3.81 (s, 3H), 3.79 – 3.76 (m, 1H), 2.50 (s, 3H). **^{13}C NMR** (100 MHz, $CDCl_3$) δ 198.5, 159.2, 150.1, 144.2, 140.8, 140.3, 140.2, 137.3, 137.1, 133.1, 129.6 (2C), 129.6 (2C), 128.6 (2C), 128.6 (2C), 128.4 (2C), 128.2 (2C), 127.3, 125.2 (2C), 123.5, 121.5, 121.3, 114.1 (2C), 106.4,

55.4, 53.9, 53.7, 44.8, 21.8. **HRMS** (EI-TOF) m/z: $[M]^+$ calcd for $[C_{36}H_{31}NO_5S]^+$: 589.1917; found: 589.1914. **HPLC** (Chiralpak IF, *n*-hexane/ethanol = 95/5, flow rate = 1.0 mL/min, λ = 220 nm) t_R= 20.90 min (*trans*-major), 27.87 min (*trans*-minor), 48.91 min (*cis*-major), 58.63 min (*cis*-minor).

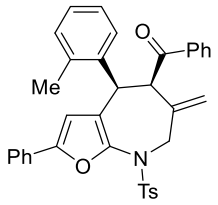


(4*R*,5*R*)-2-(4-Chlorophenyl)-6-methylene-4-phenyl-8-tosyl-5,6,7,8-tetrahydro-4*H*-furo[2,3-*b*]azepin-5-yl)(phenyl)methanone (5b): Following the general procedure **B**, compound **5b** was obtained as white solid in 80% yield (44.2 mg), 13:1 dr and 94% ee, purified by flash chromatography (petroleum ether/EtOAc = 10/1); R_f = 0.5 (petroleum ether/EtOAc = 4/1); m.p = 181-183 °C; $[\alpha]_D^{25}$ = +35.4 (*c* = 0.20, CH_2Cl_2); **^{1}H NMR** (400 MHz, $CDCl_3$) δ 7.80 (d, *J* = 8.3 Hz, 2H), 7.76 – 7.70 (m, 2H), 7.52 – 7.45 (m, 1H), 7.43 – 7.31 (m, 6H), 7.30 – 7.24 (m, 2H), 7.24 – 7.19 (m, 3H), 7.08 – 7.01 (m, 2H), 6.16 (s, 1H), 5.39 (brs, 1H), 5.08 (brs, 1H), 4.88 – 4.73 (m, 2H), 4.13 (d, *J* = 15.3 Hz, 1H), 3.75 (d, *J* = 3.3 Hz, 1H), 2.51 (s, 3H). **^{13}C NMR** (100 MHz, $CDCl_3$) δ 198.5, 148.9, 144.3, 141.8, 140.4, 140.1, 137.2, 137.0, 133.2 (2C), 129.6 (2C), 129.5 (2C), 128.9, 128.8 (5) (2C), 128.7 (2C), 128.6 (2C), 128.4 (2C), 128.4 (2C), 127.5, 125.0 (2C), 121.9, 121.8, 108.4, 54.2, 53.3, 44.8, 21.8. **HRMS** (EI-TOF) m/z: $[M]^+$ calcd for $[C_{35}H_{28}ClNO_4S]^+$: 593.1422; found: 593.1426. **HPLC** (Chiralpak IC, *n*-hexane/ethanol = 95/5, flow rate = 1.0 mL/min, λ = 254 nm) t_R=7.44 min (*trans*-minor), 8.52 min (*trans*-major), 20.07 min (*cis*-major), 52.55 min (*cis*-minor).

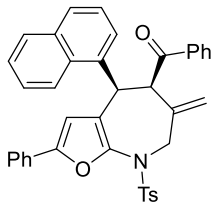


(4*R*,5*R*)-4-(4-Methoxyphenyl)-6-methylene-2-phenyl-8-tosyl-5,6,7,8-tetrahydro-4*H*-furo[2,3-*b*]azepin-5-yl)(phenyl)methanone (5c): Following the general procedure **B**, compound **5c** was obtained as a white solid in 96% yield (57.5 mg), 10:1 dr and 91% ee, purified by flash chromatography (petroleum ether/EtOAc = 10/1); R_f = 0.6 (petroleum ether/EtOAc = 4/1); m.p = 104-106 °C; $[\alpha]_D^{25}$ = -13.5 (*c* = 0.20, CH_2Cl_2); **^{1}H NMR** (400 MHz, $CDCl_3$) δ 7.85 – 7.80 (m, 2H), 7.80 – 7.74 (m, 2H), 7.53 – 7.44 (m, 3H), 7.40 – 7.33 (m, 4H), 7.33 – 7.27 (m, 2H), 7.24 – 7.18 (m, 1H), 6.97 (d, *J* = 8.7 Hz, 2H), 6.74 (d, *J* = 8.7 Hz, 2H), 6.17 (s, 1H), 5.35

(brs, 1H), 5.01 (brs, 1H), 4.87 – 4.75 (m, 2H), 4.15 (d, *J* = 15.4 Hz, 1H), 3.84 (d, *J* = 3.3 Hz, 1H), 3.75 (s, 3H), 2.50 (s, 3H). **^{13}C NMR** (100 MHz, $CDCl_3$) δ 198.6, 158.7, 149.9, 144.2, 141.4, 140.1, 137.30 137.1, 133.1, 132.2, 130.7 (2C), 130.4, 129.6 (2C), 128.7 (2C), 128.6 (2C), 128.6 (2C), 128.3 (2C), 127.5, 123.7 (2C), 121.8, 121.2, 113.5 (2C), 108.0, 55.3, 54.0, 53.9, 43.9, 21.8. **HRMS** (EI-TOF) m/z: $[M]^+$ calcd for $[C_{36}H_{31}NO_5S]^+$: 589.1917; found: 589.1921. **HPLC** (Chiralpak IC, *n*-hexane/ethanol = 95/5, flow rate = 1.0 mL/min, λ = 220 nm) t_R=9.54 min (*trans*-minor), 10.30 min (*trans*-major), 35.63 min (*cis*-major), 64.88 min (*cis*-minor).



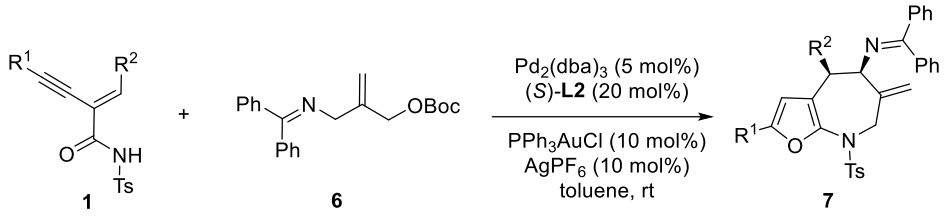
(4*R*,5*R*)-6-Methylene-2-phenyl-4-(*o*-tolyl)-8-tosyl-5,6,7,8-tetrahydro-4*H*-furo[2,3-*b*]azepin-5-yl)(phenyl)methanone (5d): Following the general procedure **B**, compound **5d** was obtained as white solid in 93% yield (53.1 mg), 8:1 dr and 84% ee, purified by flash chromatography (petroleum ether/EtOAc = 10/1); R_f = 0.5 (petroleum ether/EtOAc = 4/1); m.p = 134-136 °C; $[\alpha]_D^{25}$ = +35.5 (*c* = 0.20, CH_2Cl_2); **^{1}H NMR** (400 MHz, $CDCl_3$) δ 7.79 (d, *J* = 8.3 Hz, 2H), 7.73 – 7.66 (m, 2H), 7.52 – 7.44 (m, 3H), 7.36 – 7.26 (m, 6H), 7.24 – 7.15 (m, 2H), 7.14 – 7.03 (m, 2H), 6.99 – 6.93 (m, 1H), 6.13 (s, 1H), 5.47 (brs, 1H), 5.24 (brs, 1H), 4.77 (d, *J* = 15.1 Hz, 1H), 4.72 (d, *J* = 3.4 Hz, 1H), 4.19 – 3.99 (m, 2H), 2.44 (s, 3H), 2.12 (s, 3H). **^{13}C NMR** (100 MHz, $CDCl_3$) δ 198.4, 149.8, 144.2, 141.6, 141.5, 138.6, 137.4, 137.3 (7), 136.1, 133.1, 130.8, 130.5, 129.6 (2C), 128.8, 128.6 (2C), 128.6 (2C), 128.4 (2C), 128.3 (2C), 127.4, 127.1, 126.1, 123.7 (2C), 122.0, 121.7, 108.0, 54.1, 52.1, 40.2, 21.7, 20.1. **HRMS** (EI-TOF) m/z: $[M]^+$ calcd for $[C_{36}H_{31}NO_4S]^+$: 573.1974; found: 573.1978. **HPLC** (Chiralpak IC, *n*-hexane/ethanol = 95/5, flow rate = 1.0 mL/min, λ = 254 nm) t_R= 7.07 min (*trans*-minor), 7.67 min (*trans*-major), 24.46 min (*cis*-major), 34.59 min (*cis*-minor).



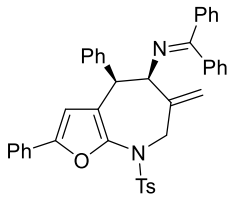
(4*R*,5*R*)-6-Methylene-4-(naphthalen-1-yl)-2-phenyl-8-tosyl-5,6,7,8-tetrahydro-4*H*-furo[2,3-*b*]azepin-5-yl)(phenyl)methanone (5e): Following the general procedure **B**, compound **5e** was obtained as white solid in 97% yield (60.9 mg), 9:1 dr and 89% ee, purified by flash chromatography (petroleum ether/EtOAc = 10/1); R_f = 0.5 (petroleum ether/EtOAc =

4/1); m.p = 144-146 °C; $[\alpha]_D^{25}$ = +87.5 (*c* = 0.20, CH_2Cl_2); **^{1}H NMR** (400 MHz, Chloroform-*d*) δ 7.89 – 7.82 (m, 3H), 7.75 – 7.69 (m, 1H), 7.67 – 7.62 (m, 2H), 7.53 – 7.41 (m, 6H), 7.38 – 7.21 (m, 8H), 7.20 – 7.14 (m, 1H), 6.07 (s, 1H), 5.56 (brs, 1H), 5.34 (brs, 1H), 4.85 (d, *J* = 3.2 Hz, 1H), 4.81 (d, *J* = 15.0 Hz, 1H), 4.68 (d, *J* = 3.2 Hz, 1H), 4.11 (d, *J* = 14.9 Hz, 1H), 2.46 (s, 3H). **^{13}C NMR** (100 MHz, $CDCl_3$) δ 198.3, 149.8, 144.3, 141.8, 141.4, 137.4, 137.2, 136.0, 134.1, 133.2, 131.5, 130.5, 129.7 (2C), 129.2, 128.7 (2C), 128.5 (2C), 128.5 (2C), 128.4 (2C), 128.0, 127.4, 126.6, 126.5, 125.8, 125.2, 123.8 (2C), 123.1, 122.6, 122.3, 108.4, 54.6, 52.0, 39.5, 21.9. **HRMS** (EI-TOF) m/z: $[M]^+$ calcd for $[C_{39}H_{31}NO_4S]^+$: 609.1968; found: 609.1976. **HPLC** (Chiralpak IC, *n*-hexane/ethanol = 95/5, flow rate = 1.0 mL/min, λ = 254 nm) t_R= 9.02 min (*trans*-minor), 9.66 min (*trans*-major), 30.31 min (*cis*-major), 46.24 min (*cis*-minor).

6. Preparation and characterization data of amino-substituted furo[2,3-*b*]azepines 7

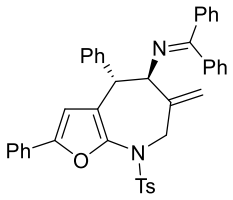


General procedure C: Under a nitrogen atmosphere, two flame dried 10 mL Schlenk tube A and B, the tube A was charged with Ph_3PAuCl (4.9 mg, 0.01 mmol, 10 mol%) and $AgPF_6$ (2.5 mg, 0.01 mmol, 10 mol%), the tube B was charged with ligand (*S*)-**L2** (10.2 mg, 0.02 mmol, 20 mol%), and $Pd_2(dba)_3$ (4.6 mg, 0.005 mmol, 5 mol%). After the tube A and B were evacuated and backfilled with nitrogen, freshly distilled toluene (1.0 mL) was added respectively, then stirred at room temperature for 15-20 minutes while the solution of tube A turned turbid and the solution of tube B turned light green. Then, enynamides **1** (0.1 mmol, 1.0 equiv) were added to tube A, and the reaction mixture immediately turned golden yellow. After 5 minutes, TMM donor **6** (42.2 mg, 0.12 mmol, 1.2 equiv) was added to tube A sequentially. The solution of tube B was then transferred to tube A at room temperature. The reaction mixture was stirred at room temperature for the indicated time, which was evaporated under reduced pressure at 30 °C. The crude residue was purified by flash chromatography (petroleum ether/EtOAc = 10/1) to give the desired products **7**.

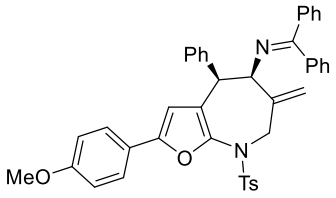


(4*R*,5*R*)-5-((Diphenyl-azaneylidene)methyl)-6-methylene-2,4-diphenyl-8-tosyl-5,6,7,8-tetrahydro-4*H*-furo[2,3-*b*]azepine (*cis*-7a) (major): Following the general procedure **C**, compound *cis*-**7a** was obtained as white solid in 60% yield (38.2 mg), and 95% ee, purified by flash chromatography (petroleum ether/EtOAc = 10/1); R_f = 0.4 (petroleum ether/EtOAc = 4/1); m.p = 104-106 °C; $[\alpha]_D^{25}$ = +131.2 (*c* = 0.20, CH_2Cl_2); **^{1}H NMR** (400 MHz, $CDCl_3$) δ 7.63 (d, *J* = 8.1 Hz, 2H), 7.60 – 7.55 (m, 2H), 7.49 – 7.43 (m, 2H), 7.38 – 7.30 (m, 4H), 7.28 – 7.20 (m, 9H), 7.19 – 7.12 (m, 2H), 7.04 – 6.87 (m, 2H), 6.43 – 6.30 (m, 2H), 6.24 (s, 1H), 5.15 (brs, 1H), 4.63 (brs, 1H), 4.60 (d, *J* = 14.5 Hz, 1H), 4.42 (d, *J* = 14.4 Hz, 1H), 3.92 (d, *J* = 2.3 Hz, 1H), 3.03 (d, *J* = 2.3 Hz, 1H), 2.45 (s, 3H). **^{13}C NMR** (100 MHz, $CDCl_3$) δ 168.4, 149.3, 145.4, 143.9, 142.4, 140.8, 139.3, 136.8, 136.1, 130.6, 130.3, 129.9 (2C), 129.3 (2C), 128.7 (2C), 128.6 (7) (2C), 128.5 (2C), 128.3 (2C), 128.2 (2C), 128.0 (4), 128.0 (2C), 127.4, 127.3 (2C),

127.1, 123.7 (2C), 120.9, 117.8, 108.9, 70.4, 51.0, 48.4, 21.7. **HRMS** (EI-TOF) m/z: $[M]^+$ calcd for $[C_{41}H_{34}N_2O_3S]^+$: 634.2285; found: 634.2291. **HPLC** (Chiralpak IA, *n*-hexane/ethanol = 95/5, flow rate = 1.0 mL/min, λ = 220 nm) t_R=8.19 min (minor), 9.88 min (major).

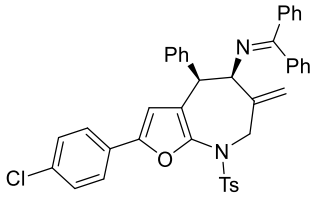


(4*S*,5*R*)-5-((Diphenyl-azaneylidene)methyl)-6-methylene-2,4-diphenyl-8-tosyl-5,6,7,8-tetrahydro-4*H*-furo[2,3-*b*]azepine (*trans*-7a) (minor): Following the general procedure **C**, compound **7a** was obtained as white solid in 15% yield (10.1 mg), and 91% ee, purified by flash chromatography (petroleum ether/EtOAc = 10/1); R_f = 0.5 (petroleum ether/EtOAc = 4/1); m.p = 202-204 °C; $[\alpha]_D^{25}$ = +40.3 (*c* = 0.20, CH_2Cl_2); **^{1}H NMR** (400 MHz, $CDCl_3$) δ 7.71 (d, *J* = 8.1 Hz, 2H), 7.51 – 7.46 (m, 2H), 7.44 – 7.38 (m, 3H), 7.38 – 7.32 (m, 3H), 7.32 – 7.27 (m, 5H), 7.27 – 7.26 (m, 1H), 7.22 – 7.16 (m, 1H), 7.15 – 7.11 (m, 3H), 6.97 – 6.78 (m, 2H), 6.53 (d, *J* = 7.3 Hz, 2H), 6.17 (s, 1H), 5.50 (brs, 1H), 5.12 (brs, 1H), 4.61 (d, *J* = 13.8 Hz, 1H), 4.34 (d, *J* = 9.2 Hz, 1H), 4.28 (d, *J* = 13.9 Hz, 1H), 3.97 (d, *J* = 9.2 Hz, 1H), 2.49 (s, 3H). **^{13}C NMR** (100 MHz, $CDCl_3$) δ 167.4, 150.1, 145.5, 143.9, 141.7, 141.2, 139.9, 137.3, 136.6, 130.3, 130.0, 129.7 (2C), 129.3 (2C), 128.7 (2C), 128.7 (2C), 128.5, 128.4 (2C), 128.2 (2C), 128.0 (2C), 128.0 (2C), 127.5, 127.4 (7) (2C), 126.7, 123.5 (2C), 119.8, 115.8, 107.9, 67.1, 56.0, 51.9, 21.8. **HRMS** (EI-TOF) m/z: $[M]^+$ calcd for $[C_{41}H_{34}N_2O_3S]^+$: 634.2285; found: 634.2291. **HPLC** (Chiralpak IA, *n*-hexane/ethanol = 95/5, flow rate = 1.0 mL/min, λ = 220 nm) t_R=9.13 min (major), 16.52 min (minor).

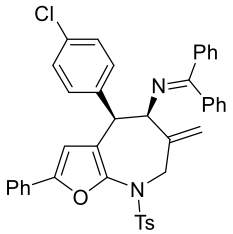


(4*R*,5*R*)-5-((Diphenyl-azaneylidene)methyl)-2-(4-methoxyphenyl)-6-methylene-4-phenyl-8-tosyl-5,6,7,8-tetrahydro-4*H*-furo[2,3-*b*]azepine (7b): Following the general procedure **C**, compound **7b** was obtained as white solid in 82% yield (44.3 mg), 4:1 dr and 95%/90% ee, purified by flash chromatography (petroleum ether/EtOAc = 10/1); R_f = 0.5 (petroleum ether/EtOAc = 4/1); m.p = 106-108 °C; $[\alpha]_D^{25}$ = +157.3 (*c* = 0.20, CH_2Cl_2); **^{1}H NMR** (400 MHz, $CDCl_3$) δ 7.62 (d, *J* = 8.0 Hz, 2H), 7.52 (d, *J* = 8.8 Hz, 2H), 7.50 – 7.42 (m, 2H), 7.35 – 7.29 (m, 1H), 7.27 – 7.20 (m, 8H), 7.20 – 7.11 (m, 2H), 7.04 – 6.94 (m, 2H), 6.88 (d, *J* = 8.8 Hz, 2H), 6.46 – 6.28 (m, 2H), 6.10 (s, 1H), 5.14 (brs, 1H), 4.65 – 4.54 (m, 2H), 4.41 (d, *J* = 14.4

Hz, 1H), 3.91 (d, *J* = 2.2 Hz, 1H), 3.83 (s, 3H), 2.99 (d, *J* = 2.2 Hz, 1H), 2.45 (s, 3H). **^{13}C NMR** (101 MHz, $CDCl_3$) δ 168.4, 159.2, 149.4, 145.4, 143.8, 141.7, 140.9, 139.4, 136.7, 136.1, 130.2, 129.9 (2C), 129.2 (2C), 128.7 (2C), 128.6 (2C), 128.2 (2C), 128.1 (2C), 128.0, 127.9 (2C), 127.3 (2C), 127.0, 125.2 (2C), 123.7, 120.8, 117.7, 114.2 (2C), 107.4, 70.4, 55.5, 51.1, 48.4, 21.7. **HRMS** (EI-TOF) m/z: $[M]^+$ calcd for $[C_{42}H_{36}N_2O_4S]^+$: 664.2390; found: 664.2380. **HPLC** (Chiralpak IA, *n*-hexane/ethanol = 95/5, flow rate = 1.0 mL/min, λ = 220 nm) t_R= 12.25 min (*cis*-minor), 13.25 (*trans*-major), 15.40 min (*cis*-major), 29.58 (*trans*-minor).

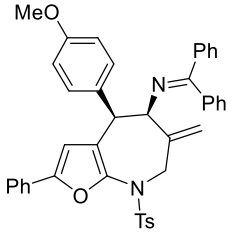


(4*R*,5*R*)-2-(4-Chlorophenyl)-5-((diphenyl-azaneylidene)methyl)-6-methylene-4-phenyl-8-tosyl-5,6,7,8-tetrahydro-4*H*-furo[2,3-*b*]azepine (7c): Following the general procedure **C**, compound **7c** was obtained as white solid in 81% yield (40.8 mg), 3:1 dr and 91%/86% ee, purified by flash chromatography (petroleum ether/EtOAc = 10/1); R_f = 0.5 (petroleum ether/EtOAc = 4/1); m.p = 111-113 °C; $[\alpha]_D^{25}$ = +156.2 (*c* = 0.20, CH_2Cl_2); **^{1}H NMR** (400 MHz, $CDCl_3$) δ 7.62 (d, *J* = 8.0 Hz, 2H), 7.54 – 7.43 (m, 4H), 7.35 – 7.27 (m, 3H), 7.28 – 7.21 (m, 8H), 7.19 – 7.12 (m, 2H), 7.01 – 6.92 (m, 2H), 6.36 (s, 2H), 6.23 (s, 1H), 5.15 (brs, 1H), 4.62 (brs, 1H), 4.59 (d, *J* = 14.6 Hz, 1H), 4.42 (d, *J* = 14.4 Hz, 1H), 3.91 (d, *J* = 2.3 Hz, 1H), 3.02 (d, *J* = 2.3 Hz, 1H), 2.46 (s, 3H). **^{13}C NMR** (100 MHz, $CDCl_3$) δ 168.6, 148.3, 145.3, 144.0, 142.7, 140.7, 139.3, 136.8, 136.0, 133.1, 130.3, 129.8 (2C), 129.3 (2C), 129.1, 128.9 (2C), 128.7 (2C), 128.5 (2C), 128.3 (2C), 128.2 (2C), 128.1, 128.0 (2C), 127.3 (2C), 127.1, 125.0 (2C), 121.0, 117.9, 109.4, 70.3, 51.0, 48.4, 21.8. **HRMS** (EI-TOF) m/z: $[M]^+$ calcd for $[C_{41}H_{33}ClN_2O_3S]^+$: 668.1895; found: 668.1895. **HPLC** (Chiralpak IC, *n*-hexane/ethanol = 95/5, flow rate = 1.0 mL/min, λ = 220 nm) t_R= 7.80 min (*trans*-major), 8.613 min (*trans*-minor), 15.62 min (*cis*-major), 17.77 min (*cis*-minor).

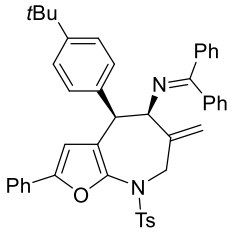


(4*R*,5*R*)-4-(4-Chlorophenyl)-5-((diphenyl-azaneylidene)methyl)-6-methylene-2-phenyl-8-tosyl-5,6,7,8-tetrahydro-4*H*-furo[2,3-*b*]azepine (7d): Following the general procedure **C**, compound **7d** was obtained as white solid in 79% yield (45.1 mg), 5:1 dr and 93%/93% ee,

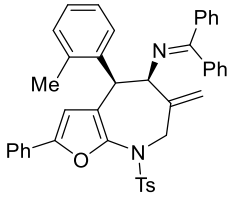
purified by flash chromatography (petroleum ether/EtOAc = 10/1); R_f = 0.5 (petroleum ether/EtOAc = 4/1); m.p = 81-83°C; $[\alpha]_D^{25}$ = +107.2 (*c* = 0.20, CH_2Cl_2); **^{1}H NMR** (400 MHz, $CDCl_3$) δ 7.66 (d, *J* = 8.3 Hz, 2H), 7.57 – 7.51 (m, 2H), 7.51 – 7.43 (m, 2H), 7.39 – 7.31 (m, 3H), 7.30 – 7.17 (m, 10H), 6.96 (d, *J* = 8.4 Hz, 2H), 6.48 (d, *J* = 7.0 Hz, 2H), 6.17 (s, 1H), 5.17 (d, *J* = 1.3 Hz, 1H), 4.66 (d, *J* = 1.4 Hz, 1H), 4.55 (d, *J* = 14.4 Hz, 1H), 4.40 (d, *J* = 14.1 Hz, 1H), 3.99 (d, *J* = 2.5 Hz, 1H), 3.17 (d, *J* = 2.5 Hz, 1H), 2.45 (s, 3H). **^{13}C NMR** (100 MHz, $CDCl_3$) δ 168.8, 149.5, 145.2, 143.9, 142.5, 139.3, 139.2, 137.0, 135.9, 132.9, 131.2 (2C), 130.4, 130.3 (9), 129.3 (2C), 128.7 (4) (2C), 128.7 (2C), 128.5 (2C), 128.3 (1) (2C), 128.3, 128.2 (2C), 128.1 (2C), 127.6, 127.3 (2C), 123.7 (2C), 120.1, 117.9, 108.6, 69.9, 51.2, 47.9, 21.7. **HRMS** (EI-TOF) m/z: $[M]^+$ calcd for $[C_{41}H_{33}ClN_2O_3S]^+$: 668.1895; found: 668.1898. **HPLC** (Chiralpak IA, *n*-hexane/ethanol = 95/5, flow rate = 1.0 mL/min, λ = 220 nm) t_R= 7.98 min (*cis*-minor), 9.30 min (*trans*-major), 10.54 min (*cis*-major), 12.95 min (*trans*-minor).



(4*R*,5*R*)-5-((Diphenyl-azaneylidene)methyl)-4-(4-methoxyphenyl)-6-methylene-2-phenyl-8-tosyl-5,6,7,8-tetrahydro-4*H*-furo[2,3-*b*]azepine (7e): Following the general procedure **D**, compound **7k** was obtained as white solid in 82% yield (47.1 mg), 6:1 dr and 97%/82% ee, purified by flash chromatography (petroleum ether/EtOAc = 10/1); R_f = 0.5 (petroleum ether/EtOAc = 4/1); m.p = 109-111 °C; $[\alpha]_D^{25}$ = +145.6 (*c* = 0.20, CH_2Cl_2); **^{1}H NMR** (400 MHz, $CDCl_3$) δ 7.64 (d, *J* = 8.3 Hz, 2H), 7.60 – 7.53 (m, 2H), 7.51 – 7.42 (m, 2H), 7.39 – 7.29 (m, 3H), 7.28 – 7.11 (m, 8H), 6.90 (d, *J* = 8.7 Hz, 2H), 6.78 (d, *J* = 8.7 Hz, 2H), 6.46 (s, 2H), 6.22 (s, 1H), 5.14 (d, *J* = 1.4 Hz, 1H), 4.61 (d, *J* = 1.5 Hz, 1H), 4.57 (d, *J* = 14.4 Hz, 1H), 4.40 (d, *J* = 14.3 Hz, 1H), 3.94 (d, *J* = 2.4 Hz, 1H), 3.80 (s, 3H), 3.03 (d, *J* = 2.3 Hz, 1H), 2.45 (s, 3H). **^{13}C NMR** (100 MHz, $CDCl_3$) δ 168.4, 158.6, 149.3, 145.4, 143.8, 142.2, 139.4, 136.8, 136.1, 133.0, 130.8 (2C), 130.6, 130.3, 129.3 (2C), 128.7 (2C), 128.6 (6) (2C), 128.5 (2C), 128.2 (2C), 128.1, 128.0 (2C), 127.4, 127.3 (6) (2C), 123.7 (2C), 121.3, 117.7, 113.6 (2C), 109.0, 70.5, 55.5, 51.1, 47.5, 21.7. **HRMS** (EI-TOF) m/z: $[M]^+$ calcd for $[C_{42}H_{36}N_2O_4S]^+$: 664.2390; found: 664.2393. **HPLC** (Chiralpak IA, *n*-hexane/ethanol = 95/5, flow rate = 1.0 mL/min, λ = 220 nm) t_R= 9.69 min (*cis*-minor), 11.21 min (*trans*-major), 13.21 min (*cis*-major) 25.98 min (*trans*-minor).

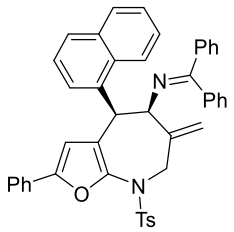


(4*R*,5*R*)-4-(4-(*tert*-Butyl)phenyl)-5-((diphenyl-azaneylidene)methyl)-6-methylene-2-phenyl-8-tosyl-5,6,7,8-tetrahydro-4*H*-furo[2,3-*b*]azepine (7f): Following the general procedure **C**, compound **7f** was obtained as white solid in 71% yield (37.1 mg), 3:1 dr and 89%/87% ee, purified by flash chromatography (petroleum ether/EtOAc = 10/1); R_f = 0.5 (petroleum ether/EtOAc = 4/1); m.p = 136-138 °C; $[\alpha]_D^{25}$ = +164.3 (*c* = 0.20, CH_2Cl_2); **^{1}H NMR** (400 MHz, $CDCl_3$) δ 7.69 – 7.54 (m, 4H), 7.49 – 7.41 (m, 2H), 7.40 – 7.29 (m, 3H), 7.29 – 7.18 (m, 8H), 7.17 – 7.05 (m, 2H), 6.86 (d, *J* = 8.1 Hz, 2H), 6.46 – 6.16 (m, 3H), 5.16 (brs, 1H), 4.83 – 4.54 (m, 2H), 4.43 (d, *J* = 14.3 Hz, 1H), 3.80 (d, *J* = 2.2 Hz, 1H), 2.88 (d, *J* = 2.2 Hz, 1H), 2.45 (s, 3H), 1.33 (s, 9H). **^{13}C NMR** (100 MHz, $CDCl_3$) δ 168.2, 150.1, 149.3, 145.6, 143.9, 142.3, 139.4, 137.7, 136.6, 136.1, 130.6, 130.2, 129.5 (2C), 129.2 (2C), 128.7 (1) (2C), 128.7 (2C), 128.6 (2C), 128.2 (2C), 128.0, 127.8 (2C), 127.4, 127.3 (2C), 125.1 (2C), 123.8 (2C), 121.1, 117.8, 109.1, 70.9, 50.9, 47.8, 34.6, 31.6 (3C), 21.7. **HRMS** (EI-TOF) m/z: $[M]^+$ calcd for $[C_{45}H_{42}N_2O_3S]^+$: 690.2911; found: 690.2908. **HPLC** (Chiralpak IC, *n*-hexane/ethanol = 95/5, flow rate = 1.0 mL/min, λ = 220 nm) t_R= 6.70 min (*trans*-major), 7.50 min (*trans*-minor), 13.52 min (*cis*-major), 15.01 min (*cis*-minor).



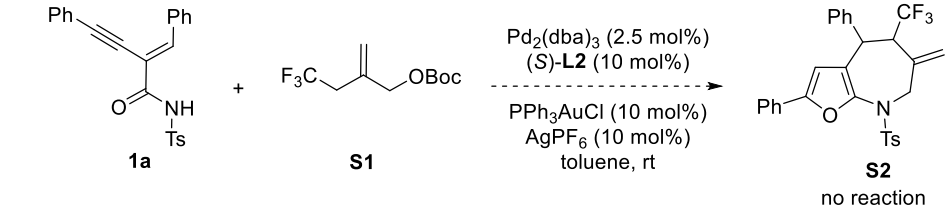
(4*R*,5*R*)-5-((Diphenyl-azaneylidene)methyl)-6-methylene-2-phenyl-4-(*o*-tolyl)-8-tosyl-5,6,7,8-tetrahydro-4*H*-furo[2,3-*b*]azepine (7g): Following the general procedure **C**, compound **7g** was obtained as white solid in 86% yield (55.8 mg), 95%/86% ee, purified by flash chromatography (petroleum ether/EtOAc = 10/1); R_f = 0.5 (petroleum ether/EtOAc = 4/1); m.p = 105-107 °C; $[\alpha]_D^{25}$ = +172.6 (*c* = 0.20, CH_2Cl_2); **^{1}H NMR** (400 MHz, $CDCl_3$) δ 7.66 – 7.56 (m, 4H), 7.48 – 7.43 (m, 2H), 7.41 – 7.28 (m, 3H), 7.27 – 7.17 (m, 7H), 7.17 – 7.01 (m, 5H), 6.32 – 6.19 (m, 3H), 5.16 (brs, 1H), 4.69 – 4.60 (m, 2H), 4.51 (d, *J* = 14.3 Hz, 1H), 3.84 (d, *J* = 2.5 Hz, 1H), 3.52 (d, *J* = 2.5 Hz, 1H), 2.38 (s, 3H), 1.78 (s, 3H). **^{13}C NMR** (100 MHz, $CDCl_3$) δ 168.6, 149.1, 145.6, 143.8, 142.7, 139.2, 138.6, 137.1, 136.1, 136.0, 130.8, 130.6, 130.4, 130.2, 129.3 (2C), 128.7 (2C), 128.6 (7) (2C), 128.4 (2C), 128.1 (2C), 128.0, 127.8 (2C), 127.4, 127.2 (2C), 126.7, 125.3, 123.7 (2C), 120.4, 117.2, 109.2, 68.9, 50.7, 42.9, 21.6, 19.5.

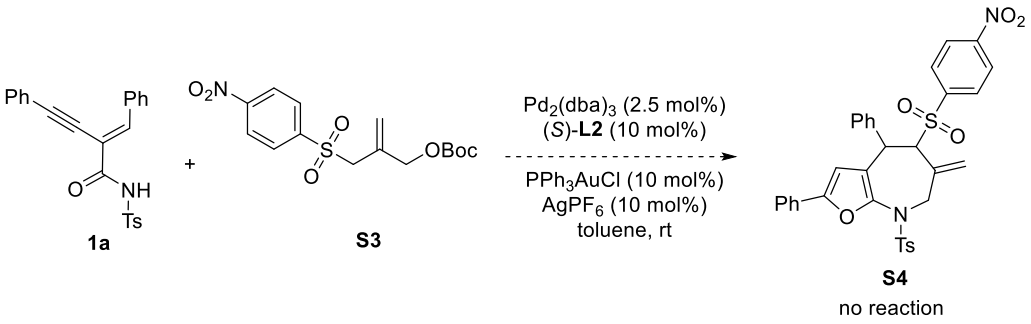
HRMS (EI-TOF) m/z: $[M]^+$ calcd for $[C_{42}H_{36}N_2O_3S]^+$: 648.2441; found: 648.2442. **HPLC** (Chiralpak IF, *n*-hexane/ethanol = 95/5, flow rate = 1.0 mL/min, λ = 220 nm) t_R=11.25 min (*trans*-major), 12.62 min (*trans*-minor), 13.75 min (*cis*-minor), 16.82 min (*cis*-major).



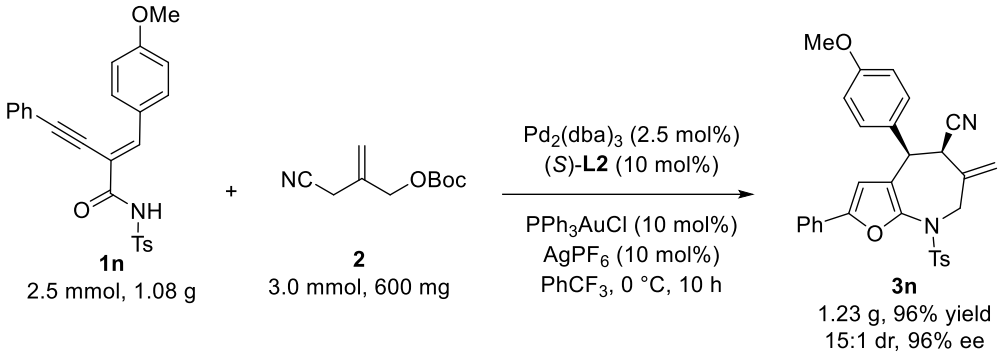
(4*R*,5*R*)-5-((Diphenyl-azaneylidene)methyl)-6-methylene-4-(naphthalen-1-yl)-2-phenyl-8-tosyl-5,6,7,8-tetrahydro-4*H*-furo[2,3-*b*]azepine (7h): Following the general procedure **C**, compound **7h** was obtained as white solid in 83% yield (46.3 mg), 4:1 dr and 90%/84% ee, purified by flash chromatography (petroleum ether/EtOAc = 10/1); R_f = 0.5 (petroleum ether/EtOAc = 4/1); m.p = 118-120 °C; $[\alpha]_D^{25}$ = +183.2 (*c* = 0.20, CH_2Cl_2); **^{1}H NMR** (400 MHz, $CDCl_3$) δ 7.87 (d, *J* = 8.2 Hz, 1H), 7.78 (d, *J* = 8.2 Hz, 1H), 7.70 (d, *J* = 7.9 Hz, 2H), 7.59 (d, *J* = 7.7 Hz, 2H), 7.46 (d, *J* = 7.8 Hz, 4H), 7.41 – 7.20 (m, 11H), 7.11 – 7.01 (m, 1H), 6.95 – 6.80 (m, 2H), 6.30 (s, 1H), 6.22 – 5.88 (m, 2H), 5.21 (brs, 1H), 4.73 – 4.65 (m, 2H), 4.59 (d, *J* = 14.3 Hz, 1H), 4.16 (d, *J* = 2.4 Hz, 1H), 4.01 (d, *J* = 2.4 Hz, 1H), 2.46 (s, 3H). **^{13}C NMR** (100 MHz, $CDCl_3$) δ 168.7, 149.2, 145.4, 143.9, 142.8, 139.1, 137.2, 136.2, 135.7, 134.0, 131.6, 130.4, 130.1, 129.3 (2C), 128.9, 128.6 (2) (2C), 128.6, 128.6 (1) (2C), 128.6, 128.4 (2C), 128.0 (4), 128.0 (2C), 127.7, 127.5 (2C), 127.4, 127.3, 126.9 (2C), 126.0, 125.3, 124.9, 123.6 (2C), 120.5, 117.3, 109.1, 68.9, 50.8, 21.7. **HRMS** (EI-TOF) m/z: $[M]^+$ calcd for $[C_{45}H_{36}N_2O_3S]^+$: 684.2441; found: 684.2449. **HPLC** (Chiralpak IC, *n*-hexane/ethanol = 95/5, flow rate = 1.0 mL/min, λ = 220 nm) t_R=8.60 min (*trans*-major), 9.60 min (*trans*-minor), 17.09 min (*cis*-major), 18.59 min (*cis*-minor).

7. The attempt of other substituted TMM donors



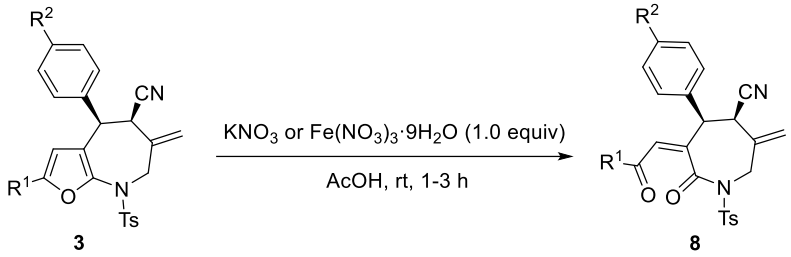


8. Gram-scale experiment

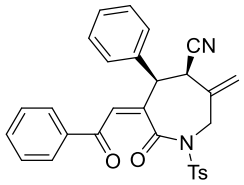


Under a nitrogen atmosphere, two flame dried 10 mL Schlenk flask A and B, The A flask was charged with Ph_3PAuCl (123 mg, 0.25 mmol, 10 mol%) and $AgPF_6$ (62.5 mg, 0.25 mmol, 10 mol%), the B flask charged with ligand (*S*)-**L2** (128 mg, 0.25 mmol, 10 mol%), and $Pd_2(dba)_3$ (58 mg, 0.06 mmol, 2.5 mol%). After the A and B flask was evacuated and backfilled with nitrogen, freshly distilled $PhCF_3$ (25 mL) was added respectively, then stirred at room temperature for 30 minutes while the solution of A flask turned white turbid and the solution of B flask turned green. Then, ynamide **1n** (1.08 g, 2.5 mmol) was added to A flask, and the reaction mixture immediately turned golden yellow. After 5 minutes, TMM donor **2** (600 mg, 3.0 mmol, 1.2 equiv) was added to A flask sequentially. The flask A and B were placed at 0 ℃ for 10 minutes, then added the solution of flask B to flask A at 0 ℃. The reaction mixture was stirred at 0 ℃ until ynamide **1n** was consumed (monitored by TLC), which was evaporated under reduced pressure at 30 ℃. The crude residue was purified by flash chromatography (petroleum ether/EtOAc = 10/1) to give the desired product **3n** in 96% yield (1.23 g, 15:1 dr, 96% ee).

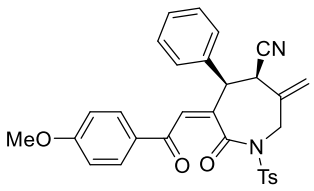
9. Cleavage of the furan moiety to synthesize polysubstituted azepines 8



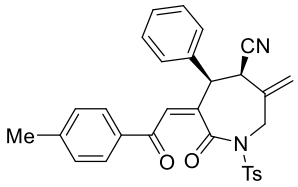
General procedure D: To a solution of cycloadducts **3** (0.1 mmol) in acetic acid (1.0 mL) was added KNO_3 (10.1 mg, 0.1 mmol, 1.0 equiv) or $Fe(NO_3)_3·9H_2O$ (40.4 mg, 0.1 mmol, 1.0 equiv). The resulting mixture was stirred at room temperature until **3** were consumed (monitored by TLC). The crude residue was purified by flash chromatography (CH_2Cl_2/MeOH = 50:1) to give the desired products **8**.



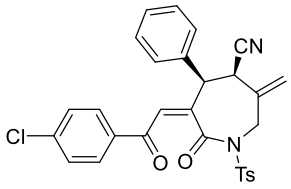
(4*R*,5*R*,*Z*)-3-Methylene-7-oxo-6-(2-oxo-2-phenylethylidene)-5-phenyl-1-tosylazepane-4-carbonitrile (8a): Following the general procedure **D**, compound **8a** was obtained as a white solid in 91% yield (45.1 mg), 14:1 dr and 97% ee, R_f = 0.6 (CH_2Cl_2/MeOH = 50/1); mp = 105-107 °C; $[\alpha]_D^{25}$ = +11.3 (*c* = 0.20, CH_2Cl_2); **^{1}H NMR** (400 MHz, $CDCl_3$) δ 7.96 (d, *J* = 8.4 Hz, 2H), 7.68 – 7.64 (m, 2H), 7.54 – 7.49 (m, 1H), 7.42 – 7.33 (m, 7H), 7.29 (dd, *J* = 6.7, 3.0 Hz, 2H), 6.67 (d, *J* = 1.8 Hz, 1H), 5.68 (s, 1H), 5.55 (d, *J* = 1.4 Hz, 1H), 5.06 (d, *J* = 16.8 Hz, 1H), 4.58 (d, *J* = 17.7 Hz, 1H), 4.16 (d, *J* = 3.2 Hz, 1H), 4.04 (d, *J* = 4.9 Hz, 1H), 2.47 (s, 3H).**^{13}C NMR** (100 MHz, $CDCl_3$) δ 189.0, 168.7, 150.7, 145.4, 136.1, 135.6, 135.5, 135.4, 134.0, 129.7(2C), 129.3(2C), 129.0, 128.8(1)(2C), 128.8(0)(2C), 128.7(2C), 128.6(2C), 127.6, 121.2, 116.7, 48.9, 48.4, 41.4, 21.9. **HRMS** (EI-TOF) m/z: $[M]^+$ calcd for $[C_{29}H_{24}N_2O_5S]^+$: 496.1451; found: 496.1460. **HPLC** (Chiralpak IF, *n*-hexane/ethanol = 80/20, flow rate = 1.0 mL/min, λ = 220 nm) t_R = 20.85 min (*trans*-major), 26.35 (*trans*-minor), 27.63 min (*cis*-minor), 34.58 min (*cis*-major).



(4*R*,5*R*,*Z*)-6-(2-(4-Methoxyphenyl)-2-oxoethylidene)-3-methylene-7-oxo-5-phenyl-1-tosylazepane-4-carbonitrile (8b): Following the general procedure **D**, compound **8b** was obtained as a white solid in 91% yield (47.8 mg), 8:1 dr and 97% ee, R_f = 0.4 (CH_2Cl_2/MeOH = 50/1); mp = 101-103 °C; $[\alpha]_D^{25}$ = +35.2 (*c* = 0.20, CH_2Cl_2); **^{1}H NMR** (400 MHz, $CDCl_3$) δ 7.96 (d, *J* = 7.9 Hz, 2H), 7.65 (d, *J* = 8.4 Hz, 2H), 7.42 – 7.26 (m, 7H), 6.83 (d, *J* = 8.4 Hz, 2H), 6.65 (s, 1H), 5.66 (s, 1H), 5.54 (s, 1H), 5.04 (d, *J* = 16.8 Hz, 1H), 4.59 (d, *J* = 17.0 Hz, 1H), 4.13 (d, *J* = 4.9 Hz, 1H), 4.01 (d, *J* = 5.0 Hz, 1H), 3.82 (s, 3H), 2.46 (s, 3H).**^{13}C NMR** (100 MHz, $CDCl_3$) δ 187.1, 168.7, 164.2, 149.7, 145.1, 135.6, 135.6, 135.5, 131.1(2C), 129.5(2C), 129.2, 129.1(6)(2C), 128.9, 128.8, 128.5(2C), 128.4(9)(2C), 120.9, 116.7, 113.9(2C), 55.5, 48.8, 48.3, 41.3, 21.7. **HRMS** (EI-TOF) m/z: $[M]^+$ calcd for $[C_{30}H_{26}N_2O_5S]^+$: 526.1557; found: 526.1560. **HPLC** (Chiralpak IA, *n*-hexane/ethanol = 80/20, flow rate = 1.0 mL/min, λ = 220 nm) t_R = 40.32 min (minor), 48.58 min (major).

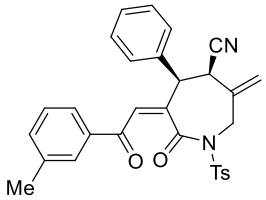


(4*R*,5*R*,*Z*)-3-Methylene-7-oxo-6-(2-oxo-2-(p-tolyl)ethylidene)-5-phenyl-1-tosylazepane-4-carbonitrile (8c): Following the general procedure **D**, compound **8c** was obtained as a white solid in 85% yield (43.4 mg), 12:1 dr and 97% ee, R_f = 0.5 (CH_2Cl_2/MeOH = 50/1); mp = 95-97 °C; $[\alpha]_D^{25}$ = +27.7 (*c* = 0.20, CH_2Cl_2); **^{1}H NMR** (400 MHz, $CDCl_3$) δ 7.96 (d, *J* = 8.4 Hz, 2H), 7.56 (d, *J* = 8.3 Hz, 2H), 7.40 – 7.33 (m, 5H), 7.29 – 7.27 (m, 2H), 7.16 (d, *J* = 7.9 Hz, 2H), 6.66 (s, 1H), 5.67 (s, 1H), 5.55 (d, *J* = 1.5 Hz, 1H), 5.05 (d, *J* = 16.9 Hz, 1H), 4.58 (d, *J* = 16.9 Hz, 1H), 4.15 (dd, *J* = 5.0, 1.8 Hz, 1H), 4.02 (d, *J* = 4.9 Hz, 1H), 2.47 (s, 3H), 2.36 (s, 3H).**^{13}C NMR** (100 MHz, $CDCl_3$) δ 188.5, 168.8, 150.3, 145.3, 145.1, 135.6, 135.6, 135.4, 133.7, 129.7(2C), 129.5(2C), 129.3(2C), 129.0(2C), 128.9, 128.7(2C), 128.6(2C), 127.6, 121.1, 116.8, 48.9, 48.4, 41.4, 21.9(1), 21.8(9). **HRMS** (EI-TOF) m/z: $[M]^+$ calcd for $[C_{30}H_{26}N_2O_4S]^+$: 510.1608; found: 510.1615. **HPLC** (Chiralpak IF, *n*-hexane/ethanol = 80/20, flow rate = 1.0 mL/min, λ = 220 nm) t_R = 24.12 min (*trans*-major), 31.26 (*trans*-minor), 34.98 min (*cis*-minor), 39.78 min (*cis*-major).

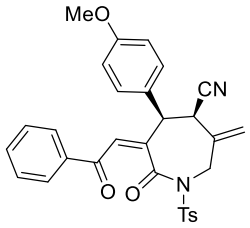


(4*R*,5*R*,*Z*)-6-(2-(4-Chlorophenyl)-2-oxoethylidene)-3-methylene-7-oxo-5-phenyl-1-

tosylazepane-4-carbonitrile (8d): Following the general procedure **D**, compound **8d** was obtained as a white solid in 90% yield (47.7 mg), 13:1 dr and 98% ee, R_f = 0.6 (CH_2Cl_2/MeOH = 50/1); mp = 137-139 °C; $[\alpha]_D^{25}$ = +30.5 (*c* = 0.20, CH_2Cl_2); **^{1}H NMR** (400 MHz, $CDCl_3$) δ 77.95 (d, *J* = 8.1 Hz, 2H), 7.59 (d, *J* = 8.3 Hz, 2H), 7.40 – 7.36 (m, 4H), 7.35 (d, *J* = 2.3 Hz, 2H), 7.33 (s, 1H), 7.30– 7.28 (m, 2H), 6.61 (s, 1H), 5.68 (s, 1H), 5.55 (s, 1H), 5.05 (d, *J* = 16.8 Hz, 1H), 4.55 (d, *J* = 16.9 Hz, 1H), 4.15 (d, *J* = 4.9 Hz, 1H), 4.04 (d, *J* = 4.9 Hz, 1H), 2.47 (s, 3H).**^{13}C NMR** (100 MHz, $CDCl_3$) δ 187.9, 168.6, 151.3, 145.4, 140.6, 135.5, 135.5, 135.3, 134.5, 130.2(2C), 129.7(2C), 129.4(2C), 129.2(2C), 129.0, 128.7(2C), 128.5(4)(2C), 128.48, 121.4, 116.7, 48.8, 48.4, 41.5, 21.9. **HRMS** (EI-TOF) m/z: $[M]^+$ calcd for $[C_{29}H_{23}ClN_2O_4S]^+$: 530.1062; found: 530.1063. **HPLC** (Chiralpak IF, *n*-hexane/ethanol = 90/10, flow rate = 1.0 mL/min, λ = 220 nm) t_R = 21.19 min (*trans*-major), 26.60 (*trans*-minor), 32.28 min (*cis*-minor), 36.68 min (*cis*-major).



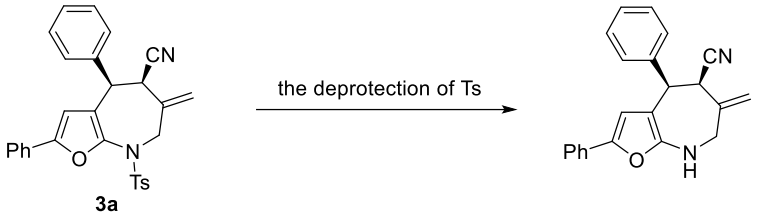
(4*R*,5*R*,*Z*)-3-Methylene-7-oxo-6-(2-oxo-2-(*m*-tolyl)ethylidene)-5-phenyl-1-tosylazepane-4-carbonitrile (8e): Following the general procedure **D**, compound **8e** was obtained as a white solid in 87% yield (44.9 mg), 16:1 dr and 98% ee, R_f = 0.5 (CH_2Cl_2/MeOH = 50/1); mp = 104-106 °C; $[\alpha]_D^{25}$ = +58.2 (*c* = 0.20, CH_2Cl_2); **^{1}H NMR** (400 MHz, $CDCl_3$) δ 7.96 (d, *J* = 8.4 Hz, 2H), 7.49 (s, 1H), 7.43 (d, *J* = 7.8 Hz, 1H), 7.40 – 7.34 (m, 5H), 7.34 – 7.27 (m, 3H), 7.23 (d, *J* = 7.6 Hz, 1H), 6.67 (s, 1H), 5.67 (s, 1H), 5.55 (d, *J* = 1.5 Hz, 1H), 5.04 (d, *J* = 16.9 Hz, 1H), 4.59 (d, *J* = 16.9 Hz, 1H), 4.16 (dd, *J* = 5.0, 1.8 Hz, 1H), 4.03 (d, *J* = 5.0 Hz, 1H), 2.47 (s, 3H), 2.32 (s, 3H). **^{13}C NMR** (100 MHz, $CDCl_3$) δ 189.1, 168.6, 150.3, 145.2, 138.6, 136.1, 135.5, 135.4, 135.3, 134.7, 129.6(2C), 129.2, 129.1(9)(2C), 129.1(4), 128.8, 128.5(4)(2C), 128.5(2)(2C), 125.9, 121.0, 116.6, 48.8, 48.3, 41.4, 41.4, 21.8, 21.3. **HRMS** (EI-TOF) m/z: $[M]^+$ calcd for $[C_{30}H_{26}N_2O_4S]^+$: 510.1608; found: 510.1609. **HPLC** (Chiralpak IF, *n*-hexane/ethanol = 80/20, flow rate = 1.0 mL/min, λ = 220 nm) t_R = 20.85 min (*trans*-minor), 25.58 (*trans*-major), 27.40 min (*cis*-minor), 35.35 min (*cis*-major).



(4*R*,5*R*,*Z*)-5-(4-Methoxyphenyl)-3-methylene-7-oxo-6-(2-oxo-2-phenylethylidene)-1-tosylazepane-4-carbonitrile (8f): Following the general procedure **D**, compound **8f** was obtained as a white solid in 83% yield (43.6 mg), >20:1 dr and 96% ee, R_f = 0.6 (CH_2Cl_2/MeOH = 50:1); mp = 93-95 °C; $[\alpha]_D^{25}$ = +24.7 (*c* = 0.20, CH_2Cl_2); **^{1}H NMR** (400 MHz, $CDCl_3$) δ 7.96 (d, *J* = 8.0 Hz, 2H), 7.71 – 7.62 (m, 2H), 7.56 – 7.48 (m, 1H), 7.38 (t, *J* = 7.8 Hz, 4H), 7.19 (d, *J* = 8.3 Hz, 2H), 6.89 (d, *J* = 8.5 Hz, 2H), 6.68 (s, 1H), 5.66 (s, 1H), 5.54 (s, 1H), 5.05 (d, *J* = 17.1 Hz, 1H), 4.58 (d, *J* = 16.9 Hz, 1H), 4.12 (d, *J* = 5.1 Hz, 1H), 3.98 (d, *J* = 5.1 Hz, 1H), 3.82 (s, 3H), 2.47 (s, 3H).**^{13}C NMR** (100 MHz, $CDCl_3$) δ 188.9, 168.6, 159.7, 151.1, 145.3, 136.0, 135.4, 135.2, 133.9, 129.7(2C), 129.6(2C), 128.7(2)(2C), 128.7(0)(2C), 128.6(2C), 128.4, 127.1, 120.7, 116.7, 114.5(2C), 55.3, 48.9, 47.7, 41.4, 21.8. **HRMS** (EI-TOF) m/z: $[M]^+$ calcd for $[C_{30}H_{26}N_2O_5S]^+$: 526.1557; found: 526.1559. **HPLC** (Chiralpak IF, *n*-hexane/ethanol = 80/20, flow rate = 1.0 mL/min, λ = 220 nm) t_R=36.64 (minor), 45.97 (major).

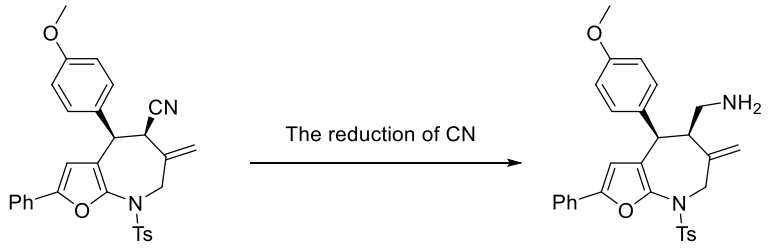
10. The attempt of other transformations of products

The deprotection of Ts group



Reaction conditions	Results
HBr, PhOH, 120 °C, 12 h	Complex reaction
SmI_2 (5.0 equiv), THF, rt, 12 h	No reaction
TBAF (3.0 equiv), THF, rt, 12 h	Complex reaction
Na (20.0 equiv), naphthalene (20.0 equiv), THF, -78 °C, 0.5 h	Complex reaction

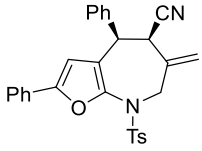
The reduction of CN group

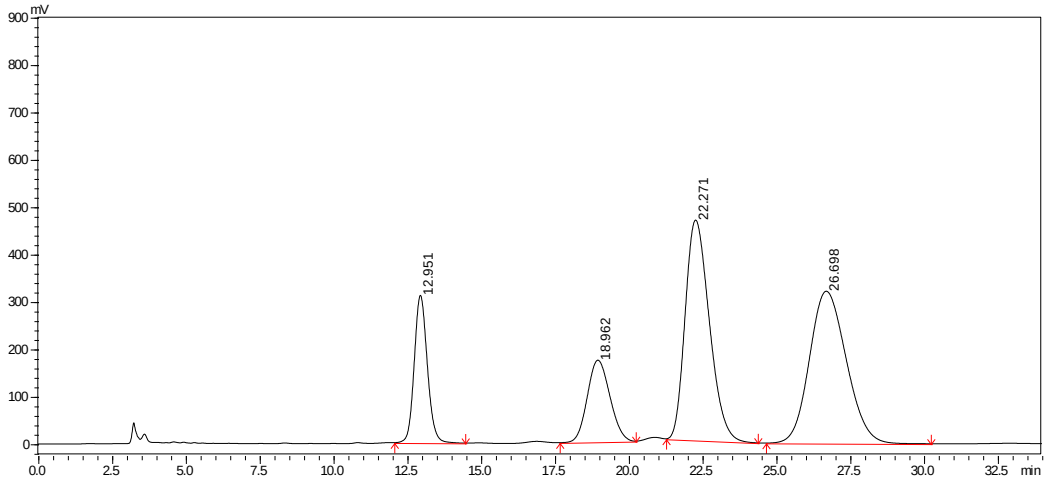


Reaction conditions	Results
$LiAlH_4$ (1.0 equiv), Et_2O, 0 °C to rt, 12 h	No reaction
$NiCl_2 \cdot 6H_2O$ (6.0 equiv), $NaBH_4$ (10 equiv), MeOH, 0 °C to rt, 12 h	No product
DIBAL-H (1.2 equiv), THF, -25 °C to rt, 24 h	No product
Raney Ni/H_2, MeOH, rt, 12 h	Complex reaction

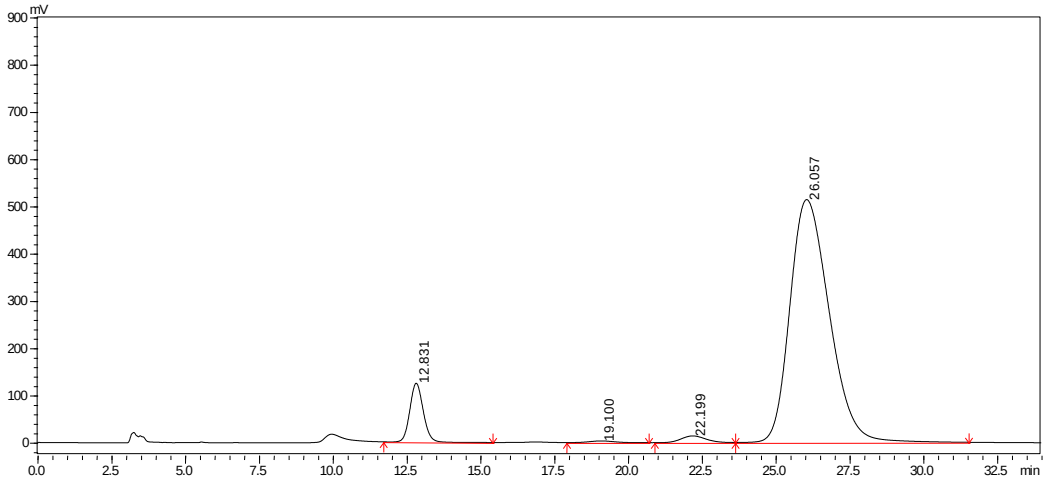
11. HPLC chromatograms

HPLC chromatogram of compound **3a** (13:1 dr and 97% ee)



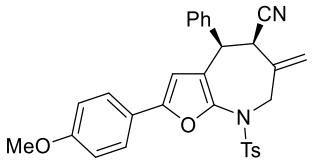


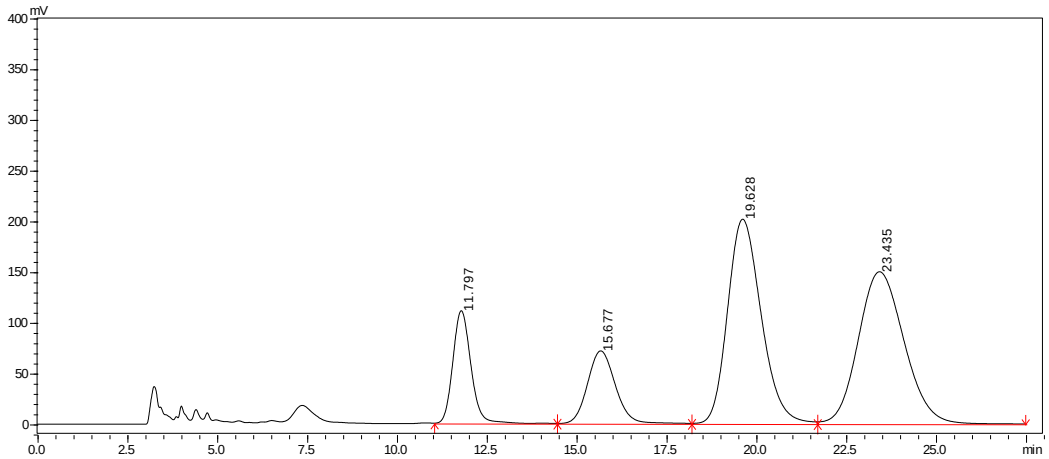
#	Ret Time (min)	Height (mV)	Area (mV.sec)	Area (%)
1	12.951	311139	9570152	13.122
2	18.962	172458	9144120	12.538
3	22.271	464356	26431143	36.242
4	26.698	320869	27784388	38.097
Total		1268823	72929802	100.000



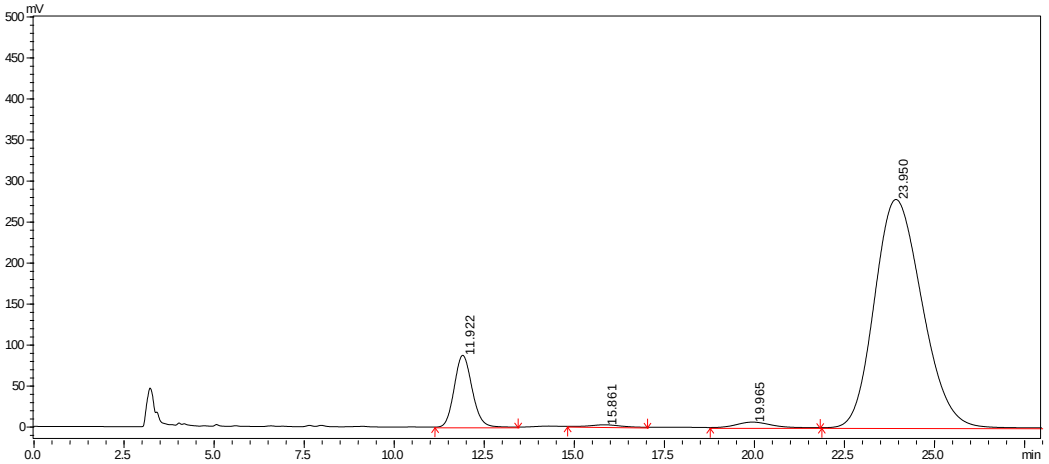
#	Ret Time (min)	Height (mV)	Area (mV.sec)	Area (%)
1	12.831	124459	3893556	7.416
2	19.100	3486	202264	0.385
3	22.199	14282	823870	1.569
4	26.057	514021	47579584	90.629
Total		656248	52499274	100.000

HPLC chromatogram of compound **3b** (8:1 dr and 97% ee)



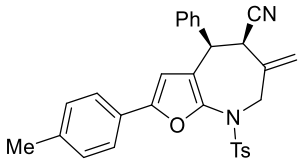


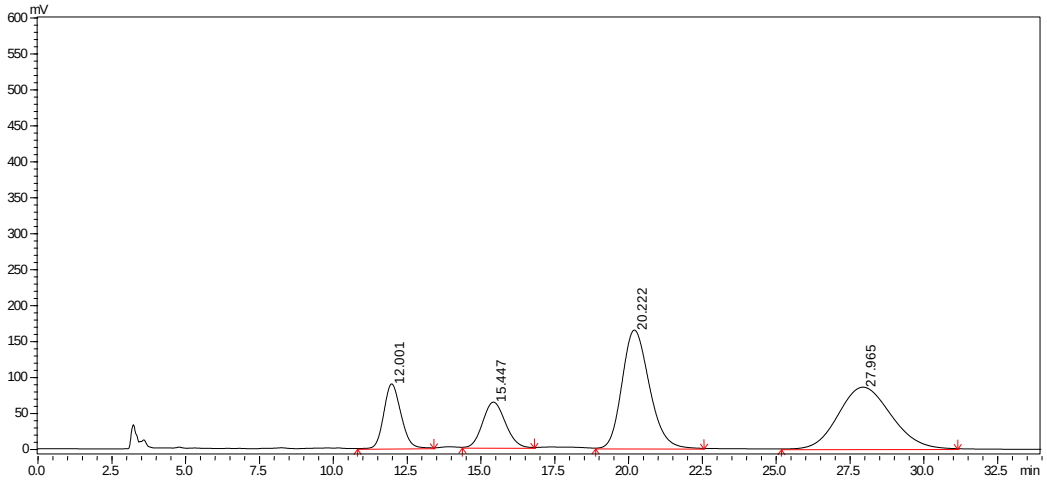
#	Ret Time (min)	Height (mV)	Area (mV.sec)	Area (%)
1	11.797	110905	3854262	11.337
2	15.677	71554	3829073	11.263
3	19.628	201471	13086983	38.496
4	23.435	149830	13225387	38.903
Total		533759	33995705	100.000



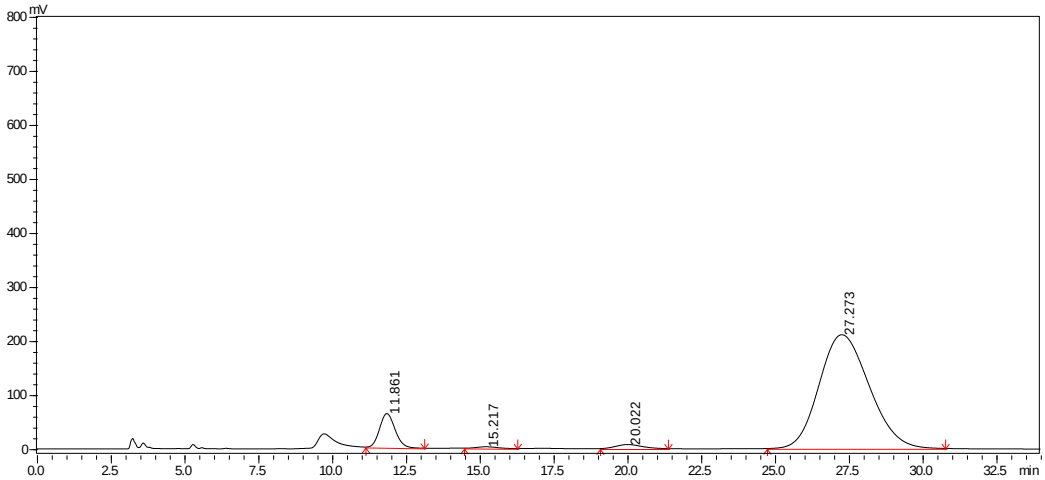
#	Ret Time (min)	Height (mV)	Area (mV.sec)	Area (%)
1	11.922	87514	3004587	10.340
2	15.861	2435	127615	0.439
3	19.965	6699	424150	1.460
4	23.950	278273	25502265	87.761
Total		374922	29058618	100.000

HPLC chromatogram of compound **3c** (11:1 dr and 96% ee)



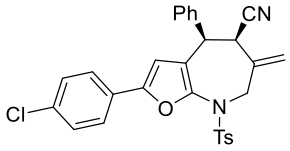


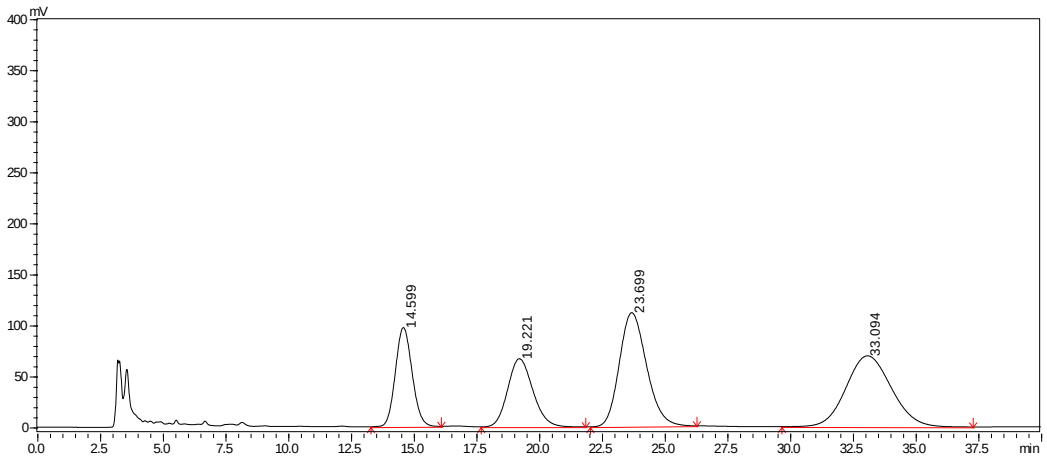
#	Ret Time (min)	Height (mV)	Area (mV.sec)	Area (%)
1	12.001	89449	3563879	12.748
2	15.447	62945	3315546	11.860
3	20.222	164217	10507934	37.588
4	27.965	85692	10568391	37.804
Total		402303	27955749	100.000



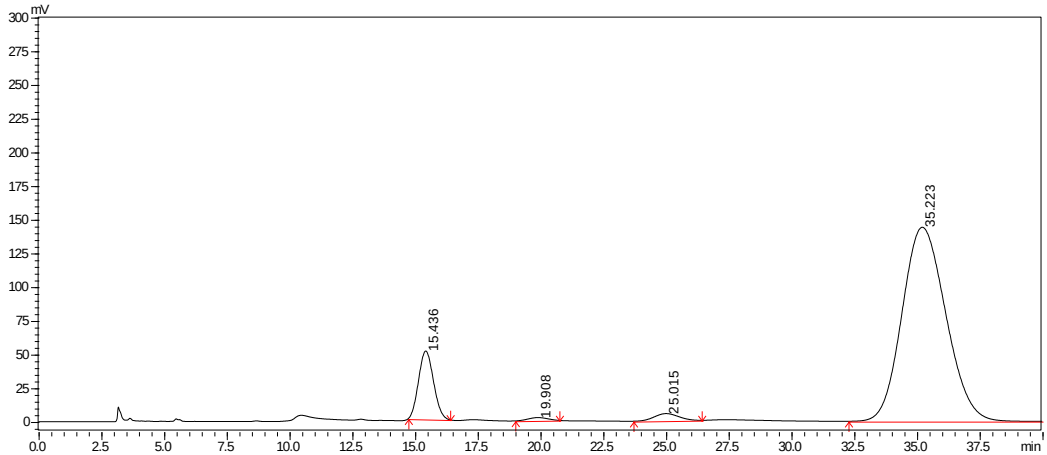
#	Ret Time (min)	Height (mV)	Area (mV.sec)	Area (%)
1	11.861	62739	2259128	8.173
2	15.217	2855	130107	0.471
3	20.022	7513	451983	1.635
4	27.273	210536	24801240	89.722
Total		283643	27642458	100.000

HPLC chromatogram of compound **3d** (8:1 dr and 96% ee)



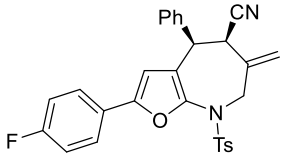


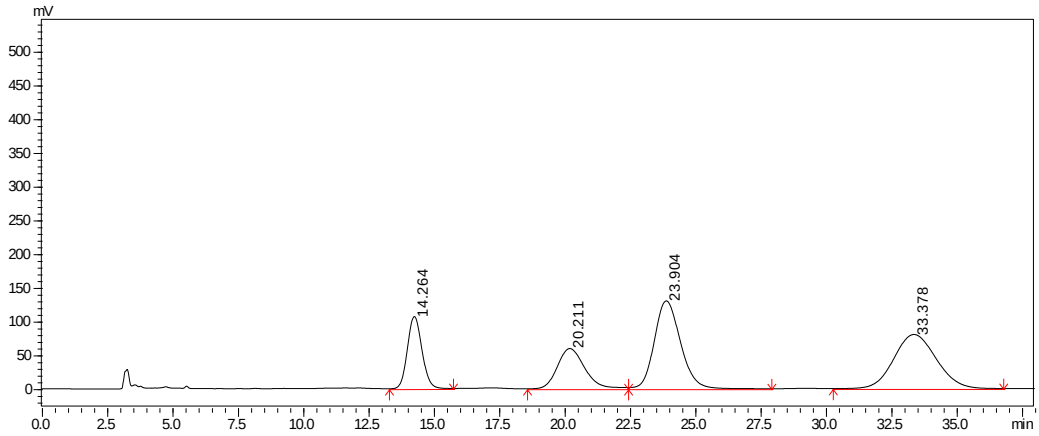
#	Ret Time (min)	Height (mV)	Area (mV.sec)	Area (%)
1	14.599	97001	4494092	17.134
2	19.221	66736	4634231	17.668
3	23.699	111445	8395740	32.009
4	33.094	69497	8705085	33.189
Total		344679	26229147	100.000



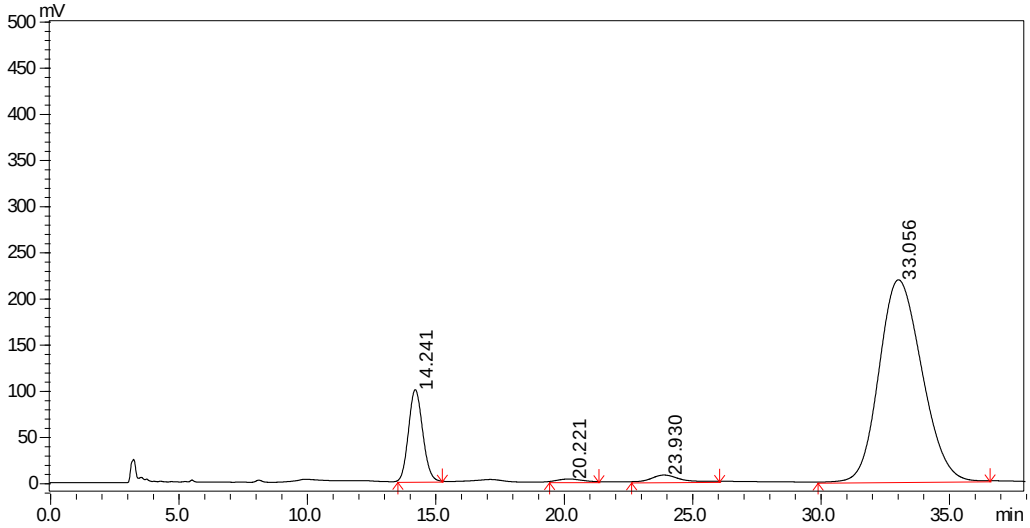
#	Ret Time (min)	Height (mV)	Area (mV.sec)	Area (%)
1	15.436	50569	2096987	10.470
2	19.908	2284	121514	0.607
3	25.015	5330	355888	1.777
4	35.223	143927	17453558	87.146
Total		202110	20027946	100.000

HPLC chromatogram of compound **3e** (6:1 dr and 96% ee)



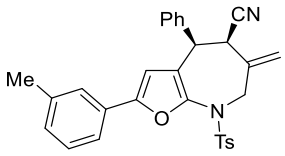


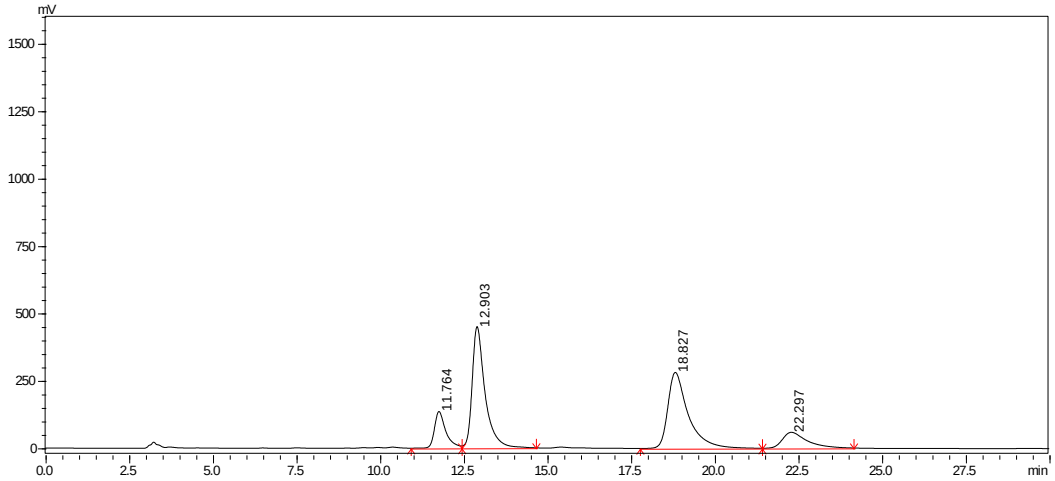
#	Ret Time (min)	Height (mV)	Area (mV.sec)	Area (%)
1	14.264	106897	4125518	15.560
2	20.211	59649	4329232	16.328
3	23.904	130209	9041857	34.103
4	33.378	80102	9017132	34.009
Total		376856	26513739	100.000



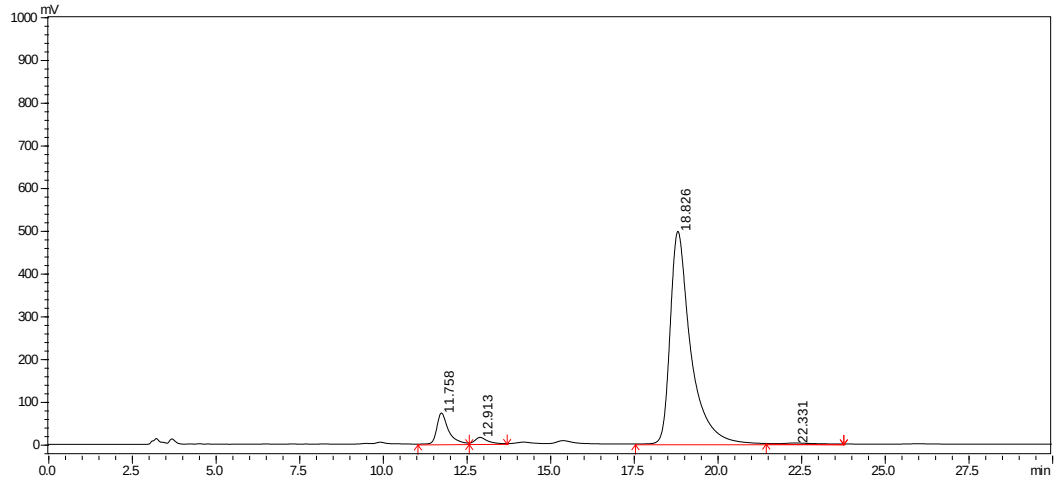
#	Ret Time (min)	Height (mV)	Area (mV.sec)	Area (%)
1	14.241	99046	3779008	12.770
2	20.221	2874	170125	0.575
3	23.930	7056	463949	1.568
4	33.056	218507	25178650	85.087
Total		327483	29591732	100.000

HPLC chromatogram of compound **3f** (12:1 dr and 96% ee)



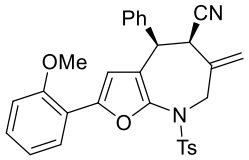


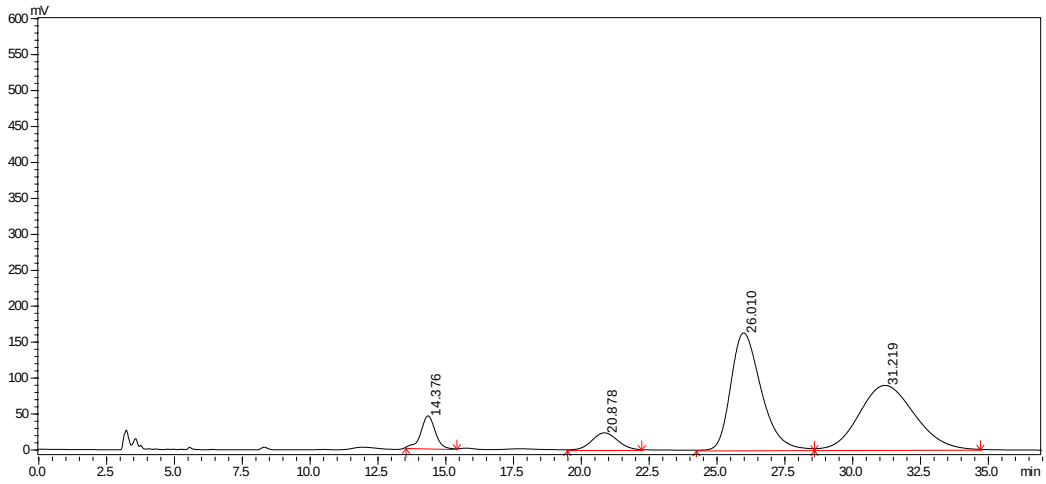
#	Ret Time (min)	Height (mV)	Area (mV.sec)	Area (%)
1	11.764	135640	3174811	10.560
2	12.903	449962	12049961	40.079
3	18.827	281687	11859527	39.446
4	22.297	58860	2981242	9.916
Total		926148	30065540	100.000



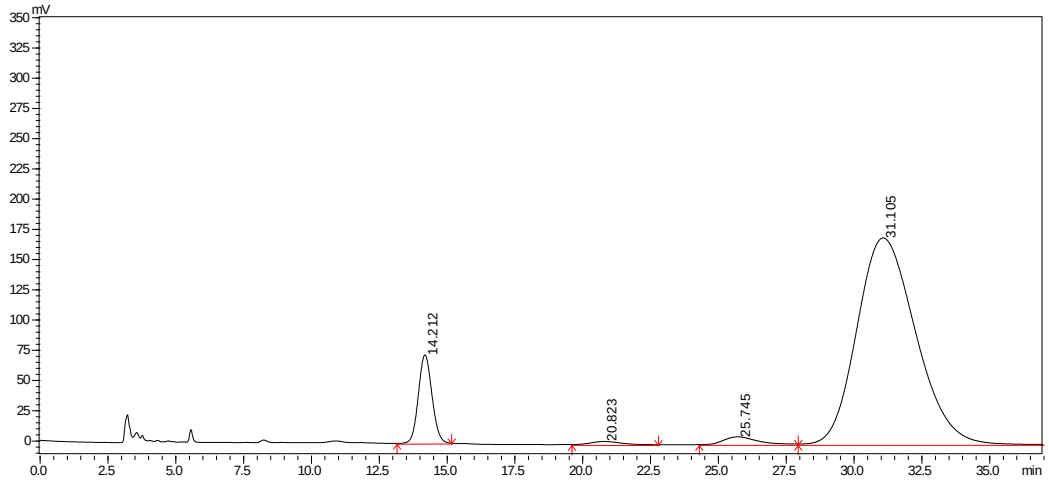
#	Ret Time (min)	Height (mV)	Area (mV.sec)	Area (%)
1	11.758	72454	1723979	7.349
2	12.913	14965	380394	1.622
3	18.826	497457	21291080	90.758
4	22.331	1638	63707	0.272
Total		586514	23459160	100.000

HPLC chromatogram of compound **3g** (10:1 dr and 96% ee)



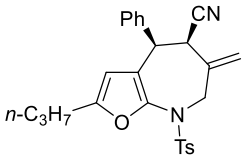


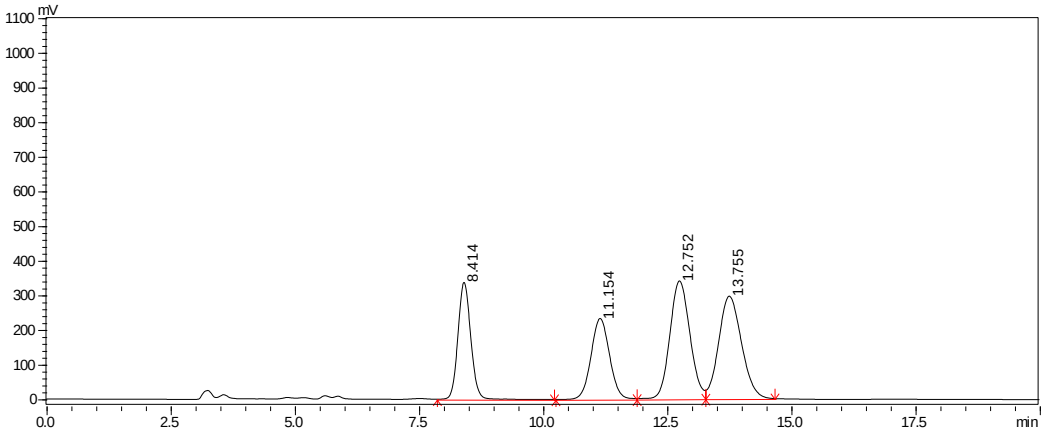
#	Ret Time (min)	Height (mV)	Area (mV.sec)	Area (%)
1	14.376	44914	1611909	5.686
2	20.878	23418	1510196	5.327
3	26.010	162791	12622522	44.525
4	31.219	89356	12604619	44.462
Total		320479	28349246	100.000



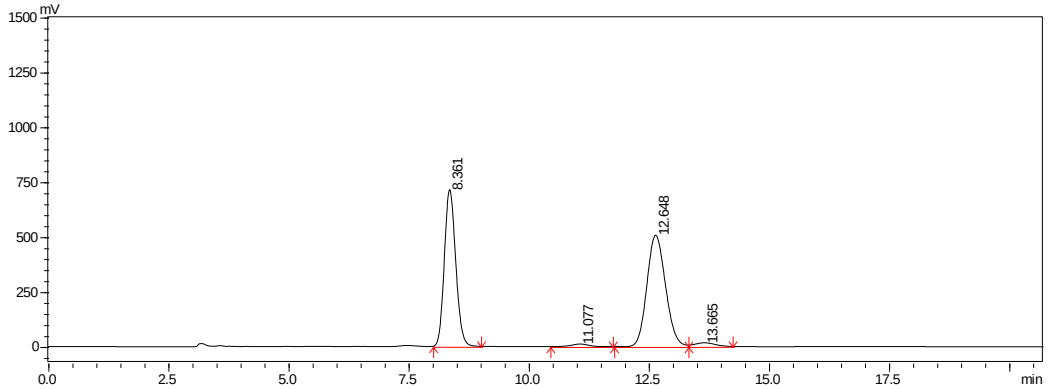
#	Ret Time (min)	Height (mV)	Area (mV.sec)	Area (%)
1	14.212	73114	2549332	8.797
2	20.823	2587	189011	0.652
3	25.745	6455	550413	1.899
4	31.105	170860	25691767	88.652
Total		253016	28980523	100.000

HPLC chromatogram of compound **3h** (1.5:1 dr and 93%/95%ee)



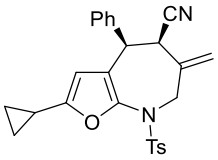


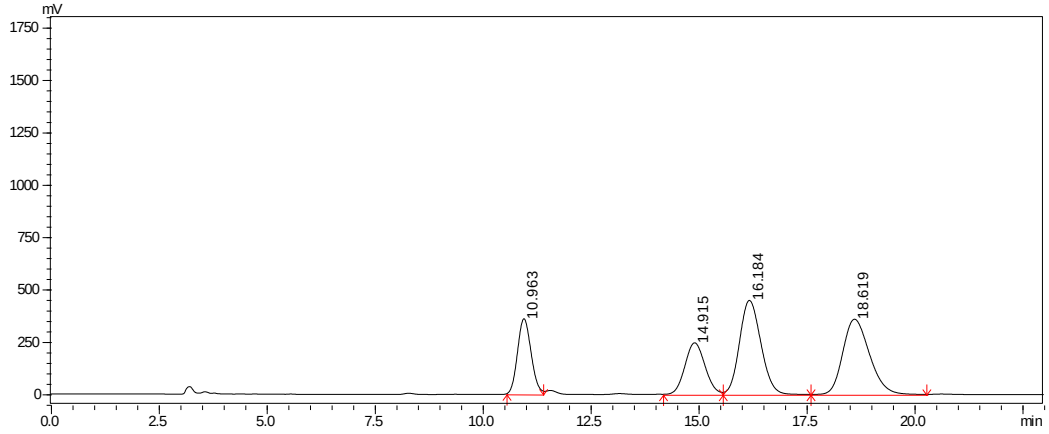
#	Ret Time (min)	Height (mV)	Area (mV.sec)	Area (%)
1	8.414	337260	6005591	19.371
2	11.154	232962	6015837	19.404
3	12.752	340639	9521698	30.712
4	13.755	296080	9460283	30.514
Total		1206940	31003408	100.000



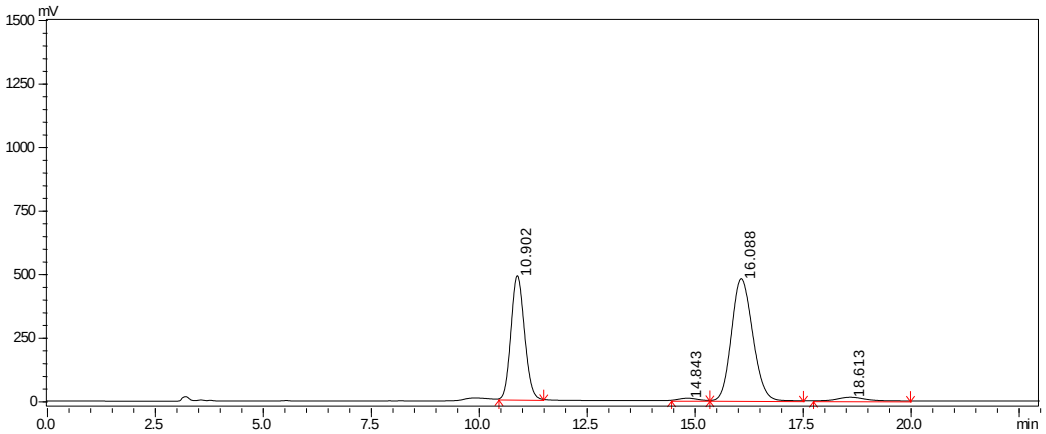
#	Ret Time (min)	Height (mV)	Area (mV.sec)	Area (%)
1	8.361	713097	11750238	44.867
2	11.077	11670	299046	1.142
3	12.648	506935	13643825	52.098
4	13.665	16914	495866	1.893
Total		1248616	26188975	100.000

HPLC chromatogram of compound **3i** (1.5:1 dr and 93%/96%ee)



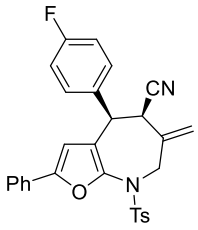


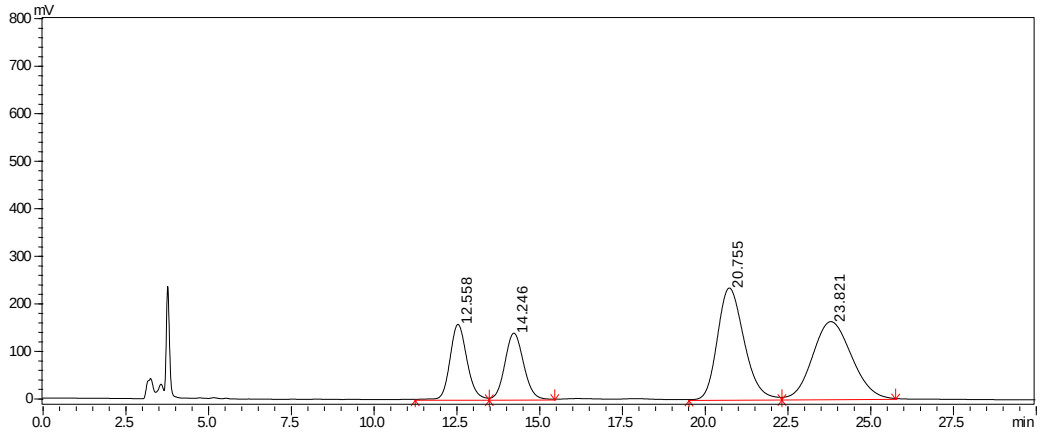
#	Ret Time (min)	Height (mV)	Area (mV.sec)	Area (%)
1	10.963	359701	7838438	16.878
2	14.915	245599	7912473	17.038
3	16.184	448098	15371527	33.099
4	18.619	358587	15318710	32.985
Total		1411985	46441148	100.000



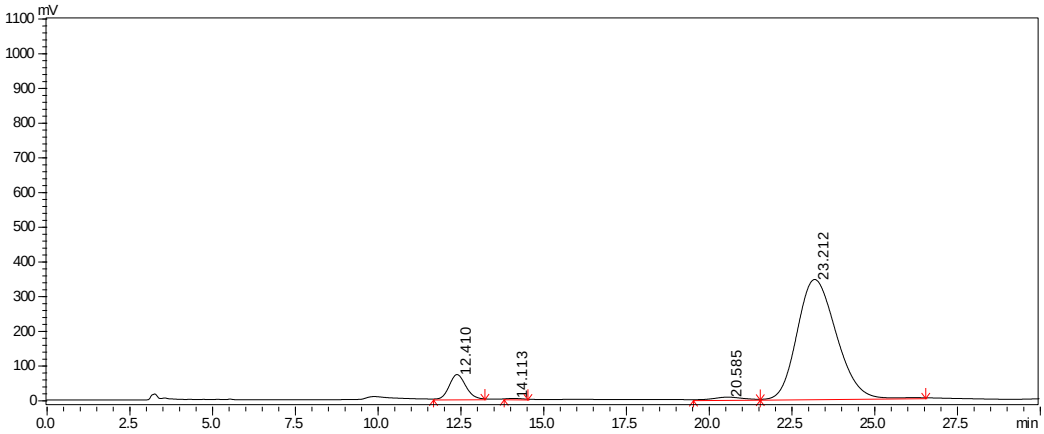
#	Ret Time (min)	Height (mV)	Area (mV.sec)	Area (%)
1	10.902	485556	10518412	38.074
2	14.843	8540	232758	0.843
3	16.088	479285	16292701	58.975
4	18.613	14067	582678	2.109
Total		987449	27626549	100.000

HPLC chromatogram of compound **3j** (12:1 dr and 98% ee)



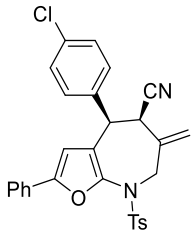


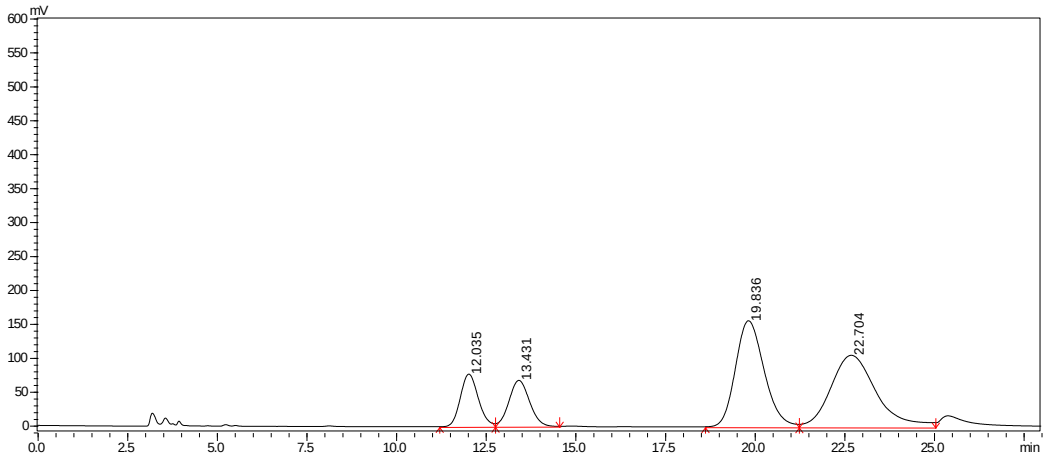
#	Ret Time (min)	Height (mV)	Area (mV.sec)	Area (%)
1	12.558	157508	5533146	14.873
2	14.246	139043	5402487	14.522
3	20.755	234332	13040059	35.052
4	23.821	162382	13226011	35.552
Total		693265	37201703	100.000



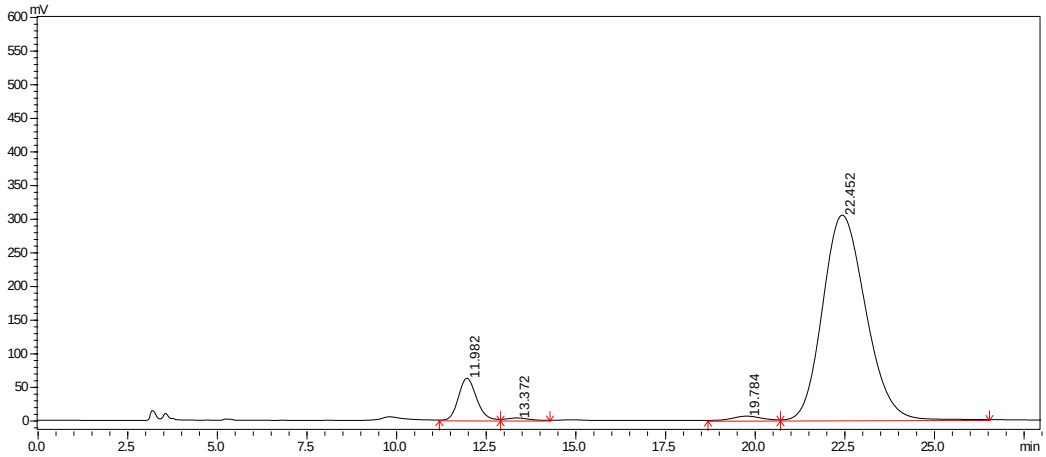
#	Ret Time (min)	Height (mV)	Area (mV.sec)	Area (%)
1	12.410	70232	2376436	7.740
2	14.113	1747	44434	0.145
3	20.585	6741	344155	1.121
4	23.212	343759	27937704	90.994
Total		422479	30702729	100.000

HPLC chromatogram of compound **3k** (11:1 dr and 97% ee)



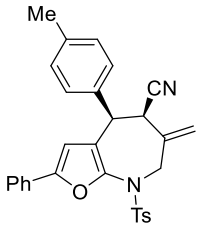


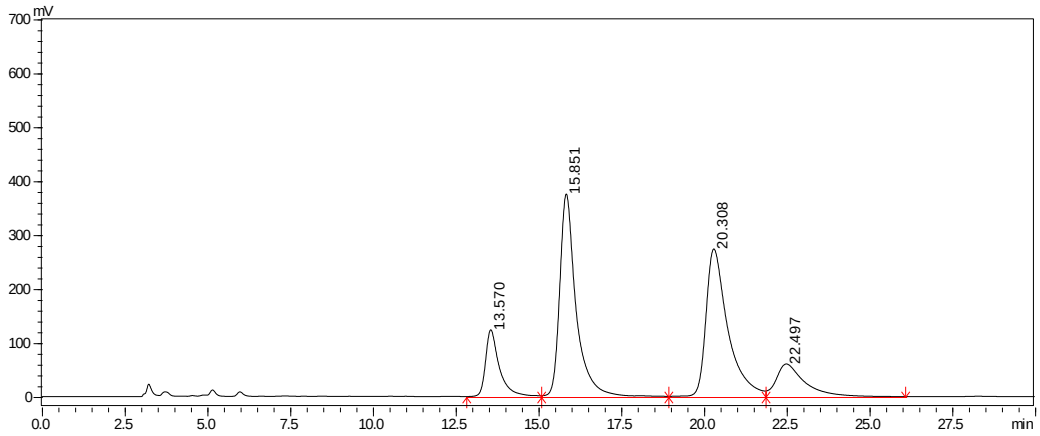
#	Ret Time (min)	Height (mV)	Area (mV.sec)	Area (%)
1	12.035	77453	2694399	12.213
2	13.431	67894	2700308	12.240
3	19.836	155100	8466078	38.376
4	22.704	101465	8200267	37.171
Total		401912	22061052	100.000



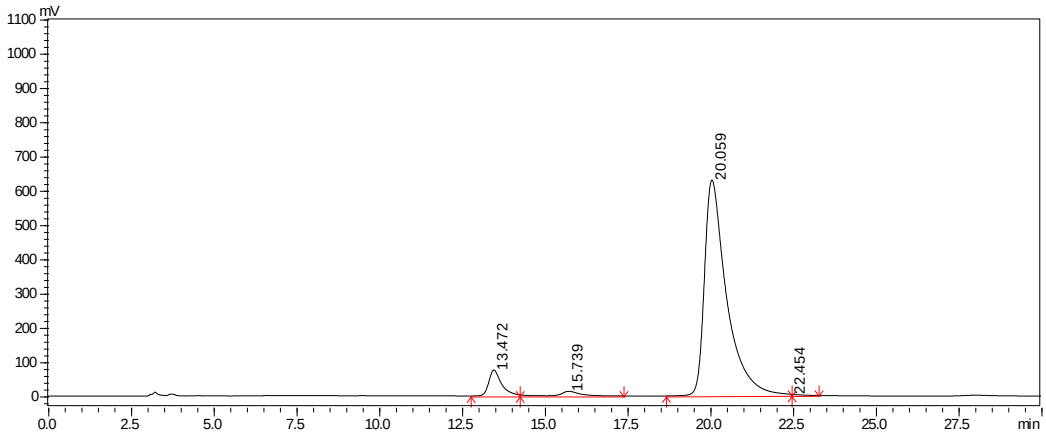
#	Ret Time (min)	Height (mV)	Area (mV.sec)	Area (%)
1	11.982	62173	2164686	7.660
2	13.372	3426	135290	0.479
3	19.784	6240	335546	1.187
4	22.452	305079	25624713	90.674
Total		376918	28260235	100.000

HPLC chromatogram of compound **3l** (14:1 dr and 96% ee)



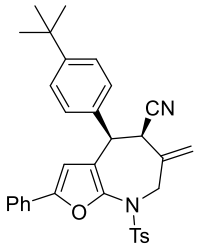


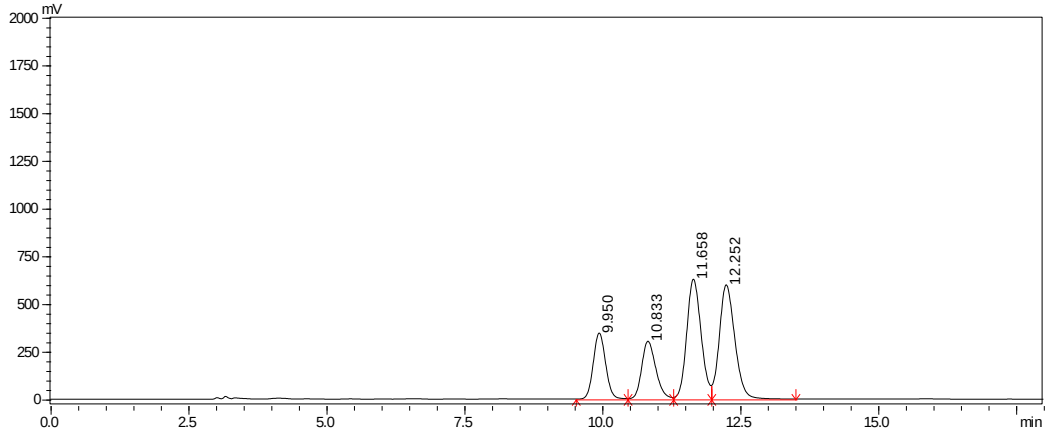
#	Ret Time (min)	Height (mV)	Area (mV.sec)	Area (%)
1	13.570	123688	3574558	10.981
2	15.851	375487	12872212	39.544
3	20.308	273694	12513073	38.441
4	22.497	60381	3591854	11.034
Total		833249	32551698	100.000



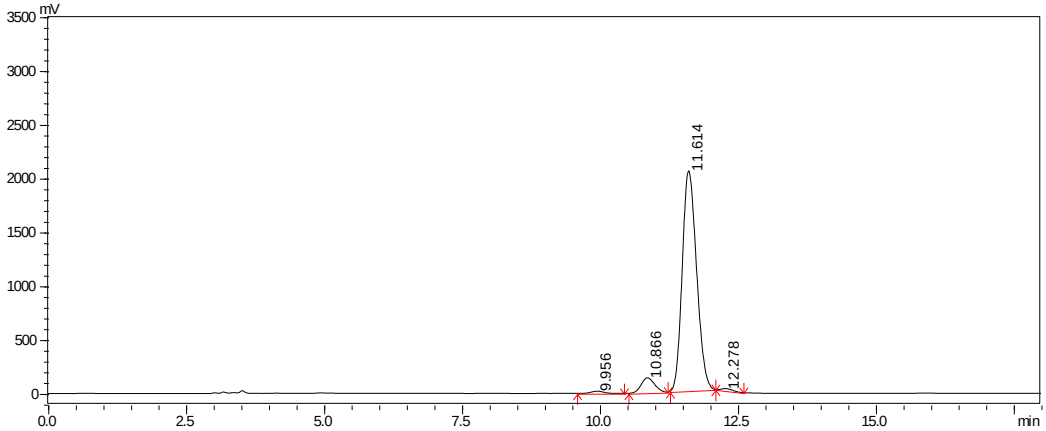
#	Ret Time (min)	Height (mV)	Area (mV.sec)	Area (%)
1	13.472	75514	2027059	6.349
2	15.739	13698	571495	1.790
3	20.059	629476	29255152	91.633
4	22.454	3981	72825	0.228
Total		722668	31926532	100.000

HPLC chromatogram of compound **3m** (14:1 dr and 99% ee)



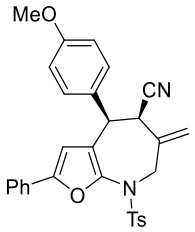


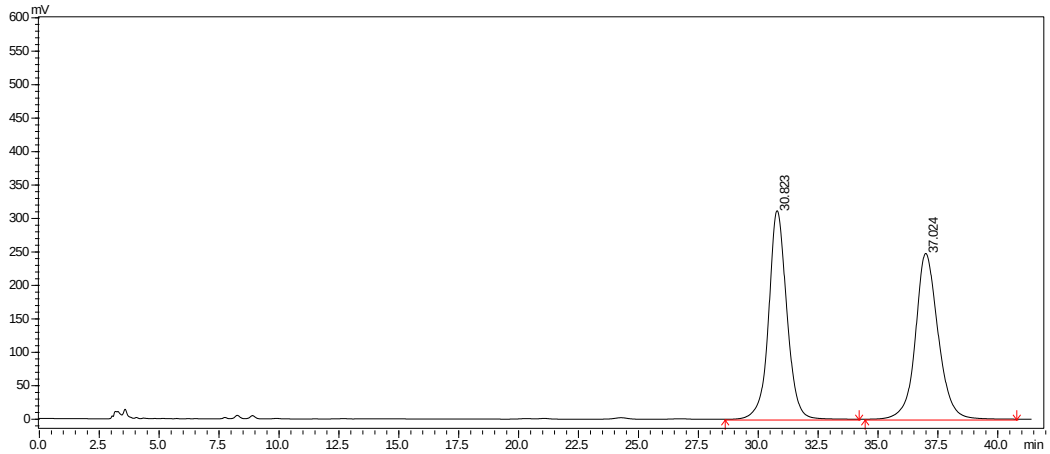
#	Ret Time (min)	Height (mV)	Area (mV.sec)	Area (%)
1	9.950	345853	5357439	15.861
2	10.833	303094	5373200	15.907
3	11.658	627617	11371443	33.665
4	12.252	598243	11675912	34.567
Total		1874807	33777994	100.000



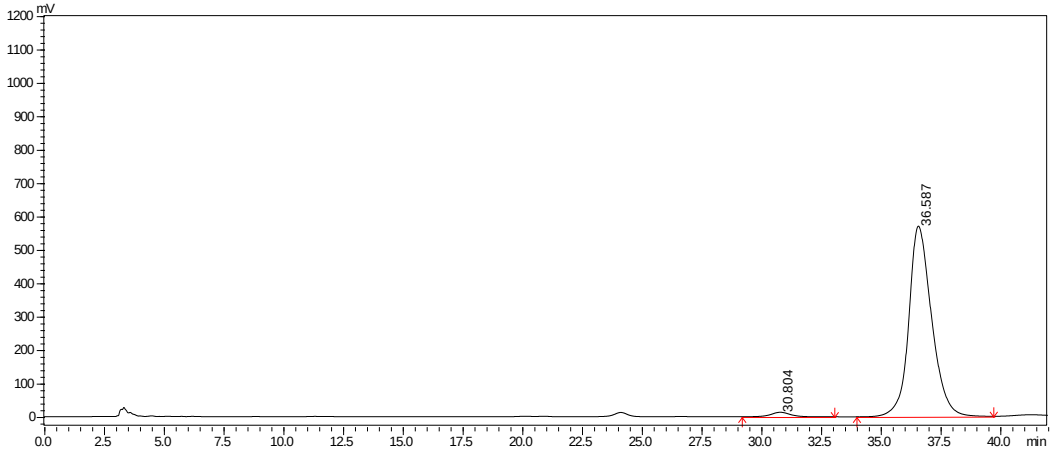
#	Ret Time (min)	Height (mV)	Area (mV.sec)	Area (%)
1	9.956	20750	315366	0.792
2	10.866	138131	2320001	5.829
3	11.614	2043310	36913057	92.736
4	12.278	19062	255925	0.643
Total		2221254	39804349	100.000

HPLC chromatogram of compound **3n** (96% ee)



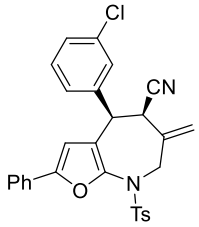


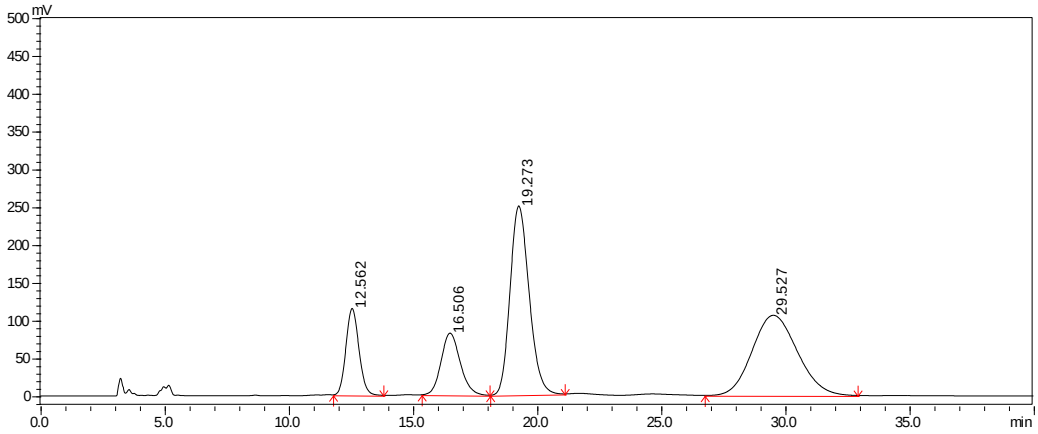
#	Ret Time (min)	Height (mV)	Area (mV.sec)	Area (%)
1	30.823	311568	16387816	50.159
2	37.024	247746	16283898	49.841
Total		559314	32671713	100.000



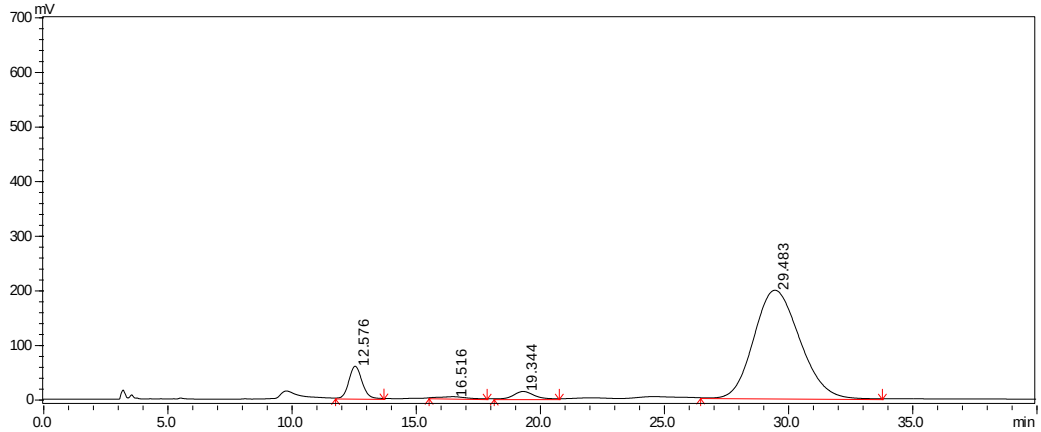
#	Ret Time (min)	Height (mV)	Area (mV.sec)	Area (%)
1	30.804	13455	752459	1.947
2	36.587	570138	37892016	98.053
Total		583593	38644475	100.000

HPLC chromatogram of compound **3o** (12:1 dr and 95% ee)



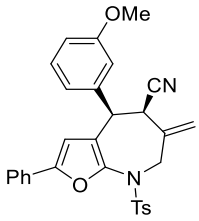


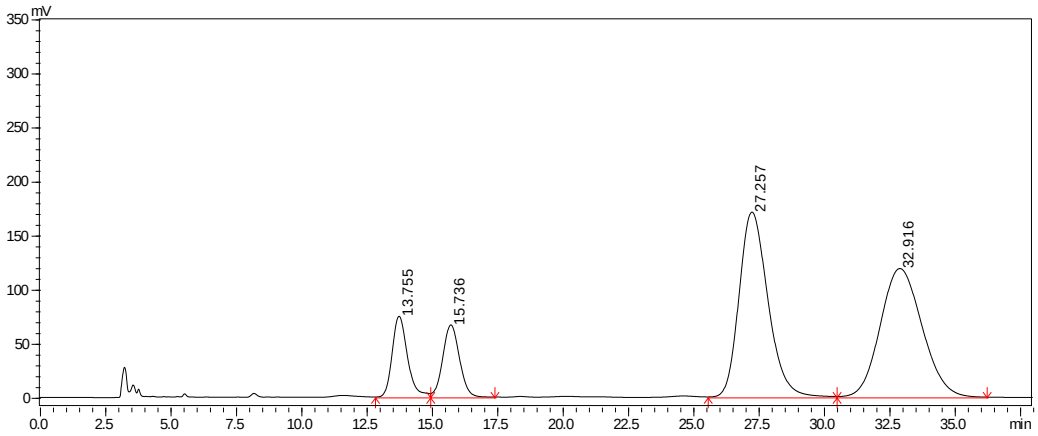
#	Ret Time (min)	Height (mV)	Area (mV.sec)	Area (%)
1	12.562	114405	4138871	11.766
2	16.506	81809	4350577	12.368
3	19.273	249570	13319314	37.864
4	29.527	105951	13367853	38.002
Total		551735	35176615	100.000



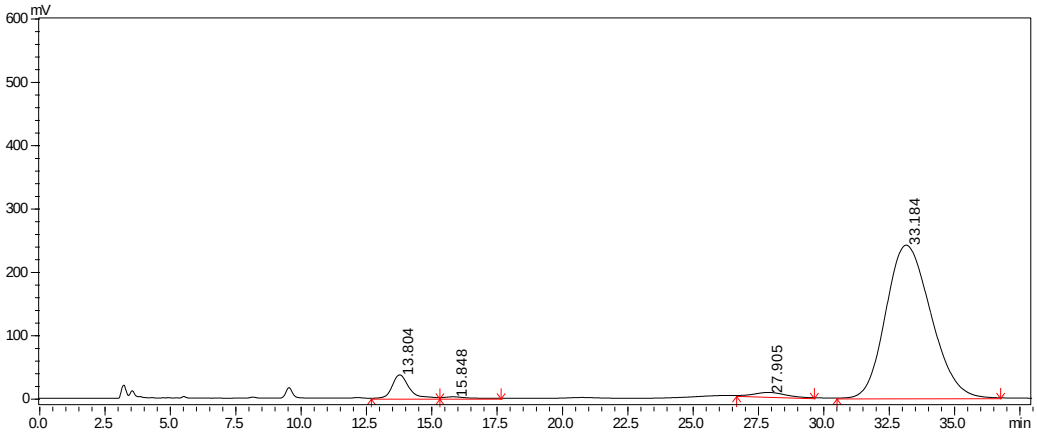
#	Ret Time (min)	Height (mV)	Area (mV.sec)	Area (%)
1	12.576	58651	2100193	7.452
2	16.516	2923	181596	0.644
3	19.344	13383	700452	2.485
4	29.483	197650	25200598	89.418
Total		272608	28182839	100.000

HPLC chromatogram of compound **3p** (17:1 dr and 97% ee)



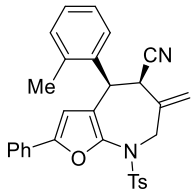


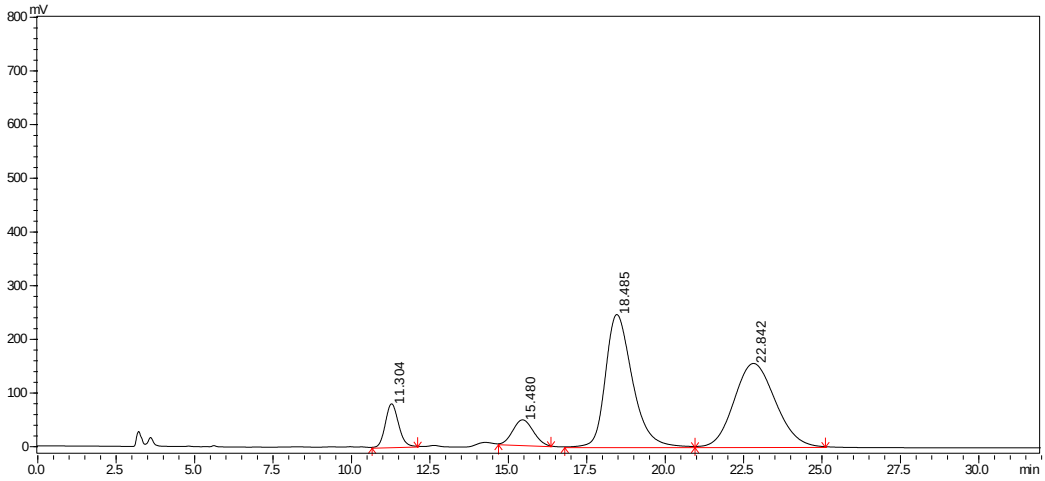
#	Ret Time (min)	Height (mV)	Area (mV.sec)	Area (%)
1	13.755	74626	3035124	9.394
2	15.736	66709	2955131	9.146
3	27.257	170965	13096962	40.536
4	32.916	118846	13222488	40.924
Total		431145	32309706	100.000



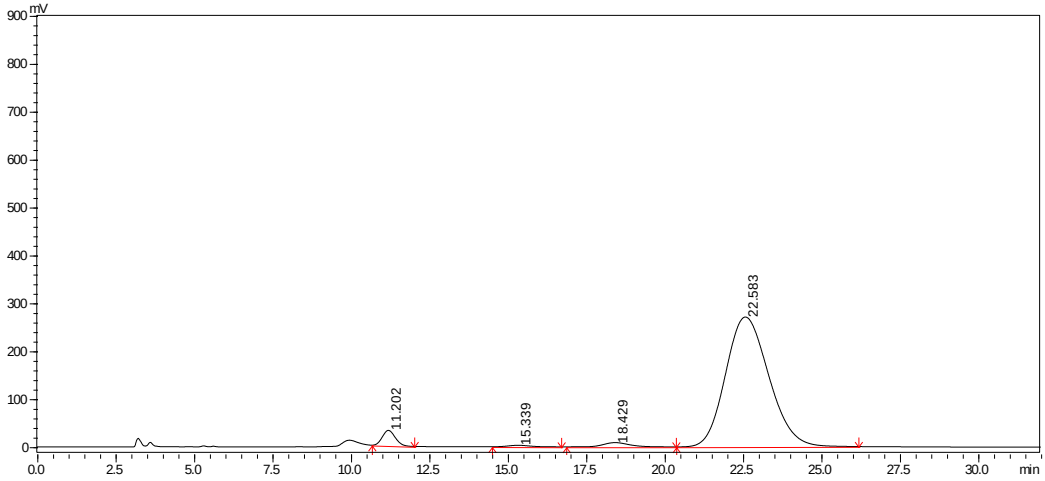
#	Ret Time (min)	Height (mV)	Area (mV.sec)	Area (%)
1	13.804	36866	1614777	5.208
2	15.848	2258	115004	0.371
3	27.905	6304	472147	1.523
4	33.184	241161	28804334	92.898
Total		286588	31006262	100.000

HPLC chromatogram of compound **3q** (>20:1 dr and 96% ee)



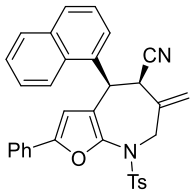


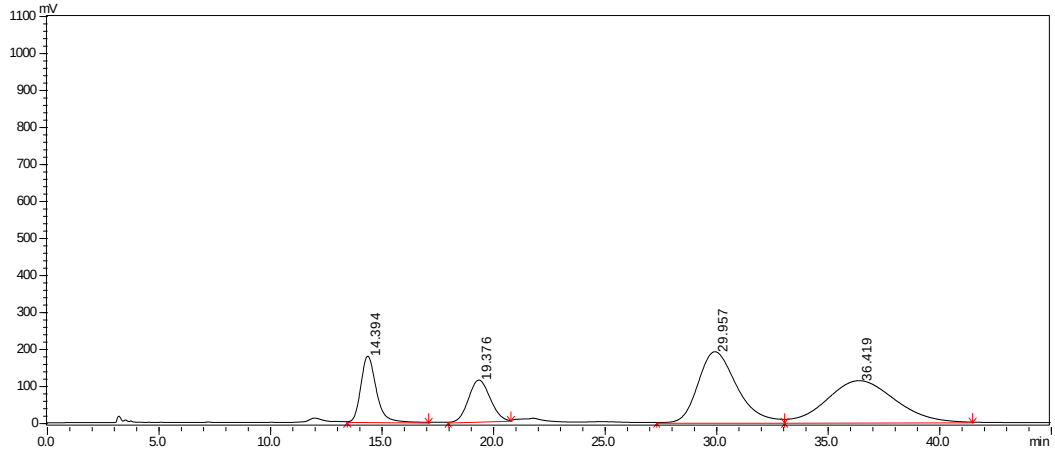
#	Ret Time (min)	Height (mV)	Area (mV.sec)	Area (%)
1	11.304	80102	2303003	6.961
2	15.480	46505	2064050	6.239
3	18.485	246530	14624911	44.206
4	22.842	155168	14091912	42.595
Total		528306	33083876	100.000



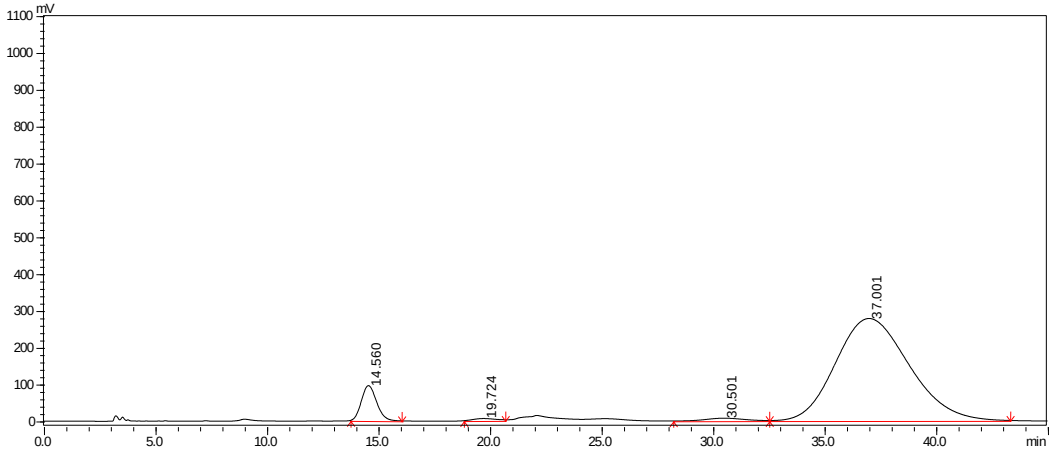
#	Ret Time (min)	Height (mV)	Area (mV.sec)	Area (%)
1	11.202	31827	906406	3.295
2	15.339	2993	138364	0.503
3	18.429	8794	499670	1.817
4	22.583	270724	25961381	94.385
Total		314339	27505821	100.000

HPLC chromatogram of compound **3r** (13:1 dr and 97% ee)



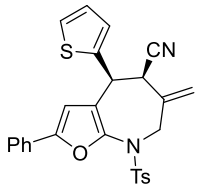


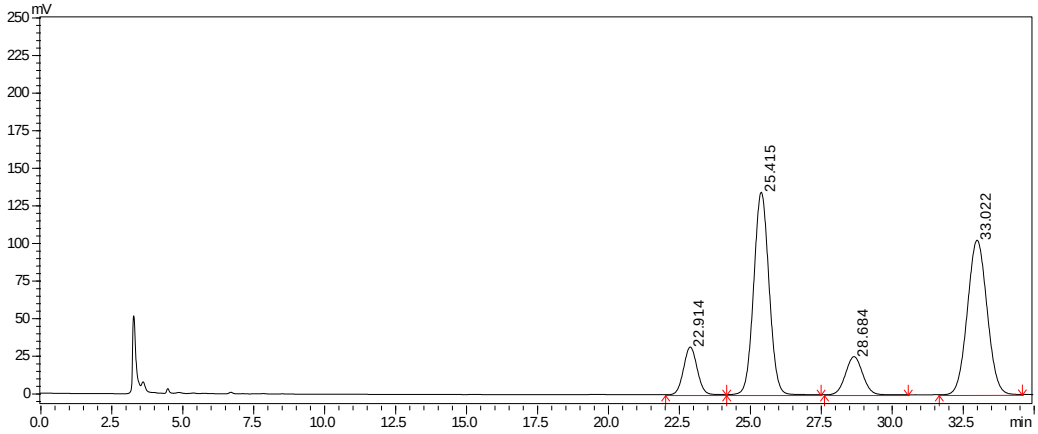
#	Ret Time (min)	Height (mV)	Area (mV.sec)	Area (%)
1	14.394	177612	8382237	13.484
2	19.376	111570	7401773	11.907
3	29.957	191068	22828278	36.722
4	36.419	112329	23553524	37.888
Total		592580	62165812	100.000



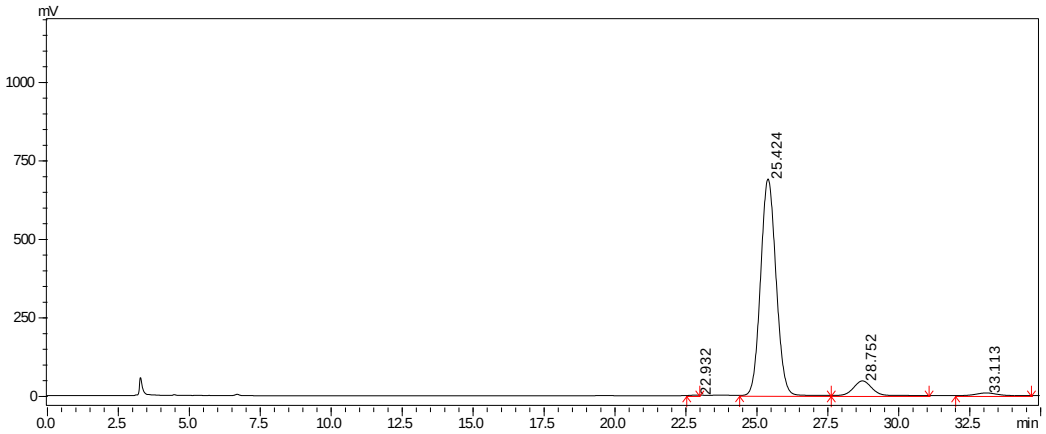
#	Ret Time (min)	Height (mV)	Area (mV.sec)	Area (%)
1	14.560	95028	4479482	6.472
2	19.724	5888	419334	0.606
3	30.501	7318	846875	1.224
4	37.001	277299	63468201	91.699
Total		385533	69213893	100.000

HPLC chromatogram of compound **3s** (13:1 dr and 97% ee)



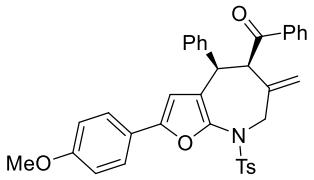


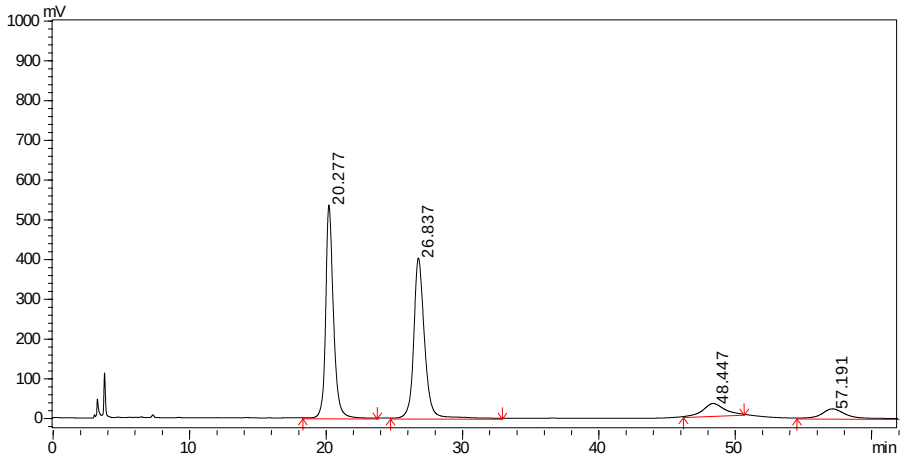
#	Ret Time (min)	Height (mV)	Area (mV.sec)	Area (%)
1	22.914	31695	1059704	8.747
2	25.415	134652	5044403	41.638
3	28.684	25317	1061857	8.765
4	33.022	102656	4948848	40.850
Total		294320	12114813	100.000



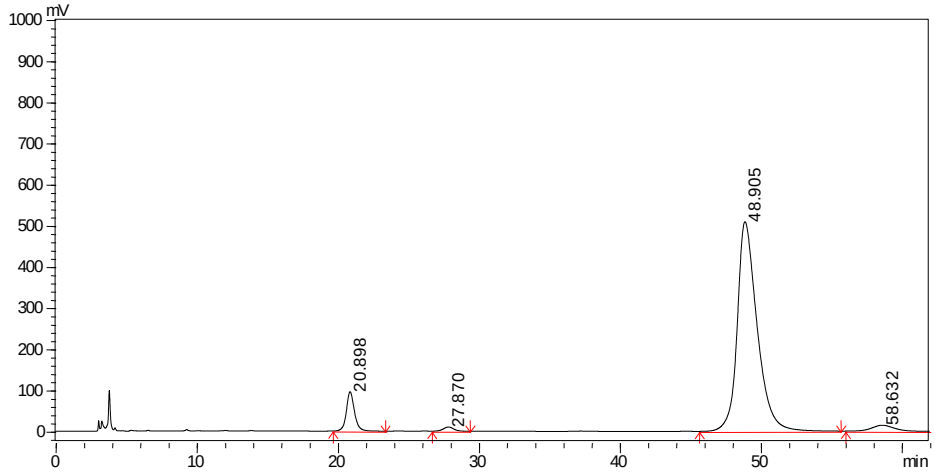
#	Ret Time (min)	Height (mV)	Area (mV.sec)	Area (%)
1	22.932	1717	30089	0.106
2	25.424	689584	25958674	91.313
3	28.752	46494	2030769	7.144
4	33.113	8401	408614	1.437
Total		746195	28428146	100.000

HPLC chromatogram of compound **5a** (12:1 dr and 94% ee)



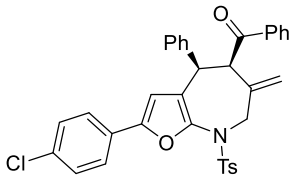


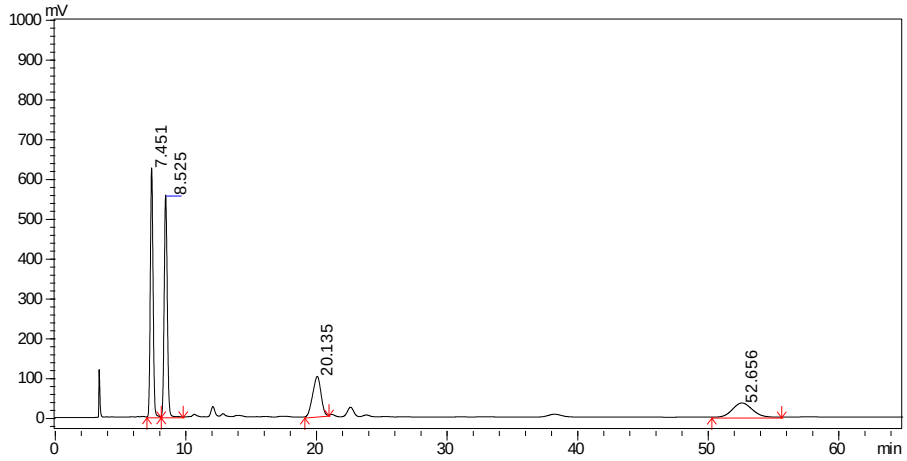
#	Ret Time (min)	Height (mV)	Area (mV.sec)	Area (%)
1	20.277	536013	21073955	43.336
2	26.837	402809	21887858	45.010
3	48.447	29981	3123423	6.423
4	57.191	23405	2543982	5.231
Total		992208	48629218	100.000



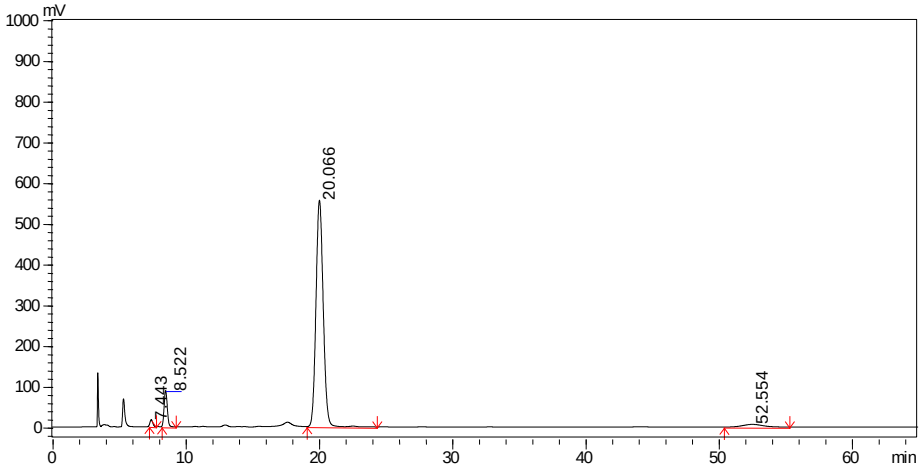
#	Ret Time (min)	Height (mV)	Area (mV.sec)	Area (%)
1	20.898	95745	3835980	6.861
2	27.870	10158	521959	0.934
3	48.905	509125	49921792	89.295
4	58.632	14531	1626912	2.910
Total		629559	55906643	100.000

HPLC chromatogram of compound **5b** (13:1 dr and 94% ee)



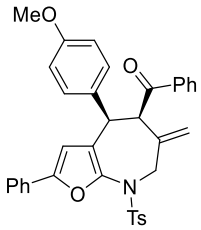


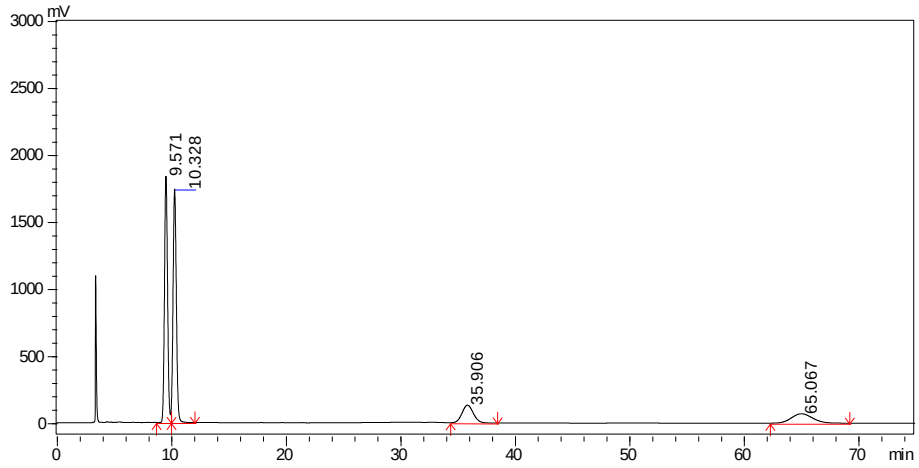
#	Ret Time (min)	Height (mV)	Area (mV.sec)	Area (%)
1	7.451	625644	9173074	34.762
2	8.525	557087	9177216	34.778
3	20.135	99537	4347932	16.477
4	52.656	35584	3690128	13.984
Total		1317851	26388350	100.000



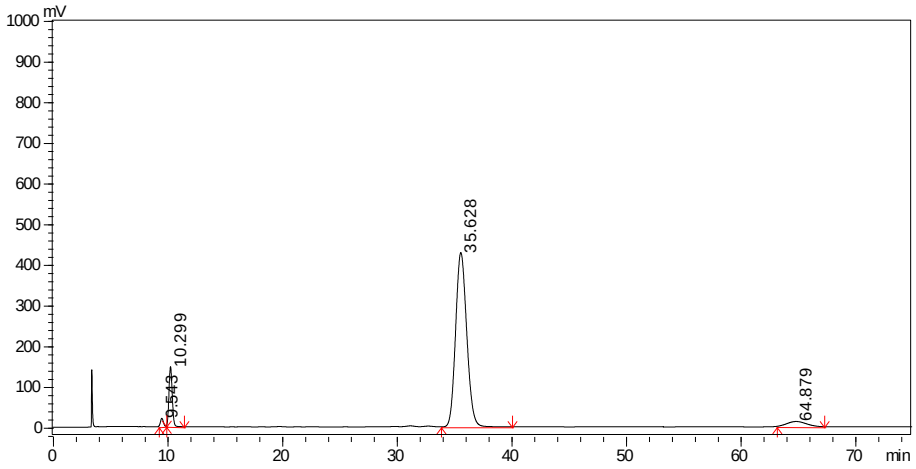
#	Ret Time (min)	Height (mV)	Area (mV.sec)	Area (%)
1	7.443	16704	235457	1.011
2	8.522	88975	1466232	6.293
3	20.066	556164	20942370	89.878
4	52.554	6362	656766	2.819
Total		668206	23300826	100.000

HPLC chromatogram of compound **5c** (10:1 dr and 91% ee)



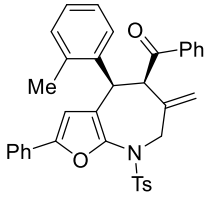


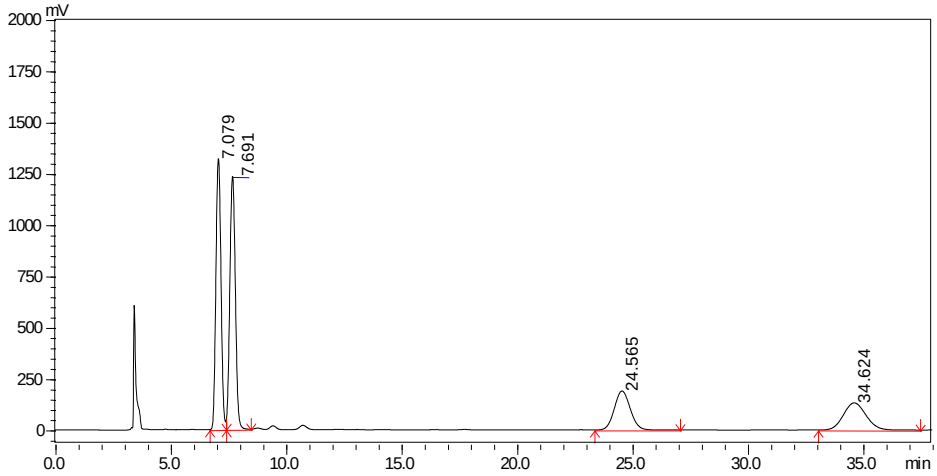
#	Ret Time (min)	Height (mV)	Area (mV.sec)	Area (%)
1	9.571	1836652	34190089	39.333
2	10.328	1742827	34819615	40.058
3	35.906	131703	8982252	10.333
4	65.067	70008	8931926	10.276
Total		3781191	86923882	100.000



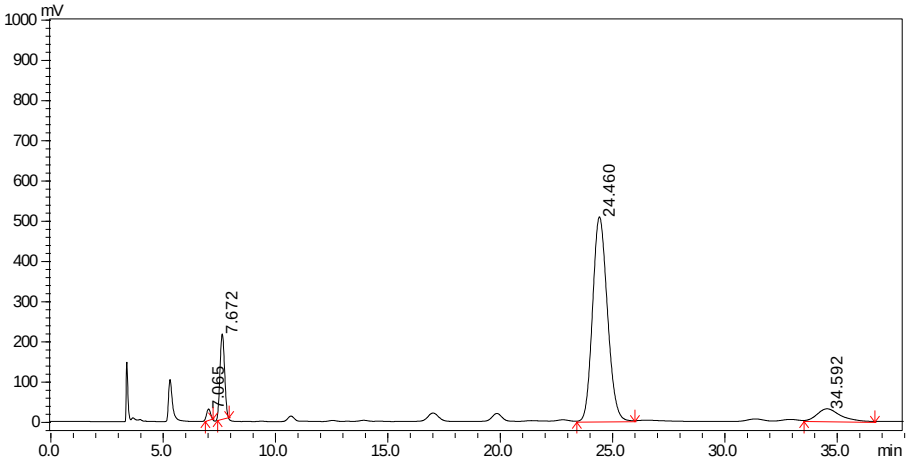
#	Ret Time (min)	Height (mV)	Area (mV.sec)	Area (%)
1	9.543	20079	350464	1.045
2	10.299	146727	2884909	8.603
3	35.628	428181	28875075	86.104
4	64.879	12286	1424772	4.249
Total		607274	33535220	100.000

HPLC chromatogram of compound **5d** (8:1 dr and 84% ee)



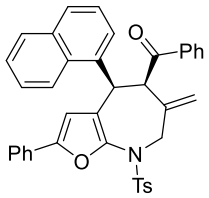


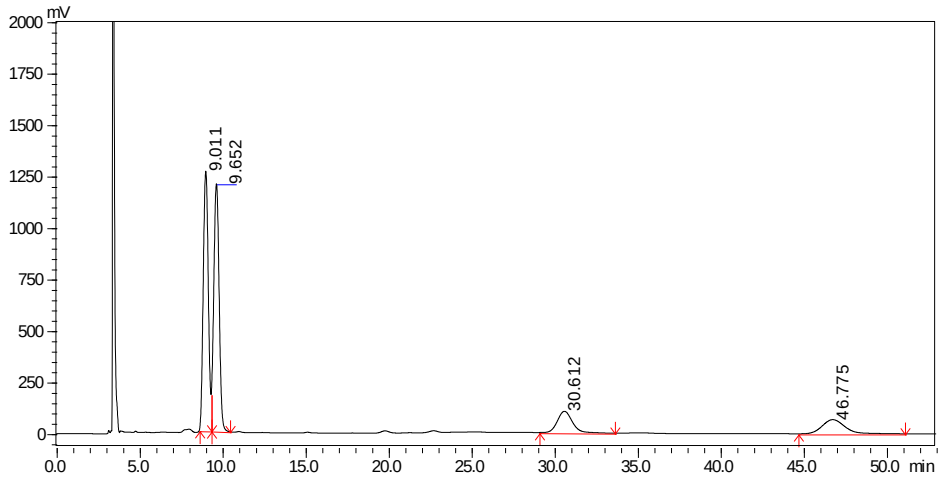
#	Ret Time (min)	Height (mV)	Area (mV.sec)	Area (%)
1	7.079	1319894	20317508	34.459
2	7.691	1233112	20597107	34.933
3	24.565	189868	9078211	15.397
4	34.624	132395	8969052	15.212
Total		2875269	58961878	100.000



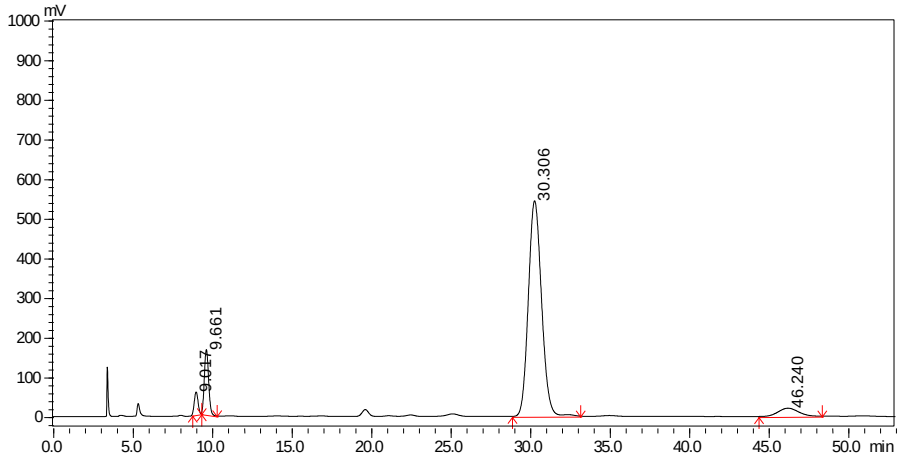
#	Ret Time (min)	Height (mV)	Area (mV.sec)	Area (%)
1	7.065	25124	282143	0.993
2	7.672	209139	2943600	10.364
3	24.460	507687	23147801	81.499
4	34.592	29819	2028995	7.144
Total		771768	28402539	100.000

HPLC chromatogram of compound **5e** (9:1 dr and 89% ee)



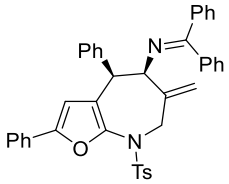


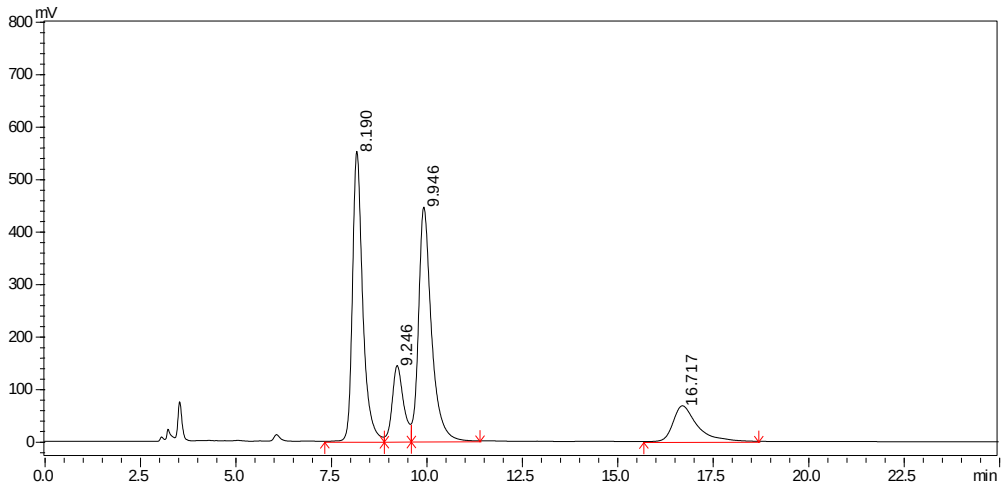
#	Ret Time (min)	Height (mV)	Area (mV.sec)	Area (%)
1	9.011	1261699	26448062	39.624
2	9.652	1202211	27262905	40.845
3	30.612	104240	6531046	9.785
4	46.775	68758	6504960	9.746
Total		2636908	66746973	100.000



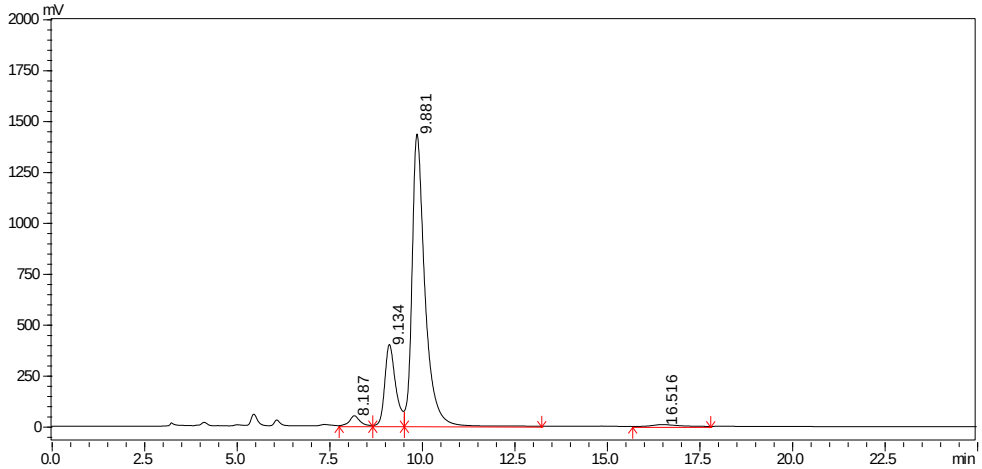
#	Ret Time (min)	Height (mV)	Area (mV.sec)	Area (%)
1	9.017	57030	920641	2.483
2	9.661	163445	3041863	8.202
3	30.306	543350	31341749	84.514
4	46.240	20472	1780402	4.801
Total		784297	37084655	100.000

HPLC chromatogram of compound **7a** (4:1 dr and 95%/91% ee)



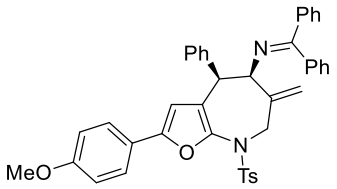


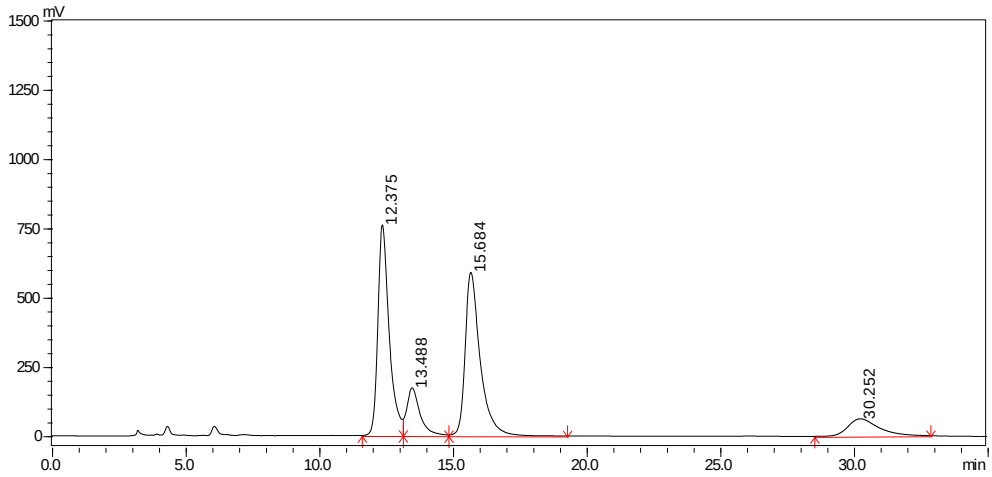
#	Ret Time (min)	Height (mV)	Area (mV.sec)	Area (%)
1	8.190	552116	10290370	38.636
2	9.246	144036	2927408	10.991
3	9.946	445765	10455413	39.256
4	16.717	68008	2960941	11.117
Total		1209924	26634133	100.000



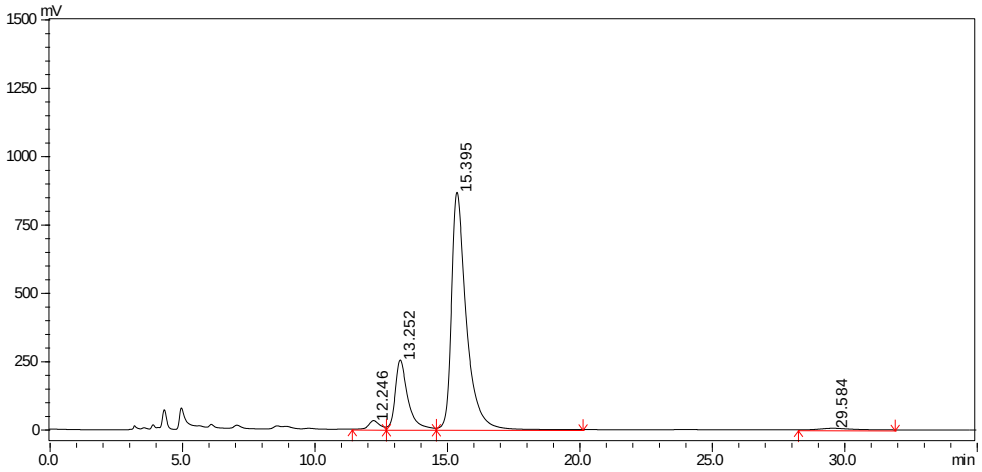
#	Ret Time (min)	Height (mV)	Area (mV.sec)	Area (%)
1	8.187	48924	928569	2.118
2	9.134	399475	8065675	18.400
3	9.881	1433840	34454875	78.602
4	16.516	8995	385246	0.879
Total		1891234	43834365	100.000

HPLC chromatogram of compound **7b** (4:1 dr and 95%/90% ee)



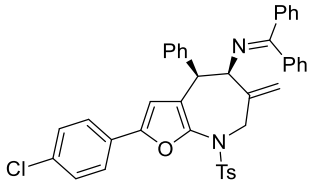


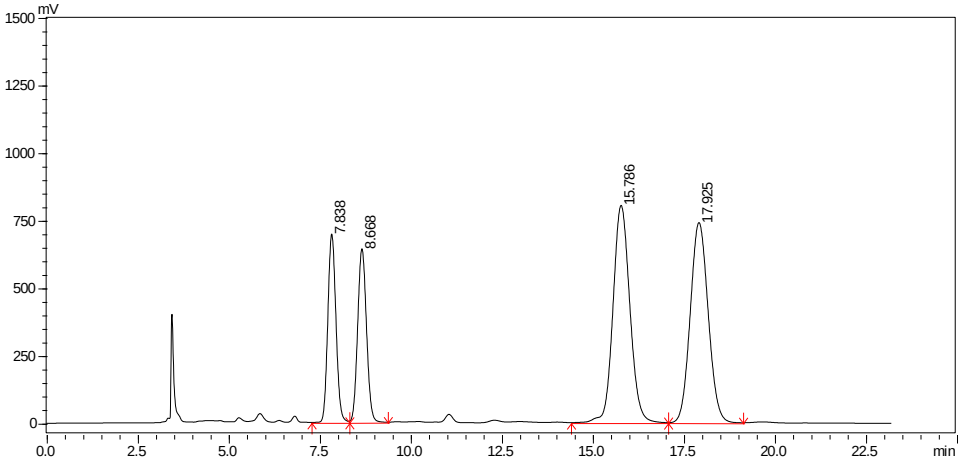
#	Ret Time (min)	Height (mV)	Area (mV.sec)	Area (%)
1	12.375	759795	22300572	39.629
2	13.488	172419	6012866	10.685
3	15.684	589714	23004747	40.880
4	30.252	62434	4955506	8.806
Total		1584363	56273691	100.000



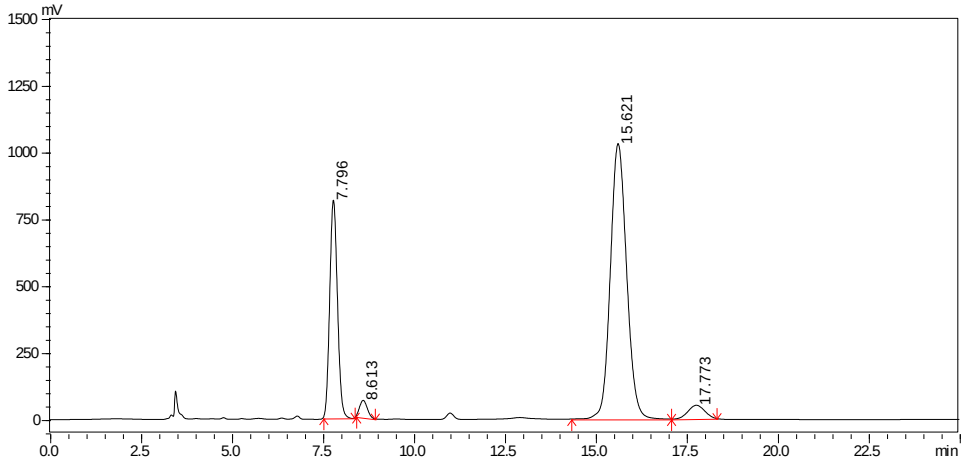
#	Ret Time (min)	Height (mV)	Area (mV.sec)	Area (%)
1	12.246	31659	892600	2.068
2	13.252	253520	8312493	19.257
3	15.395	867139	33508003	77.628
4	29.584	5878	451993	1.047
Total		1158196	43165090	100.000

HPLC chromatogram of compound **7c** (3:1 dr and 91%/86% ee)



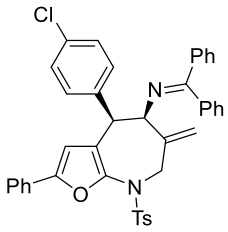


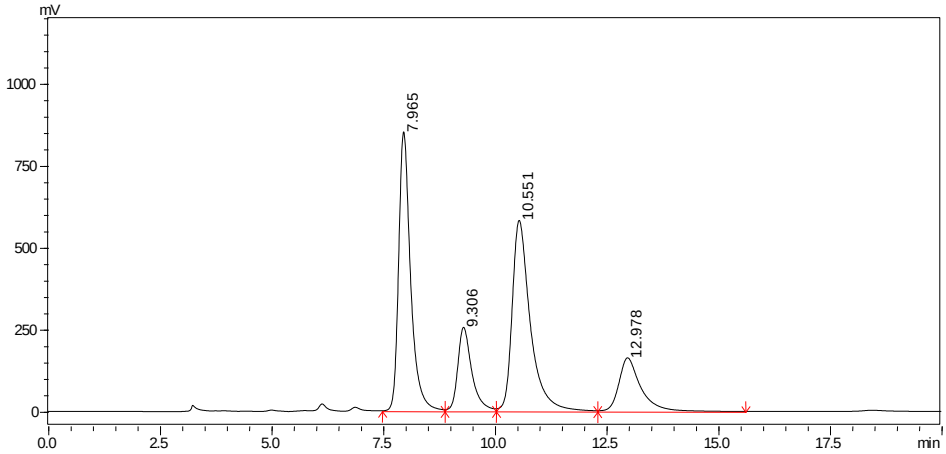
#	Ret Time (min)	Height (mV)	Area (mV.sec)	Area (%)
1	7.838	696268	10808416	14.853
2	8.668	641686	10817070	14.865
3	15.786	803366	25843099	35.515
4	17.925	740083	25298602	34.766
Total		2881403	72767186	100.000



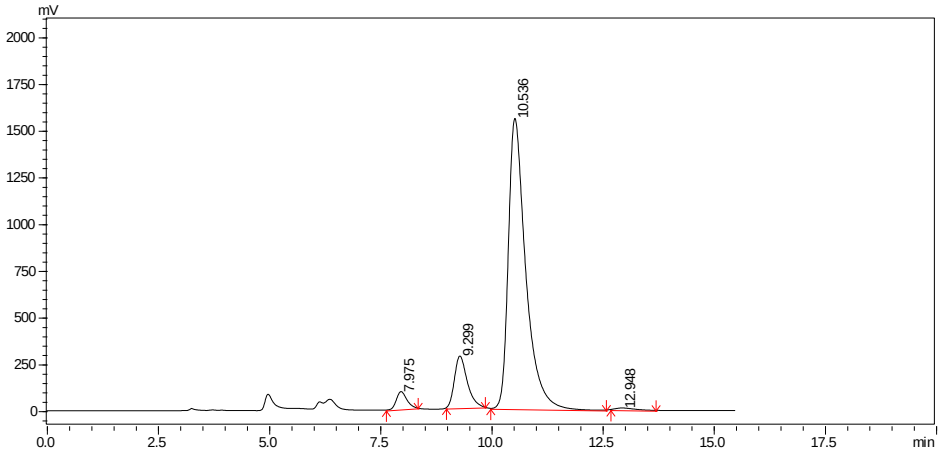
#	Ret Time (min)	Height (mV)	Area (mV.sec)	Area (%)
1	7.796	814802	11984428	25.785
2	8.613	63595	922624	1.985
3	15.621	1030333	31993100	68.834
4	17.773	50284	1578340	3.396
Total		1959013	46478493	100.000

HPLC chromatogram of compound **7d** (5:1 dr and 93%/93% ee)



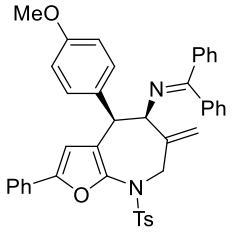


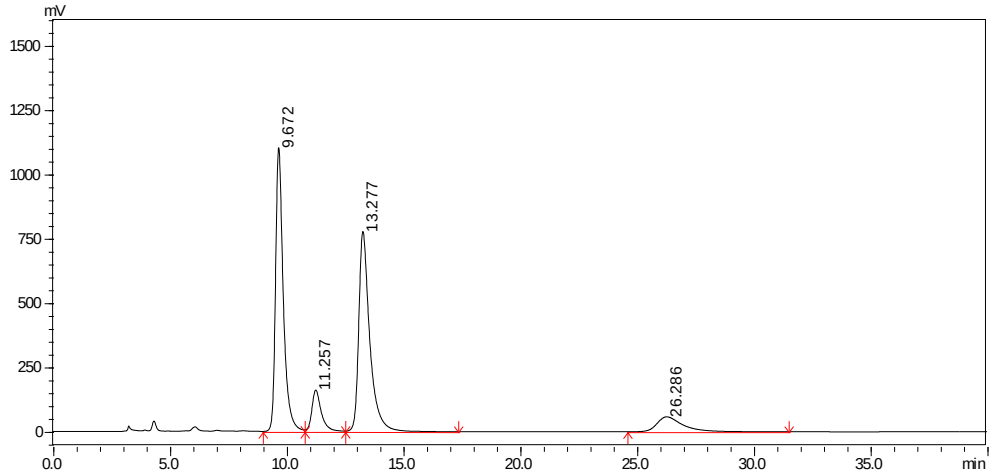
#	Ret Time (min)	Height (mV)	Area (mV.sec)	Area (%)
1	7.965	851046	15772416	36.522
2	9.306	255012	5553895	12.860
3	10.551	581290	16368229	37.901
4	12.978	162823	5492106	12.717
Total		1850173	43186646	100.000



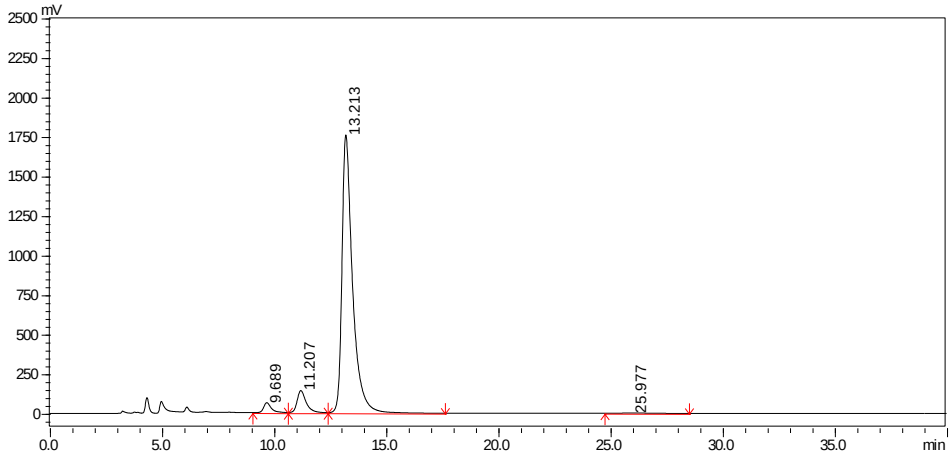
#	Ret Time (min)	Height (mV)	Area (mV.sec)	Area (%)
1	7.975	93484	1500688	3.046
2	9.299	276728	5496445	15.155
3	10.536	1553100	42009241	81.260
4	12.948	9838	265475	0.539
Total		1933150	49271849	100.000

HPLC chromatogram of compound **7e** (6:1 dr and 97%/82% ee)



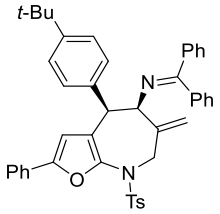


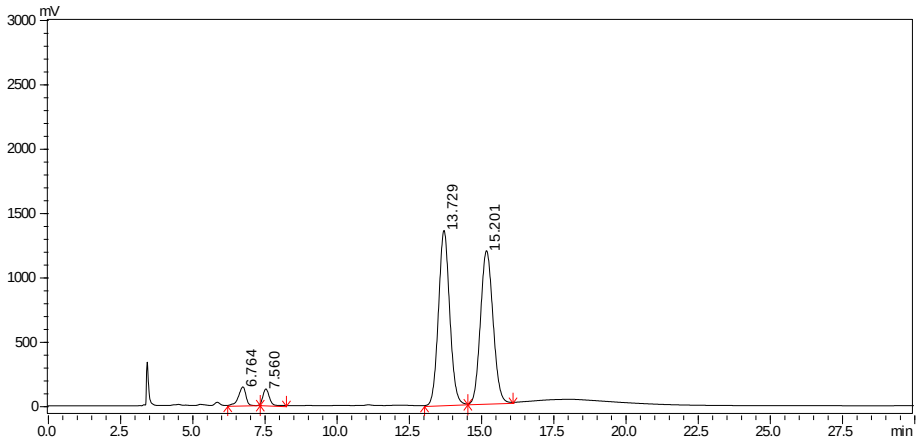
#	Ret Time (min)	Height (mV)	Area (mV.sec)	Area (%)
1	9.672	1102985	25378718	42.364
2	11.257	161090	4556014	7.605
3	13.277	777397	25468201	42.514
4	26.286	58047	4502957	7.517
Total		2099519	59905890	100.000



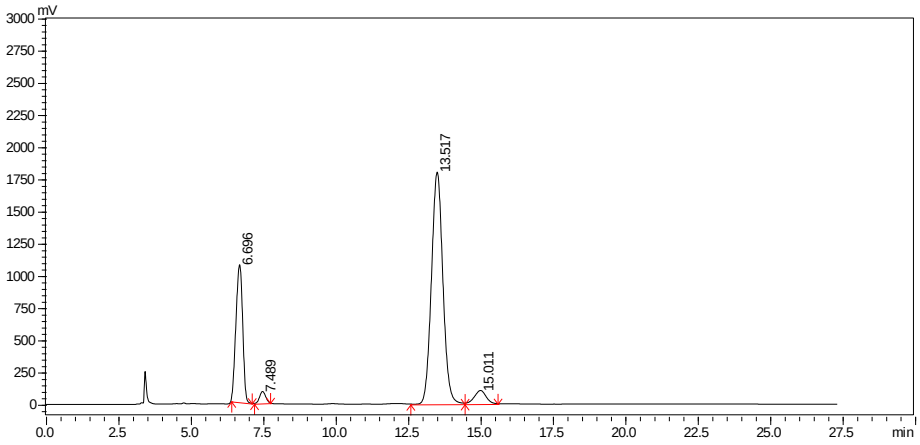
#	Ret Time (min)	Height (mV)	Area (mV.sec)	Area (%)
1	9.689	63453	1521048	1.405
2	11.207	140467	3975221	13.286
3	13.213	1758531	57548217	85.994
4	25.977	2713	199657	1.316
Total		1965164	63244143	100.000

HPLC chromatogram of compound **7f** (3:1 dr and 89%/87% ee)



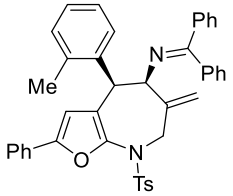


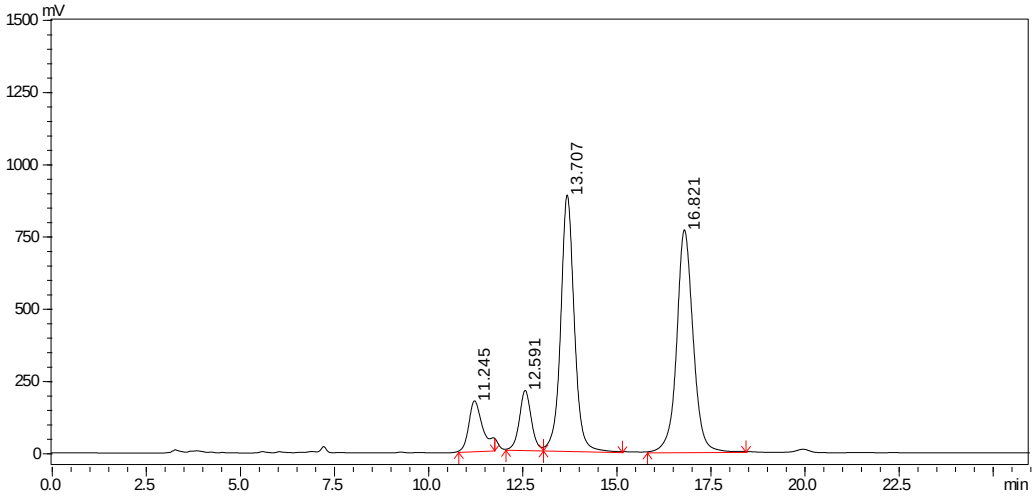
#	Ret Time (min)	Height (mV)	Area (mV.sec)	Area (%)
1	6.764	141311	2328503	3.058
2	7.560	123950	1808219	2.375
3	13.729	1354213	36371216	47.771
4	15.201	1185427	35627927	46.795
Total		2804902	76135864	100.000



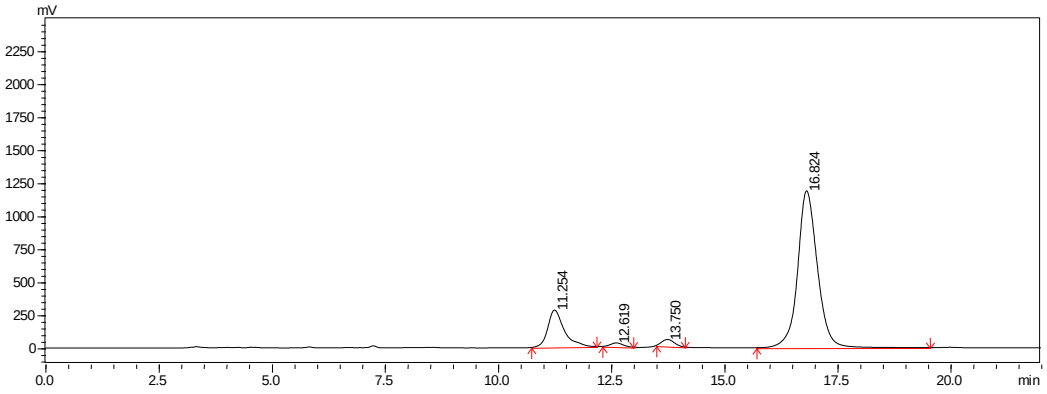
#	Ret Time (min)	Height (mV)	Area (mV.sec)	Area (%)
1	6.696	1066679	17236940	24.385
2	7.489	89114	1249539	1.768
3	13.517	1801231	49337119	69.796
4	15.011	103087	2864428	4.052
Total		3060111	70688025	100.000

HPLC chromatogram of compound **7g** (5:1 dr and 95%/86% ee)



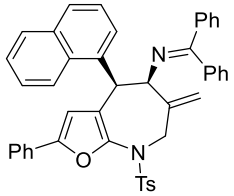


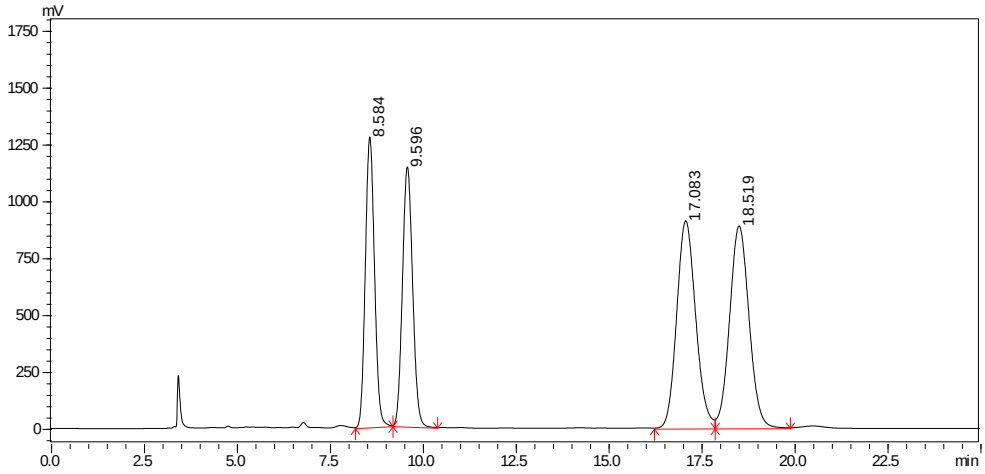
#	Ret Time (min)	Height (mV)	Area (mV.sec)	Area (%)
1	11.245	172932	4383840	8.132
2	12.591	205323	4428669	8.216
3	13.707	884873	21995188	40.803
4	16.821	767926	23097796	42.849
Total		2031055	53905493	100.000



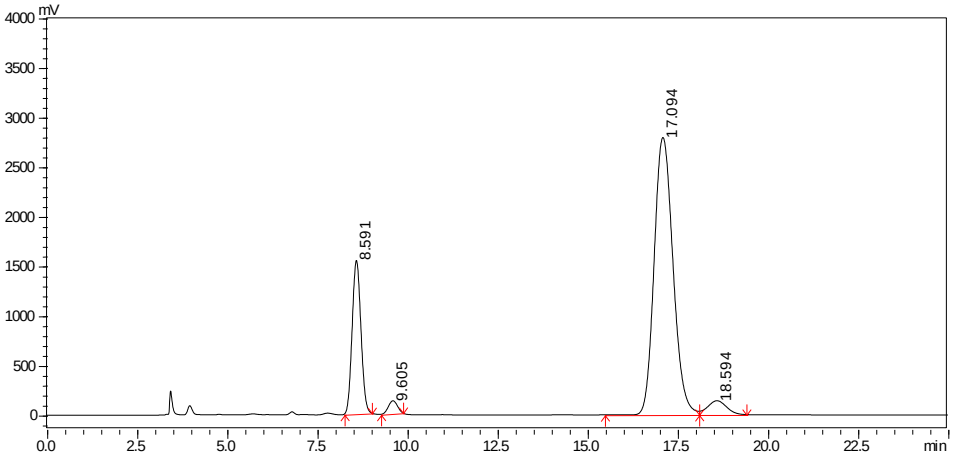
#	Ret Time (min)	Height (mV)	Area (mV.sec)	Area (%)
1	11.254	281045	7045811	15.821
2	12.619	28953	537252	1.206
3	13.750	50740	957501	2.150
4	16.824	1187607	35994582	80.823
Total		1548346	44535145	100.000

HPLC chromatogram of compound **7h** (4:1 dr and 90%/84% ee)



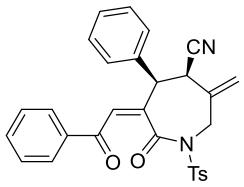


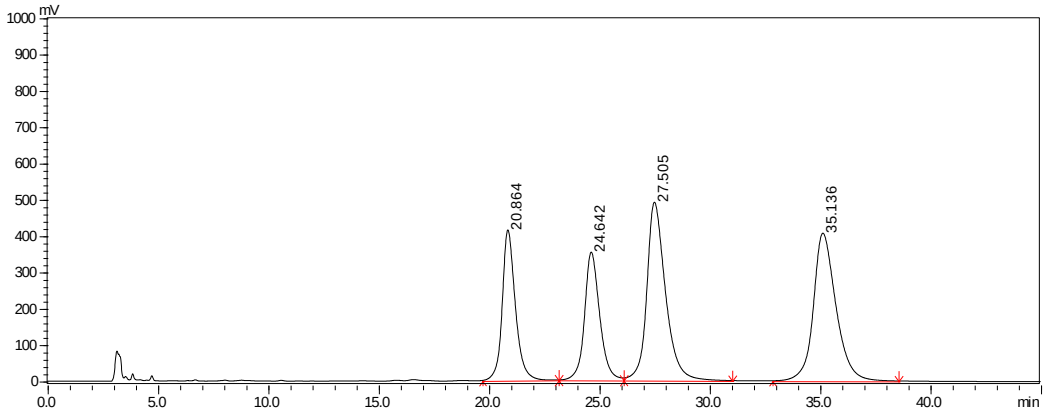
#	Ret Time (min)	Height (mV)	Area (mV.sec)	Area (%)
1	8.584	1275114	21781208	20.193
2	9.596	1140762	21693236	20.111
3	17.083	911170	32171643	29.826
4	18.519	888213	32219974	29.870
Total		4215259	107866061	100.000



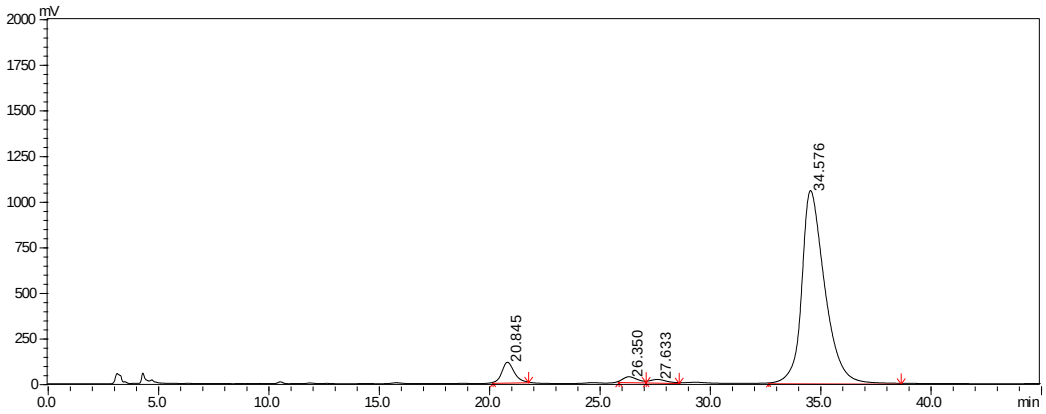
#	Ret Time (min)	Height (mV)	Area (mV.sec)	Area (%)
1	8.591	1543912	26120773	19.376
2	9.605	128296	2201973	1.633
3	17.094	2793514	101359875	75.187
4	18.594	139982	5127659	3.804
Total		4605704	134810279	100.000

HPLC chromatogram of compound **8a** (14:1 dr and 97% ee)



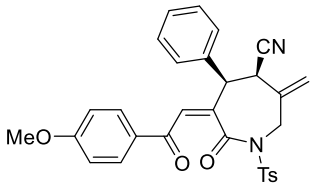


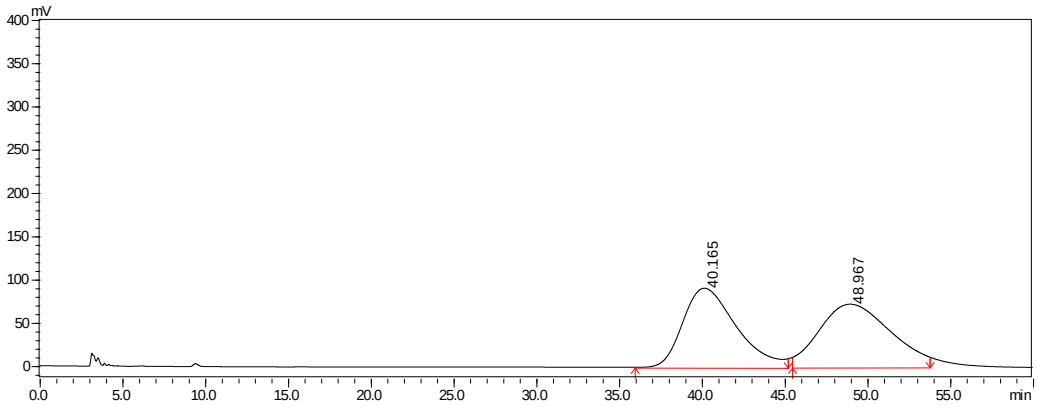
#	Ret Time (min)	Height (mV)	Area (mV.sec)	Area (%)
1	20.864	413780	17024450	18.614
2	24.642	352300	16734831	18.297
3	27.505	490290	28809530	31.499
4	35.136	406701	28893535	31.591
Total		1663070	91462346	100.000



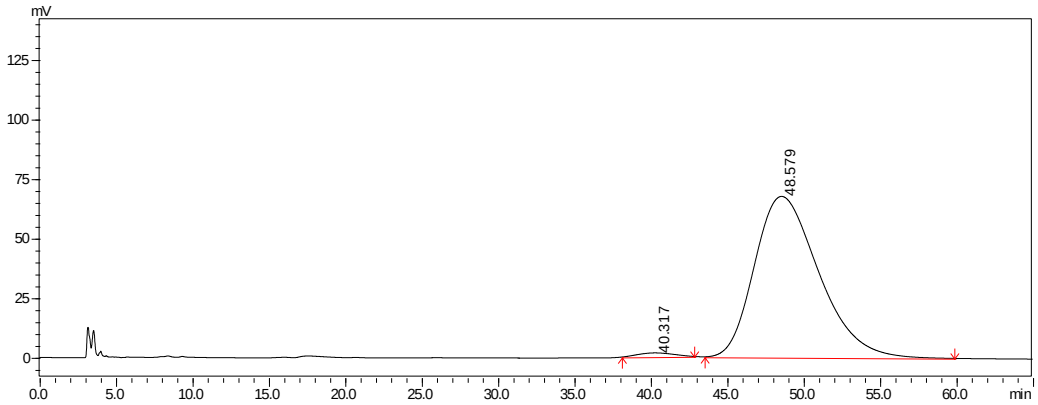
#	Ret Time (min)	Height (mV)	Area (mV.sec)	Area (%)
1	20.845	109732	4108155	5.032
2	26.350	27119	1117142	1.368
3	27.633	15145	687592	0.842
4	34.576	1054606	75732285	92.758
Total		1206602	81645175	100.000

HPLC chromatogram of compound **8b** (97% ee)



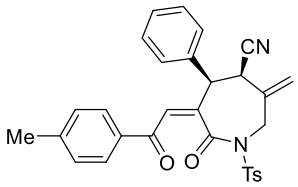


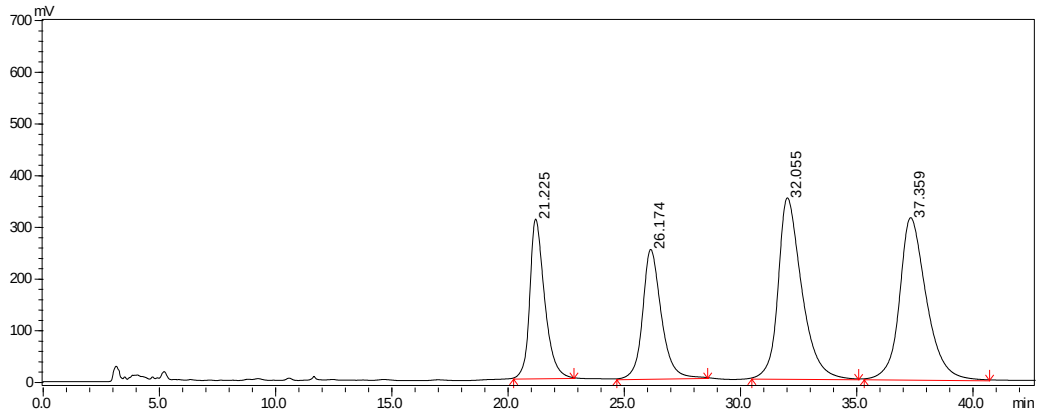
#	Ret Time (min)	Height (mV)	Area (mV.sec)	Area (%)
1	40.165	91464	20466480	48.608
2	48.967	72856	21638464	51.392
Total		164320	42104944	100.000



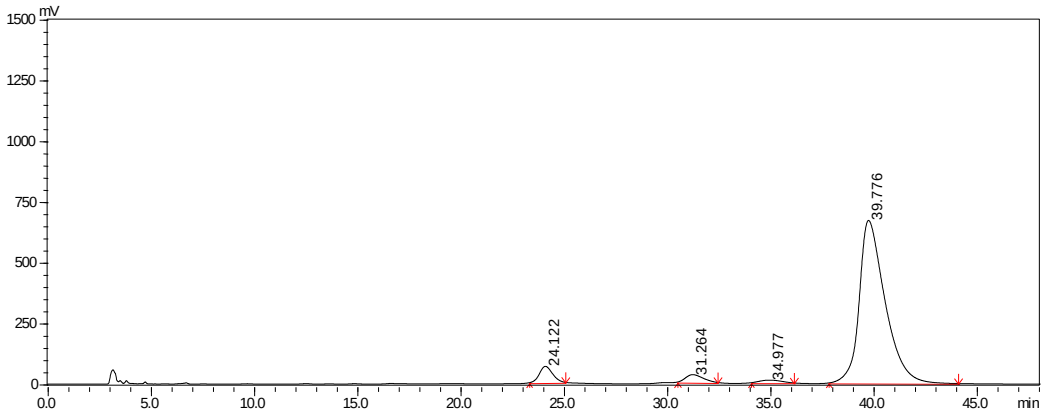
#	Ret Time (min)	Height (mV)	Area (mV.sec)	Area (%)
1	40.317	1632	260188	1.301
2	48.579	67496	19745642	98.699
Total		69128	20005830	100.000

HPLC chromatogram of compound **8c** (12:1 dr and 97% ee)



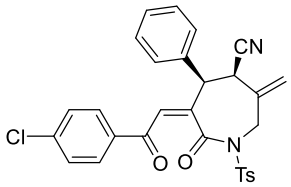


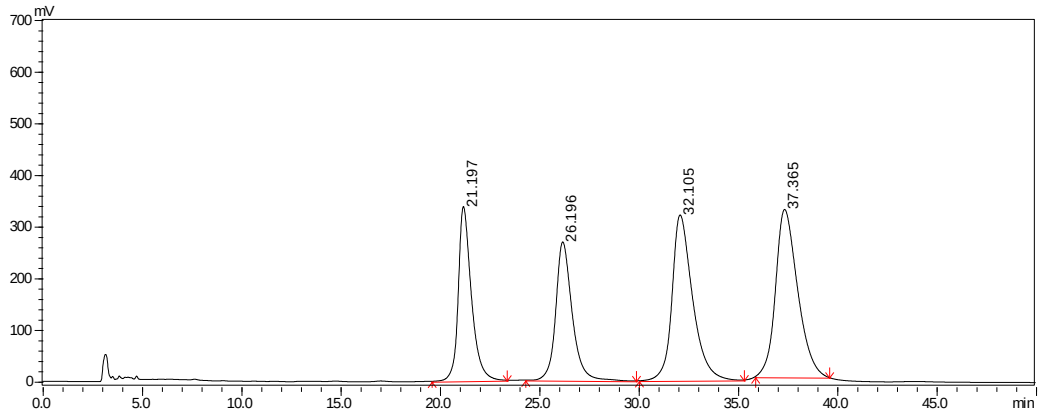
#	Ret Time (min)	Height (mV)	Area (mV.sec)	Area (%)
1	21.225	307283	13499403	17.622
2	26.174	249428	13760642	17.963
3	32.055	349286	24479576	31.955
4	37.359	312592	24866310	32.460
Total		1218590	76605931	100.000



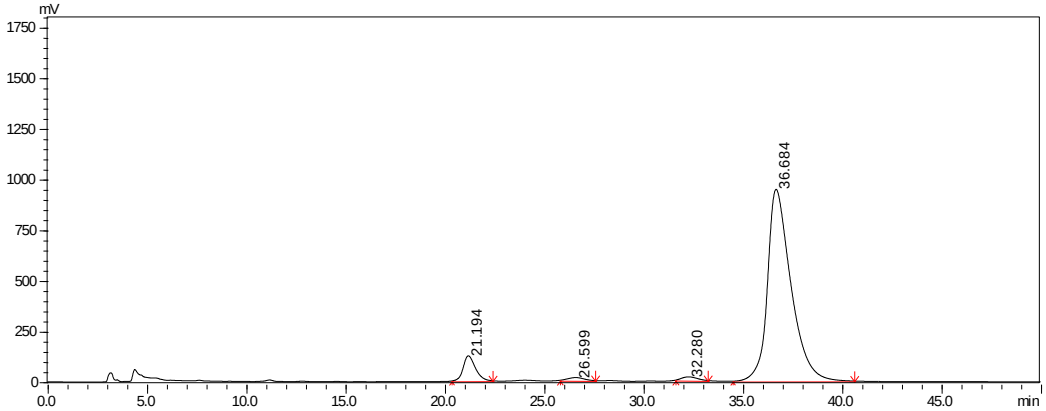
#	Ret Time (min)	Height (mV)	Area (mV.sec)	Area (%)
1	24.122	66722	2906151	4.560
2	31.264	31332	1793237	2.814
3	34.977	11033	783205	1.229
4	39.776	669639	58248563	91.397
Total		778727	63731155	100.000

HPLC chromatogram of compound **8d** (13:1 dr and 98% ee)



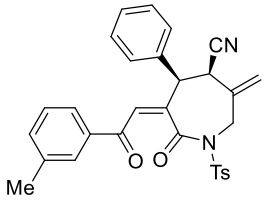


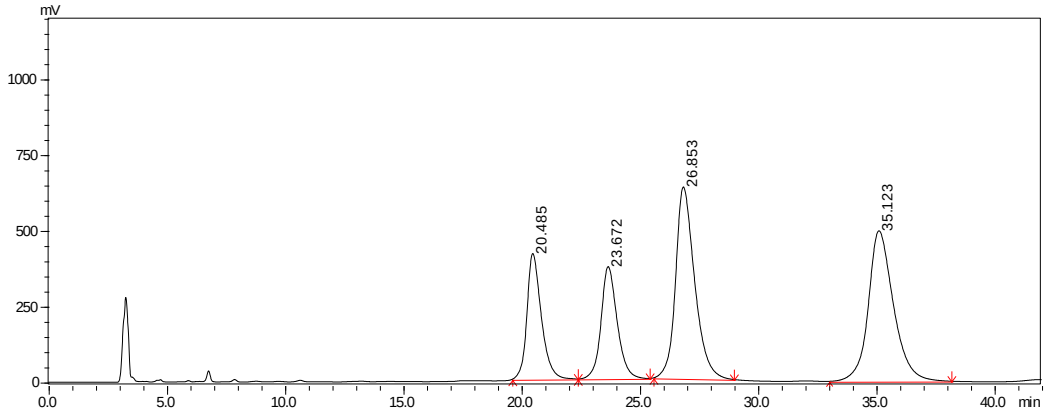
#	Ret Time (min)	Height (mV)	Area (mV.sec)	Area (%)
1	21.197	337359	15433232	19.591
2	26.196	267990	15284503	19.402
3	32.105	320476	22968557	29.156
4	37.365	324449	25090528	31.850
Total		1250274	78776820	100.00



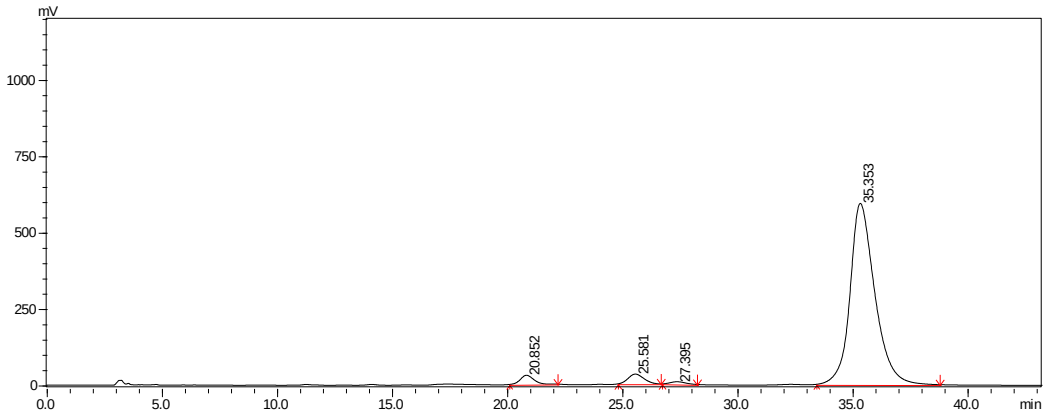
#	Ret Time (min)	Height (mV)	Area (mV.sec)	Area (%)
1	21.194	124138	5255187	6.202
2	26.599	14313	783419	0.925
3	32.280	17275	896592	1.058
4	36.684	946700	77803604	91.816
Total		1102426	84738802	100.000

HPLC chromatogram of compound **8e** (16:1 dr and 98% ee)



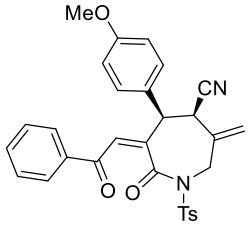


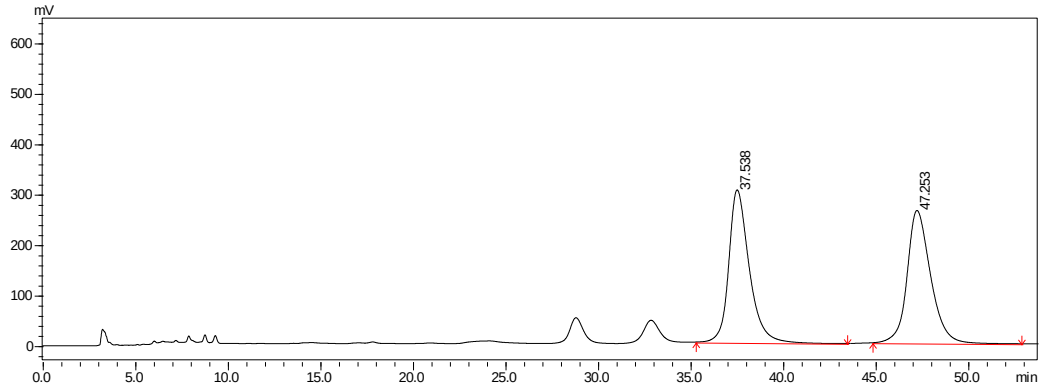
#	Ret Time (min)	Height (mV)	Area (mV.sec)	Area (%)
1	20.485	415080	17503109	16.340
2	23.672	369979	17464149	16.303
3	26.853	631803	35449704	33.093
4	35.123	496386	36703580	34.264
Total		1913248	107120542	100.000



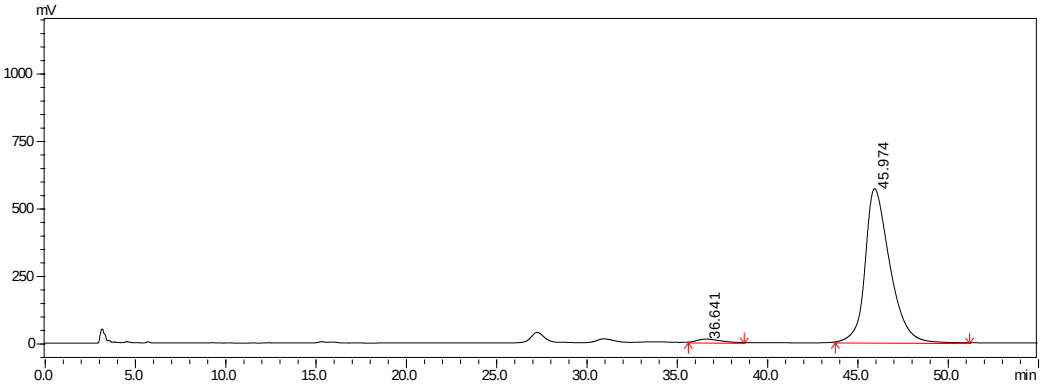
#	Ret Time (min)	Height (mV)	Area (mV.sec)	Area (%)
1	20.852	29864	1197705	2.527
2	25.581	32120	1520363	3.207
3	27.395	7870	346486	0.731
4	35.353	592920	44338955	93.535
Total		662773	47403510	100.000

HPLC chromatogram of compound **8f** (>20:1 dr and 96% ee)





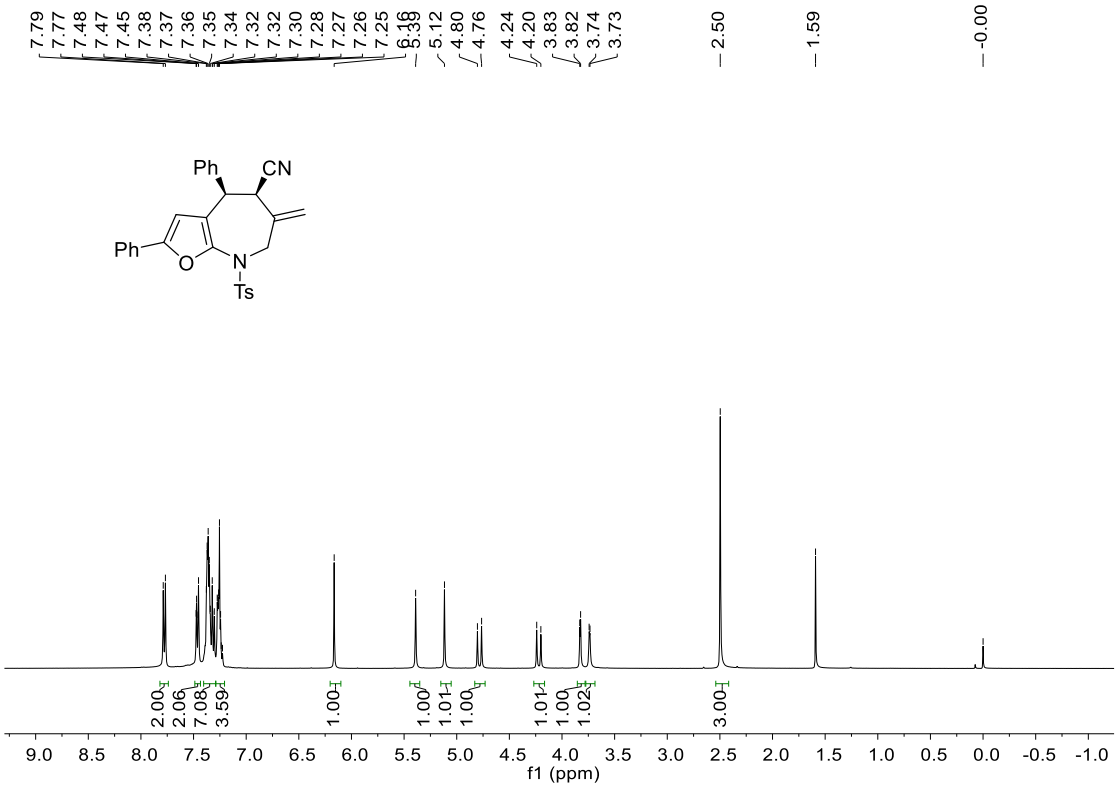
#	Ret Time (min)	Height (mV)	Area (mV.sec)	Area (%)
1	37.538	302581	23148450	50.041
2	47.253	262936	23110077	49.959
Total		565517	46258527	100.000



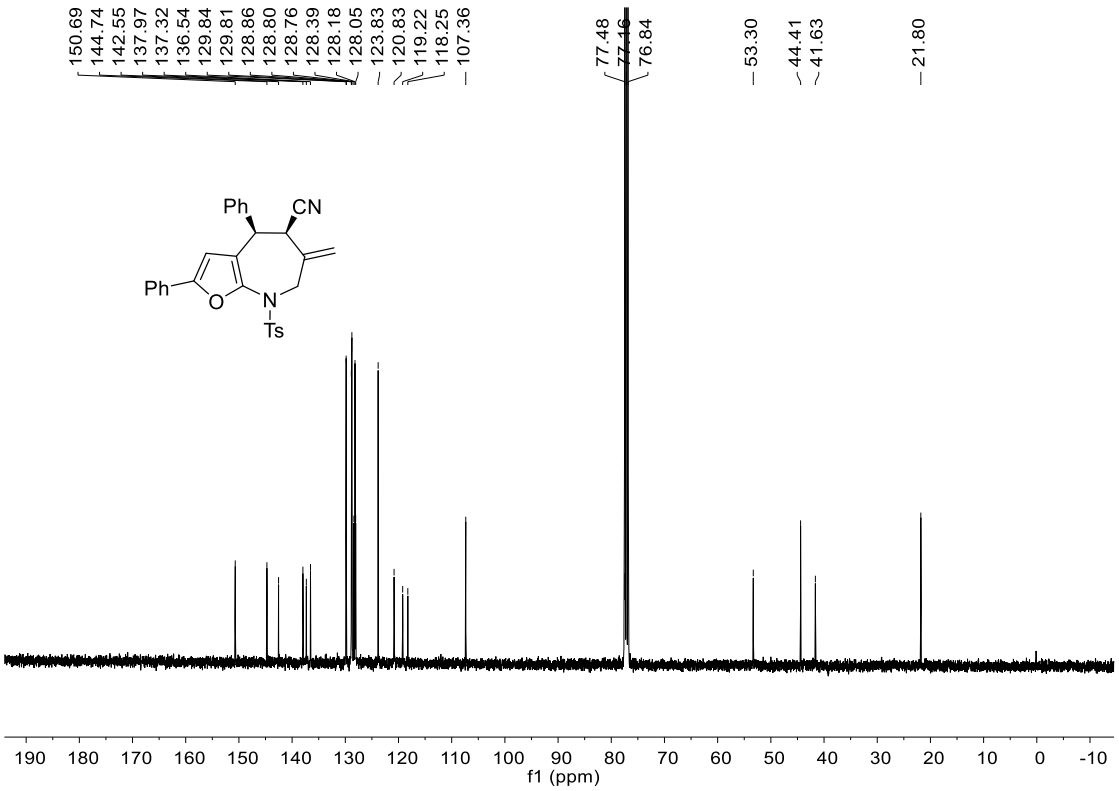
#	Ret Time (min)	Height (mV)	Area (mV.sec)	Area (%)
1	36.641	11901	988467	1.808
2	45.974	569069	53671124	98.192
Total		580971	54659591	100.000

12. ^{1}H NMR, ^{13}C NMR and ^{19}F NMR spectra

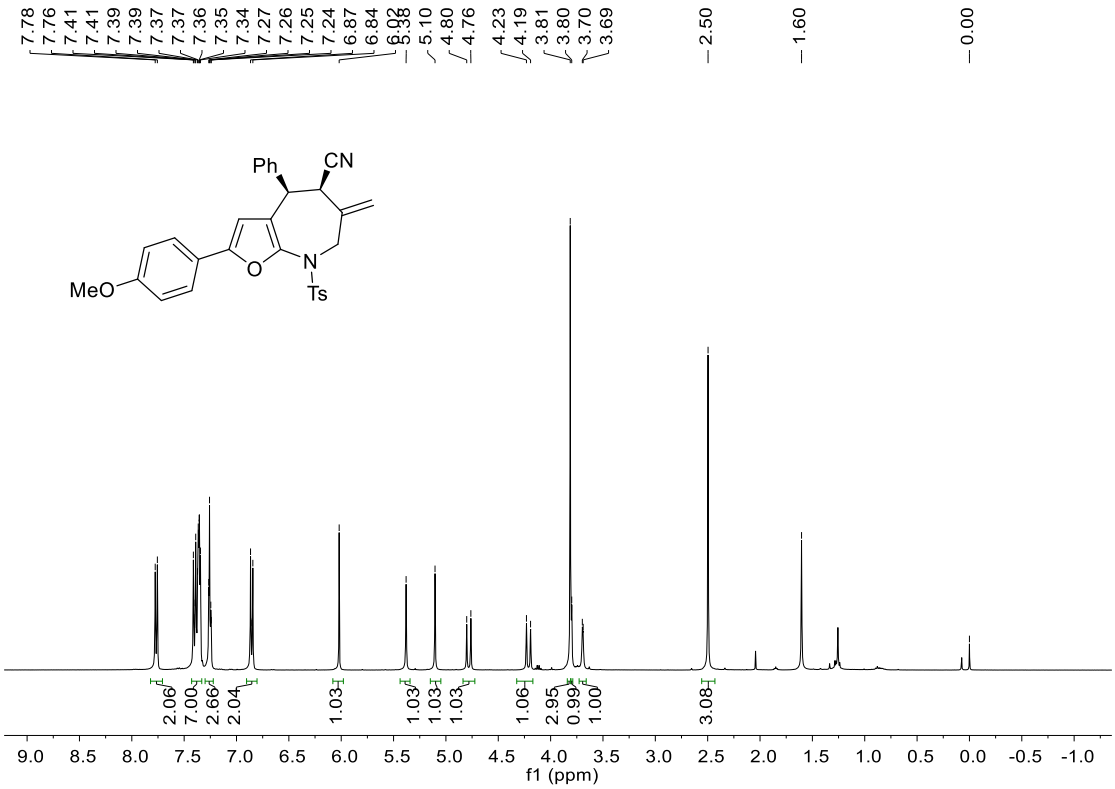
^{1}H NMR (400 MHz) of **3a** in $CDCl_3$



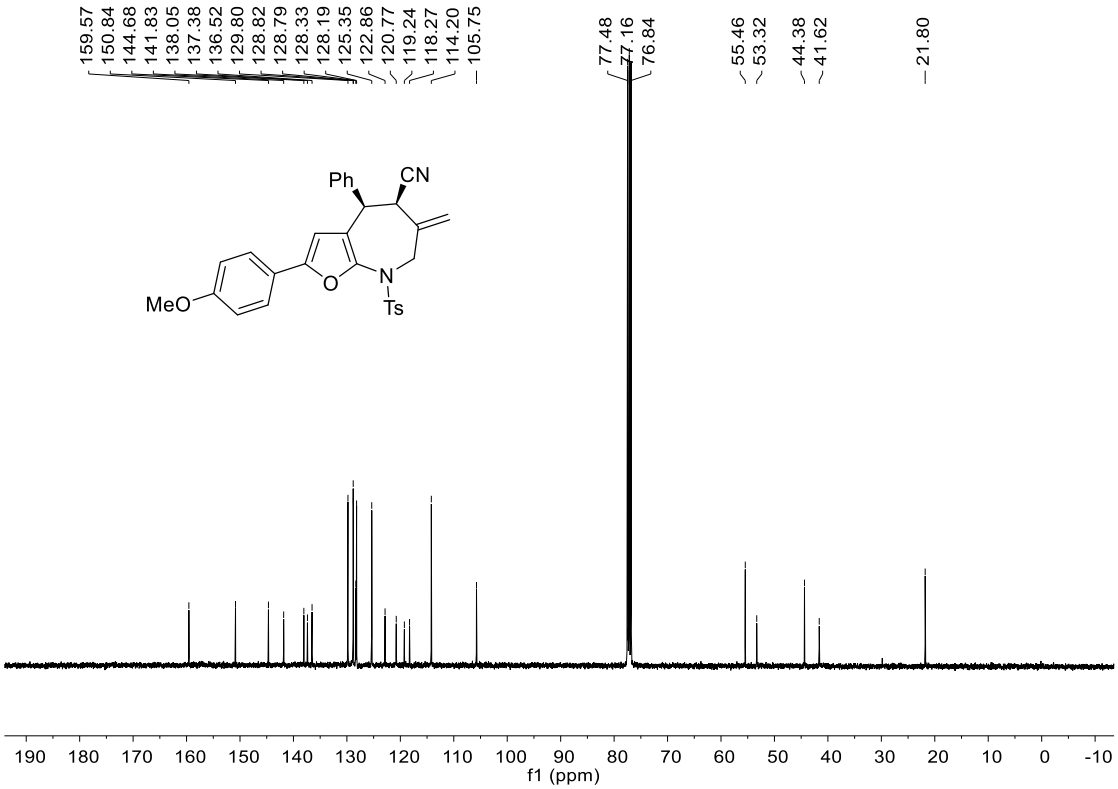
^{13}C NMR (100 MHz) of **3a** in $CDCl_3$



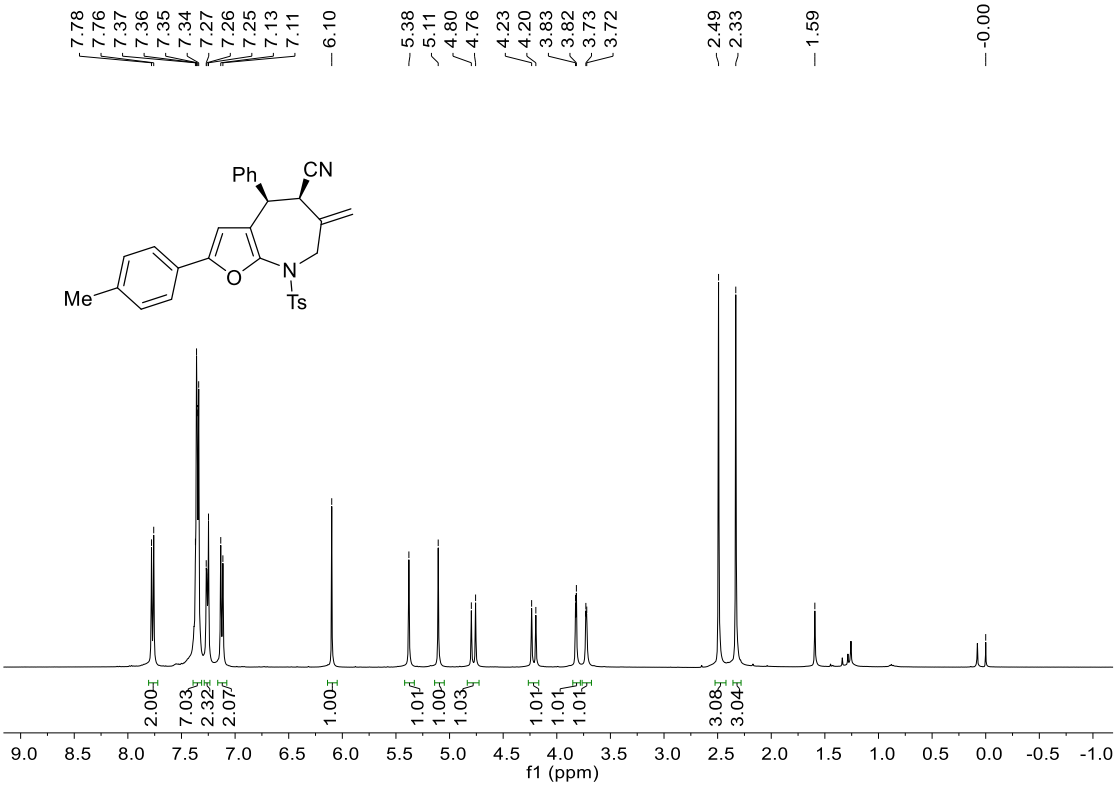
^{1}H NMR (400 MHz) of **3b** in $CDCl_3$



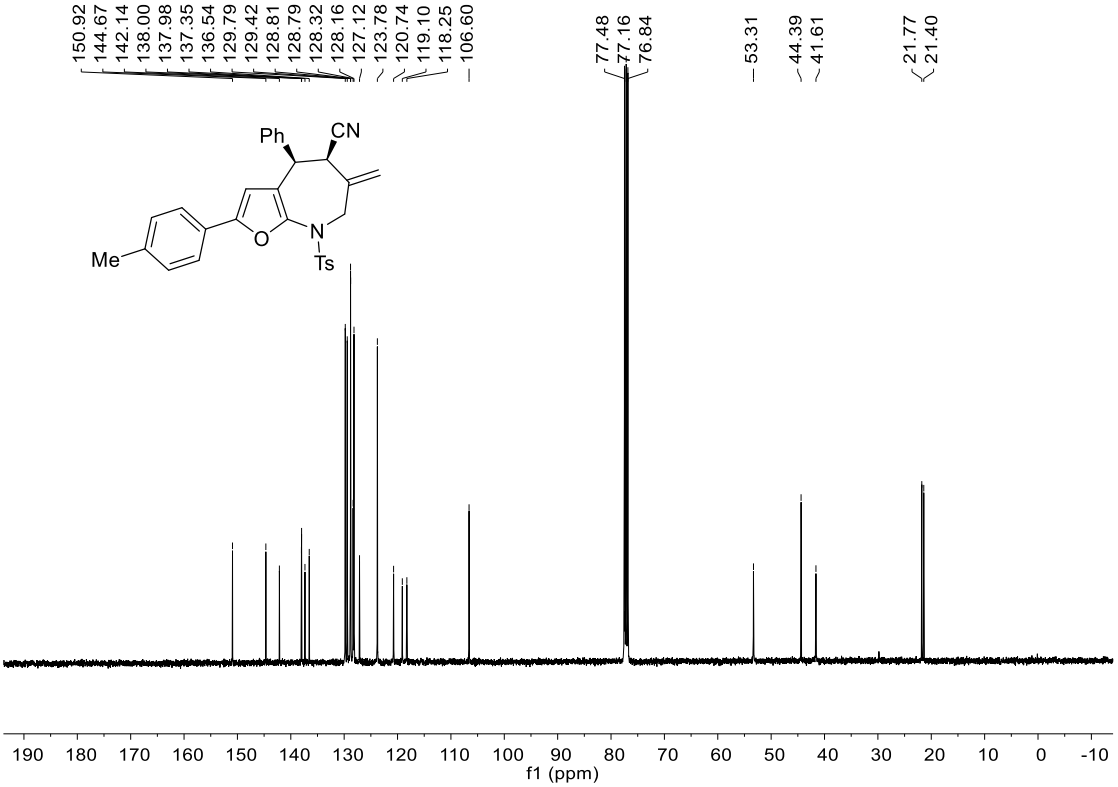
^{13}C NMR (100 MHz) of **3b** in $CDCl_3$



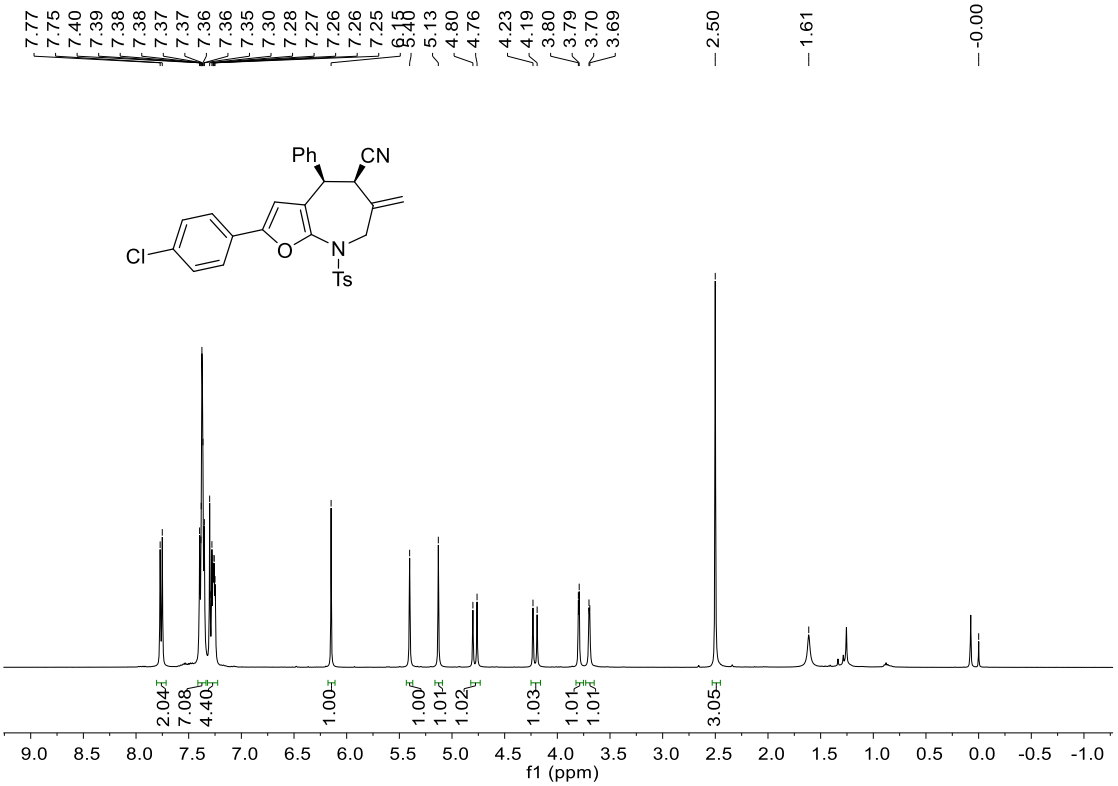
^{1}H NMR (400 MHz) of **3c** in $CDCl_3$



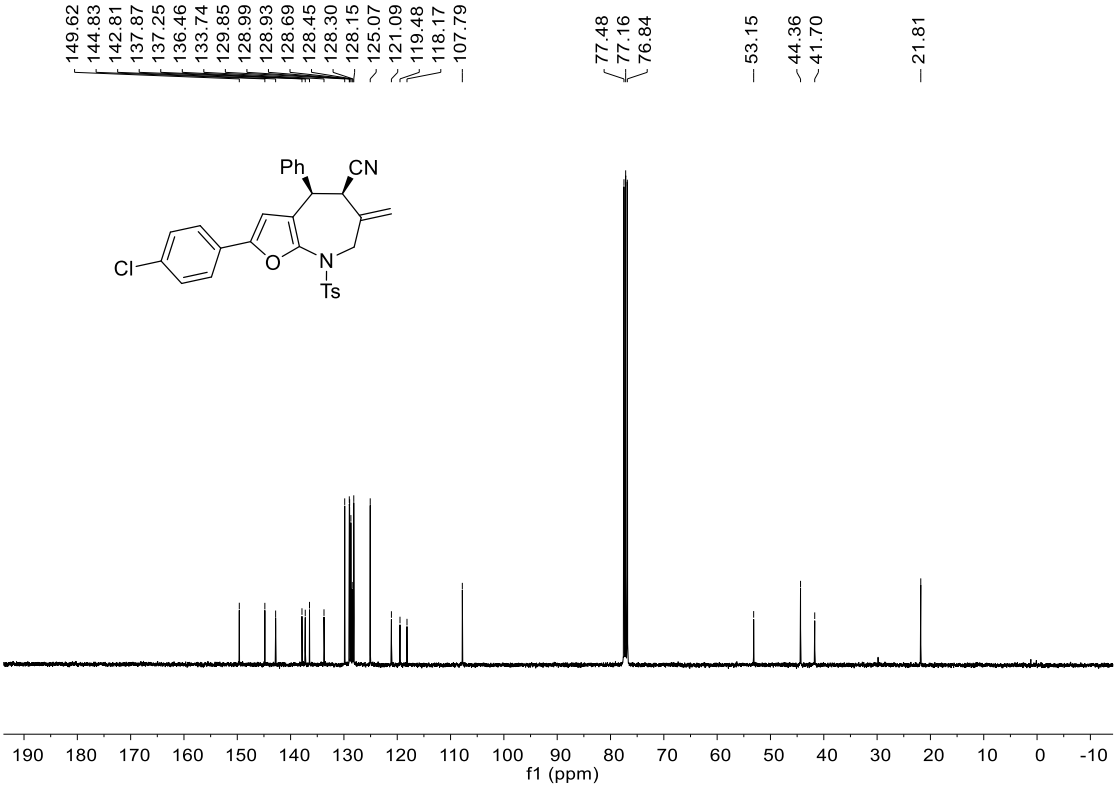
^{13}C NMR (100 MHz) of **3c** in $CDCl_3$



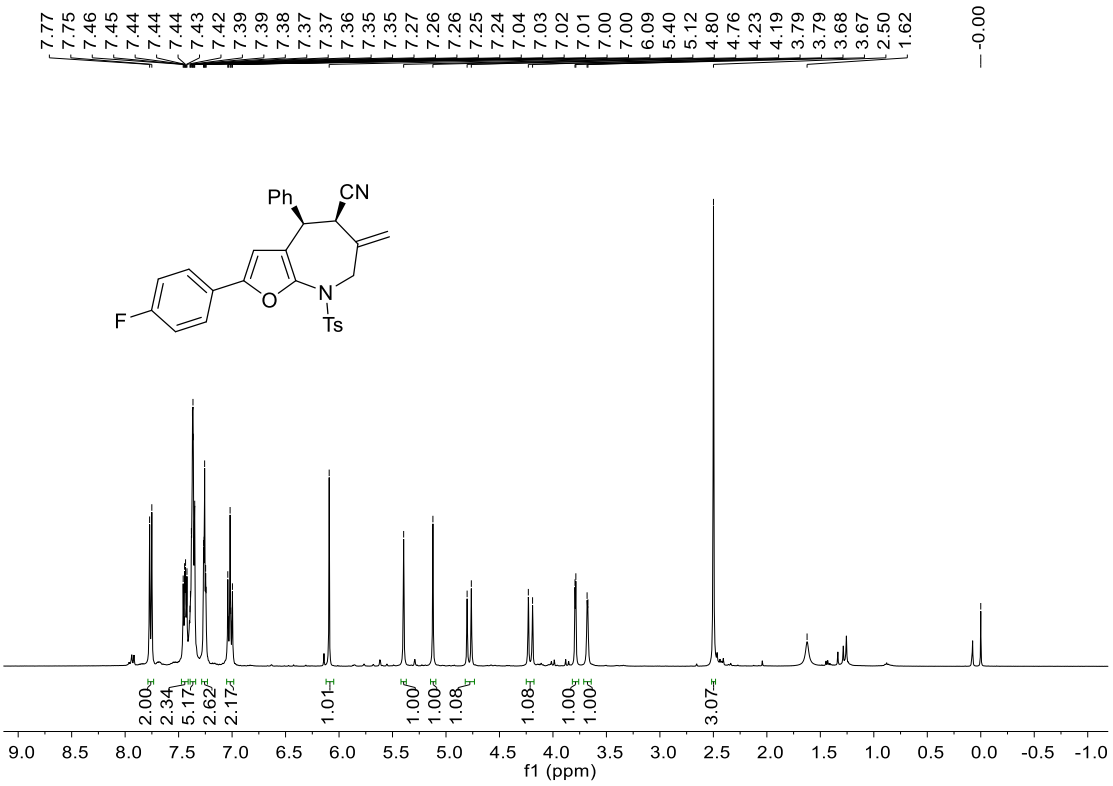
^{1}H NMR (400 MHz) of **3d** in $CDCl_3$



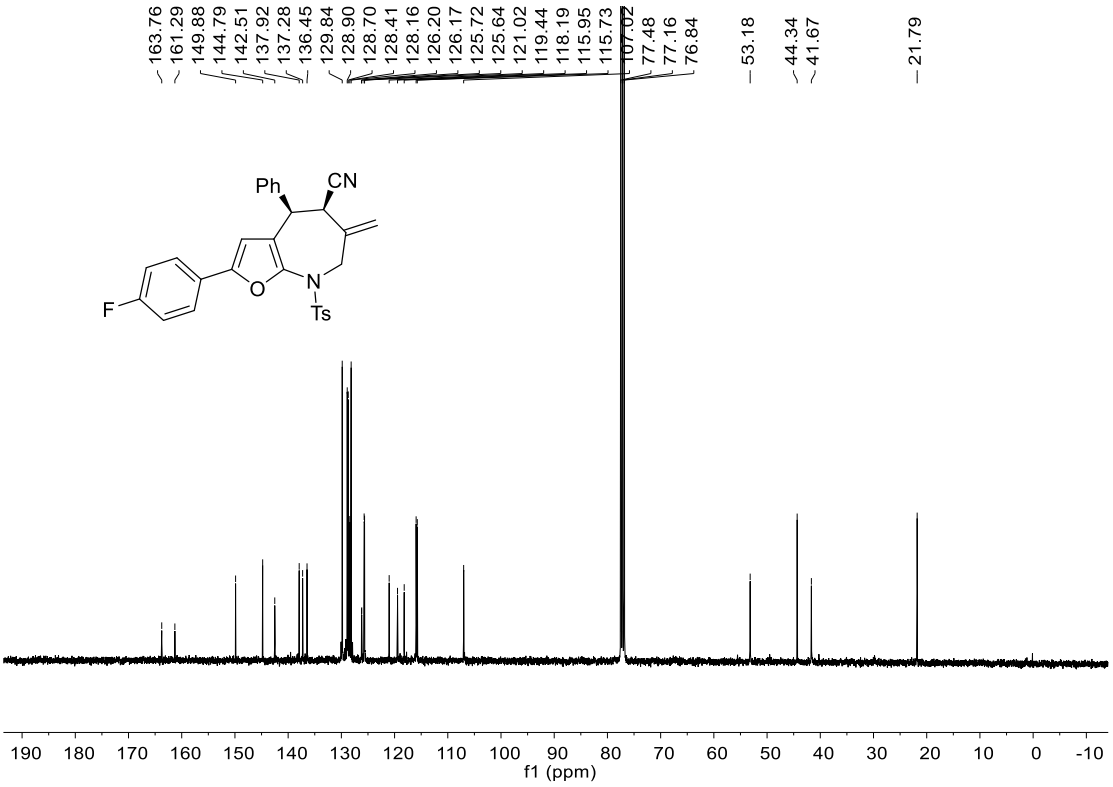
^{13}C NMR (100 MHz) of **3d** in $CDCl_3$



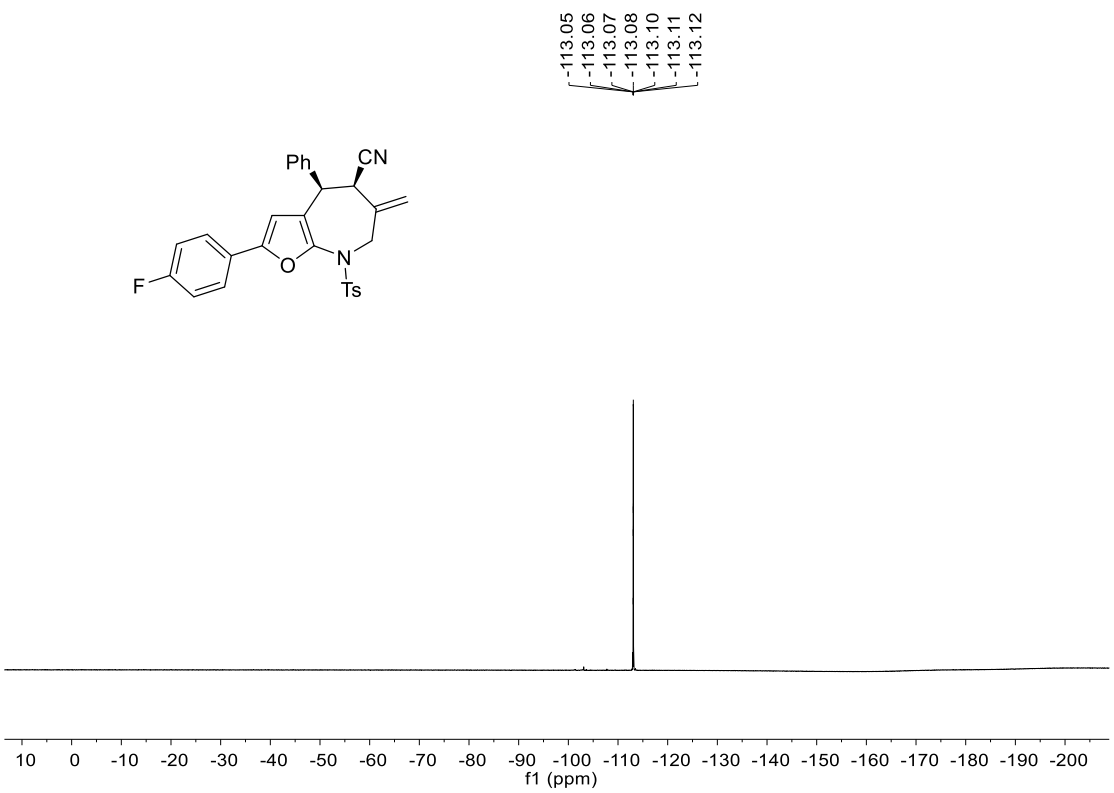
^{1}H NMR (400 MHz) of **3e** in $CDCl_3$



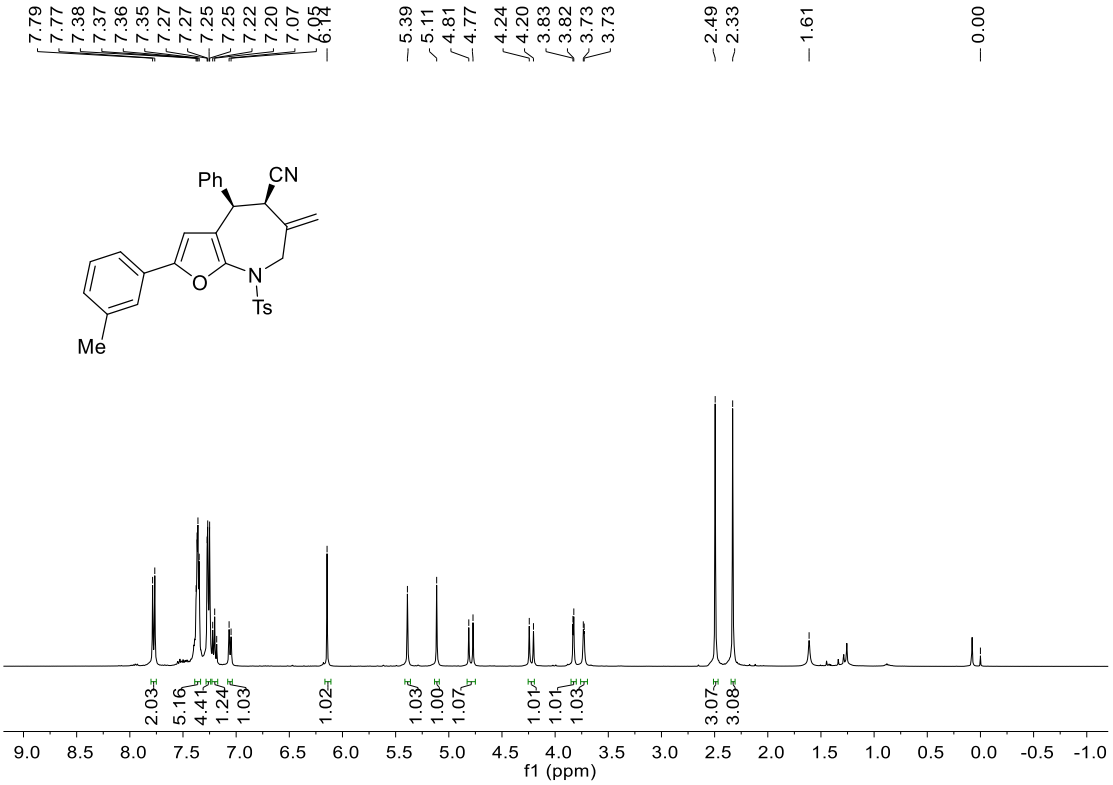
^{13}C NMR (100 MHz) of **3e** in $CDCl_3$



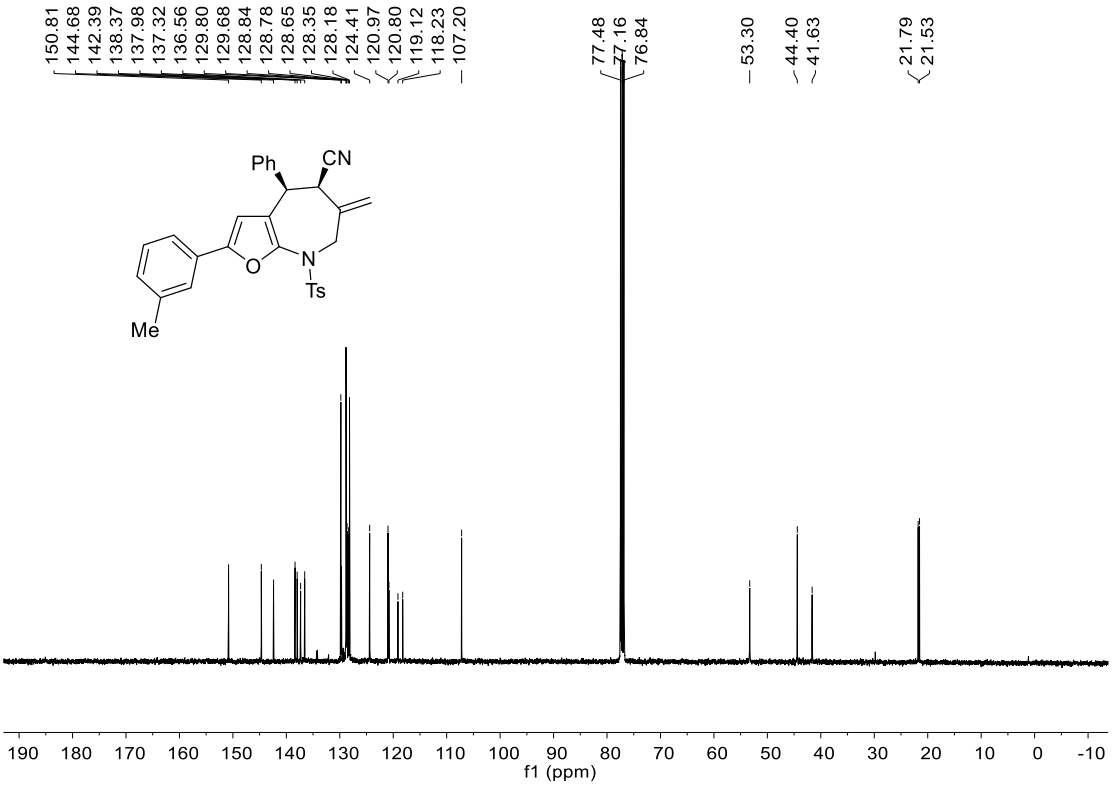
^{19}F NMR (376 MHz) of **3e** in $CDCl_3$



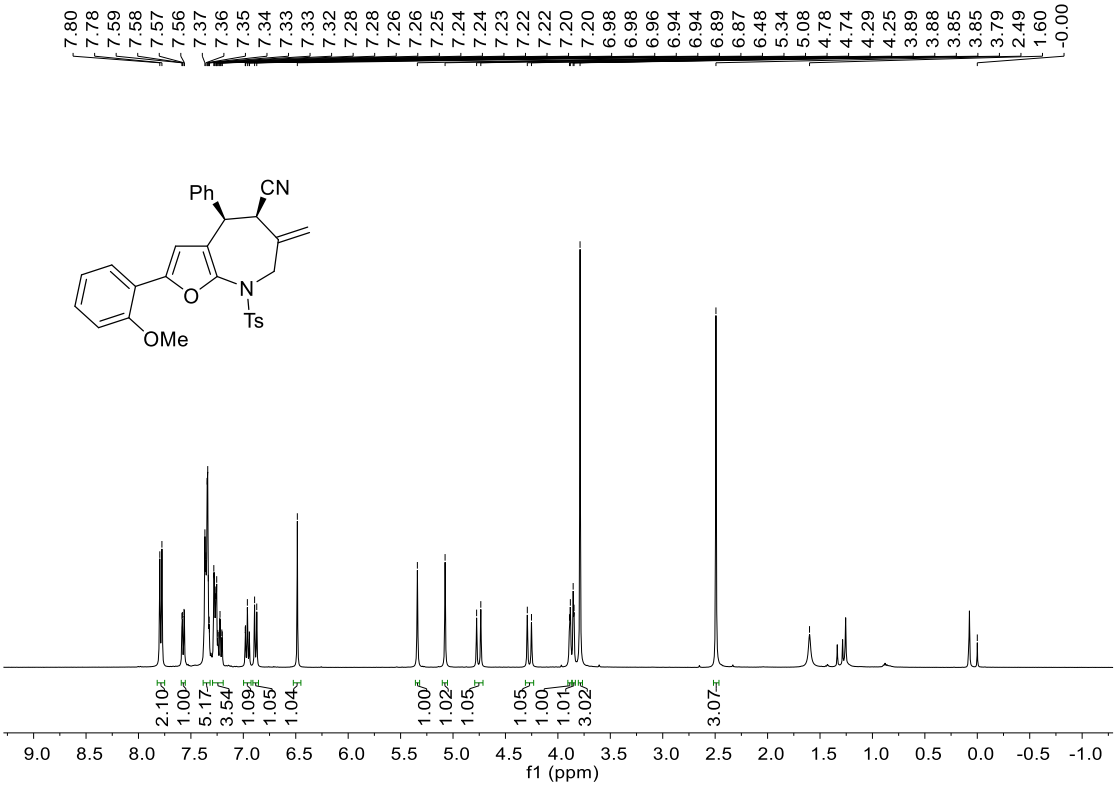
^{1}H NMR (400 MHz) of **3f** in $CDCl_3$



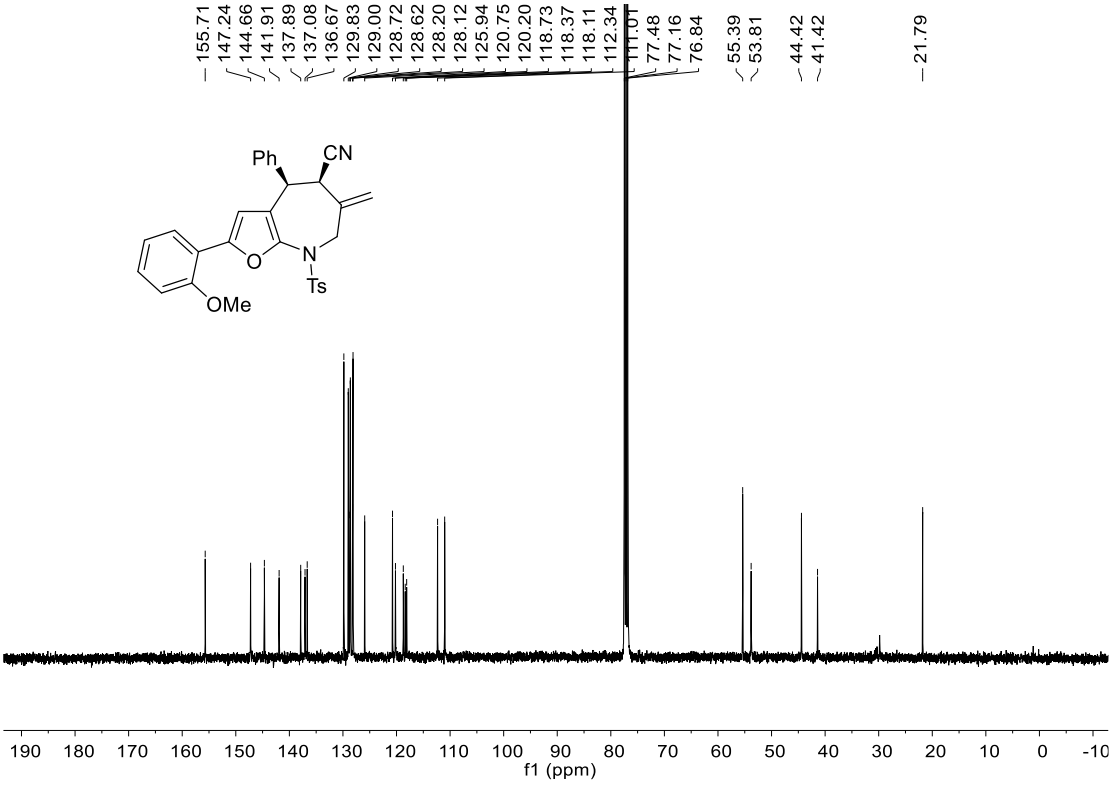
^{13}C NMR (100 MHz) of **3f** in $CDCl_3$



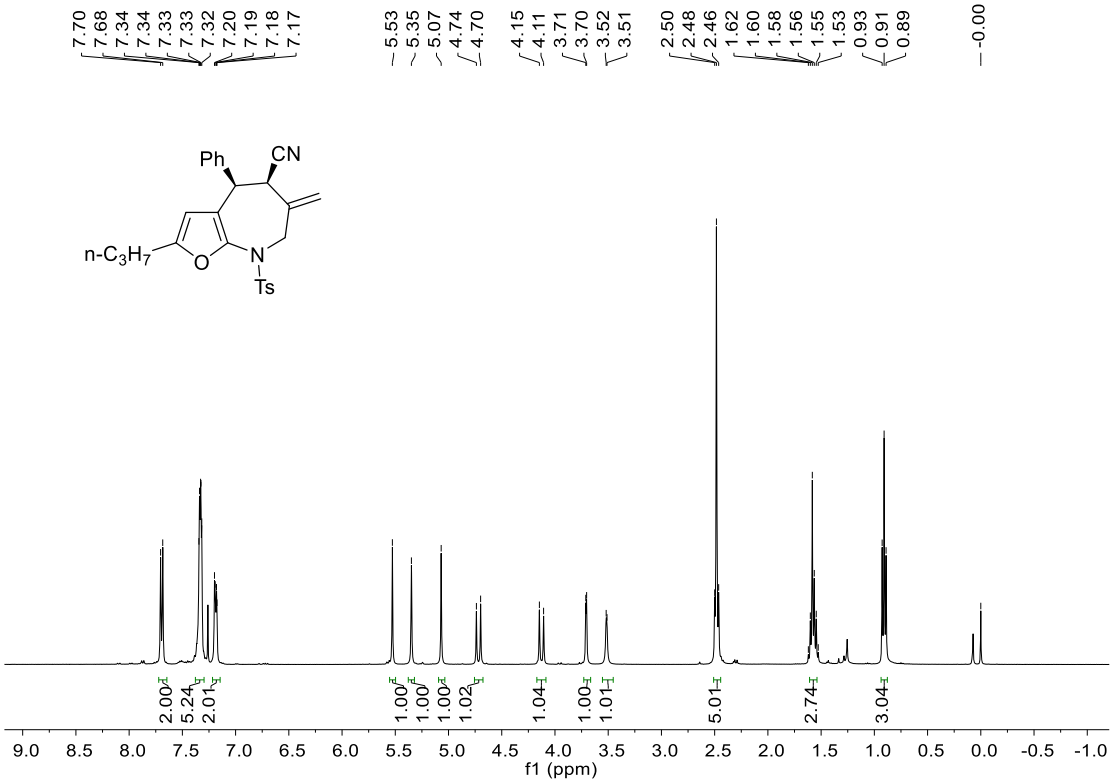
^{1}H NMR (400 MHz) of **3g** in $CDCl_3$



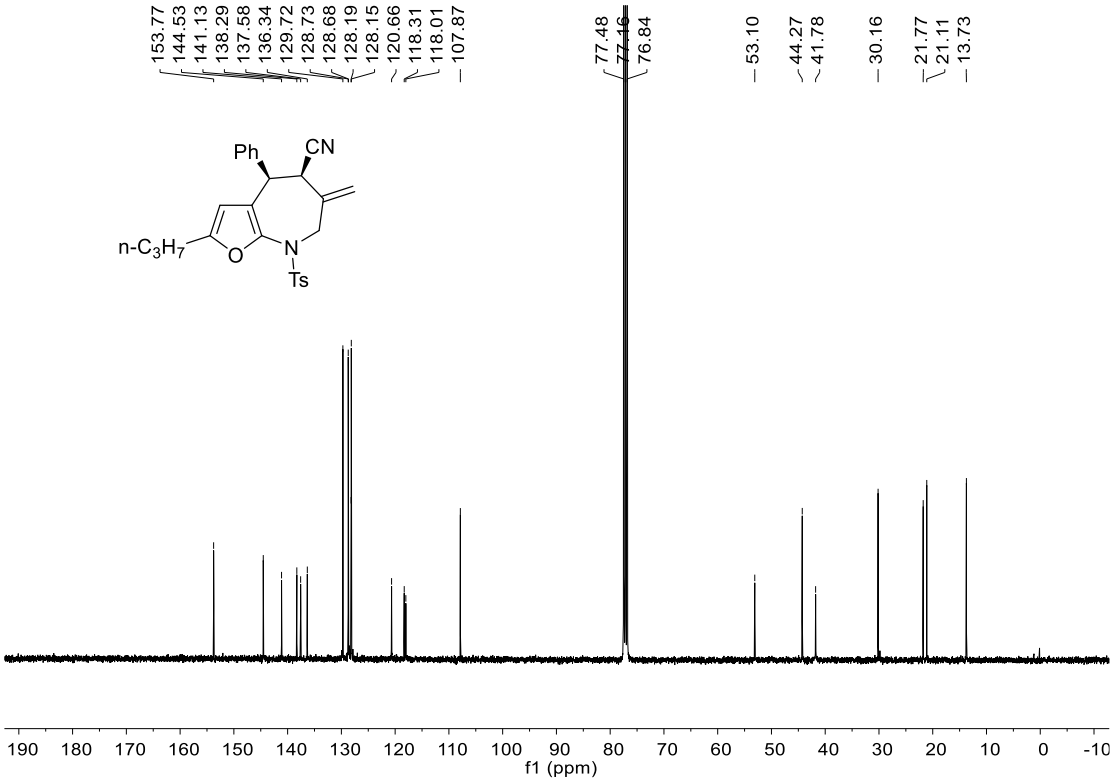
^{13}C NMR (100 MHz) of **3g** in $CDCl_3$



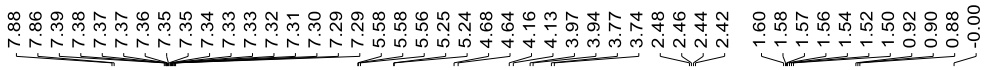
^{1}H NMR (400 MHz) of *cis*-**3h** in $CDCl_3$

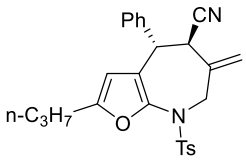


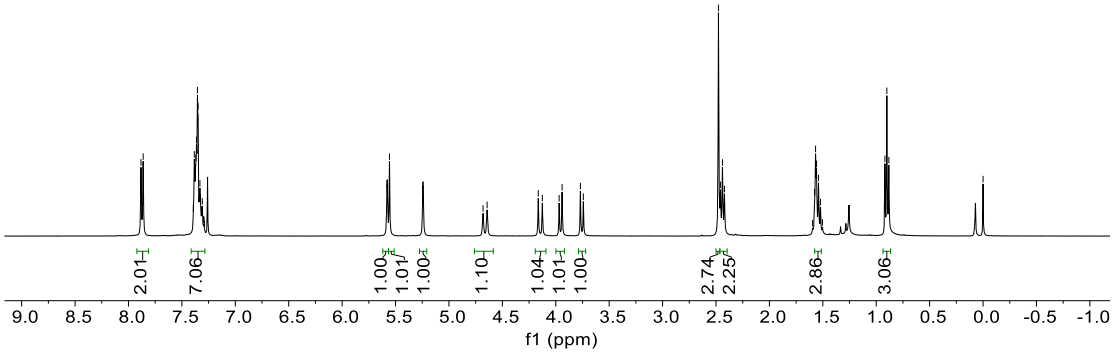
^{13}C NMR (100 MHz) of *cis*-**3h** in $CDCl_3$



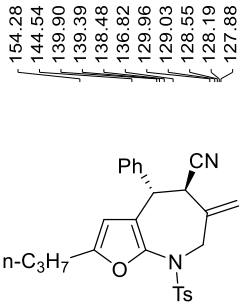
^{1}H NMR (400 MHz) of *trans*-**3h** in $CDCl_3$



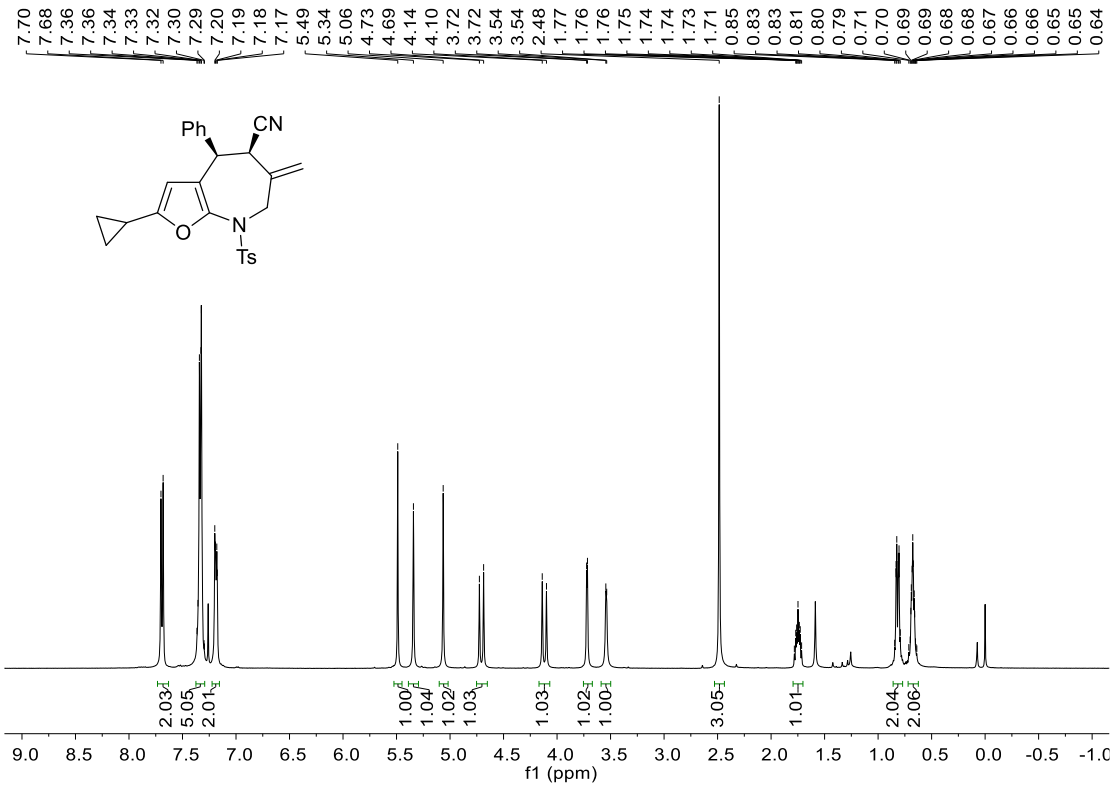




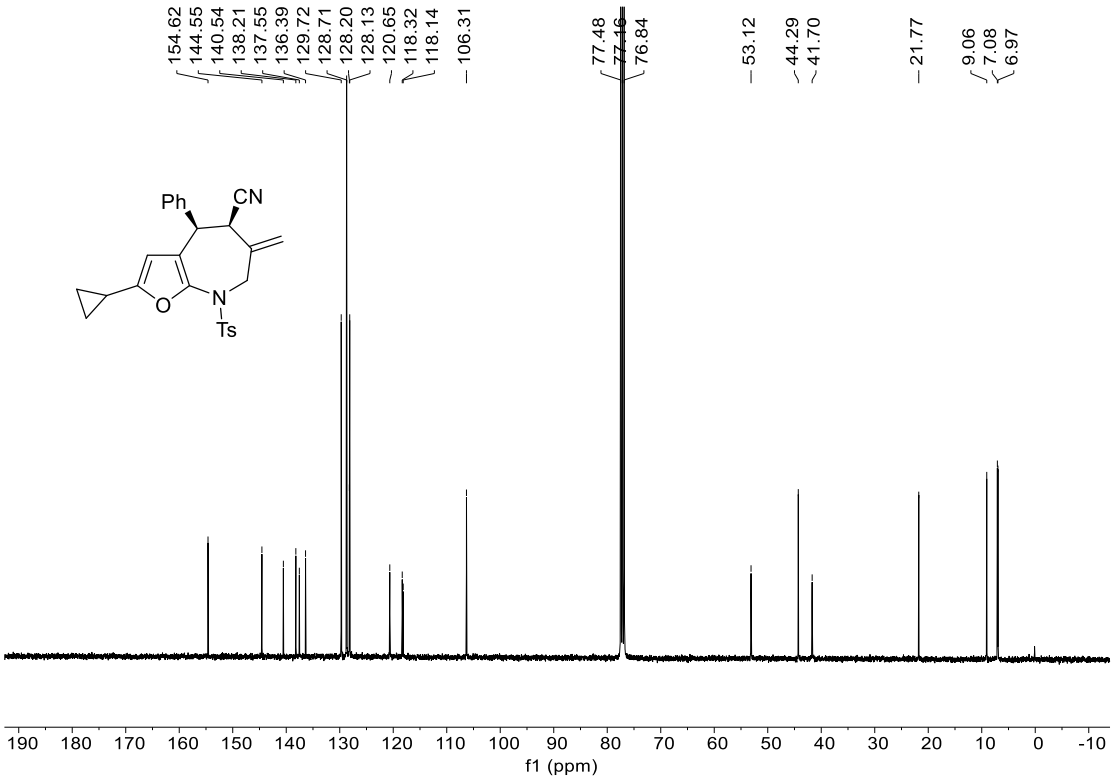
^{13}C NMR (100 MHz) of *trans*-**3h** in $CDCl_3$



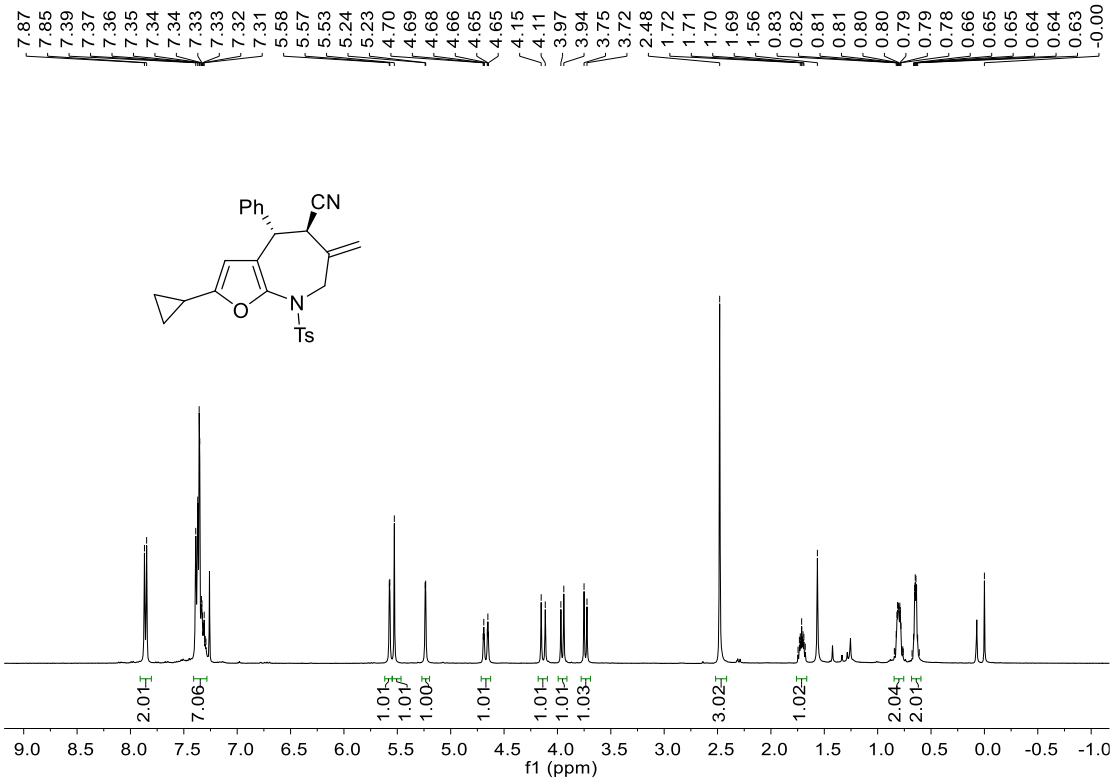
^{1}H NMR (400 MHz) of *cis*-**3i** in $CDCl_3$



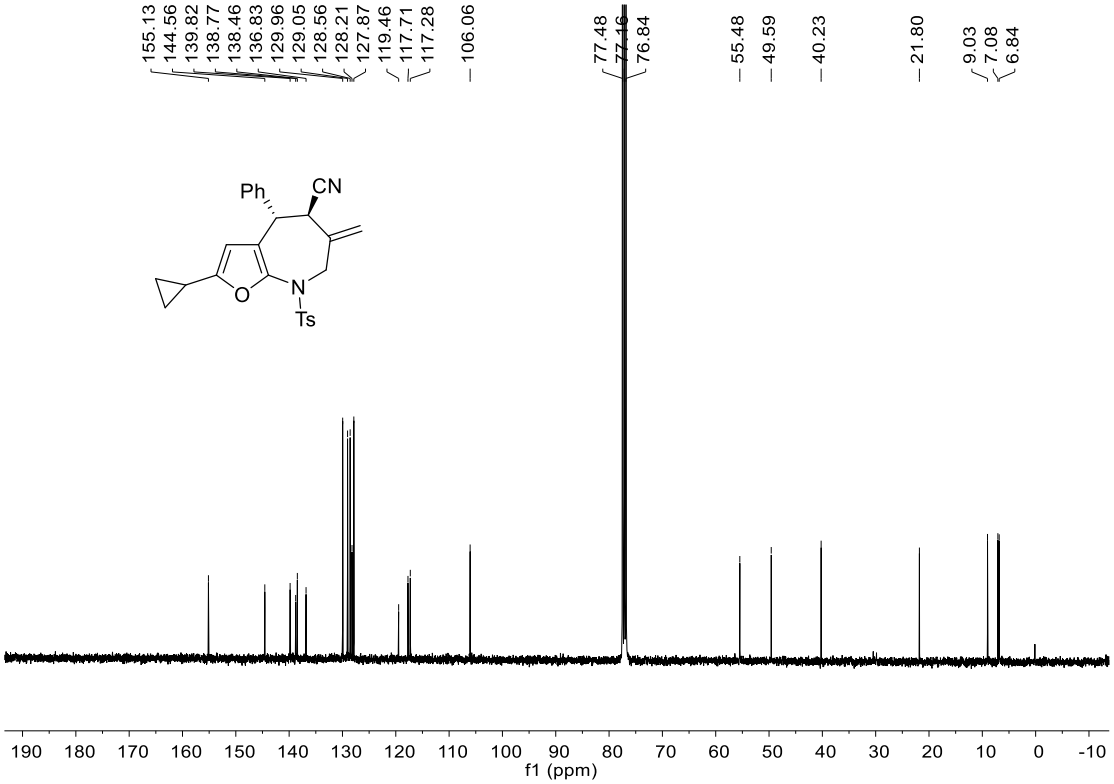
^{13}C NMR (100 MHz) of *cis*-**3i** in $CDCl_3$



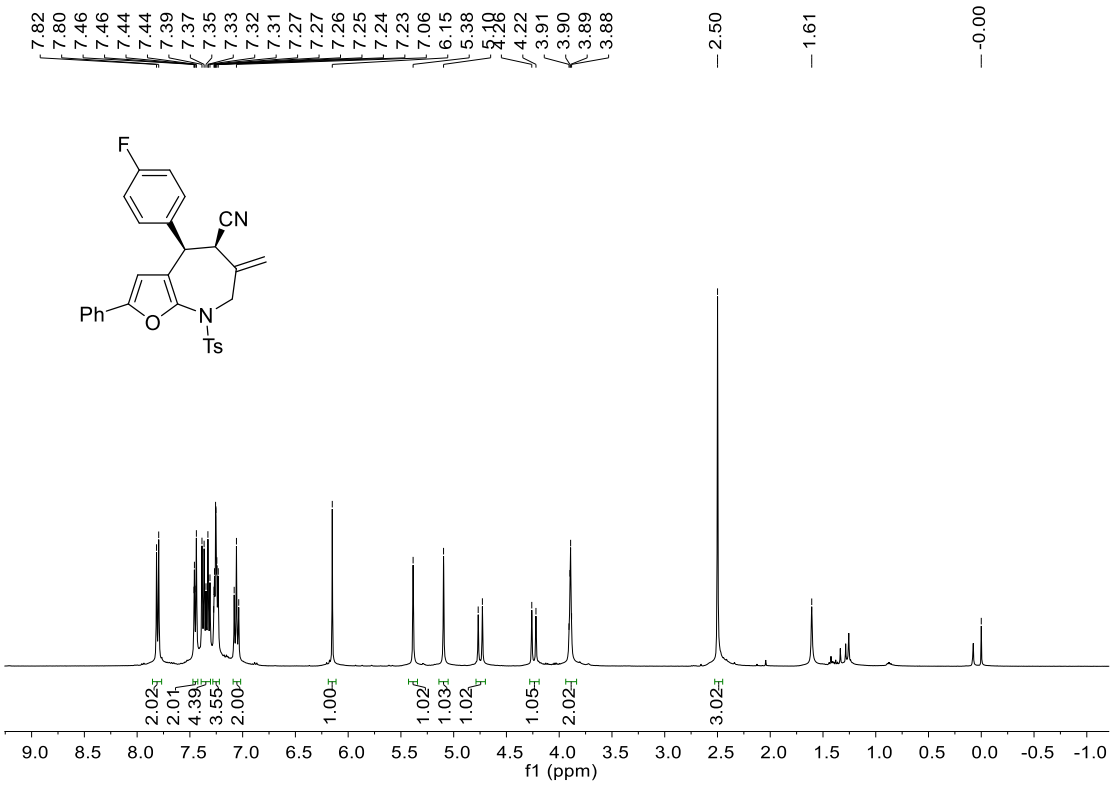
^{1}H NMR (400 MHz) of *trans*-**3i** in $CDCl_3$



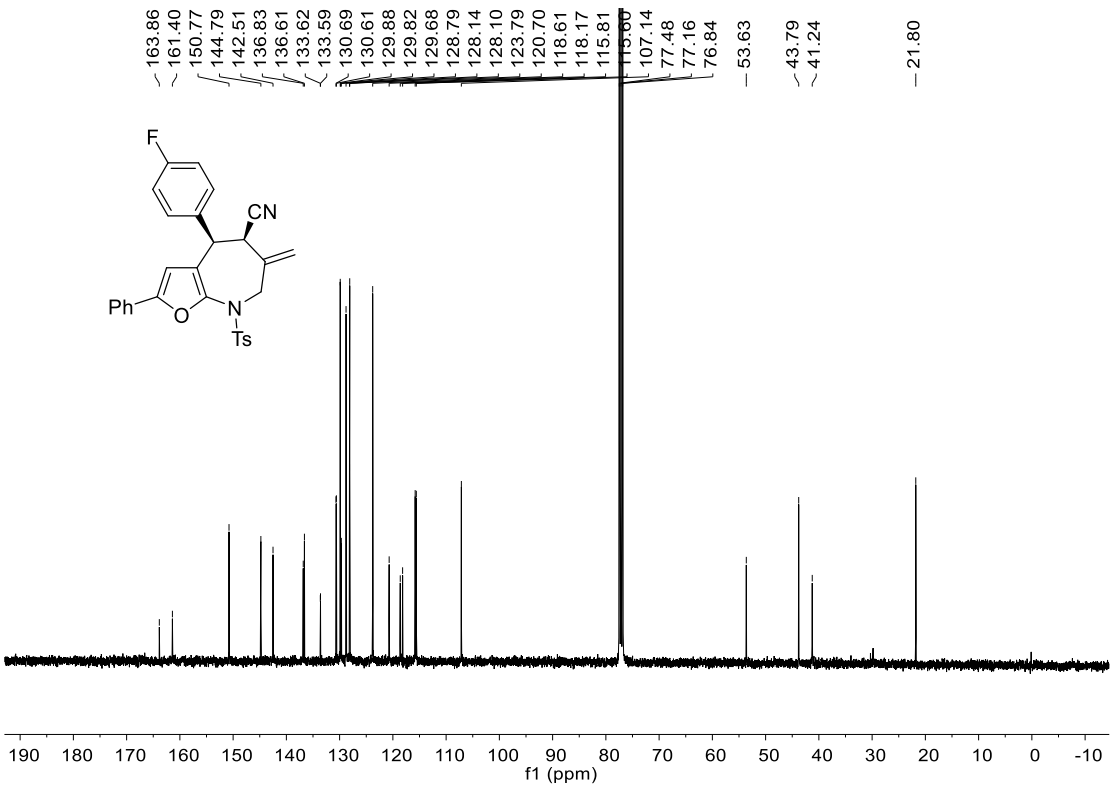
^{13}C NMR (100 MHz) of *trans*-**3i** in $CDCl_3$



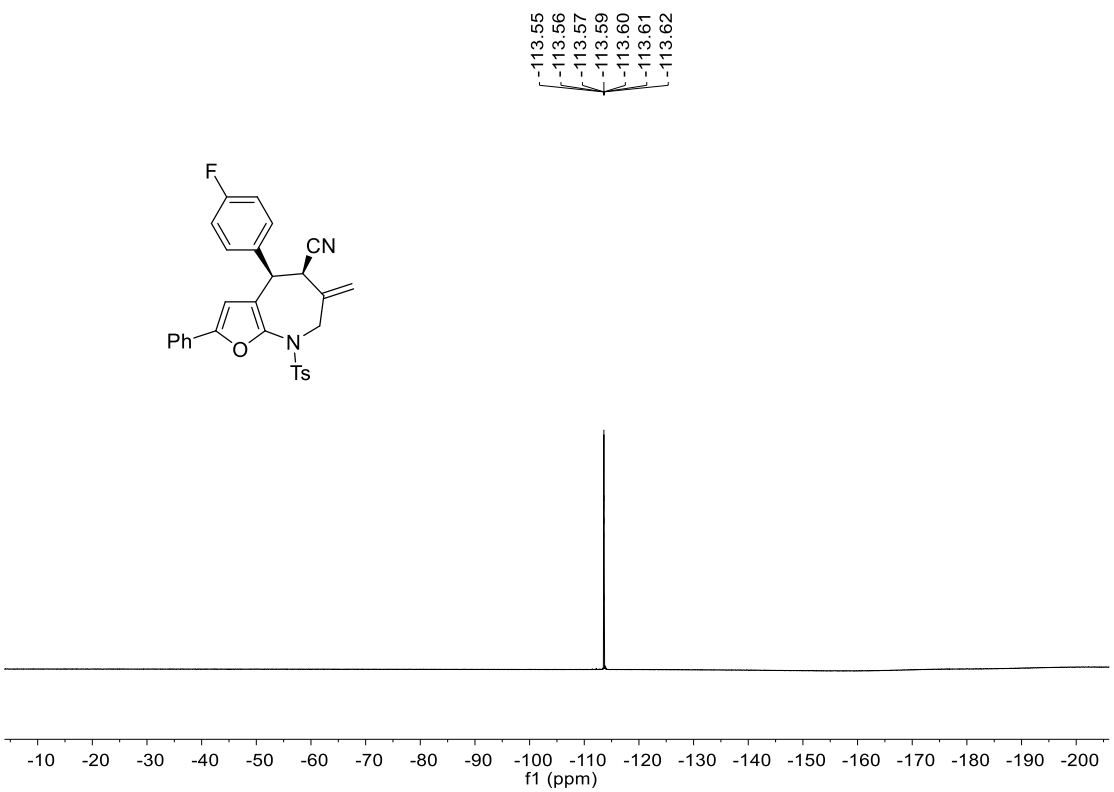
^{1}H NMR (400 MHz) of **3j** in $CDCl_3$



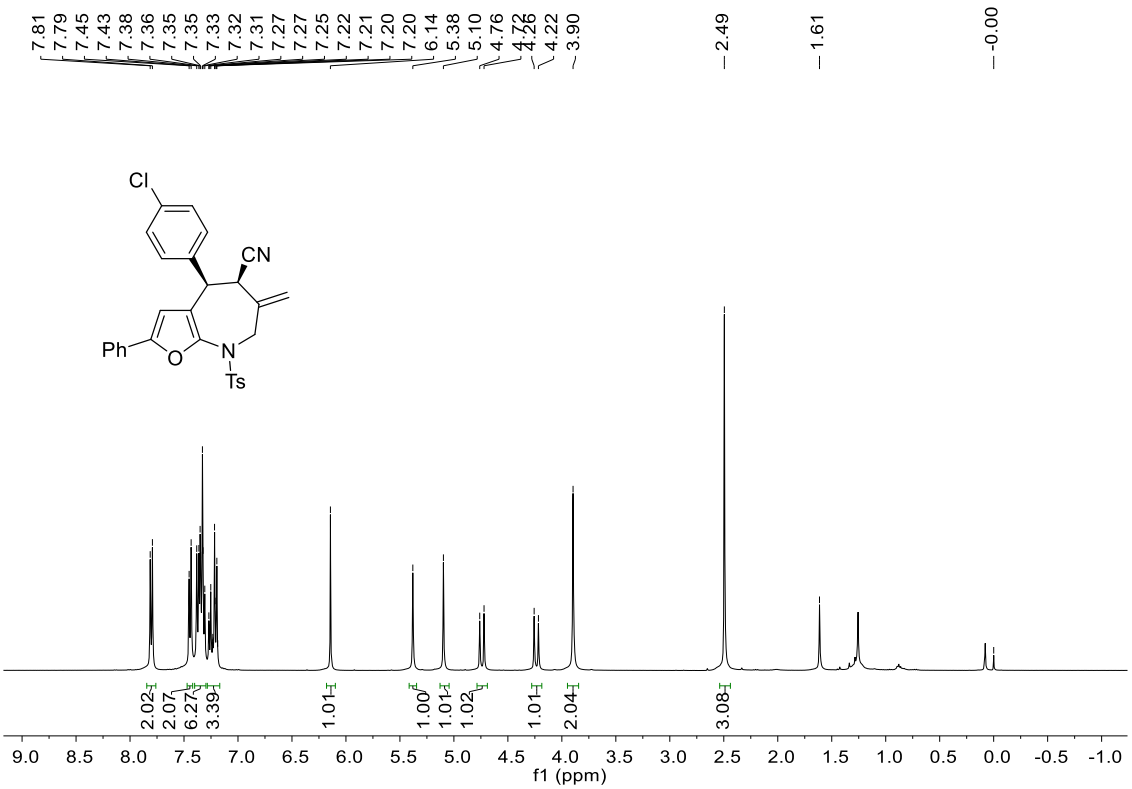
^{13}C NMR (100 MHz) of **3j** in $CDCl_3$



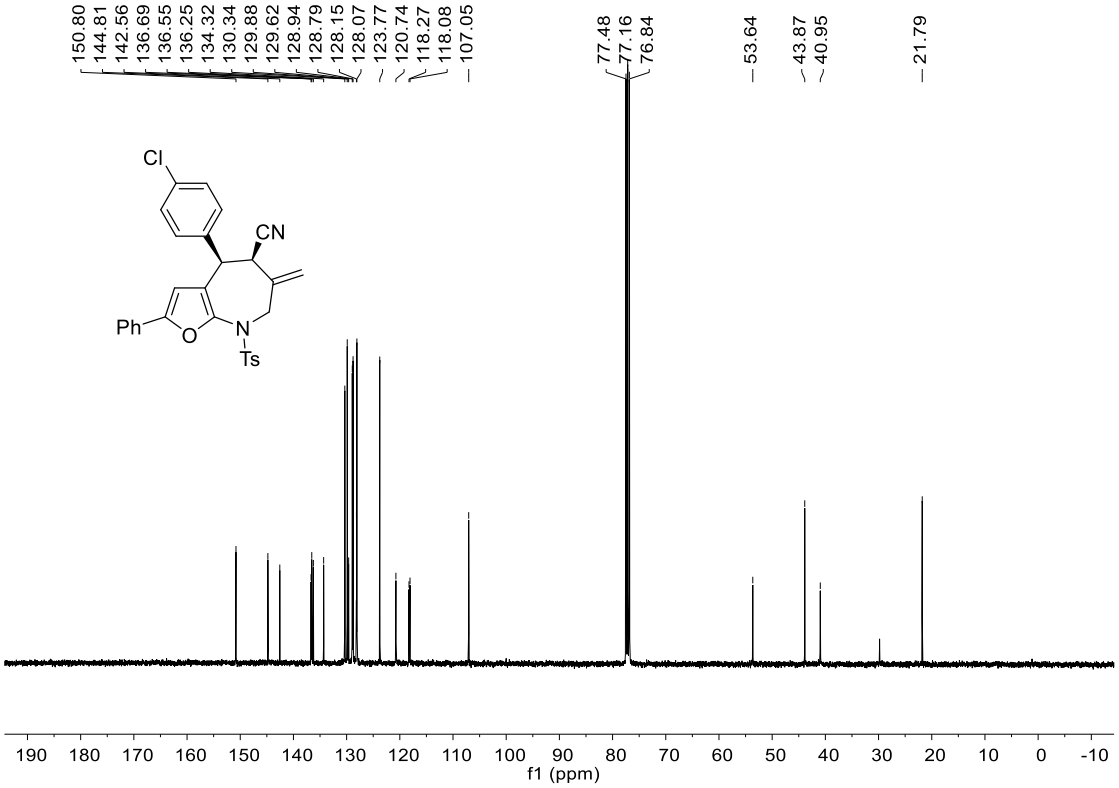
^{19}F NMR (376 MHz) of **3j** in $CDCl_3$



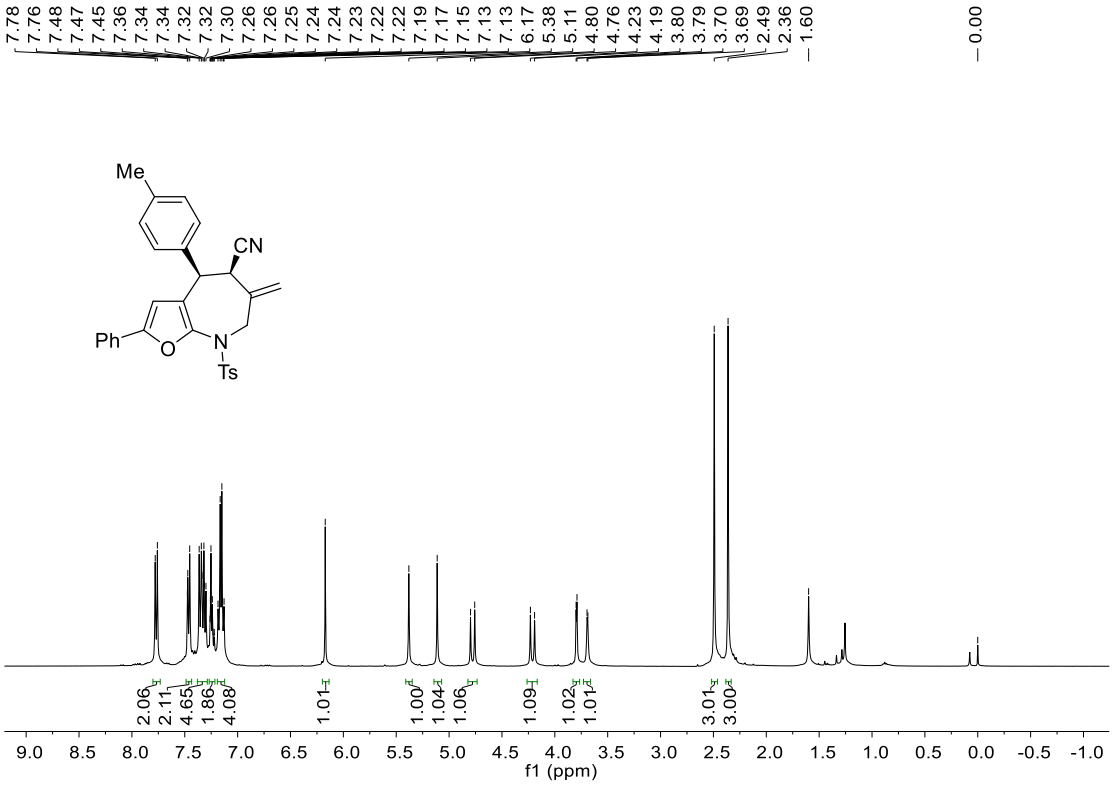
^{1}H NMR (400 MHz) of **3k** in $CDCl_3$



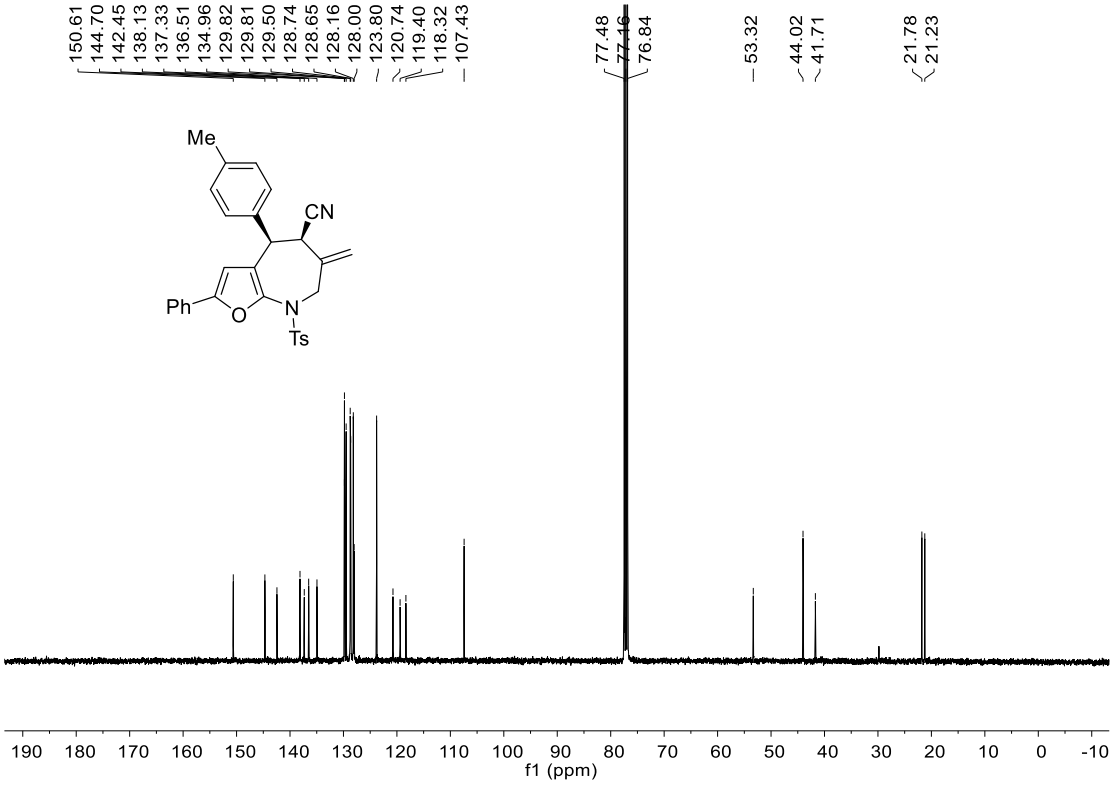
^{13}C NMR (150 MHz, 50 ℃) of **3k** in $CDCl_3$



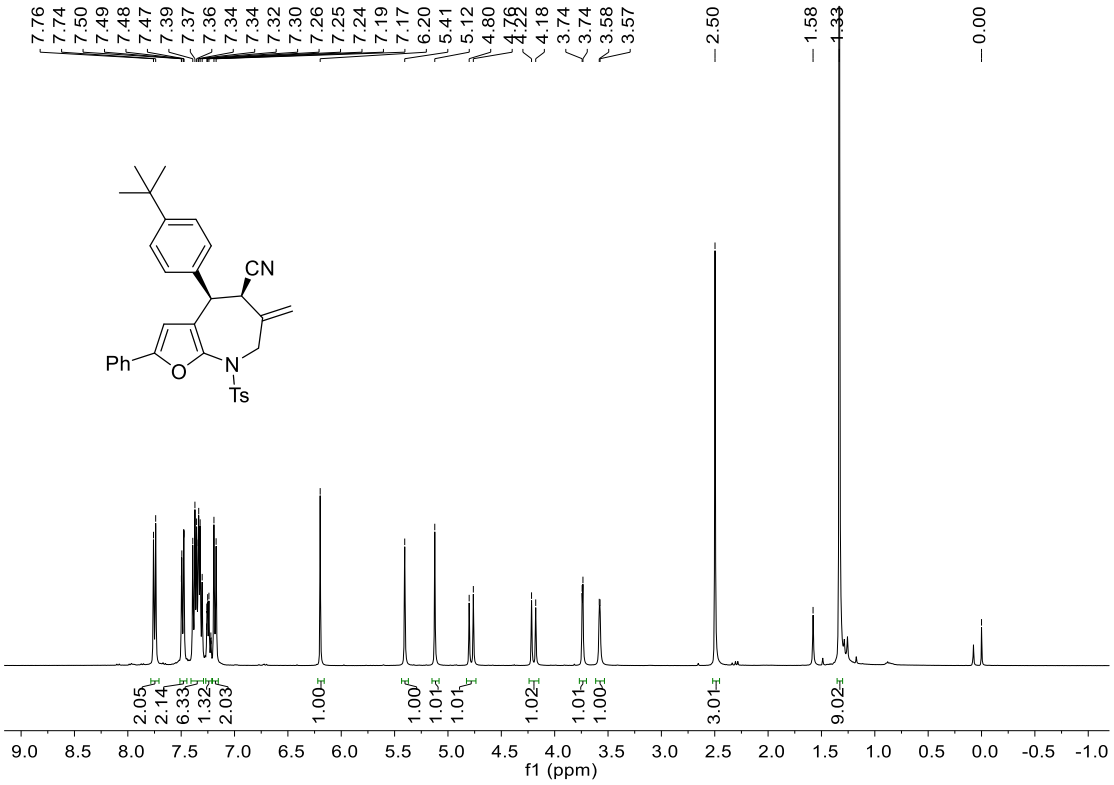
^{1}H NMR (400 MHz) of **3l** in $CDCl_3$



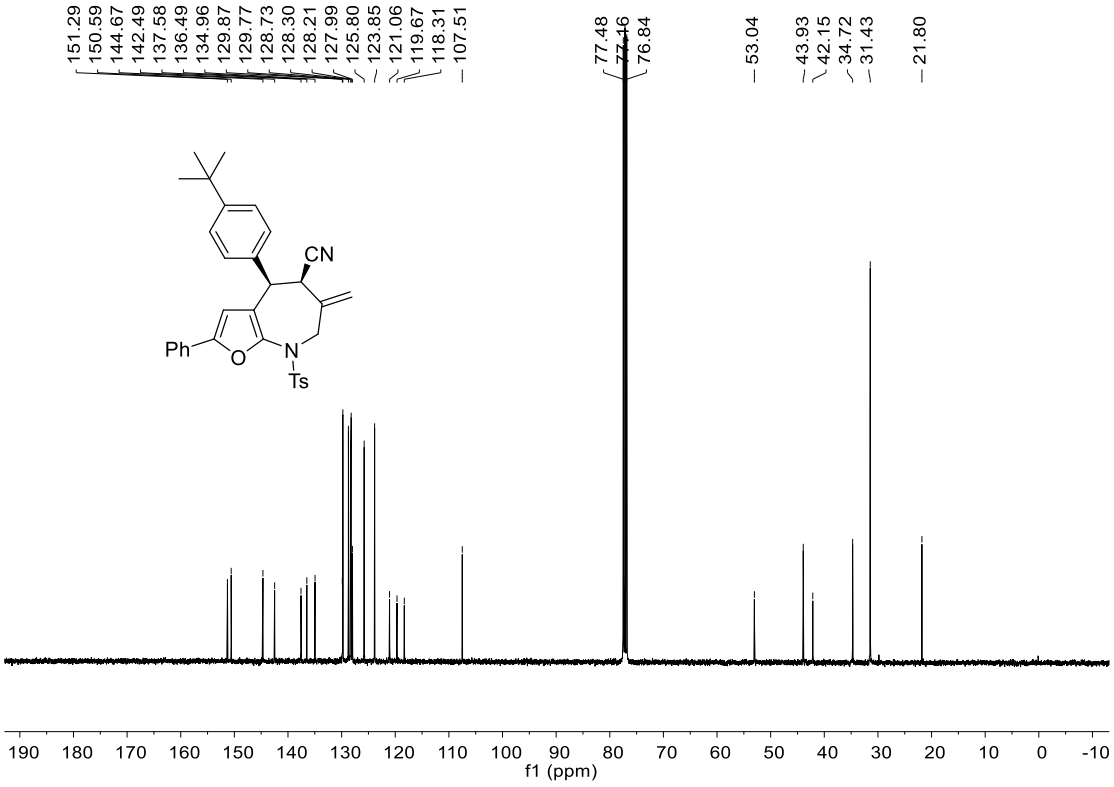
^{13}C NMR (100 MHz) of **3l** in $CDCl_3$



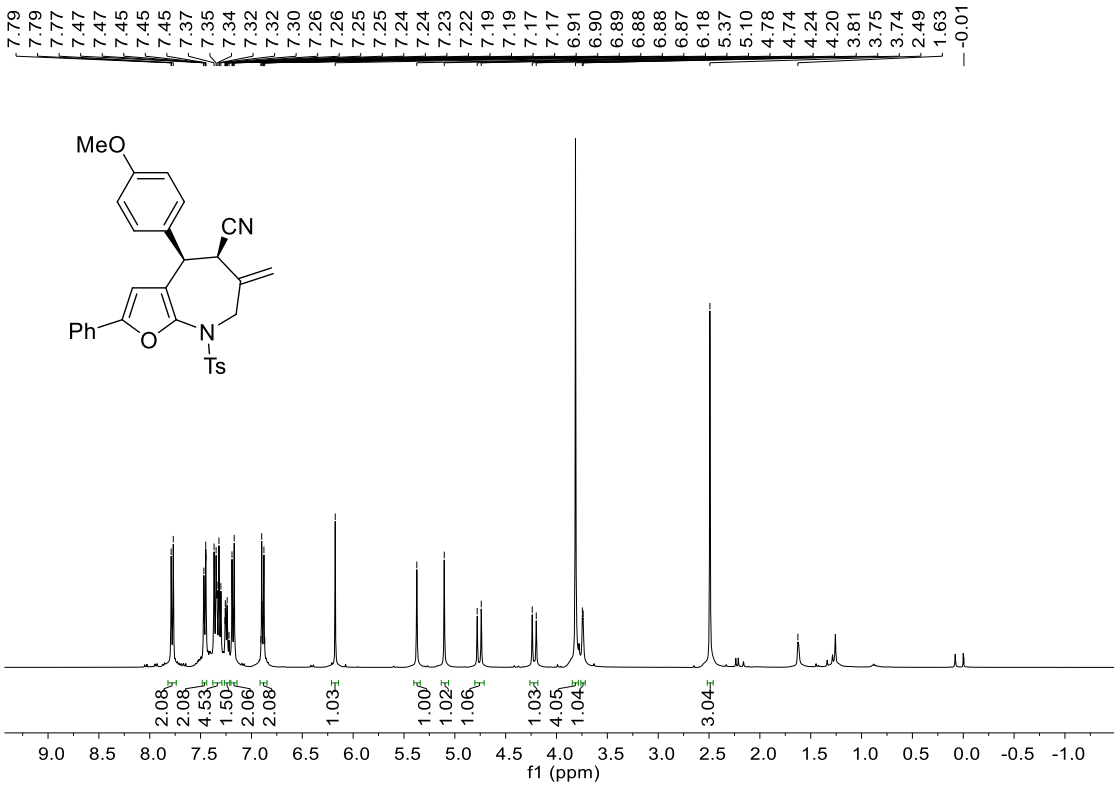
^{1}H NMR (400 MHz) of **3m** in $CDCl_3$



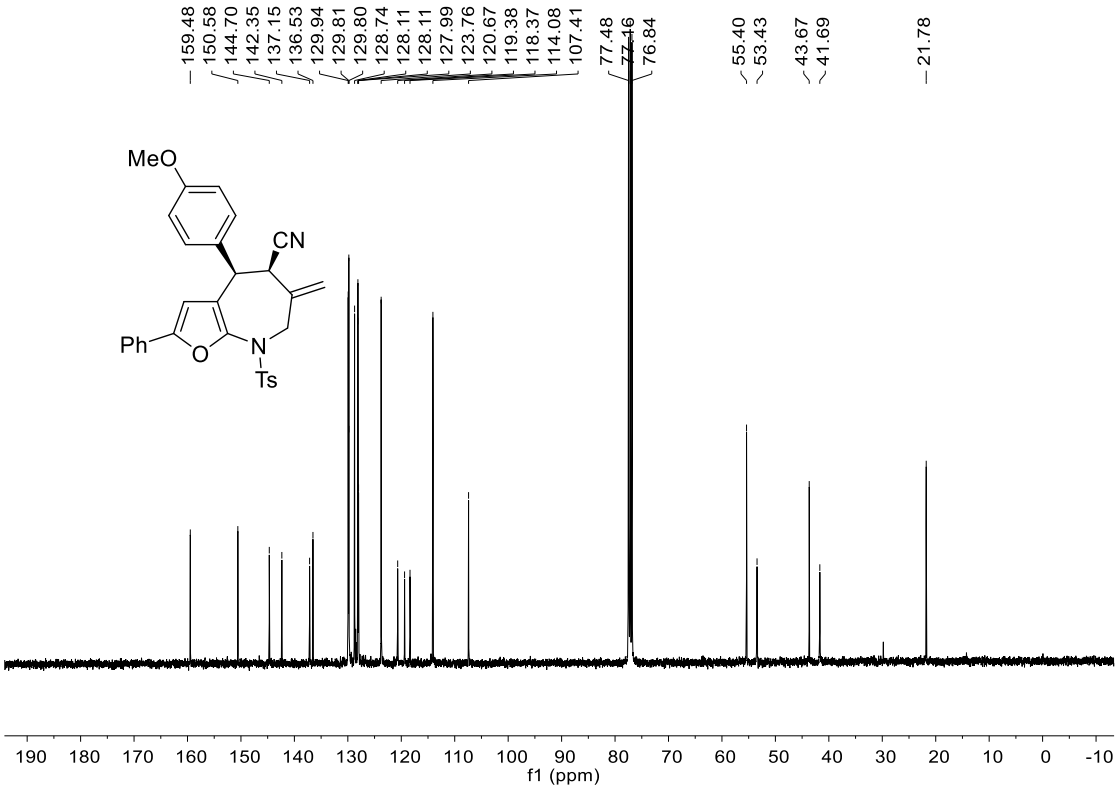
^{13}C NMR (100 MHz) of **3m** in $CDCl_3$



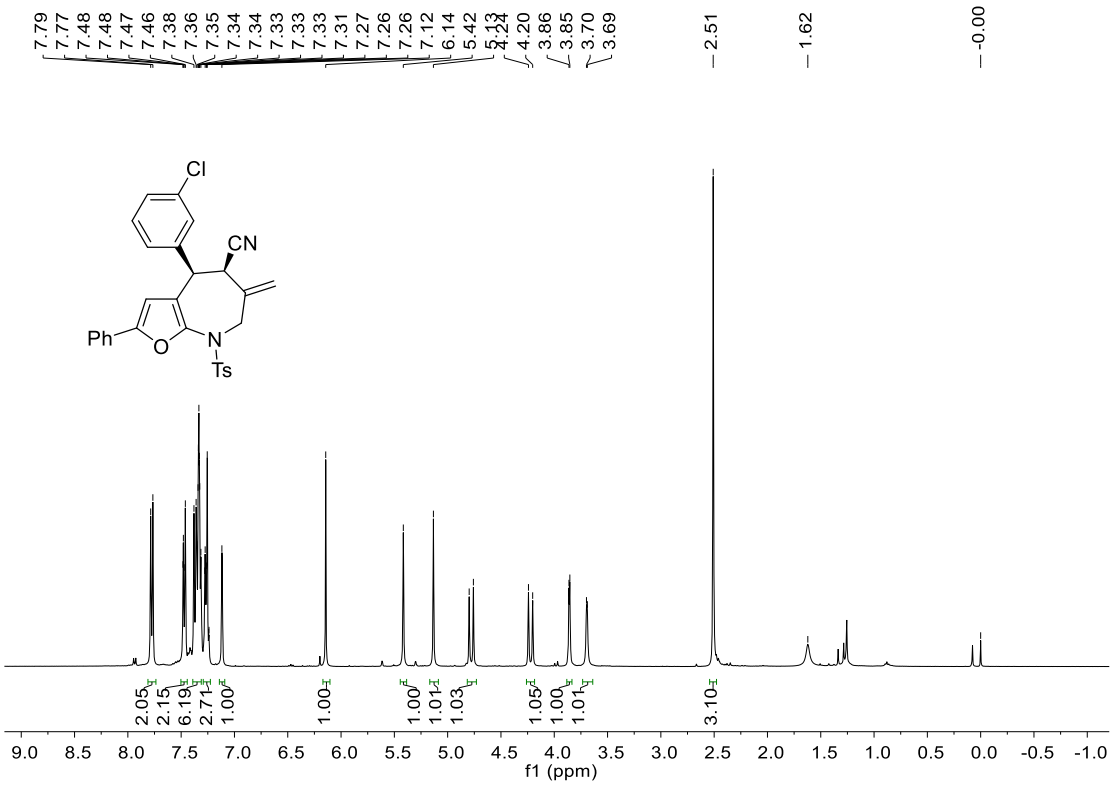
^{1}H NMR (400 MHz) of **3n** in $CDCl_3$



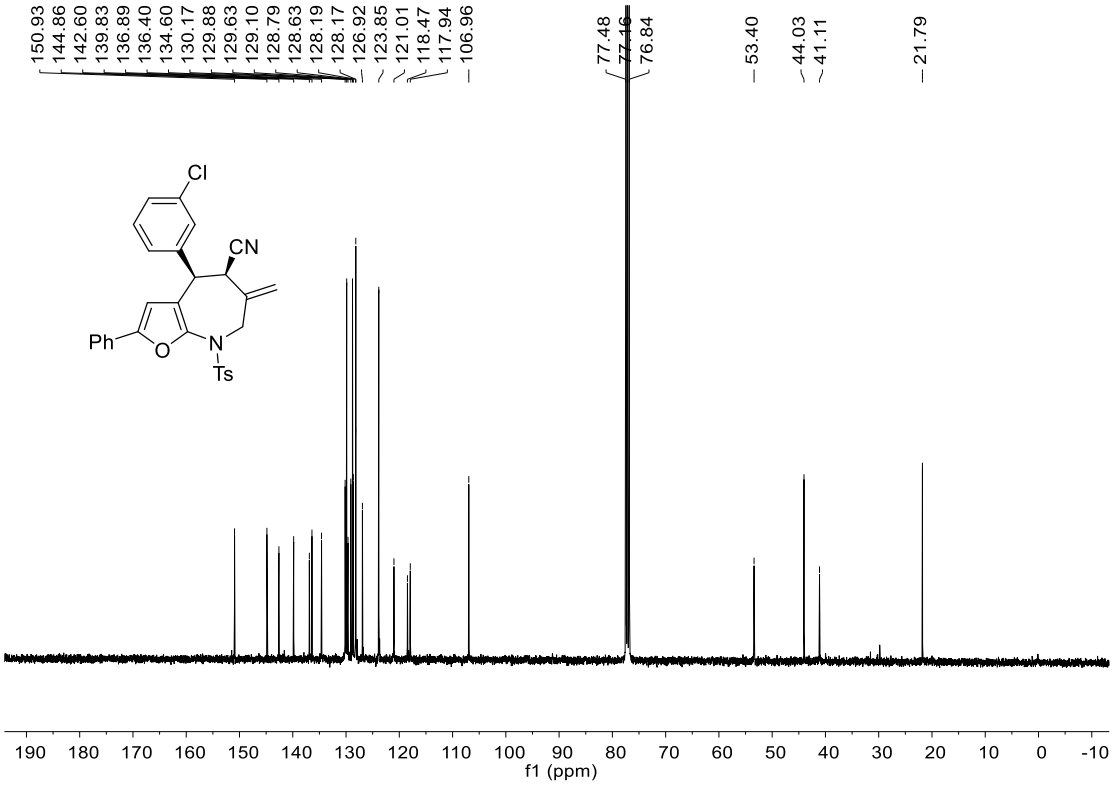
^{13}C NMR (100 MHz) of **3n** in $CDCl_3$



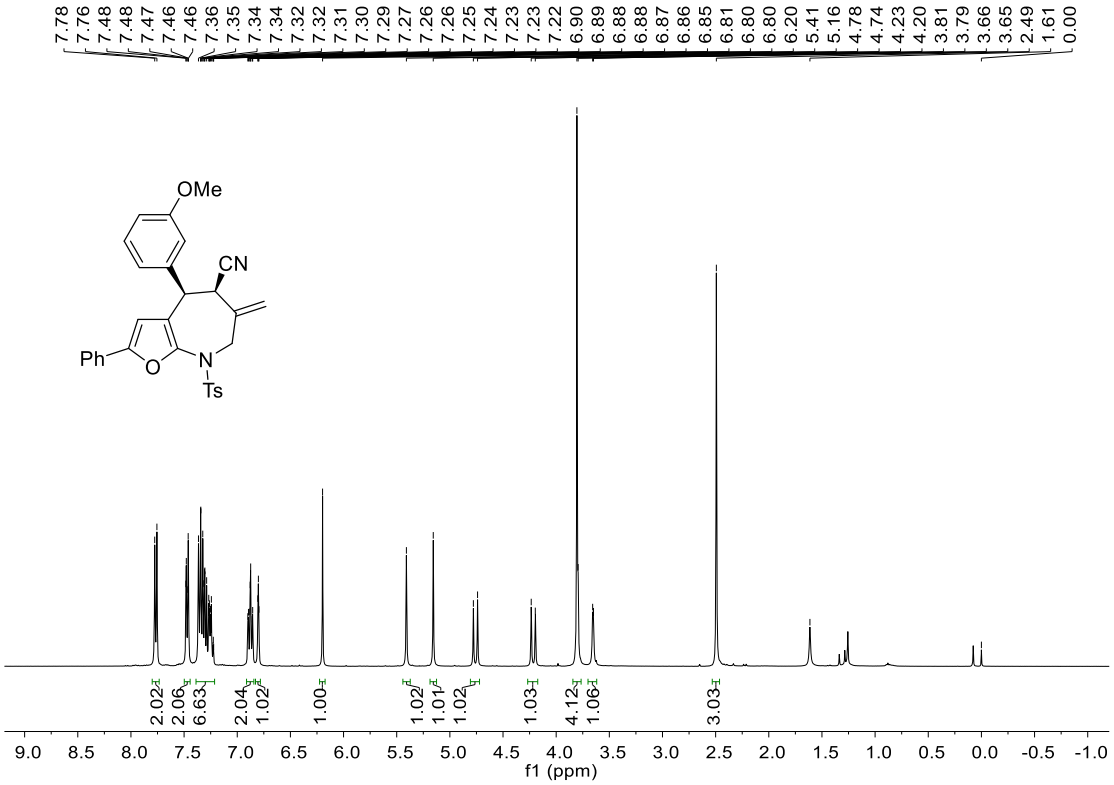
^{1}H NMR (400 MHz) of **3o** in $CDCl_3$



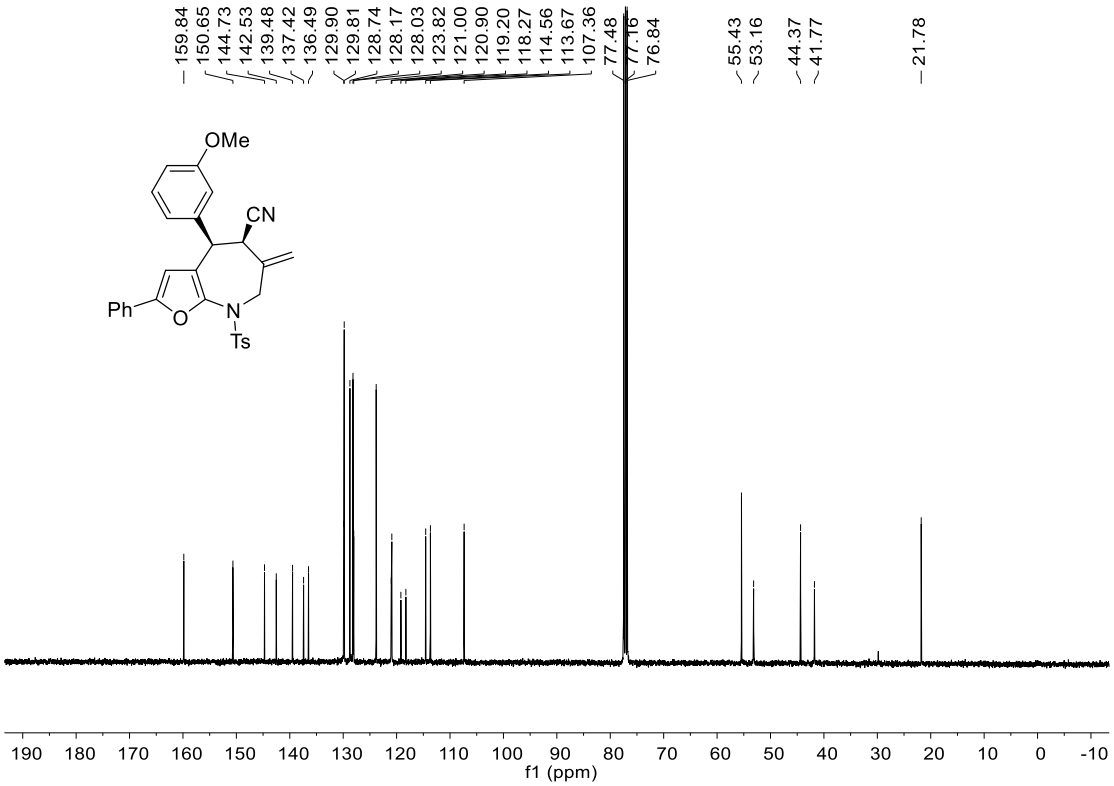
^{13}C NMR (100 MHz) of **3o** in $CDCl_3$



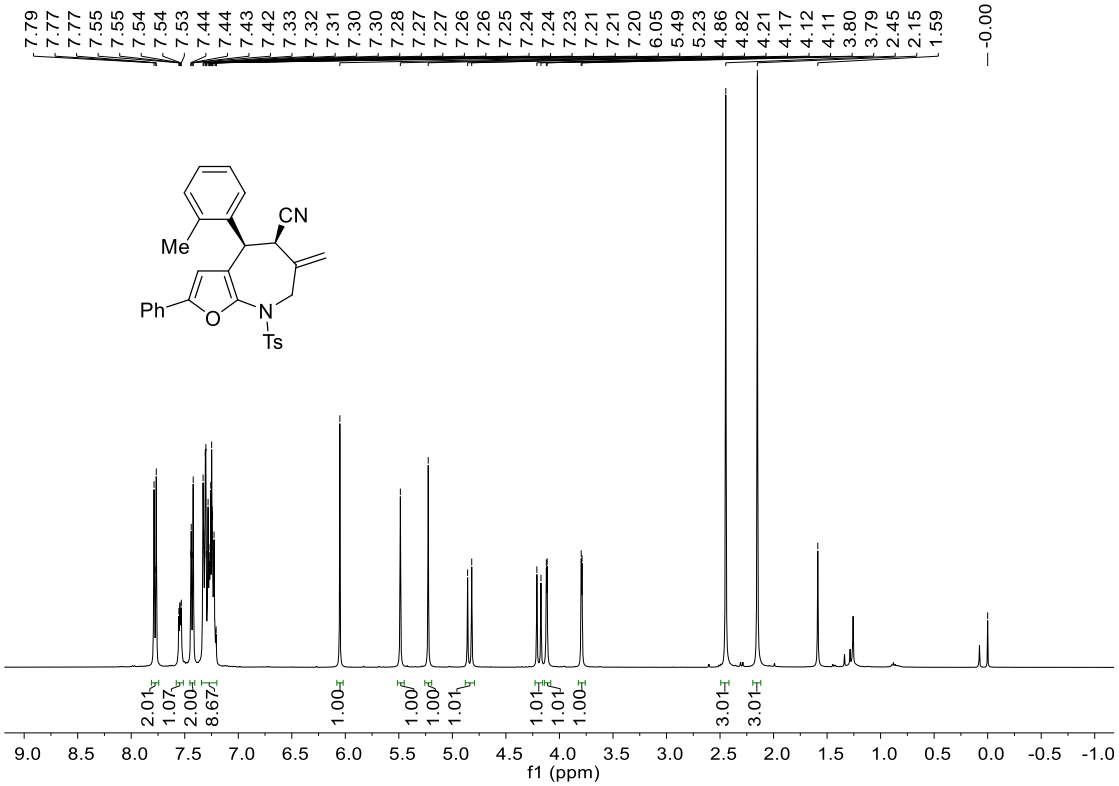
^{1}H NMR (400 MHz) of **3p** in $CDCl_3$



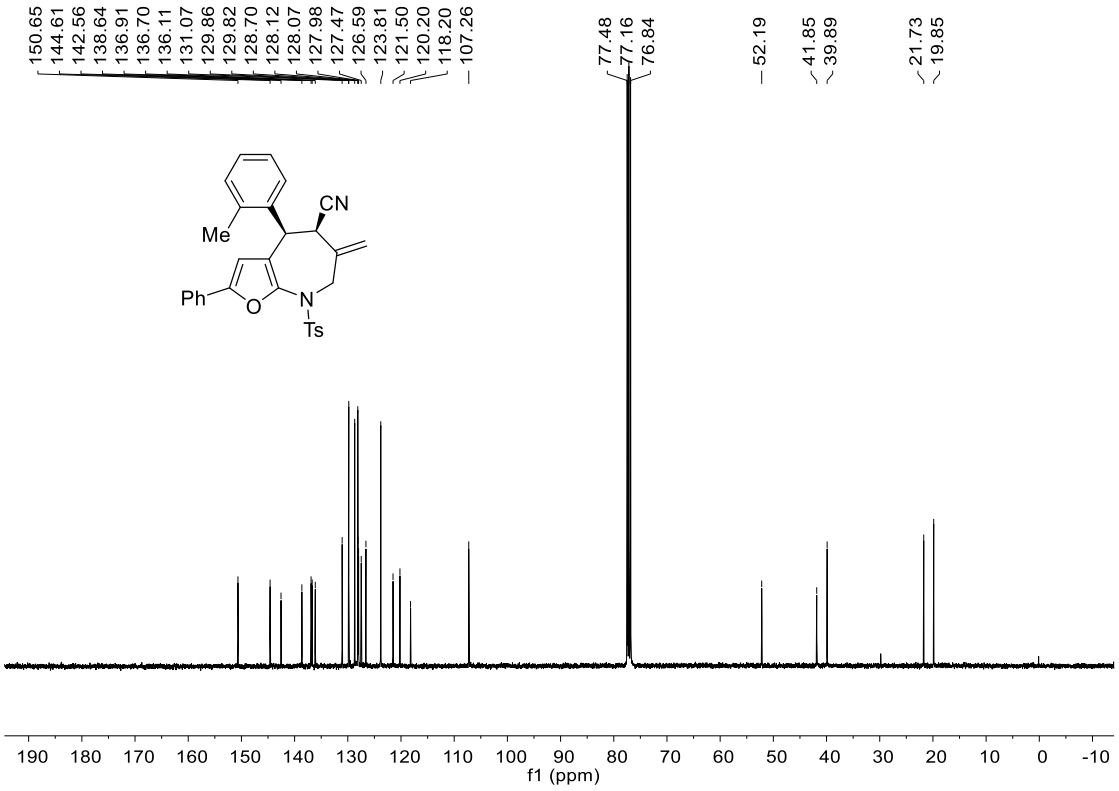
^{13}C NMR (100 MHz) of **3p** in $CDCl_3$



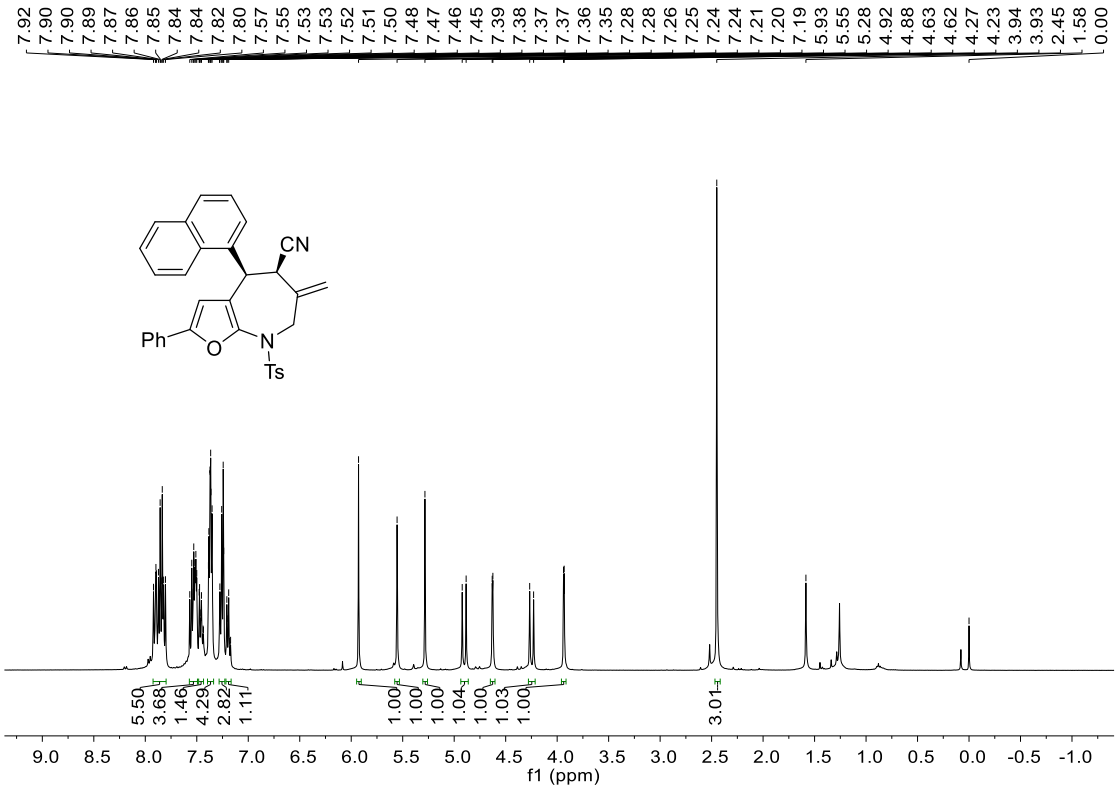
^{1}H NMR (400 MHz) of **3q** in $CDCl_3$



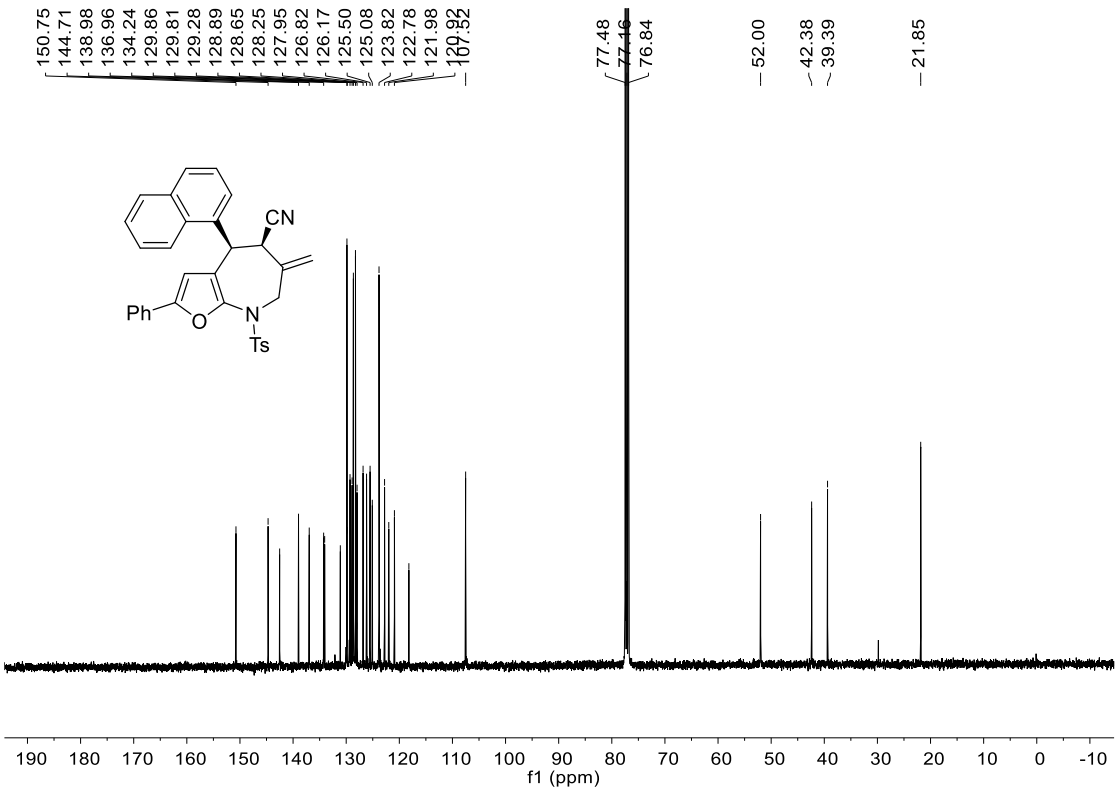
^{13}C NMR (100 MHz) of **3q** in $CDCl_3$



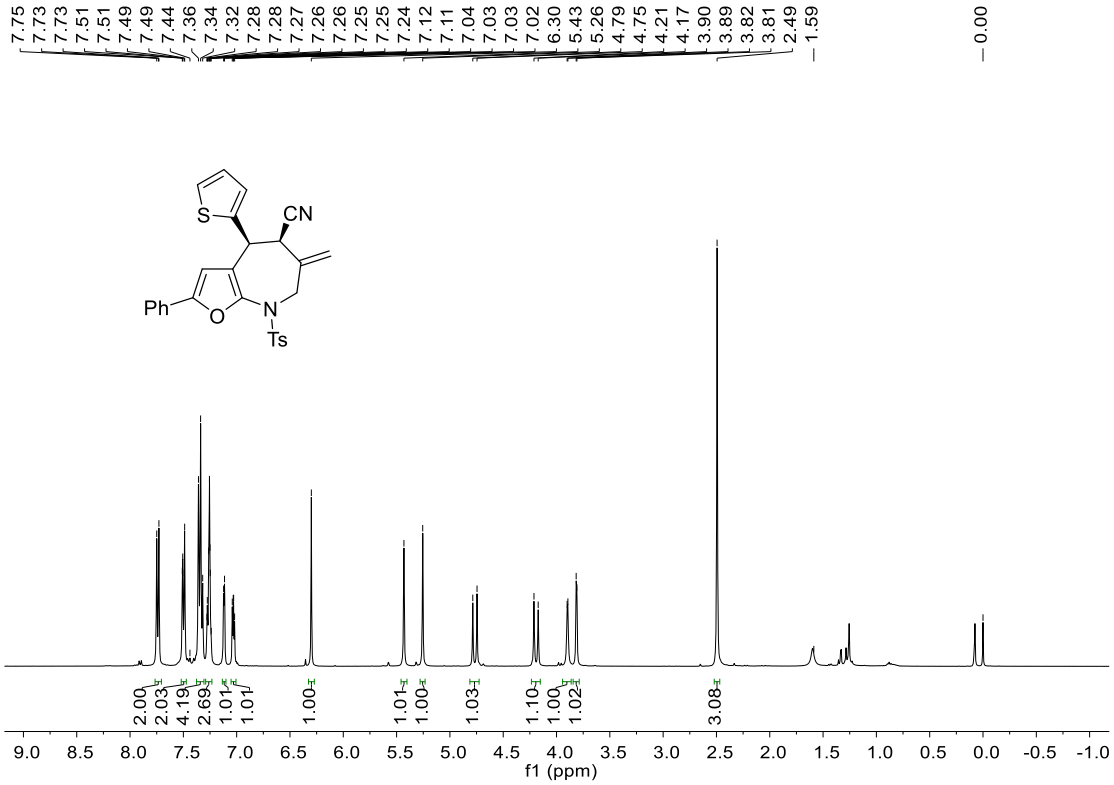
^{1}H NMR (400 MHz) of **3r** in $CDCl_3$



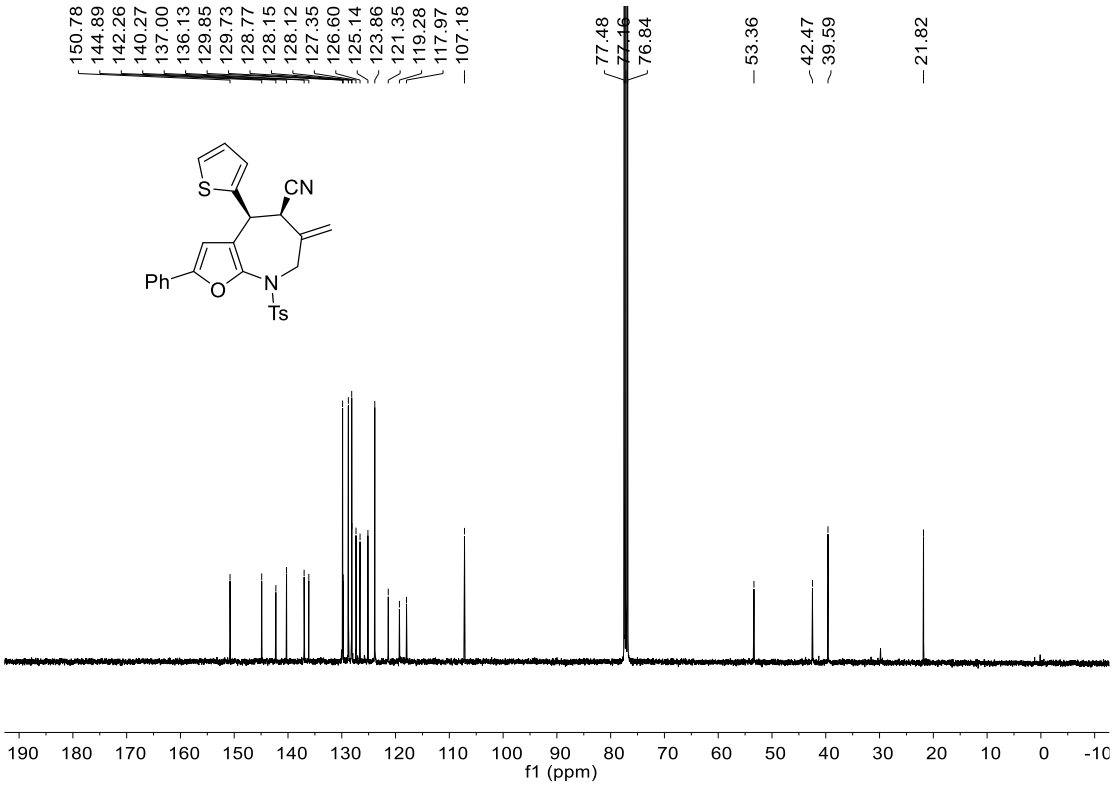
^{13}C NMR (100 MHz) of **3r** in $CDCl_3$



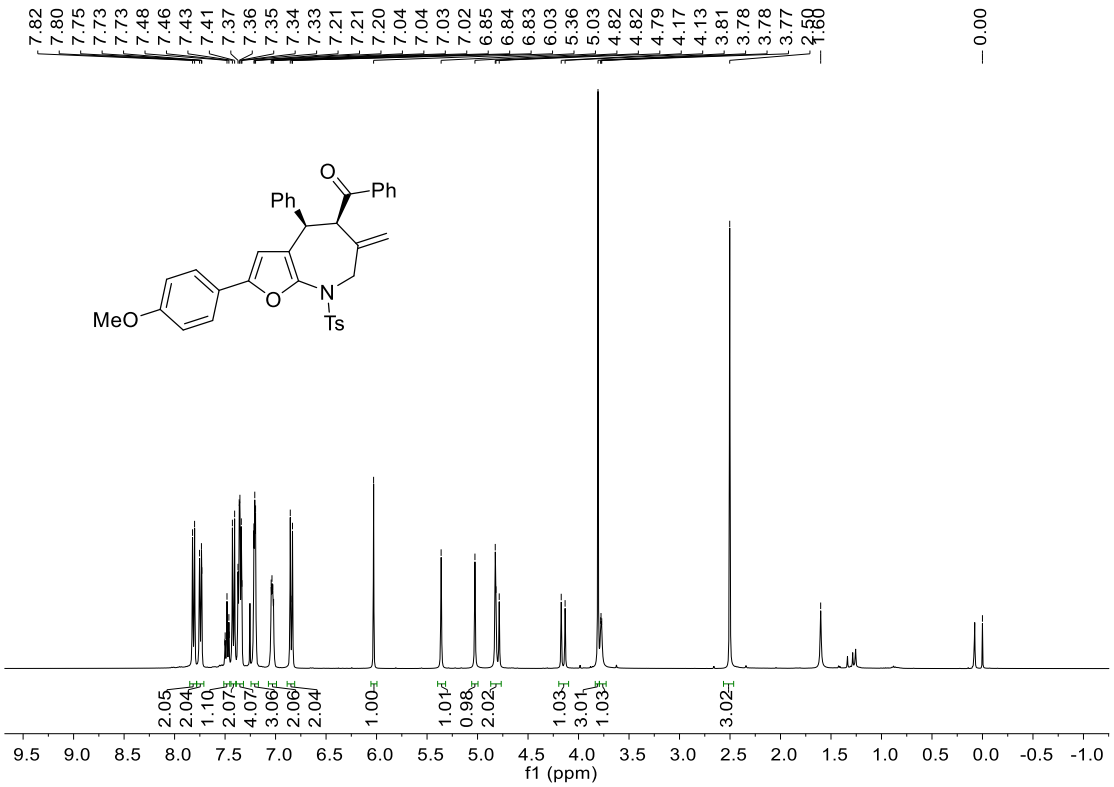
^{1}H NMR (400 MHz) of **3s** in $CDCl_3$



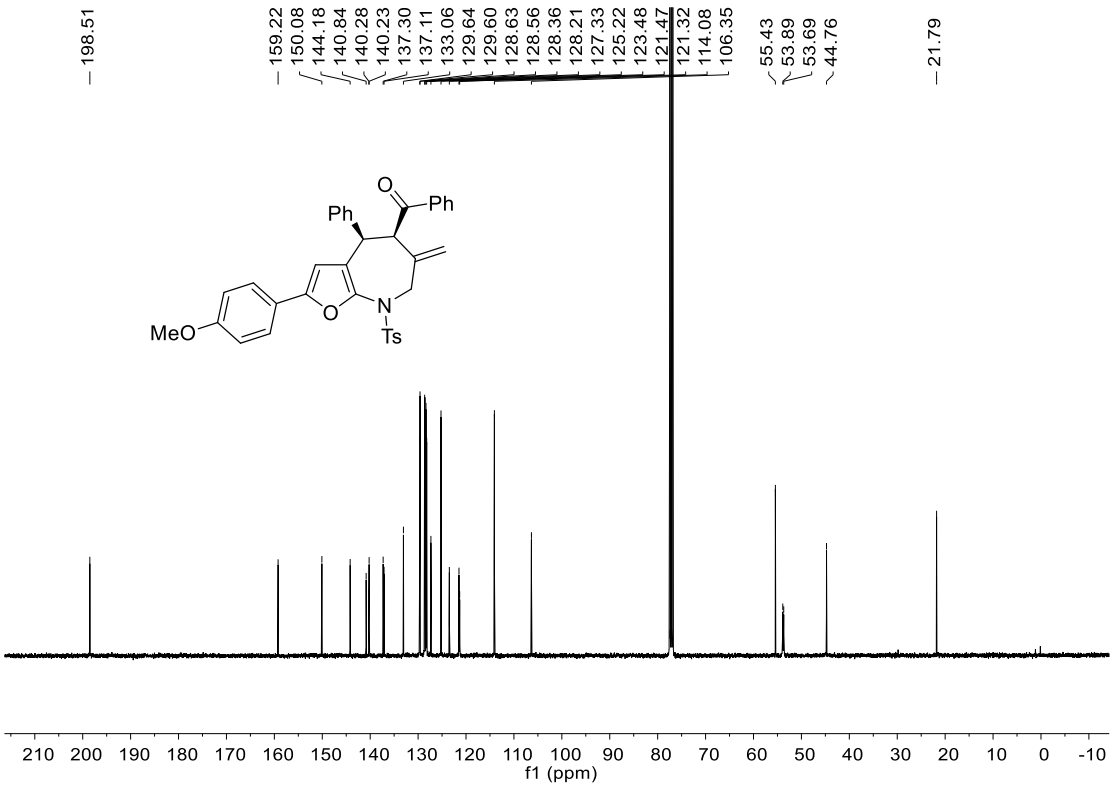
^{13}C NMR (100 MHz) of **3s** in $CDCl_3$



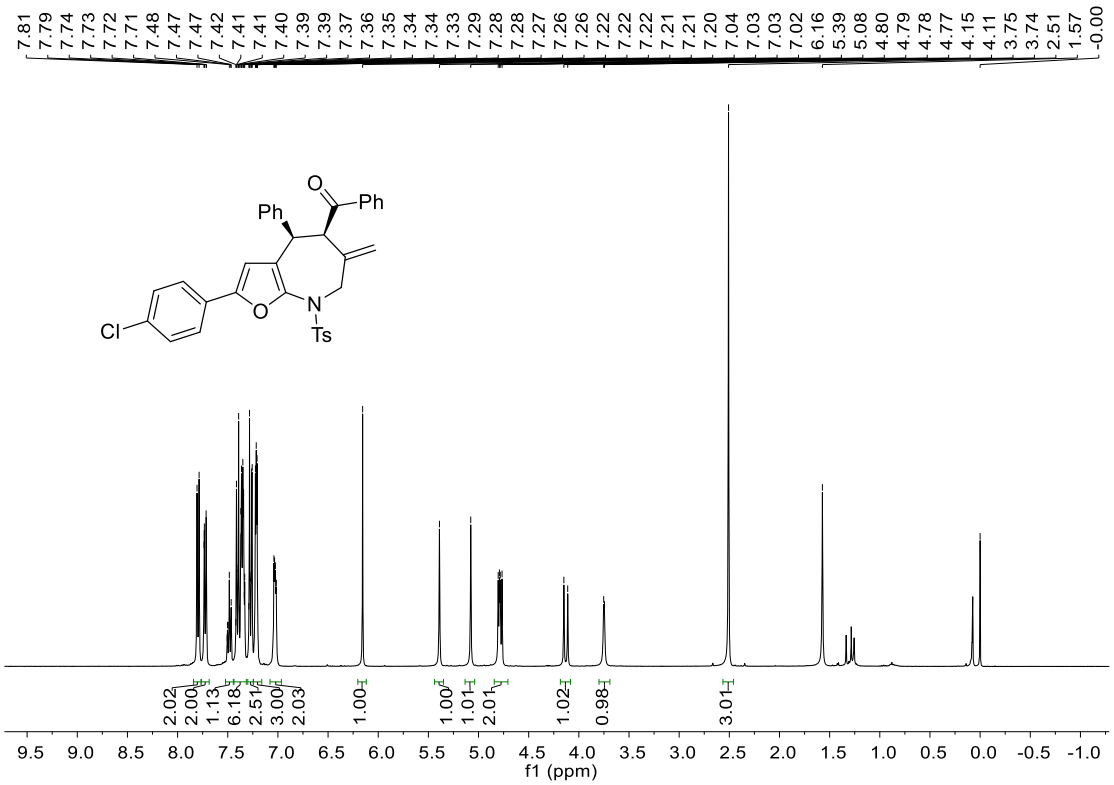
^{1}H NMR (400 MHz) of **5a** in $CDCl_3$



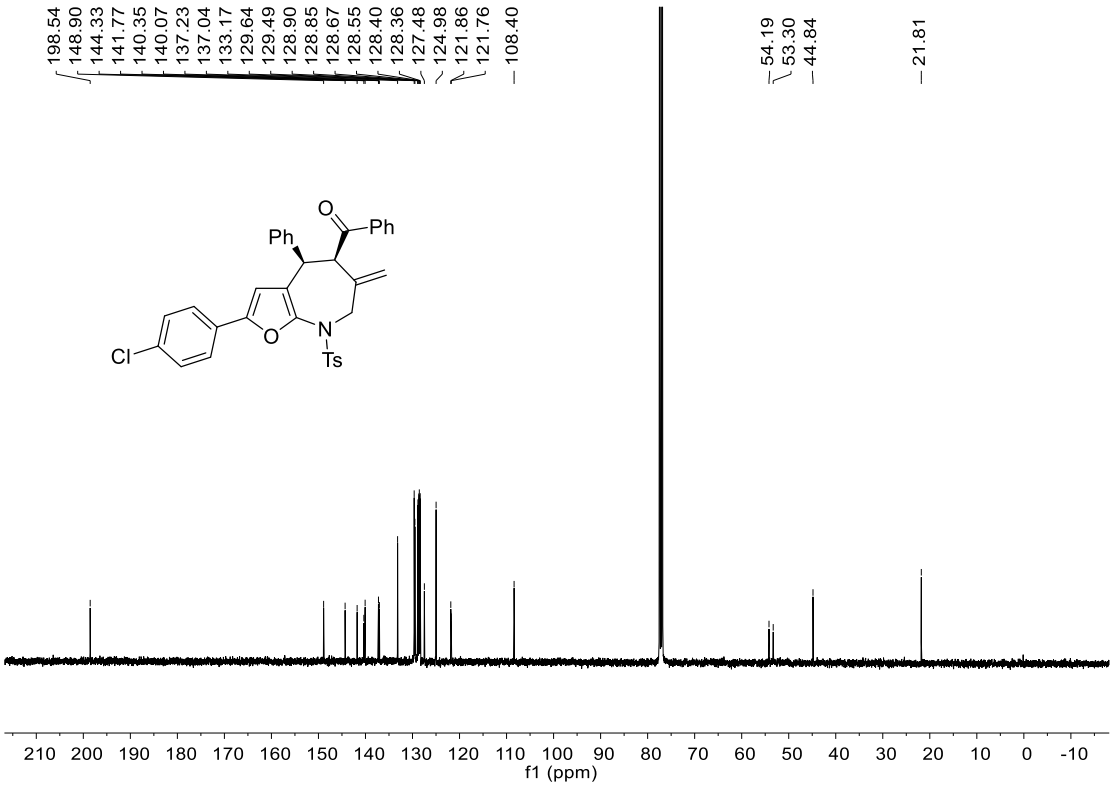
^{13}C NMR (100 MHz) of **5a** in $CDCl_3$



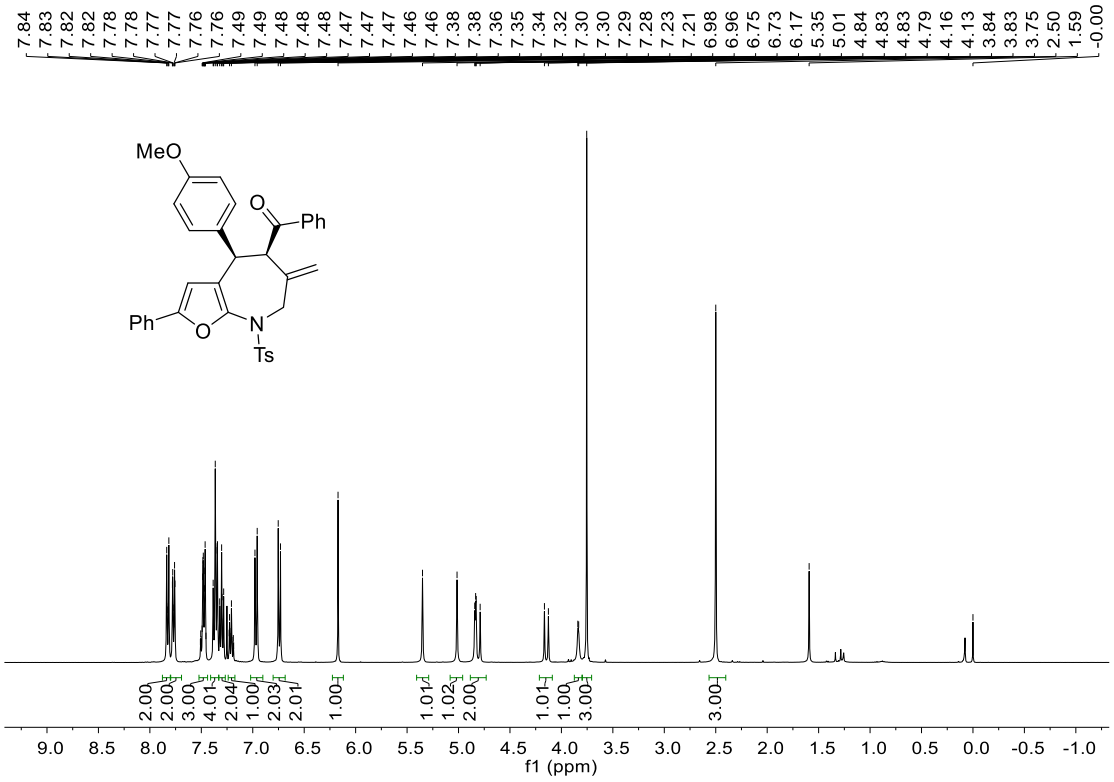
^{1}H NMR (400 MHz) of **5b** in $CDCl_3$



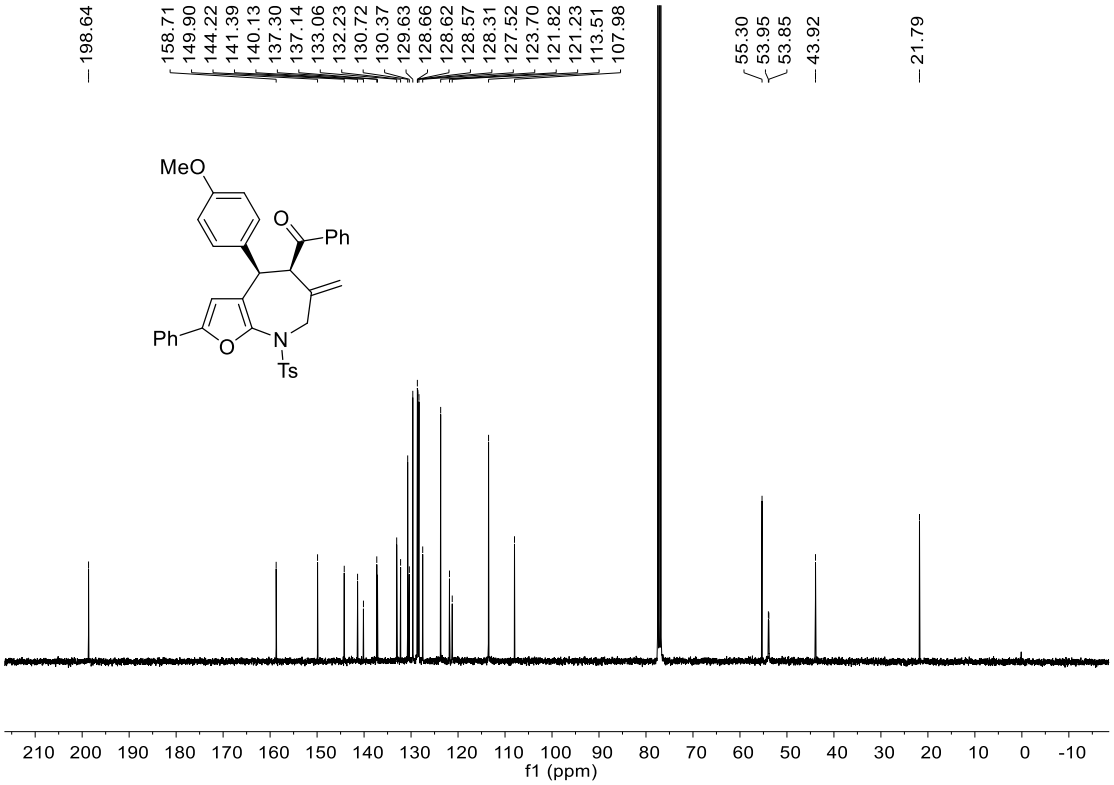
^{13}C NMR (100 MHz) of **5b** in $CDCl_3$



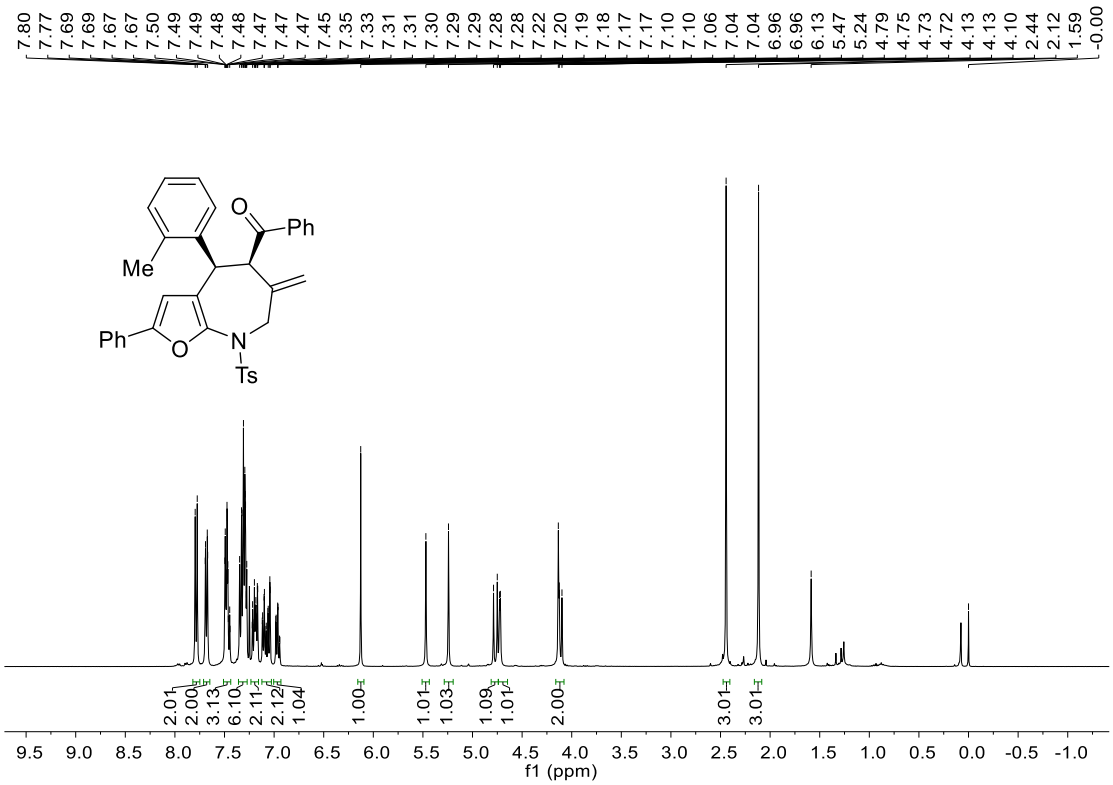
^{1}H NMR (400 MHz) of **5c** in $CDCl_3$



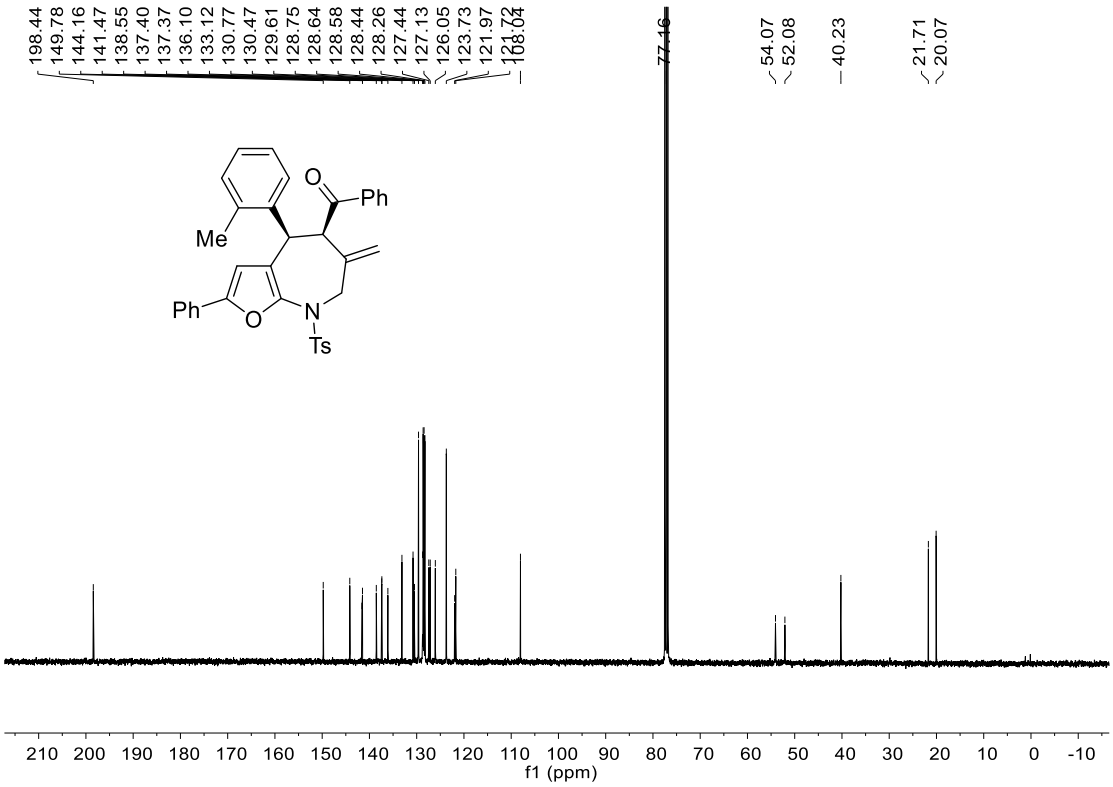
^{13}C NMR (100 MHz) of **5c** in $CDCl_3$



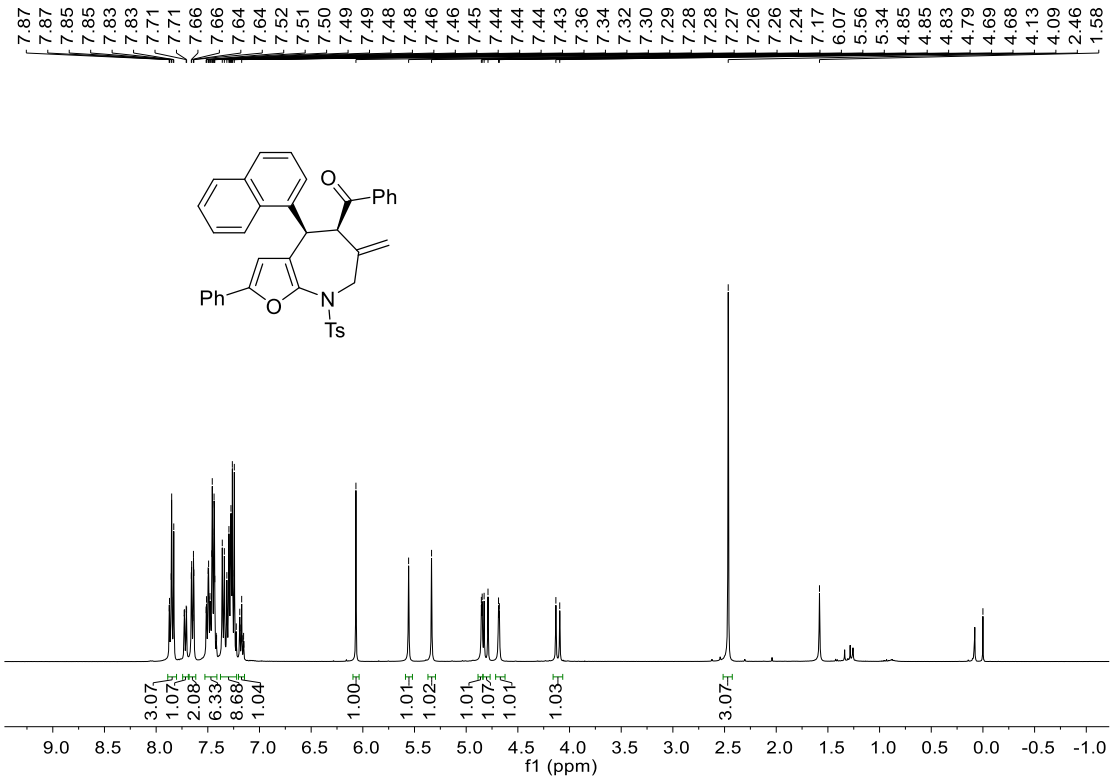
^{1}H NMR (400 MHz) of **5d** in $CDCl_3$



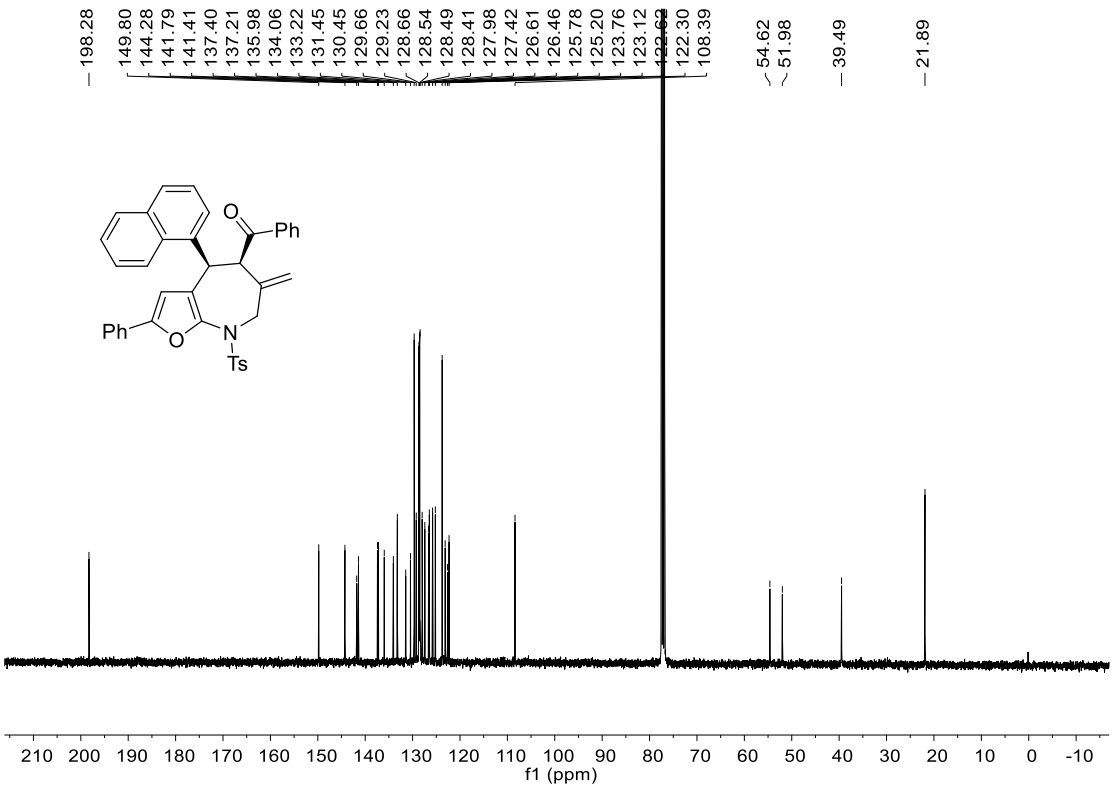
^{13}C NMR (100 MHz) of **5d** in $CDCl_3$



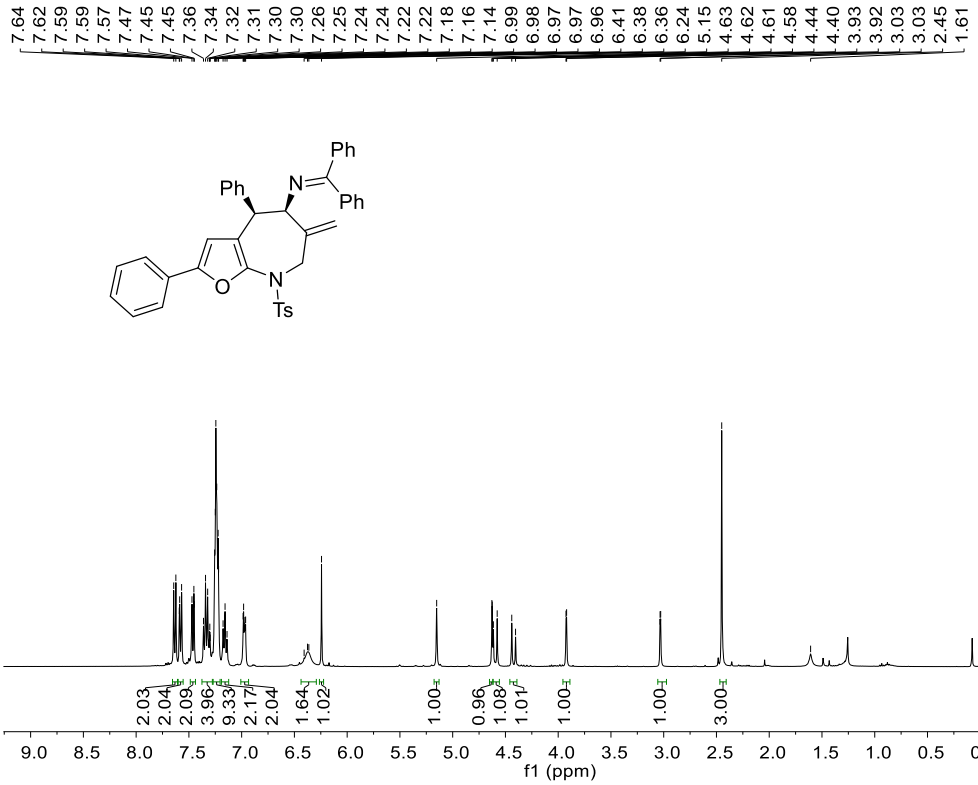
^{1}H NMR (400 MHz) of **5e** in $CDCl_3$



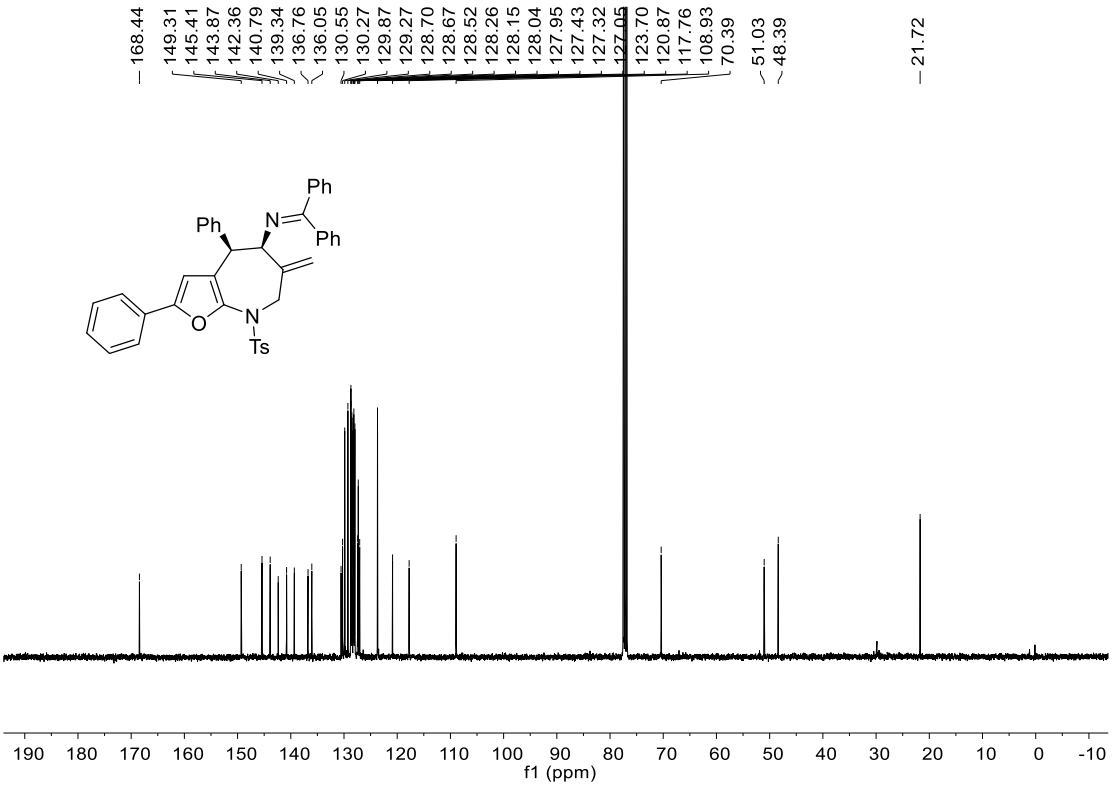
^{13}C NMR (100 MHz) of **5e** in $CDCl_3$



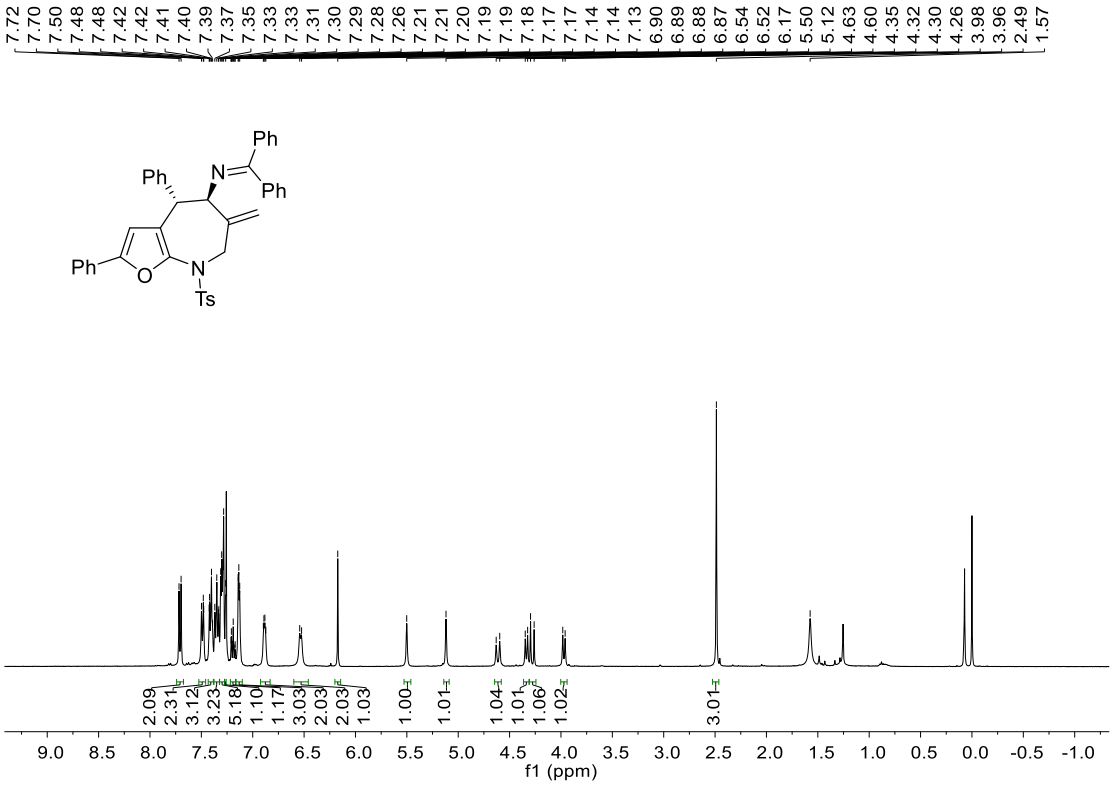
^{1}H NMR (400 MHz) of *cis*-**7a** in $CDCl_3$



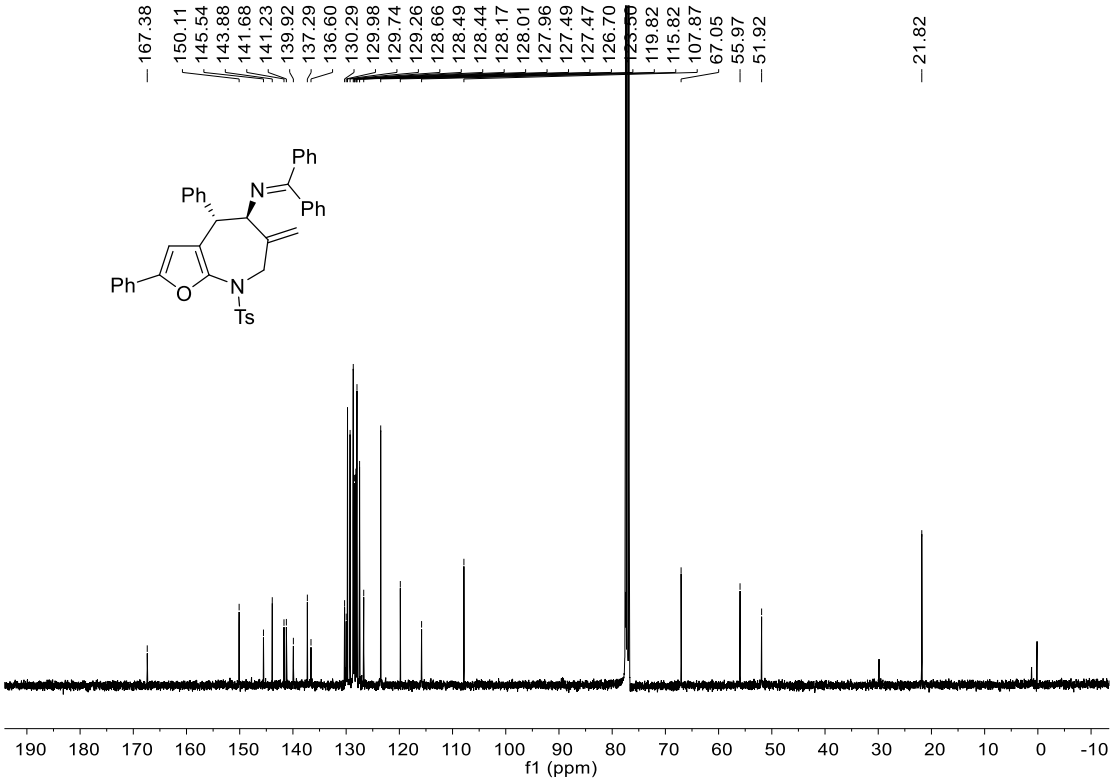
^{13}C NMR (100 MHz) of *cis*-**7a** in $CDCl_3$



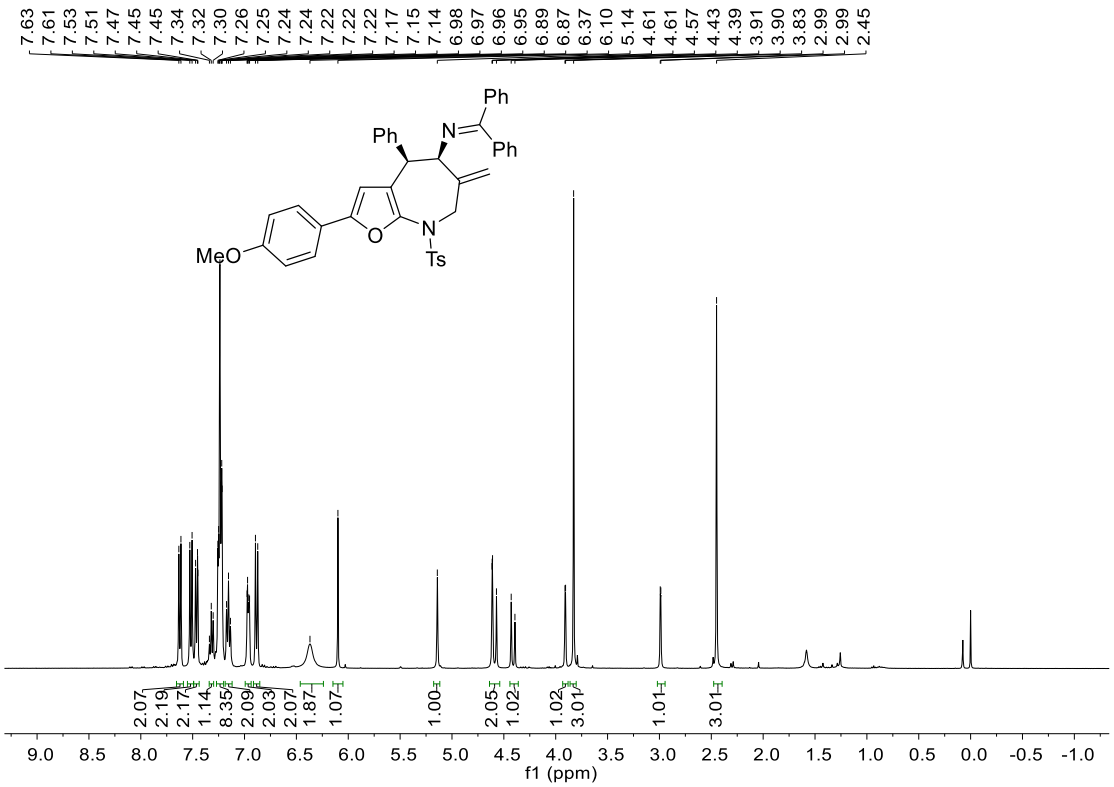
^{1}H NMR (400 MHz) of *trans*-**7a** in $CDCl_3$



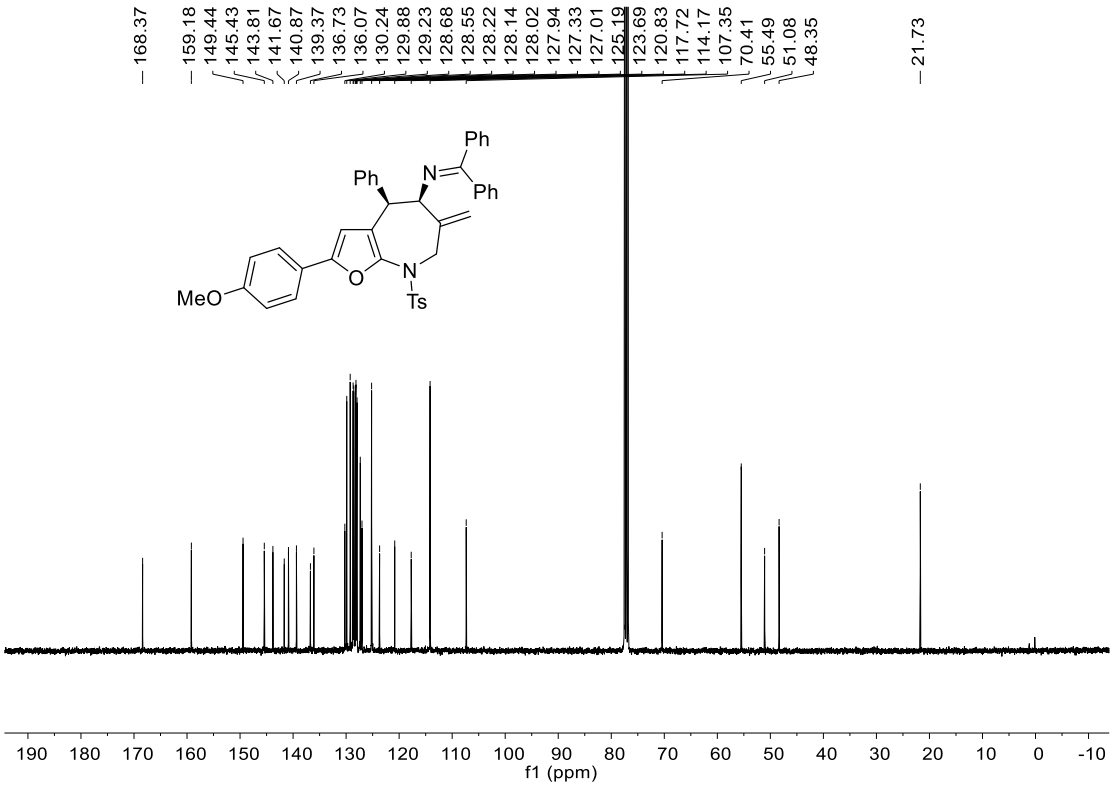
^{13}C NMR (100 MHz) of *trans*-**7a** in $CDCl_3$



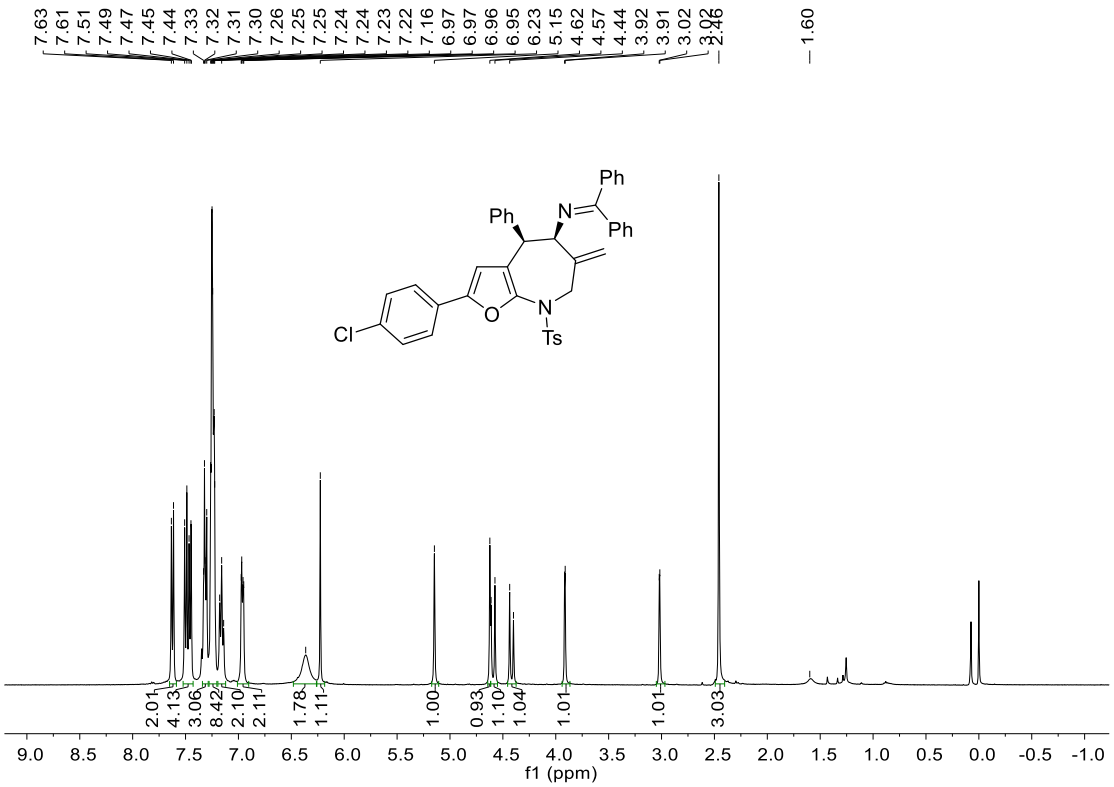
^{1}H NMR (400 MHz) of **7b** in $CDCl_3$



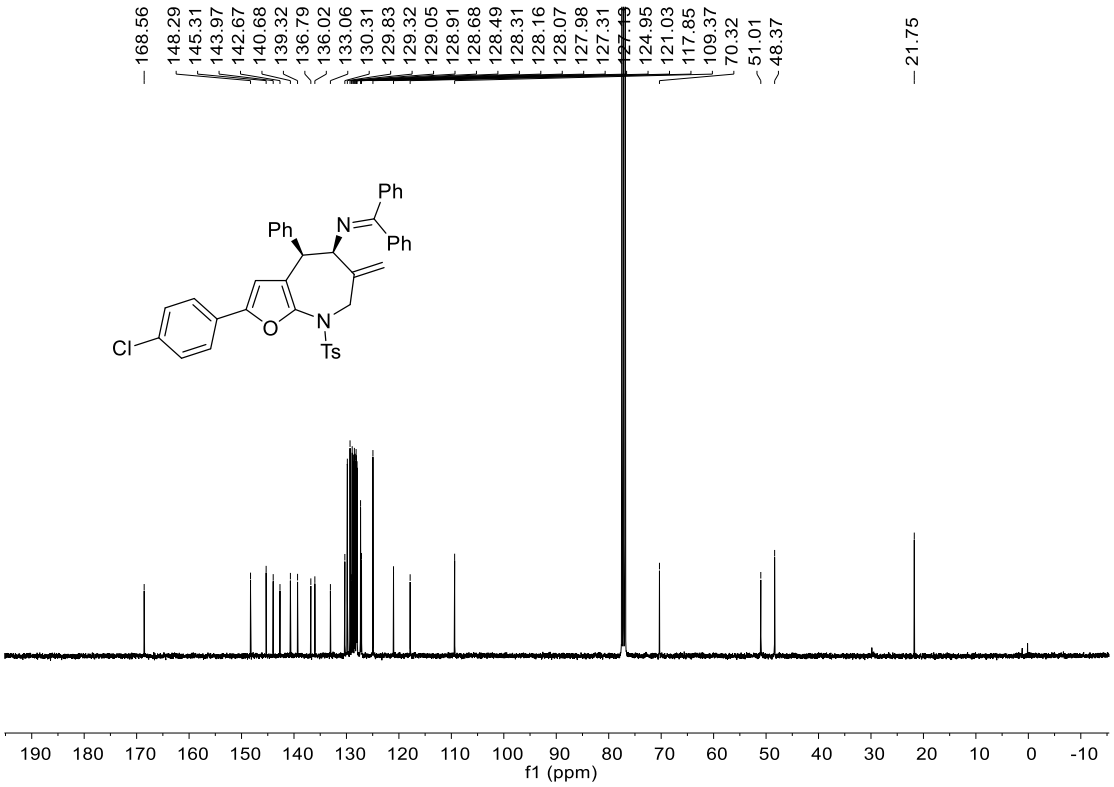
^{13}C NMR (100 MHz) of **7b** in $CDCl_3$



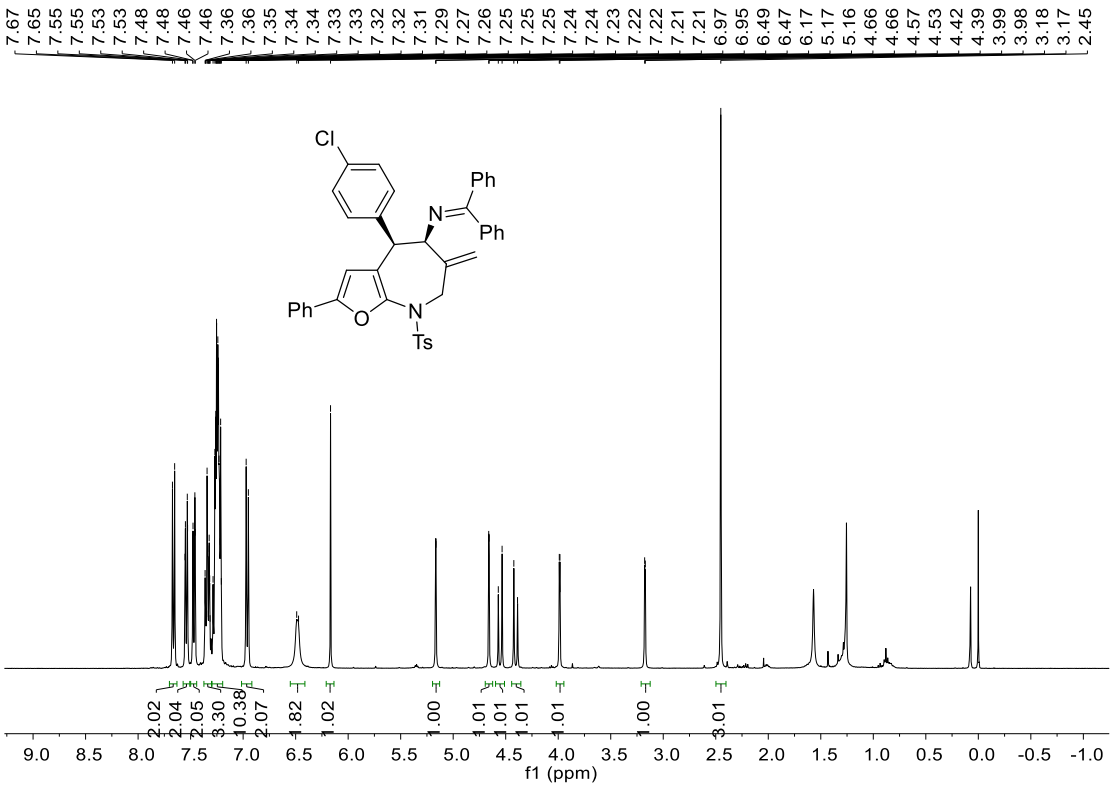
^{1}H NMR (400 MHz) of **7c** in $CDCl_3$



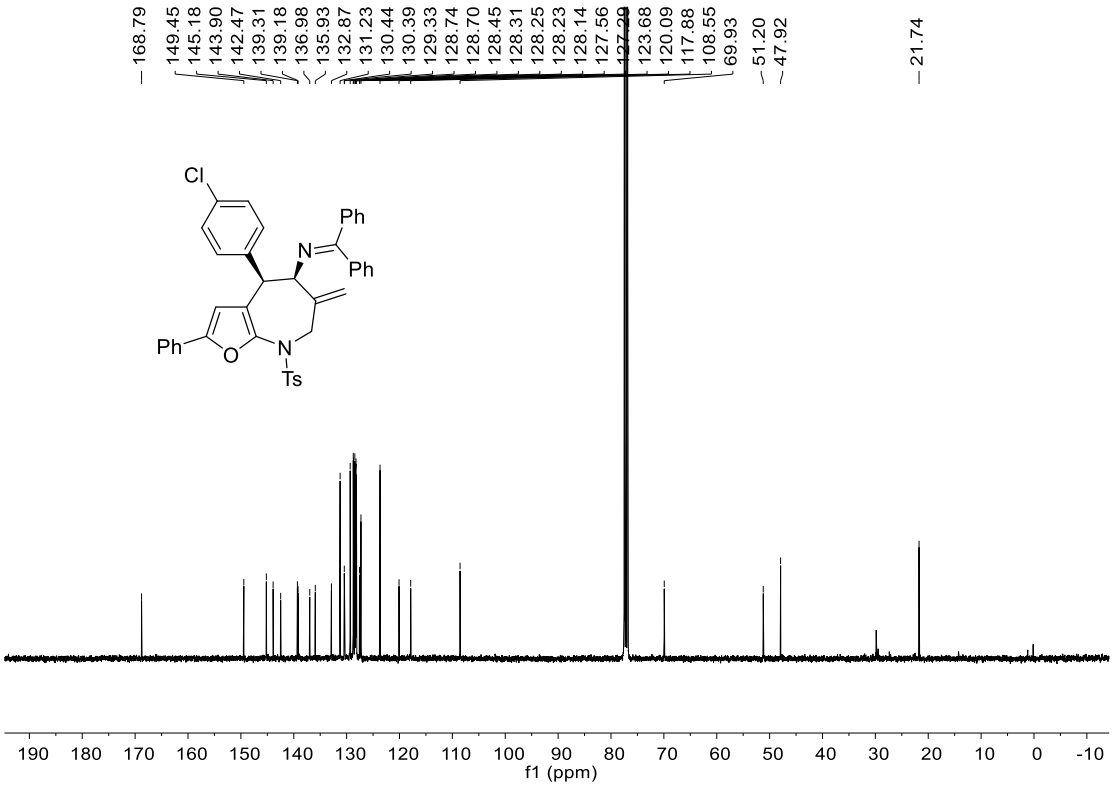
^{13}C NMR (100 MHz) of **7c** in $CDCl_3$



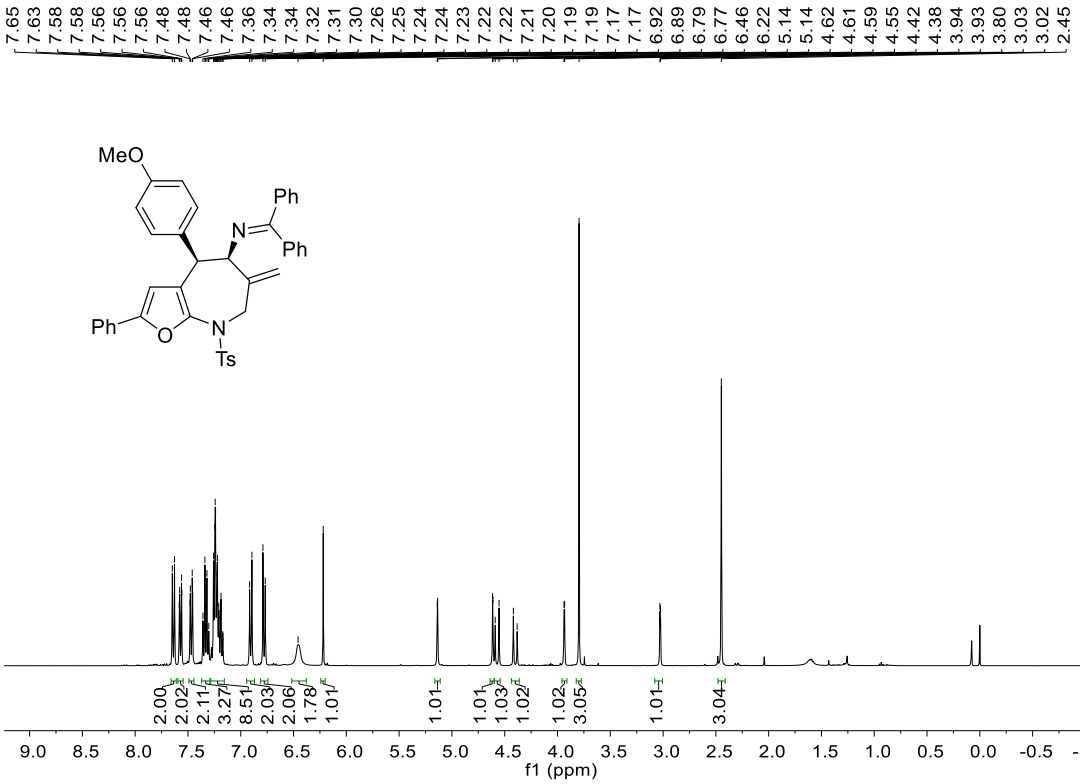
^{1}H NMR (400 MHz) of **7d** in $CDCl_3$



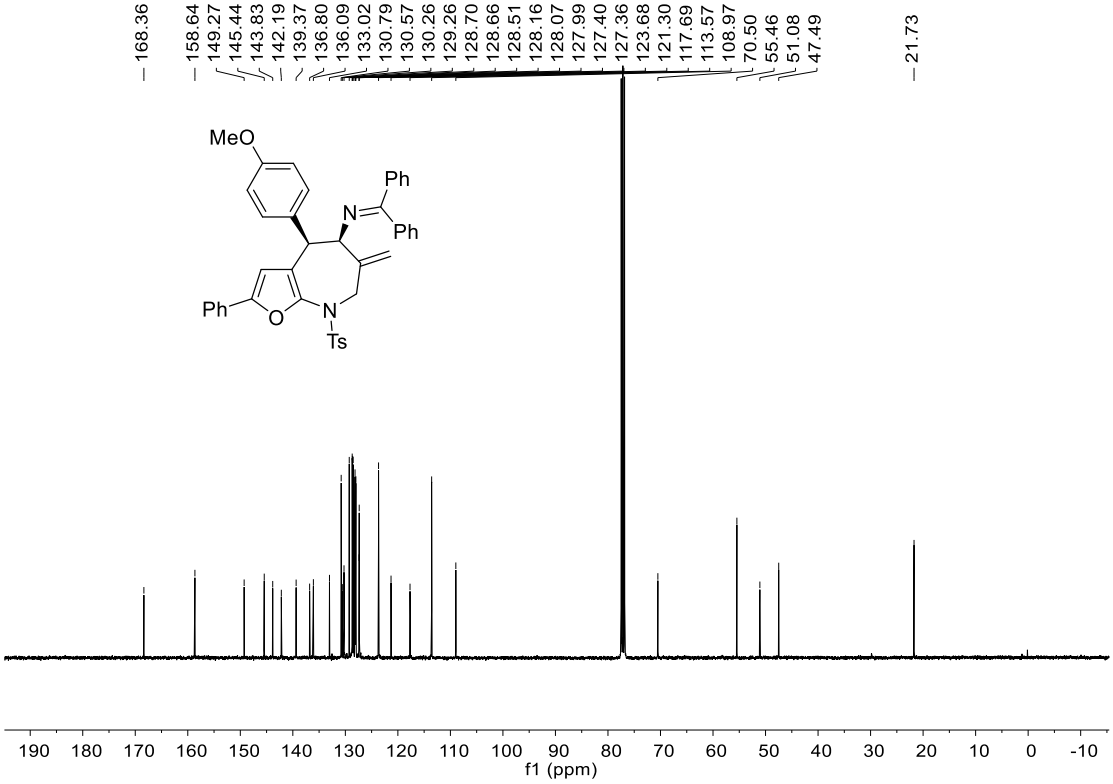
^{13}C NMR (100 MHz) of **7d** in $CDCl_3$



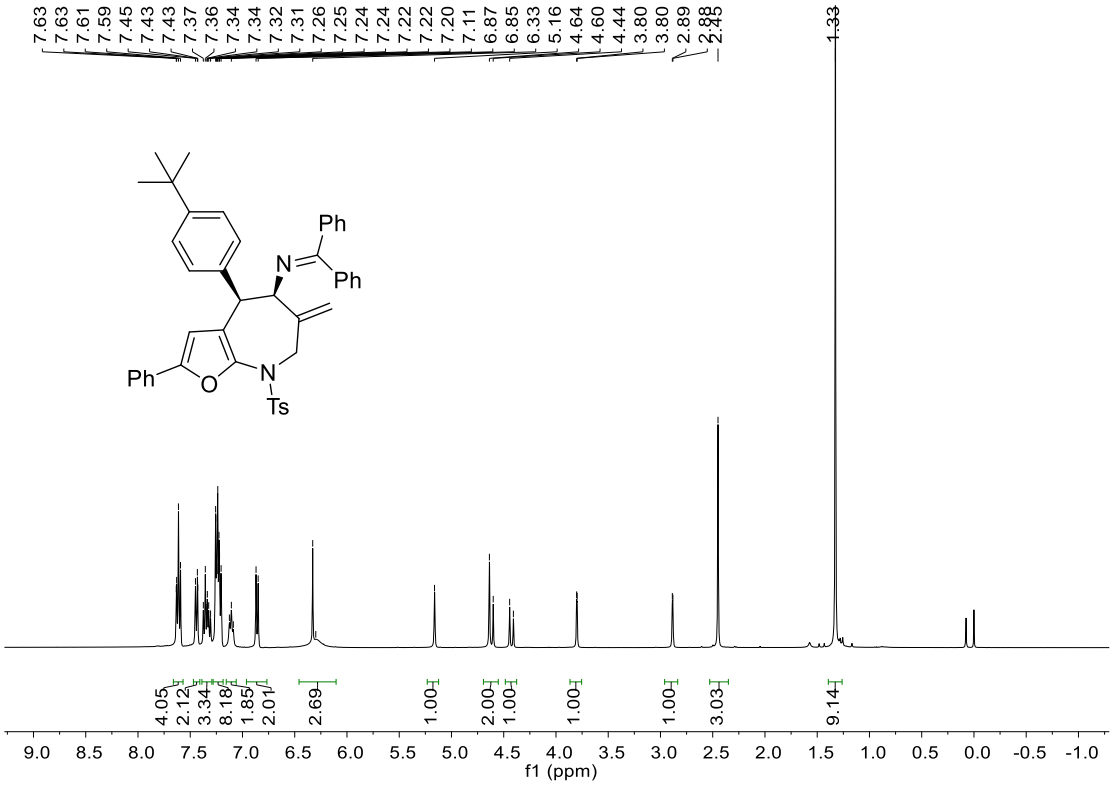
^{1}H NMR (400 MHz) of **7e** in $CDCl_3$



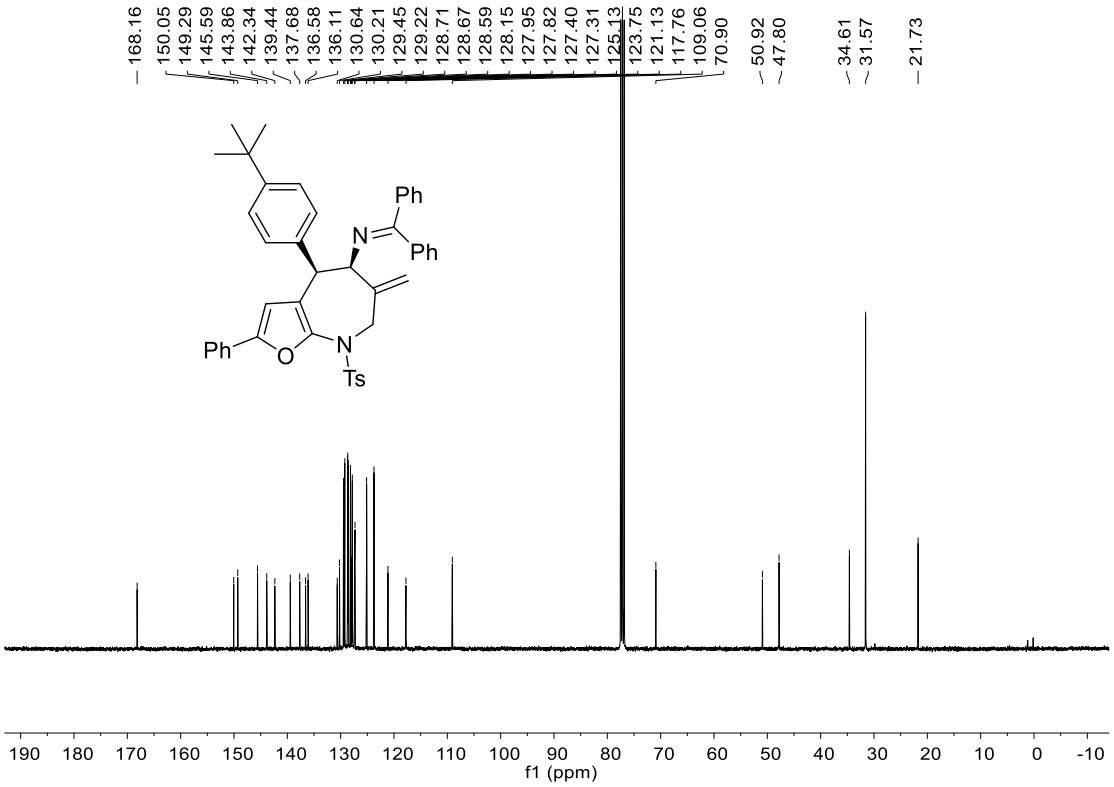
^{13}C NMR (100 MHz) of **7e** in $CDCl_3$



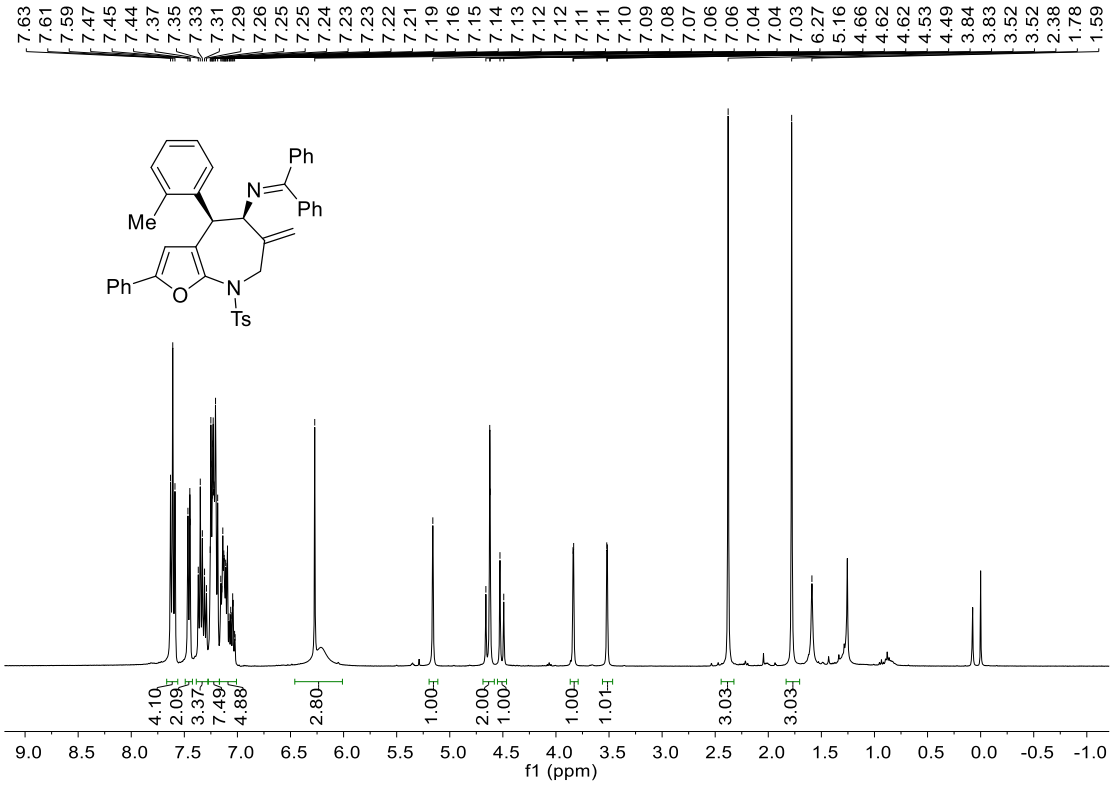
^{1}H NMR (400 MHz) of **7f** in $CDCl_3$



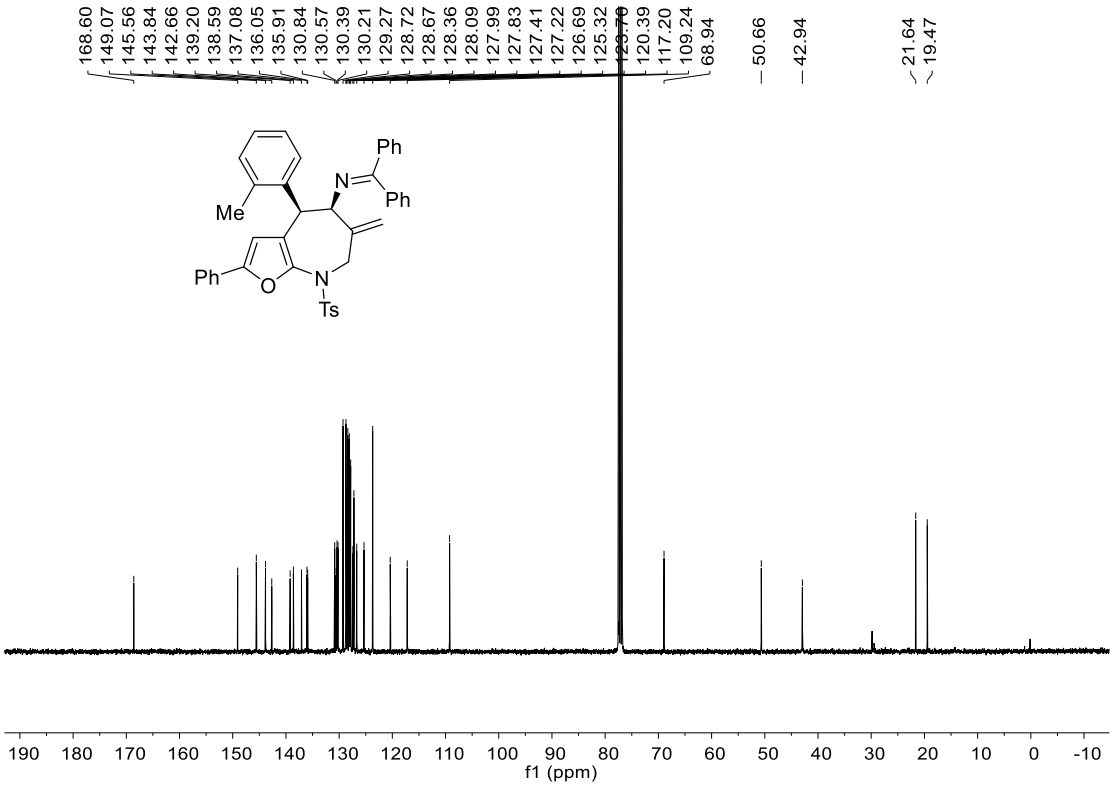
^{13}C NMR (100 MHz) of **7f** in $CDCl_3$



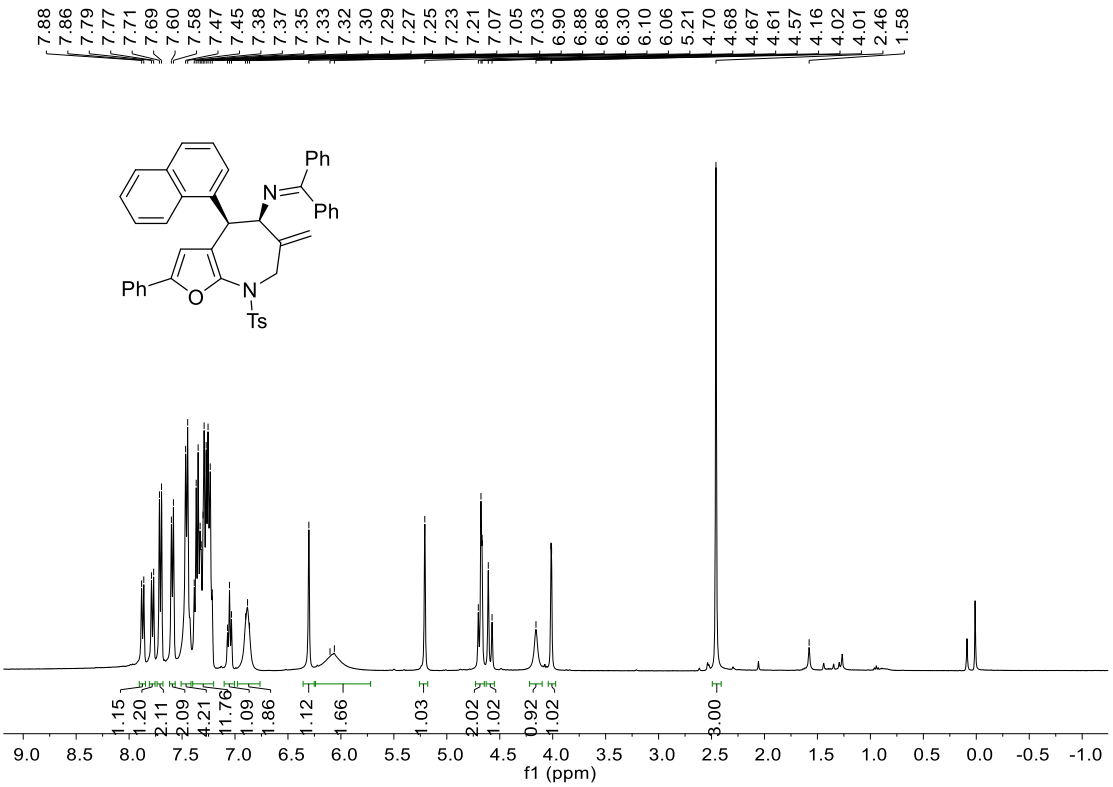
^{1}H NMR (400 MHz) of **7g** in $CDCl_3$



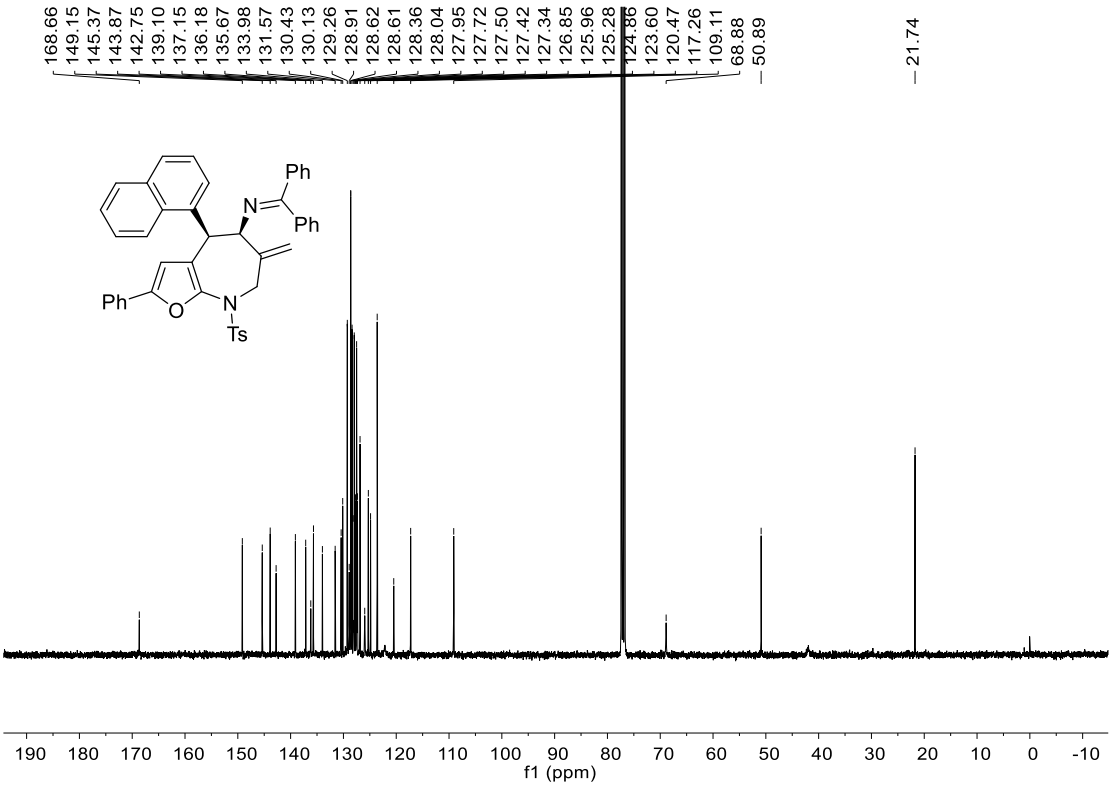
^{13}C NMR (100 MHz) of **7g** in $CDCl_3$



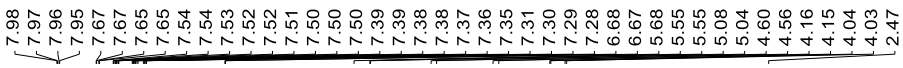
^{1}H NMR (400 MHz) of **7h** in $CDCl_3$

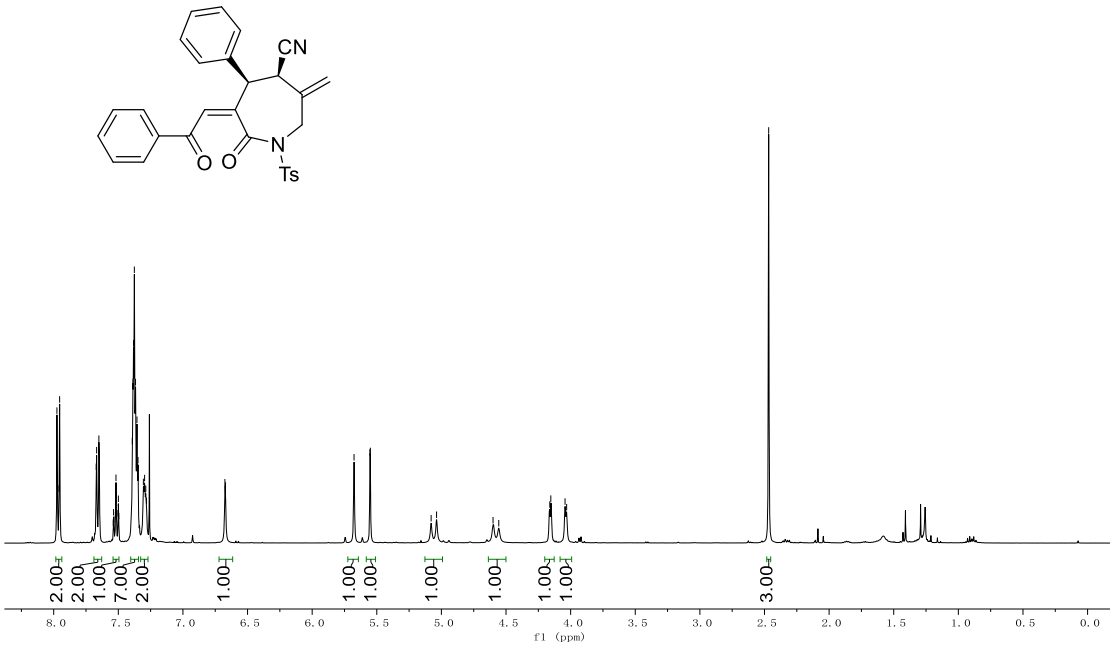


^{13}C NMR (100 MHz) of **7h** in $CDCl_3$

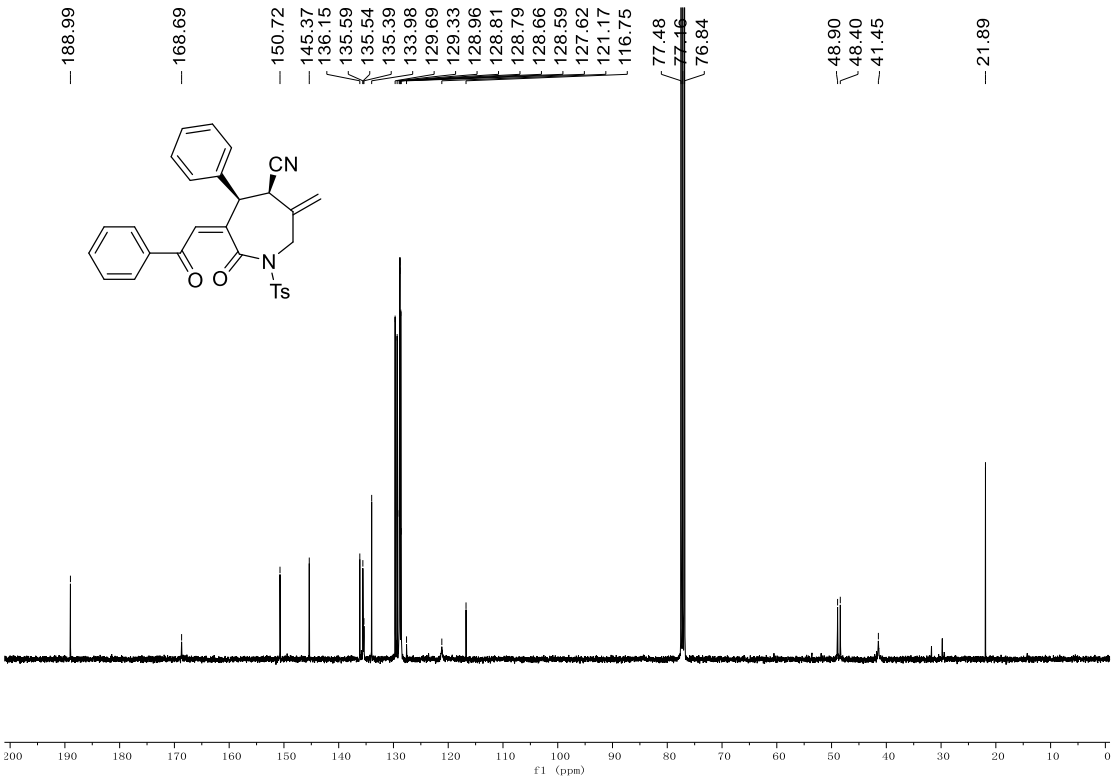


^{1}H NMR (400 MHz) of **8a** in $CDCl_3$

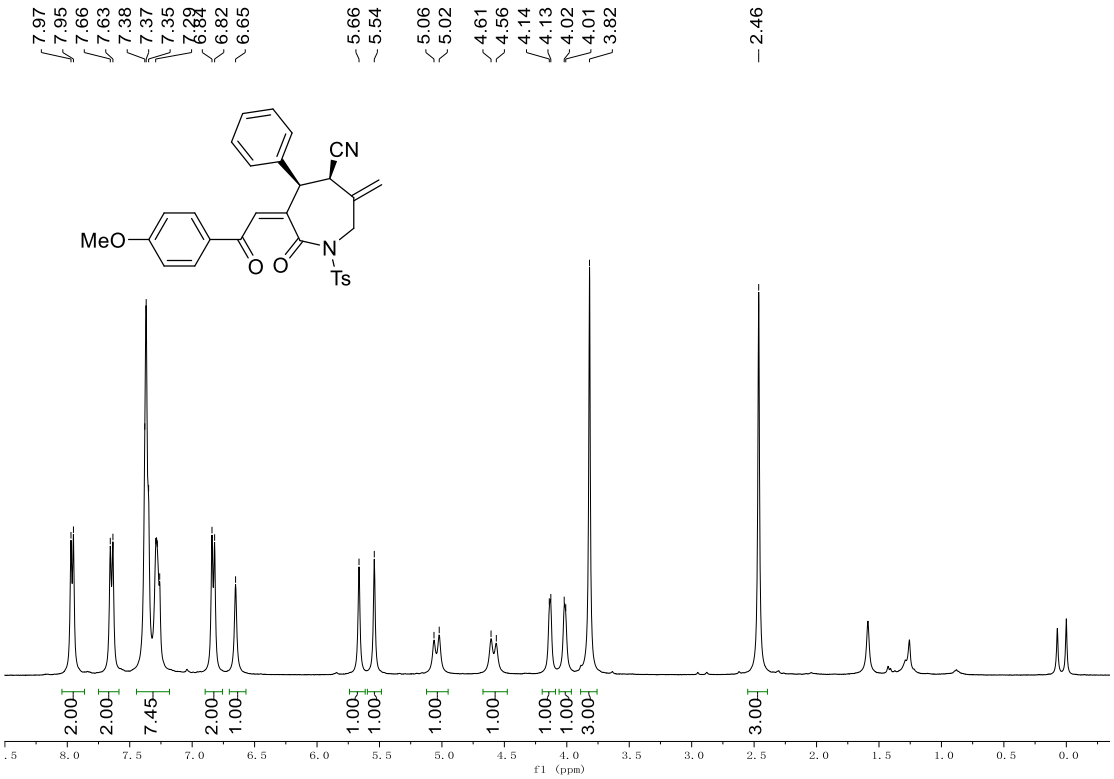




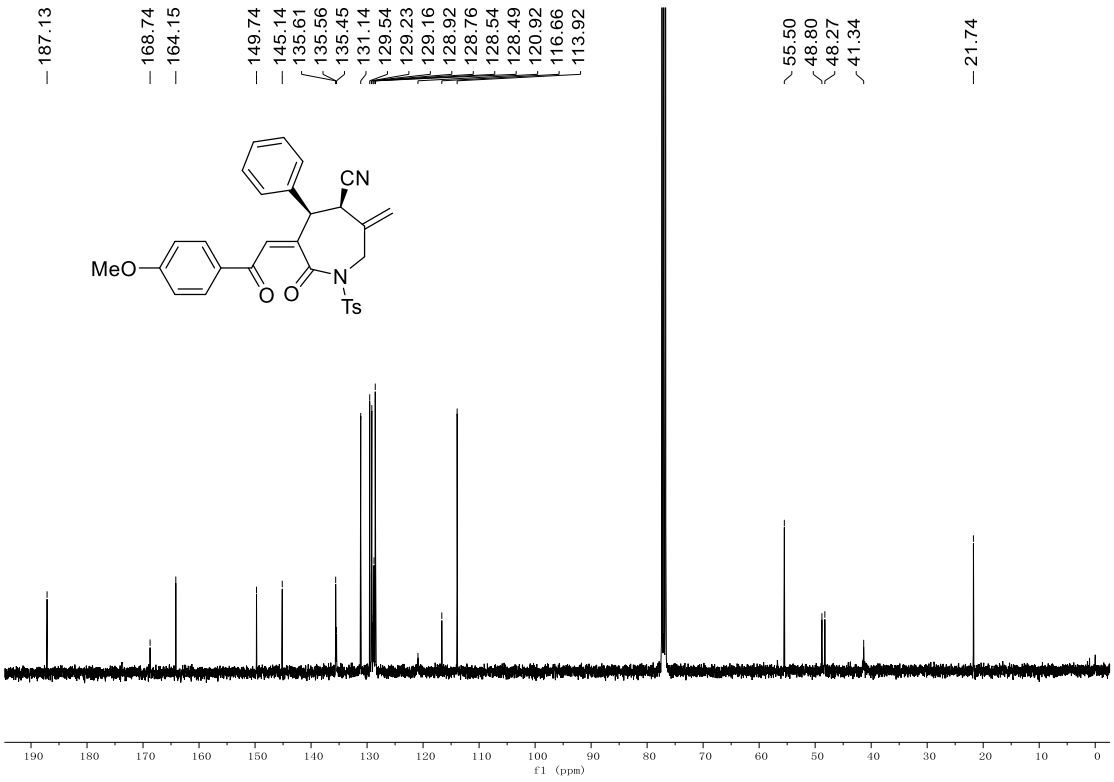
^{13}C NMR (100 MHz) of **8a** in $CDCl_3$



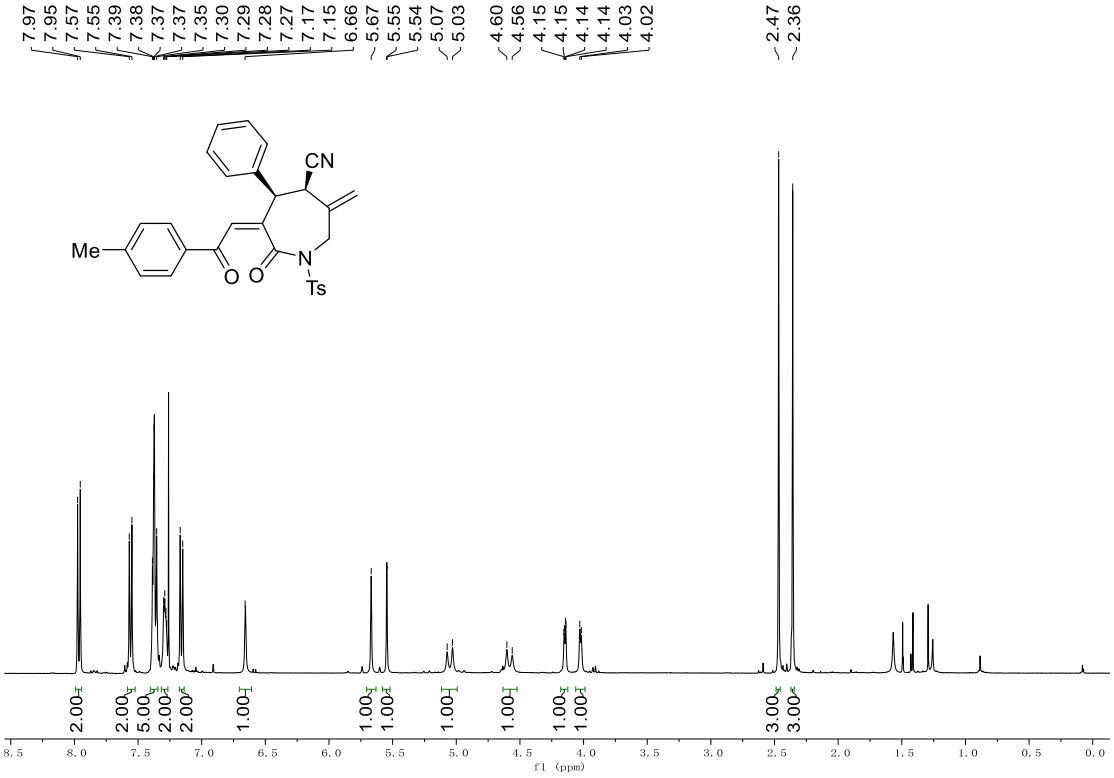
^{1}H NMR (400 MHz) of **8b** in $CDCl_3$



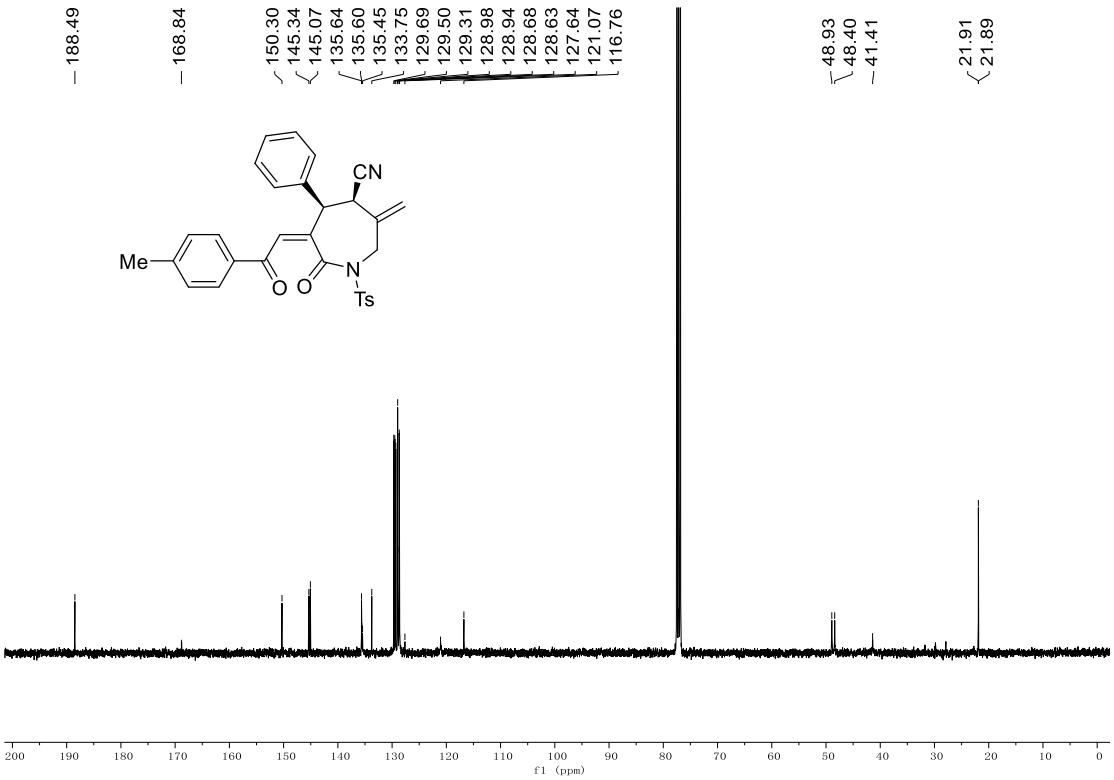
^{13}C NMR (100 MHz) of **8b** in $CDCl_3$



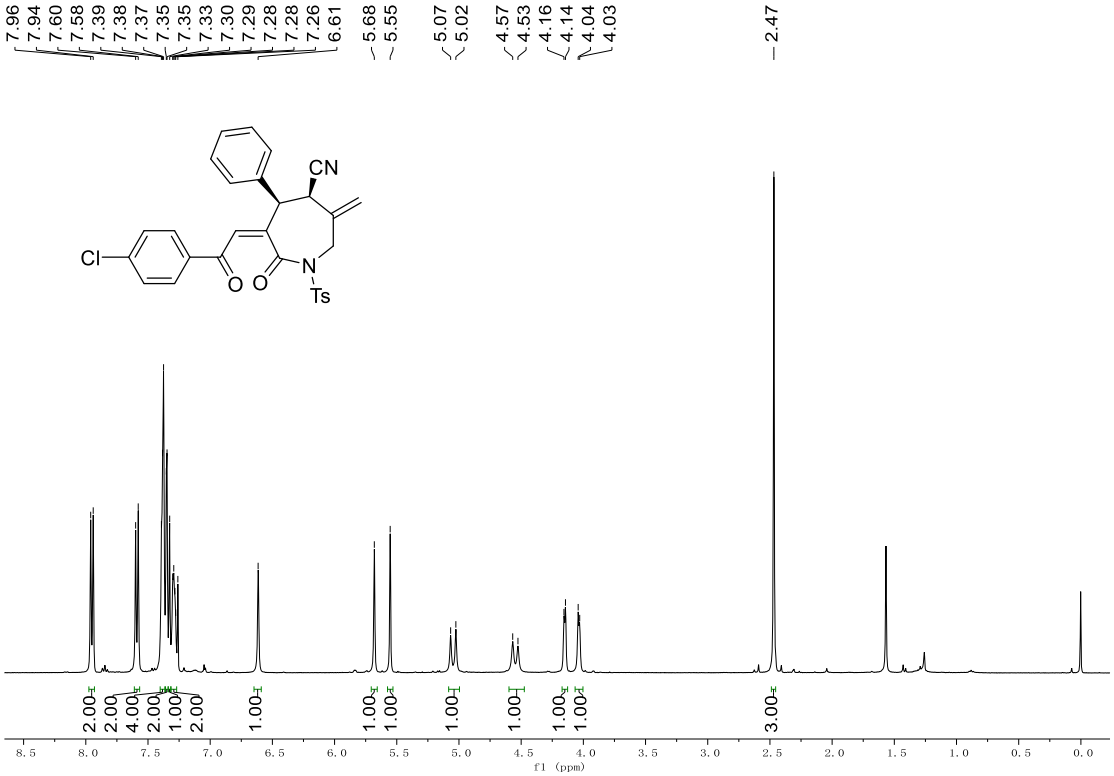
^{1}H NMR (400 MHz) of **8c** in $CDCl_3$



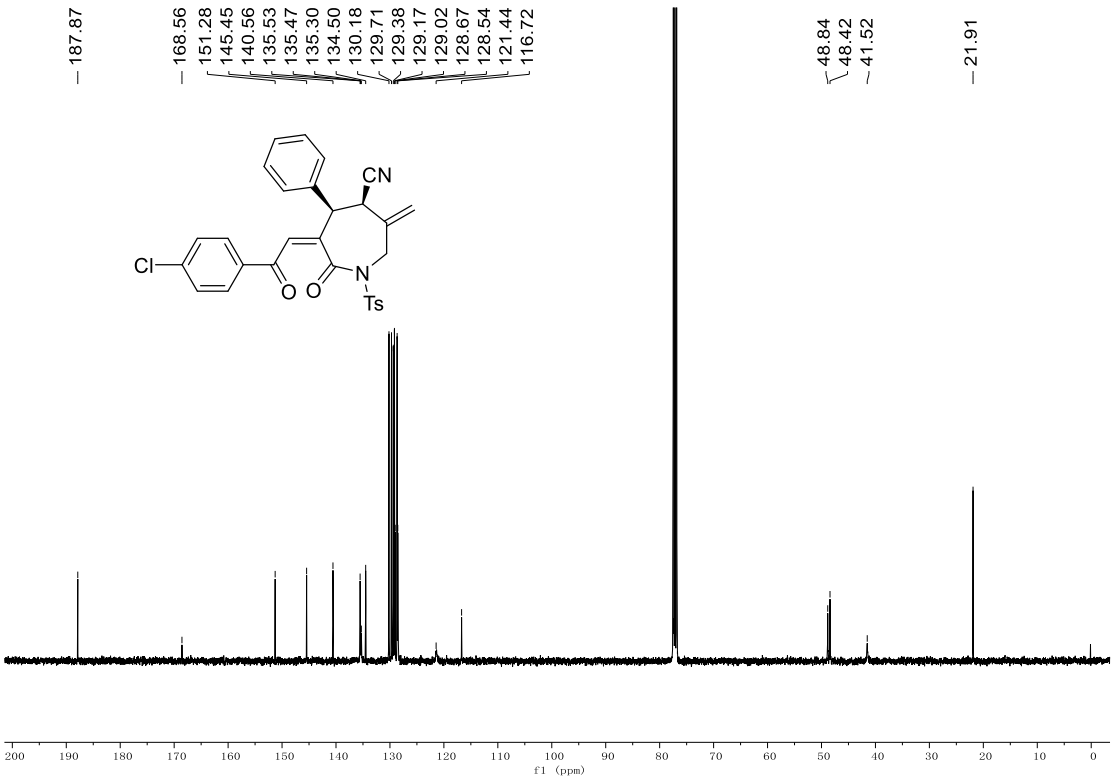
^{13}C NMR (100 MHz) of **8c** in $CDCl_3$



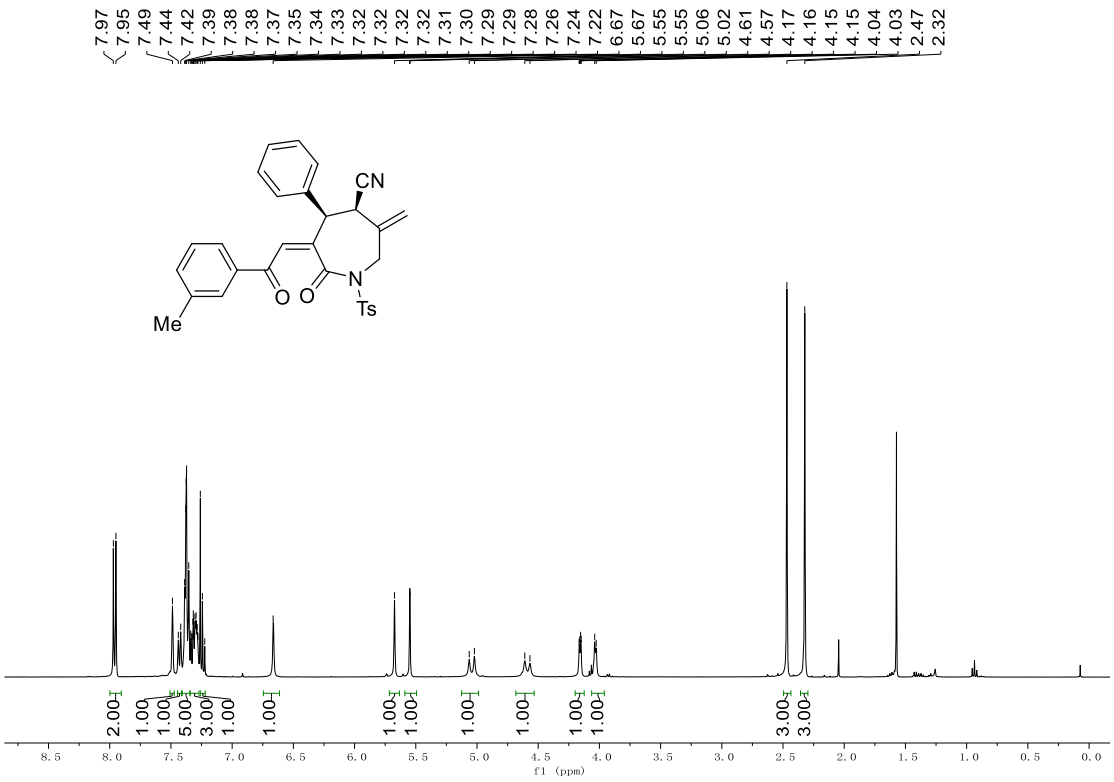
^{1}H NMR (400 MHz) of **8d** in $CDCl_3$



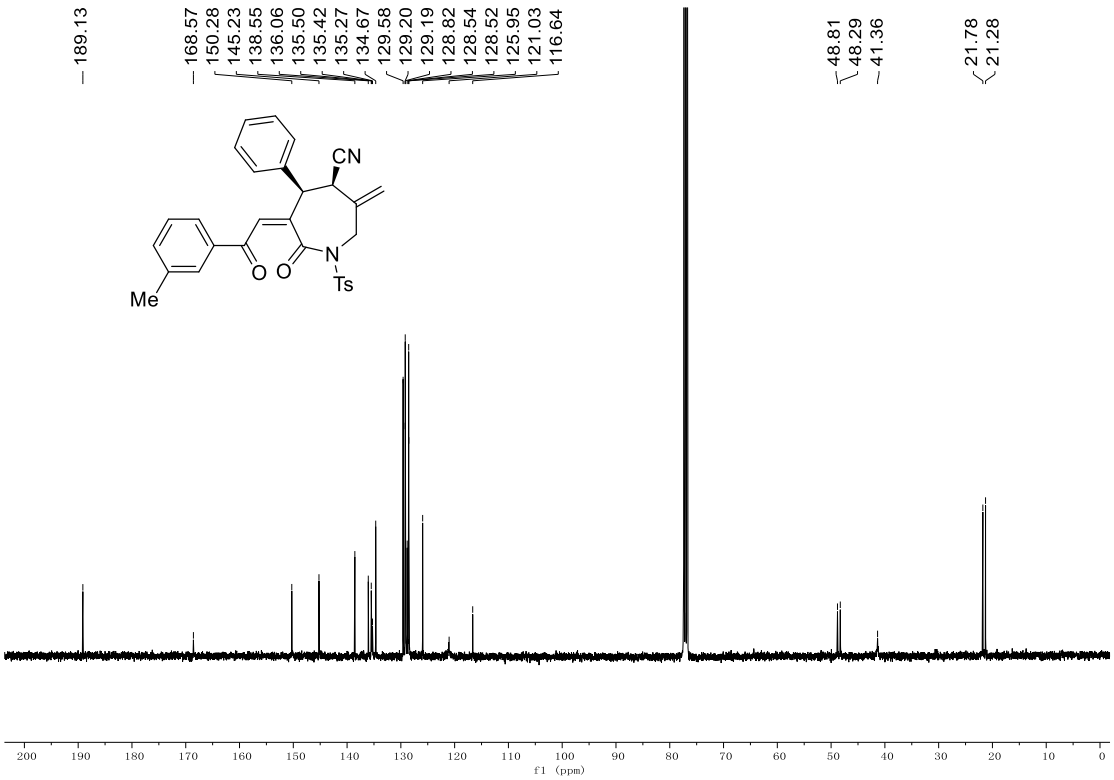
^{13}C NMR (100 MHz) of **8d** in $CDCl_3$



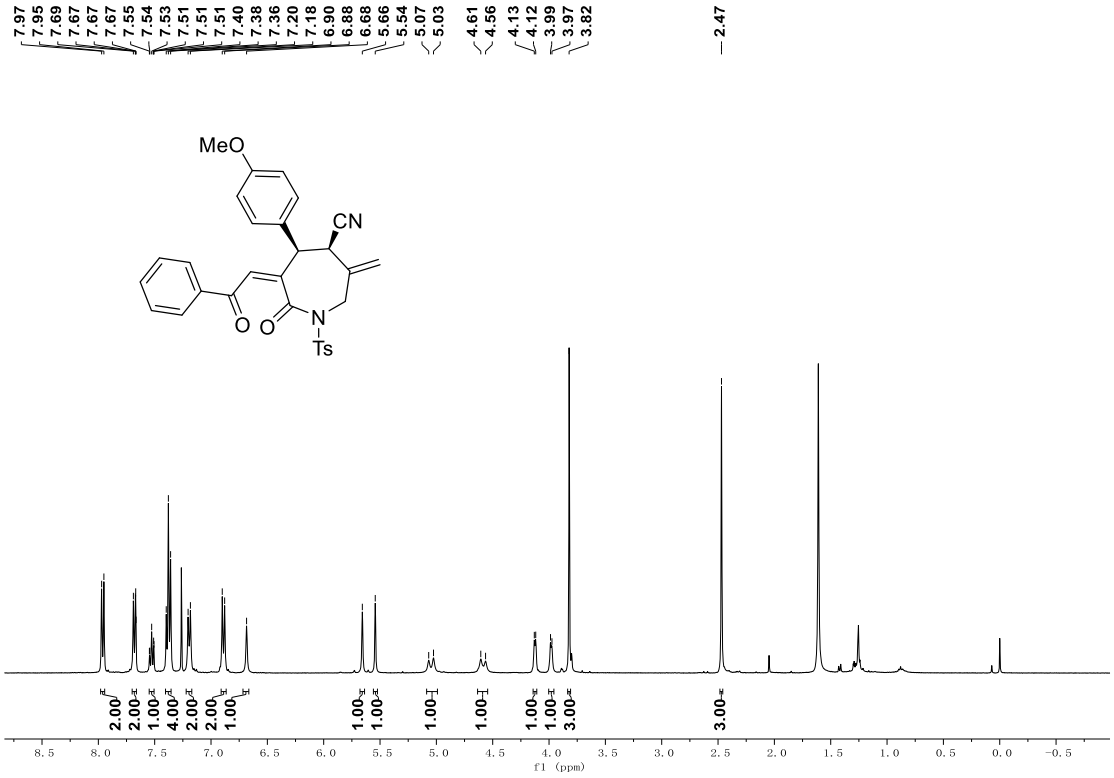
^{1}H NMR (400 MHz) of **8e** in $CDCl_3$



^{13}C NMR (100 MHz) of **8e** in $CDCl_3$



^{1}H NMR (400 MHz) of **8f** in $CDCl_3$



^{13}C NMR (100 MHz) of **8f** in $CDCl_3$