Electronic Supplementary Material (ESI) for Organic Chemistry Frontiers.

Supporting Information

Palladium-catalyzed asymmetric [4 + 3] cycloaddition of acyclic α,β-unsaturated imines with trimethylenemethane donors: access to chiral non-fused azepines

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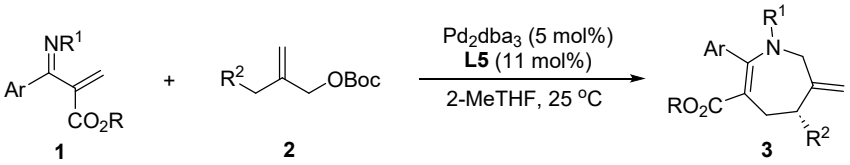
Contents

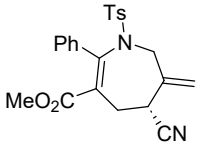
1. General information

^{1}H NMR spectra were recorded on a Bruker DPX 400 MHz or Bruker Ascend 600 MHz spectrometer in $CDCl_3$. 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, td = triplet of doublets, dt = doublet of triplets, ddd = doublet of doublet of doublets, ddt = doublet of doublet of triplets, dtd = doublet of triplet of doublets, brs = broad singlet, coupling constant (s) *J* are reported in Hz and relative integrations are reported. ^{13}C NMR spectra were recorded on a Bruker DPX 400 MHz or Bruker Ascend 600 MHz spectrometer in $CDCl_3$. Chemical shifts were reported in ppm with the internal chloroform signal at 77.16 ppm as a standard. ^{19}F NMR spectra were recorded on a Bruker Ascend 600 MHz spectrometer in $CDCl_3$ and referenced relative to $CFCl_3$. Enantiomeric excesses were determined by analysis of HPLC traces, obtained by using Chiralpak IC column with *n*-hexane and *i*-propanol as solvents. (Chiralpak IC column was purchased from Daicel. *n*-hexane and *i*-propanol were purchased from Energy.) Melting points were obtained in open capillary tubes using SGW X-4 micro melting point apparatus which were uncorrected. High-resolution mass spectra (HRMS) were recorded on a Waters GCT Premier mass spectrometer using EI-TOF (electron ionization-time of flight) or on a JEOC AccuTOF LC-plus 4G mass spectrometer using ESI (electrospray ionization). Commercially available materials were used as received. Anhydrous CH_2Cl_2 was distilled from calcium hydride, anhydrous THF and toluene was distilled from sodium/benzophenone. *α,β*-Unsaturated imines **1**[1] and trimethylenemethane（TMM）donors **2**[2] were prepared according to the literature procedure.

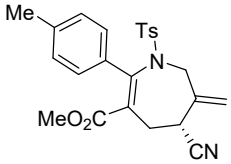
2. General procedure for the synthesis of products 3



General procedure A: To a flame-dried and N_2-purged Schlenk tube was added ligand **L5** (10.8 mg, 0.022 mmol, 11 mol%), and $Pd_2(dba)_3$ (9.2 mg, 0.01 mmol, 5 mol%) and anhydrous 2-MeTHF (2.0 mL). The resulting solution was stirred for 0.5 h at room temperature. Then the reaction tube was moved to 0 ℃. After 5 minutes, *α,β*-unsaturated imine **1** (0.2 mmol, 1.0 equiv) and trimethylenemethane（TMM）donor **2** (0.3 mmol, 1.5 equiv) was added sequentially. The resulting solution was stirred vigorously at 0 ℃. Once starting material was consumed (monitored by TLC), the mixture was concentrated and purified by column chromatography (PE/EA/DCM = 6:1:1) to give the corresponding product **3**.

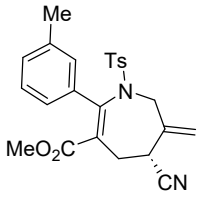


Methyl (*R*)-5-cyano-6-methylene-2-phenyl-1-tosyl-4,5,6,7-tetrahydro-1*H*-azepine-3-carboxylate (3a): Following the general procedure **A**, compound **3a** was obtained as a white solid in 90% yield (79.0 mg) and 96% *ee*; R_f = 0.4 (petroleum ether/EtOAc/DCM = 6/1/1, v/v/v); m.p.: 117-119 °C; **^{1}H NMR** (600 MHz, $CDCl_3$) δ 7.35–7.28 (m, 1H), 7.25–7.16 (m, 4H), 7.14–7.00 (m, 4H), 5.45 (s, 1H), 5.42 (s, 1H), 4.54–4.27 (m, 2H), 3.62–3.49 (m, 1H), 3.42 (s, 3H), 2.99–2.94 (m, 1H), 2.88 (dd, *J* = 14.4, 8.9 Hz, 1H), 2.38 (s, 3H), **^{13}C NMR** (150 MHz, $CDCl_3$) δ 168.5, 150.1, 144.0, 137.6, 137.2, 136.1, 129.5(3C), 129.0(2C), 127.9(2C), 127.2(2C), 125.7, 119.2, 118.5, 55.2, 52.1, 33.2, 32.6, 21.6; **HRMS** (ESI-TOF) calcd for $C_{23}H_{23}N_2O_4S$ $[M+H]^+$: 423.1300, found: 423.1302. $[\alpha]_D^{20}$ = -117.8 (*c* = 0.2, CH_2Cl_2); **HPLC** (Chiralpak IC-H, *n*-hexane/*i*-propanol = 80/20, flow rate = 1.0 mL/min, λ = 254 nm) t_R= 32.692 min (major), 38.709 min (minor).

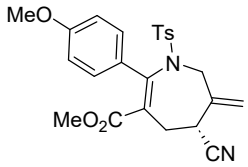


Methyl (*R*)-5-cyano-6-methylene-2-(*p*-tolyl)-1-tosyl-4,5,6,7-tetrahydro-1*H*-azepine-3-carboxylate (3b), Following the general procedure **A**, compound **3b** was obtained as a white solid in 84% yield (73.3 mg) and 96% *ee*; R_f = 0.4 (petroleum ether/EtOAc/DCM = 6/1/1, v/v/v); m.p.:121-123 °C; **^{1}H NMR** (400 MHz, $CDCl_3$) δ 7.27 (d, *J* = 8.1 Hz, 2H), 7.12 (d, *J* = 8.0 Hz, 2H), 7.00 (s, 4H), 5.45 (s, 1H), 5.43 (s, 1H), 4.53 – 4.28 (m, 2H), 3.55 – 3.49 (m, 1H),

3.47 (s, 3H), 2.94 (dd, *J* = 14.5, 3.3 Hz, 1H), 2.85 (dd, *J* = 14.6, 8.6 Hz, 1H), 2.41 (s, 3H), 2.36 (s, 3H).; **^{13}C NMR** (150 MHz, $CDCl_3$) δ 168.6, 150.4, 143.9, 139.7, 137.6, 137.3, 133.2, 129.4(2C), 128.9(2C), 128.6(2C), 127.2(2C), 124.9, 119.2, 118.6, 55.2, 52.1, 33.2, 32.6, 21.6, 21.5; **HRMS** (ESI-TOF) calcd for $C_{24}H_{25}N_2O_4S$ $[M+H]^+$: 437.1530, found: 437.1528. $[\alpha]_D^{20}$ = -101.0 (*c* = 0.2, CH_2Cl_2); **HPLC** (Chiralpak IC-H, *n*-hexane/*i*-propanol = 80/20, flow rate = 1.0 mL/min, λ = 254 nm) t_R= 36.215 min (major), 41.963 min (minor).

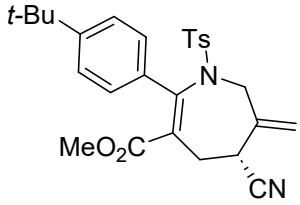


Methyl (*R*)-5-cyano-6-methylene-2-(*m*-tolyl)-1-tosyl-4,5,6,7-tetrahydro-1*H*-azepine-3-carboxylate (3c): Following the general procedure **A**, compound **3c** was obtained as a white solid in 82% yield (71.6 mg) and 97% *ee*; R_f = 0.4 (petroleum ether/EtOAc/DCM = 6/1/1, v/v/v); m.p.: 138-140 °C; **^{1}H NMR** (400 MHz, $CDCl_3$) δ 7.18 (d, *J* = 8.0 Hz, 2H), 7.12 – 7.04 (m, 4H), 6.94 (d, *J* = 6.5 Hz, 1H), 6.72 (s, 1H), 5.44 (s, 1H), 5.42 (s, 1H), 4.46 – 4.31 (m, 2H), 3.59 – 3.52 (m, 1H), 3.42 (s, 3H), 3.00 (dd, *J* = 14.5, 3.3 Hz, 1H), 2.91 (dd, *J* = 14.6, 8.5 Hz, 1H), 2.36 (s, 3H), 2.13 (s, 3H). **^{13}C NMR** (150 MHz, $CDCl_3$) δ 168.6, 150.3, 143.8, 137.8, 137.4, 137.3, 135.5, 130.3, 129.4, 129.3 (2C), 127.8, 127.1(2C), 126.6, 125.4, 119.0, 118.6, 55.3, 52.1, 33.2, 32.7, 21.6, 21.2.; **HRMS** (ESI-TOF) calcd for $C_{24}H_{25}N_2O_4S$ $[M+H]^+$: 437.1530, found: 437.1528. $[\alpha]_D^{20}$ = -88.7 (*c* = 0.4, CH_2Cl_2); **HPLC** (Chiralpak IC-H, *n*-hexane/*i*-propanol = 80/20, flow rate = 1.0 mL/min, λ = 254 nm) t_R= 30.568 min (major), 36.801 min (minor).

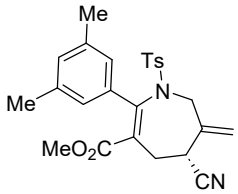


Methyl (*R*)-5-cyano-2-(4-methoxyphenyl)-6-methylene-1-tosyl-4,5,6,7-tetrahydro-1*H*-azepine-3-carboxylate (3d): Following the general procedure **A**, compound **3d** was obtained as a white solid in 88% yield (79.6 mg) and 95% *ee*; R_f = 0.2 (petroleum ether/EtOAc/DCM = 6/1/1, v/v/v); m.p.: 172-173 °C; **^{1}H NMR** (400 MHz, $CDCl_3$) δ 7.28 – 7.23 (m, 2H), 7.14 – 7.09 (m, 2H), 7.04 – 6.99 (m, 2H), 6.72 – 6.65 (m, 2H), 5.42 (d, *J* = 1.2 Hz, 1H), 5.41 (s, 1H), 4.48 – 4.28 (m, 2H), 3.79 (s, 3H), 3.51 – 3.48 (m, 1H), 3.46 (s, 3H), 2.90 (dd, *J* = 14.4, 3.3 Hz, 1H), 2.87 – 2.77 (m, 1H), 2.38 (s, 3H). **^{13}C NMR** (150 MHz, $CDCl_3$) δ 168.8, 160.8, 150.3, 143.9, 137.6, 137.4, 130.6(2C), 129.5(2C), 128.4, 127.2(2C), 124.0, 119.1, 118.6, 113.3(2C), 77.4, 77.2, 76.9, 55.4, 55.2, 52.1, 33.2, 32.6, 21.6; **HRMS** (ESI-TOF) calcd for $C_{24}H_{25}N_2O_5S$ $[M+H]^+$: 453.1479, found: 453.1483. $[\alpha]_D^{20}$ = -74.1 (*c* = 0.4, CH_2Cl_2); **HPLC**

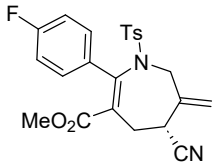
(Chiralpak IC-H, *n*-hexane/*i*-propanol = 70/30, flow rate = 1.0 mL/min, λ = 254 nm) t_R= 26.064 min (major), 31.149 min (minor).



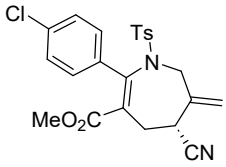
Methyl (*R*)-2-(4-(tert-butyl)phenyl)-5-cyano-6-methylene-1-tosyl-4,5,6,7-tetrahydro-1*H*-azepine-3-carboxylate (3e): Following the general procedure **A**, compound **3e** was obtained as a white solid in 73% yield (69.8 mg) and 97% *ee*; R_f = 0.4 (petroleum ether/EtOAc/DCM = 6/1/1, v/v/v); m.p.: 119-120 °C; **^{1}H NMR** (600 MHz, $CDCl_3$) δ 7.18 – 7.15 (m, 2H), 7.14 – 7.12 (m, 2H), 7.04 (d, *J* = 8.0 Hz, 2H), 6.97 – 6.94 (m, 2H), 5.44 (d, *J* = 1.2 Hz, 1H), 5.42 (s, 1H), 4.48 – 4.31 (m, 2H), 3.56 (dd, *J* = 8.6, 4.6 Hz, 1H), 3.43 (s, 3H), 3.02 (dd, *J* = 14.4, 3.3 Hz, 1H), 2.94 (dd, *J* = 14.4, 8.6 Hz, 1H), 2.35 (s, 3H), 1.29 (s, 9H).; **^{13}C NMR** (150 MHz, $CDCl_3$) δ 168.4, 152.6, 150.1, 143.5, 137.8, 137.4, 132.5, 129.3(2C), 128.7(2C), 127.1(2C), 125.2, 124.6(2C), 119.0, 118.5, 55.2, 52.0, 34.7, 33.2, 32.6, 31.3(3C), 21.5; **HRMS** (ESI-TOF) calcd for $C_{27}H_{31}N_2O_4S$ $[M+H]^+$: 479.1999, found: 479.2004. $[\alpha]_D^{20}$ = -37.5 (*c* = 0.6, CH_2Cl_2); **HPLC** (Chiralpak IC-H, *n*-hexane/*i*-propanol = 80/20, flow rate = 1.0 mL/min, λ = 254 nm) t_R= 31.497 min (major), 35.586 min (minor).



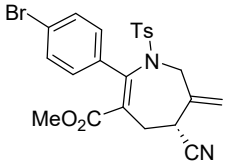
Methyl (*R*)-5-cyano-2-(3,5-dimethoxyphenyl)-6-methylene-1-tosyl-4,5,6,7-tetrahydro-1*H*-azepine-3-carboxylate (3f): Following the general procedure **A**, compound **3f** was obtained as a white solid in 83% yield (74.7 mg) and 97% *ee*; R_f = 0.4 (petroleum ether/EtOAc/DCM = 6/1/1, v/v/v); m.p.: 119-120 °C; **^{1}H NMR** (400 MHz, $CDCl_3$) δ 7.22 (d, *J* = 8.3 Hz, 2H), 7.10 (d, *J* = 8.1 Hz, 2H), 6.91 (s, 1H), 6.64 (s, 2H), 5.46 (d, *J* = 9.0 Hz, 2H), 4.42 (s, 2H), 3.58 (d, *J* = 6.3 Hz, 1H), 3.47 (s, 3H), 3.10 – 2.89 (m, 2H), 2.40 (s, 3H), 2.17 (s, 6H). **^{13}C NMR** (150 MHz, $CDCl_3$) δ 168.7, 150.4, 143.6, 137.3, 137.2, 135.1, 131.2, 129.2, 127.1(2C), 126.8(2C), 124.0, 123.8, 118.8, 118.5, 55.3, 52.0, 33.2, 32.7, 21.5, 21.0; **HRMS** (ESI-TOF) calcd for $C_{25}H_{27}N_2O_4S$ $[M+H]^+$:451.1686, found: 451.1697. $[\alpha]_D^{20}$ = -73.5 (*c* = 0.3, CH_2Cl_2); **HPLC** (Chiralpak IC-H, *n*-hexane/*i*-propanol = 80/20, flow rate = 1.0 mL/min, λ = 254 nm) t_R= 25.230 min (major), 29.476 min (minor).



Methyl (*R*)-5-cyano-2-(4-fluorophenyl)-6-methylene-1-tosyl-4,5,6,7-tetrahydro-1*H*-azepine-3-carboxylate (3g): Following the general procedure **A**, compound **3g** was obtained as a white solid in 70% yield (68.4 mg) and 95% *ee*; R_f = 0.4 (petroleum ether/EtOAc/DCM = 6/1/1, v/v/v); m.p.: 108-110 °C; **^{1}H NMR** (600 MHz, $CDCl_3$) δ 7.28 – 7.25 (m, 2H), 7.18 – 7.14 (m, 2H), 7.11 – 7.08 (m, 2H), 6.93 – 6.85 (m, 2H), 5.46 (d, *J* = 1.2 Hz, 1H), 5.44 (s, 1H), 4.45 – 4.37 (m, 2H), 3.57 – 3.52 (m, 1H), 3.48 (s, 3H), 2.95 (dd, *J* = 14.4, 3.4 Hz, 1H), 2.89 (dd, *J* = 14.5, 8.7 Hz, 1H), 2.41 (s, 3H); **^{13}C NMR** (150 MHz, $CDCl_3$) δ 168.3, 163.4 (d, J_{C-F} = 250.3 Hz), 149.2, 144.3, 137.4, 137.2, 132.2 (d, J_{C-F} = 3.3 Hz), 131.0 (d, J_{C-F} = 8.6 Hz), 129.8, 129.6, 127.1, 126.5, 125.6, 119.5, 118.5, 115.0 (d, J_{C-F} = 22.0 Hz), 55.1, 52.3, 33.1, 32.5, 21.6; **^{19}F NMR**(565 MHz, $CDCl_3$) δ -110.66. **HRMS** (ESI-TOF) calcd for $C_{24}H_{22}FN_2O_4S$ $[M+H]^+$: 441.1279, found: 441.1283. $[\alpha]_D^{20}$ = -40.0 (*c* = 0.1, CH_2Cl_2); **HPLC** (Chiralpak IC-H, *n*-hexane/*i*-propanol = 80/20, flow rate = 1.0 mL/min, λ = 254 nm) t_R= 29.526 min (major), 32.782 min (minor).

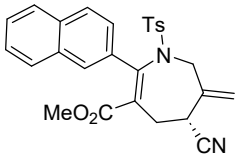


Methyl (*R*)-2-(4-chlorophenyl)-5-cyano-6-methylene-1-tosyl-4,5,6,7-tetrahydro-1H-azepine-3-carboxylate (3h). Following the general procedure **A**, compound **3h** was obtained as a colorless oil in 68% yield (62.0 mg) and 89% *ee*; R_f = 0.4 (petroleum ether/EtOAc/DCM = 6/1/1, v/v/v); **^{1}H NMR** (400 MHz, $CDCl_3$) δ 7.29 – 7.25 (m, 2H), 7.19 – 7.12 (m, 4H), 7.07 – 7.01 (m, 2H), 5.51 – 5.40 (m, 2H), 4.42 (s, 2H), 3.55 (dd, J = 8.3, 3.6 Hz, 1H), 3.49 (s, 3H), 3.03 – 2.83 (m, 2H), 2.43 (s, 3H); **^{13}C NMR** (100 MHz, $CDCl_3$) δ 168.1, 149.1, 144.3, 137.4, 137.2, 135.7, 134.6, 130.4(2C), 129.6(2C), 128.2(2C), 127.1(2C), 126.0, 119.5, 118.4, 55.2, 52.4, 33.1, 32.5, 21.7. **HRMS** (ESI-TOF) calcd for $C_{23}H_{22}ClN_2O_4S$ $[M+H]^+$: 457.0983, found: 457.0991; $[\alpha]_D^{20}$ = -153.7 (*c* = 0.1, CH_2Cl_2); **HPLC** (Chiralpak IA, *n*-hexane/*i*-propanol = 85/15, flow rate = 0.7 mL/min, λ = 254 nm) t_R=21.618 min (major), 24.773 min (minor).

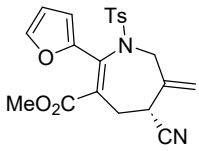


Methyl (*R*)-2-(4-bromophenyl)-5-cyano-6-methylene-1-tosyl-4,5,6,7-tetrahydro-1*H*-azepine-3-carboxylate (3i): Following the general procedure **A**, compound **3i** was obtained as a white solid in 46% yield (46.0 mg) and 90% *ee*; R_f = 0.4 (petroleum ether/EtOAc/DCM =

6/1/1, v/v/v); m.p.: 154-155 °C; **^{1}H NMR** (600 MHz, $CDCl_3$) δ 7.30 – 7.25 (m, 2H), 7.24 – 7.20 (m, 2H), 7.12 (d, *J* = 8.4 Hz, 2H), 6.94 – 6.91 (m, 2H), 5.43 (s, 1H), 5.41 (s, 1H), 4.38 (s, 2H), 3.57 – 3.50 (m, 1H), 3.46 (s, 3H), 2.93 (dd, *J* = 14.4, 3.4 Hz, 1H), 2.87 (dd, *J* = 14.5, 8.6 Hz, 1H), 2.39 (s, 3H); **^{13}C NMR** (150 MHz, $CDCl_3$) 167.9, 149.0, 144.2, 137.3, 137.1, 134.9, 131.0(2C), 130.5 (2C), 129.5(2C), 127.0(2C), 125.9, 123.8, 119.4, 118.4, 55.1, 52.2, 32.9, 32.4, 21.6; **HRMS** (ESI-TOF) calcd for $C_{23}H_{22}BrN_2O_4S$ $[M+H]^+$: 501.0478, found: 501.0483. $[\alpha]_D^{20}$ = -94.2 (*c* = 0.1, CH_2Cl_2); **HPLC** (Chiralpak IC-H, *n*-hexane/*i*-propanol = 80/20, flow rate = 1.0 mL/min, λ = 254 nm) t_R= 26.563 min (major), 30.749 min (minor).

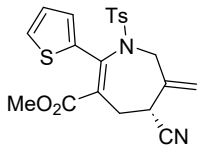


Methyl (*R*)-5-cyano-6-methylene-2-(naphthalen-2-yl)-1-tosyl-4,5,6,7-tetrahydro-1*H*-azepine-3-carboxylate (3j): Following the general procedure **A**, compound **3j** was obtained as a yellow solid in 71% yield (76.5 mg) and 91% *ee*; R_f = 0.4 (petroleum ether/EtOAc/DCM = 6/1/1, v/v/v); m.p.: 134-137 °C; **^{1}H NMR** (600 MHz, $CDCl_3$) δ 7.81 (d, *J* = 8.1 Hz, 1H), 7.67 (d, *J* = 8.5 Hz, 1H), 7.58 (d, *J* = 8.1 Hz, 1H), 7.52 (m, 1H), 7.47 (d, *J* = 7.2 Hz, 1H), 7.44 (s, 1H), 7.25 – 7.20 (m, 1H), 7.13 (d, *J* = 8.2 Hz, 2H), 6.84 (d, *J* = 8.1 Hz, 2H), 5.51 (s, 1H), 5.50 (s, 1H), 4.54 (s, 2H), 3.67 - 3.58 (m, 1H), 3.41 (s, 3H), 3.14 – 2.98 (m, 2H), 2.23 (s, 3H); **^{13}C NMR** (150 MHz, $CDCl_3$) δ 168.4, 150.4, 143.8, 137.8, 137.3, 133.5, 132.9, 132.5, 129.2(2C), 128.7, 128.4, 127.6, 127.4, 127.0, 126.9(2C), 126.5, 126.2, 125.6, 119.1, 118.5, 55.4, 52.1, 33.2, 32.7, 21.4; **HRMS** (ESI-TOF) calcd for $C_{27}H_{25}N_2O_4S$ $[M+H]^+$: 473.1530, found: 473.1536. $[\alpha]_D^{20}$ = -102.5 (*c* = 0.3, CH_2Cl_2); **HPLC** (Chiralpak IC-H, *n*-hexane/*i*-propanol = 80/20, flow rate = 1.0 mL/min, λ = 254 nm) t_R= 27.384 min (major), 28.818 min (minor).

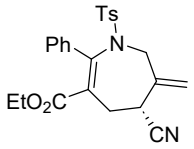


Methyl (*R*)-5-cyano-2-(furan-2-yl)-6-methylene-1-tosyl-4,5,6,7-tetrahydro-1*H*-azepine-3-carboxylate (3k): Following the general procedure **A**, compound **3k** was obtained as a yellow solid in 79% yield (65.1 mg) and 93% *ee*; R_f = 0.4 (petroleum ether/EtOAc/DCM = 6/1/1, v/v/v); m.p.: 93-95 °C; **^{1}H NMR** (600 MHz, $CDCl_3$) δ 7.55 (d, *J* = 8.2 Hz, 2H), 7.34 (d, *J* = 1.7 Hz, 1H), 7.30 – 7.27 (m, 2H), 6.55 (d, *J* = 3.5 Hz, 1H), 6.41 (dd, *J* = 3.5, 1.7 Hz, 1H), 5.42 (s, 1H), 5.41 (s, 1H), 4.43 (s, 1H), 4.28 (s, 1H), 3.69 (s, 3H), 3.41 (s, 1H), 2.72 – 2.66 (m, 1H), 2.62 – 2.50 (m, 1H), 2.45 (s, 3H); **^{13}C NMR** (150 MHz, $CDCl_3$) δ 168.1, 148.5, 144.3, 144.0, 137.8, 137.0, 137.0, 129.7(2C), 127.4(2C), 125.1, 119.5, 118.3, 114.1, 111.7, 54.3, 52.4, 33.1, 32.3, 21.6; **HRMS** (ESI-TOF) calcd for $C_{21}H_{21}N_2O_5S$ $[M+H]^+$: 413.1166, found:

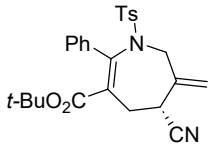
413.1173. $[\alpha]_D^{20}$ = -48.5 (*c* = 0.6, CH_2Cl_2); **HPLC** (Chiralpak IC-H, *n*-hexane/*i*-propanol = 70/30, flow rate = 0.7 mL/min, λ = 254 nm) t_R= 27.740 min (major), 31.326 min (minor).



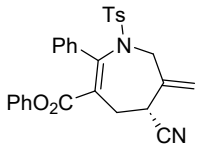
Methyl (*R*)-5-cyano-6-methylene-2-(thiophen-2-yl)-1-tosyl-4,5,6,7-tetrahydro-1*H*-azepine-3-carboxylate (3l): Following the general procedure **A**, compound **3l** was obtained as a yellow solid in 77% yield (65.9 mg) and 88% *ee*; R_f = 0.4 (petroleum ether/EtOAc/DCM = 6/1/1, v/v/v); m.p.: 107-108 °C; **^{1}H NMR** (600 MHz, $CDCl_3$) δ 7.40 (d, *J* = 8.2 Hz, 2H), 7.33 (dd, *J* = 5.1, 1.2 Hz, 1H), 7.18 (d, *J* = 8.0 Hz, 2H), 7.01 (dd, *J* = 3.7, 1.2 Hz, 1H), 6.90 (dd, *J* = 5.0, 3.6 Hz, 1H), 5.44 (s, 1H), 5.42 (s, 1H), 4.41 (br, 1H), 4.29 (br, 1H), 3.56 (s, 3H), 3.48 (s, 1H), 2.83 (dd, *J* = 14.4, 3.3 Hz, 1H), 2.73 (br, 1H), 2.40 (s, 3H); **^{13}C NMR** (150 MHz, $CDCl_3$) δ 168.3, 144.1, 142.0, 138.3, 137.2, 129.9, 129.6(2C), 128.8, 127.2(2C), 126.8, 126.6, 119.5, 118.3, 54.5, 52.4, 33.0, 32.6, 21.6; **HRMS** (ESI-TOF) calcd for $C_{21}H_{21}N_2O_4S_2$ $[M+H]^+$:429.0937, found: 429.0944. $[\alpha]_D^{20}$ = -51.6 (*c* = 0.2, CH_2Cl_2); **HPLC** (Chiralpak IC-H, *n*-hexane/*i*-propanol = 80/20, flow rate = 1.0 mL/min, λ = 254 nm) t_R= 31.441 min (major), 35.151 min (minor).



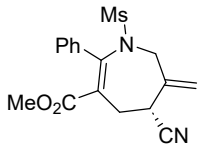
Ethyl (*R*)-5-cyano-6-methylene-2-phenyl-1-tosyl-4,5,6,7-tetrahydro-1*H*-azepine-3-carboxylate (3m): Following the general procedure **A**, compound **3m** was obtained as a white solid in 88% yield (76.8 mg) and 95% *ee*; R_f = 0.4 (petroleum ether/EtOAc/DCM = 6/1/1, v/v/v); m.p.: 128-129 °C; **^{1}H NMR** (600 MHz, $CDCl_3$) δ 7.35 – 7.30 (m, 1H), 7.25 – 7.17 (m, 4H), 7.14 – 7.09 (m, 4H), 5.47 (d, *J* = 1.3 Hz, 1H), 5.44 (d, *J* = 1.0 Hz, 1H), 4.52 – 4.34 (m, 2H), 3.96 – 3.86 (m, 2H), 3.56 (d, *J* = 6.7 Hz, 1H), 3.06 – 2.86 (m, 2H), 2.40 (s, 3H), 0.84 (t, *J* = 7.1 Hz, 3H); **^{13}C NMR** (150 MHz, $CDCl_3$) δ 168.1, 149.9, 143.9, 137.7, 137.1, 136.2, 129.5(2C), 129.4, 129.1(2C), 127.8(2C), 127.2(2C), 126.0, 119.0, 118.6, 61.3, 55.2, 33.2, 32.6, 21.6, 13.5; **HRMS** (ESI-TOF) calcd for $C_{24}H_{25}N_2O_4S$ $[M+H]^+$: 437.1530, found: 437.1535. $[\alpha]_D^{20}$ = -76.1 (*c* = 0.3, CH_2Cl_2); **HPLC** (Chiralpak IC-H, *n*-hexane/*i*-propanol = 80/20, flow rate = 1.0 mL/min, λ = 254 nm) t_R= 33.345 min (major), 37.913 min (minor).



***tert*-Butyl (*R*)-5-cyano-6-methylene-2-phenyl-1-tosyl-4,5,6,7-tetrahydro-1*H*-azepine-3-carboxylate (3n):** Following the general procedure **A**, compound **3n** was obtained as a white solid in 86% yield (79.9 mg) and 96% *ee*; R_f = 0.4 (petroleum ether/EtOAc/DCM = 6/1/1, v/v/v); m.p.: 107-109 °C; **^{1}H NMR** (600 MHz, $CDCl_3$) δ 7.31 – 7.27 (m, 1H), 7.20 – 7.14 (m, 4H), 7.10 – 7.05 (m, 4H), 5.41 (s, 1H), 5.40 (s, 1H), 4.45 – 4.21 (m, 2H), 3.62 – 3.44 (m, 1H), 3.02 – 2.76 (m, 2H), 2.36 (s, 3H), 1.09 (s, 9H); **^{13}C NMR** (150 MHz, $CDCl_3$) δ 167.1, 148.8, 143.7, 138.0, 137.3, 136.5, 129.4(2C), 129.3(2C), 129.1, 127.8(2C), 127.7, 127.1(2C), 118.9, 118.6, 81.9, 55.1, 33.2, 32.6, 27.4(3C), 21.6; **HRMS** (ESI-TOF) calcd for $C_{26}H_{29}N_2O_4S$ $[M+H]^+$: 465.1843, found: 465.1840. $[\alpha]_D^{20}$ = -138.2 (*c* = 0.7, CH_2Cl_2); **HPLC** (Chiralpak IC-H, *n*-hexane/*i*-propanol = 80/20, flow rate = 1.0 mL/min, λ = 254 nm) t_R= 20.162 min (major), 26.798 min (minor).

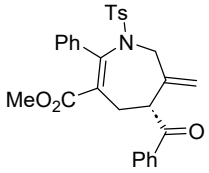


Phenyl (*R*)-5-cyano-6-methylene-2-phenyl-1-tosyl-4,5,6,7-tetrahydro-1*H*-azepine-3-carboxylate (3o): Following the general procedure **A**, compound **3o** was obtained as a white solid in 68% yield (65.9 mg) and 93% *ee*; R_f = 0.4 (petroleum ether/EtOAc/DCM = 6/1/1, v/v/v); m.p.: 126-128 °C; **^{1}H NMR** (600 MHz, $CDCl_3$) δ7.40 – 7.36 (m, 1H), 7.28 – 7.22 (m, 8H), 7.17 – 7.11 (m, 3H), 6.70 – 6.64 (m, 2H), 5.50 (d, *J* = 1.2 Hz, 1H), 5.49 (s, 1H), 4.55 (d, *J* = 14.7 Hz, 1H), 4.45 (d, *J* = 14.7 Hz, 1H), 3.67 (dd, *J* = 7.1, 3.5 Hz, 1H), 3.17 – 3.02 (m, 2H), 2.41 (s, 3H); **^{13}C NMR** (150 MHz, $CDCl_3$) δ 166.8, 151.6, 150.3, 144.1, 137.5, 137.2, 136.1, 129.9, 129.6(2C), 129.5(2C), 129.3(2C), 128.2(2C), 127.2(2C), 126.0, 124.9, 121.1(2C), 119.7, 118.5, 55.2, 33.3, 33.0, 21.6; **HRMS** (ESI-TOF) calcd for $C_{28}H_{25}N_2O_4S$ $[M+H]^+$: 485.1530, found: 485.1533. $[\alpha]_D^{20}$ = -66.7 (*c* = 0.3, CH_2Cl_2); **HPLC** (Chiralpak IC-H, *n*-hexane/*i*-propanol = 80/20, flow rate = 1.0 mL/min, λ = 254 nm) t_R= 35.724 min (major), 40.839 min (minor).

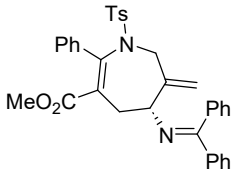


Methyl (*R*)-5-cyano-6-methylene-1-(methylsulfonyl)-2-phenyl-4,5,6,7-tetrahydro-1*H*-azepine-3-carboxylate (3p): Following the general procedure **A**, compound **3p** was obtained as a white solid in 40% yield (27.7 mg) and 93% *ee*; R_f = 0.4 (petroleum ether/EtOAc/DCM = 6/1/1, v/v/v); m.p.: 83-85 °C; **^{1}H NMR** (600 MHz, $CDCl_3$) δ 7.41 – 7.38 (m, 3H), 7.32 – 7.29 (m, 2H), 5.48 (s, 1H), 5.40 (s, 1H), 4.42 – 4.30 (m, 2H), 3.71 – 3.63 (m, 1H), 3.46 (s, 3H), 3.20 – 3.16 (m, 1H), 3.16 – 3.12 (m, 1H), 2.49 (s, 3H); **^{13}C NMR** (150 MHz, $CDCl_3$) δ 167.9, 149.8, 137.9, 136.0, 129.9, 128.9(2C), 128.3(2C), 126.2, 118.9, 118.4, 54.8, 52.1, 41.8, 33.3, 32.8; **HRMS** (ESI-

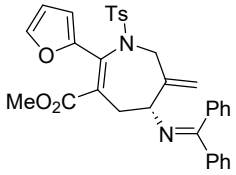
TOF) calcd for $C_{17}H_{19}N_2O_4S$ $[M+H]^+$: 347.1060, found: 347.1062. $[\alpha]_D^{20}$ = -77.0 (*c* = 0.1, CH_2Cl_2); **HPLC** (Chiralpak IC-H, *n*-hexane/*i*-propanol = 80/20, flow rate = 1.0 mL/min, λ = 254 nm) t_R=28.455 min (major), 30.833 min (minor).



Methyl (*R*)-5-benzoyl-6-methylene-2-phenyl-1-tosyl-4,5,6,7-tetrahydro-1*H*-azepine-3-carboxylate (3q): Following the general procedure **A**, compound **3q** was obtained as a yellow solid in 72% yield (77.2 mg) and 87% *ee*; R_f = 0.4 (petroleum ether/EtOAc/DCM = 6/1/1, v/v/v); m.p.: 99-100 °C; **^{1}H NMR** (400 MHz, $CDCl_3$) δ 8.02 – 7.94 (m, 2H), 7.61 – 7.56 (m, 1H), 7.48 (dd, *J* = 8.3, 7.0 Hz, 2H), 7.30 – 7.27 (m, 3H), 7.24 – 7.18 (m, 2H), 7.16 – 7.12 (m, 4H), 5.29 (s, 1H), 5.02 (s, 1H), 4.66 – 4.46 (m, 3H), 3.38 (s, 3H), 2.97 – 2.85 (m, 2H), 2.40 (s, 3H); **^{13}C NMR** (100 MHz, $CDCl_3$) δ 199.4, 169.0, 146.2, 143.5, 133.4, 129.5, 129.4(2C), 129.2, 129.0(2C), 128.9, 128.8(2C), 128.7(2C), 128.1, 127.8(2C), 127.5, 127.2(2C), 126.5, 110.9, 51.8, 47.7, 42.4, 37.4, 21.6; **HRMS** (ESI-TOF) calcd for $C_{29}H_{28}NO_5S$ $[M+H]^+$: 502.1683, found: 502.1689; $[\alpha]_D^{20}$ = -30.7 (*c* = 0.2, CH_2Cl_2); **HPLC** (Chiralpak IC-H, *n*-hexane/*i*-propanol = 70/30, flow rate = 0.7 mL/min, λ = 254 nm) t_R=12.445 min (major), 18.648 min (minor).

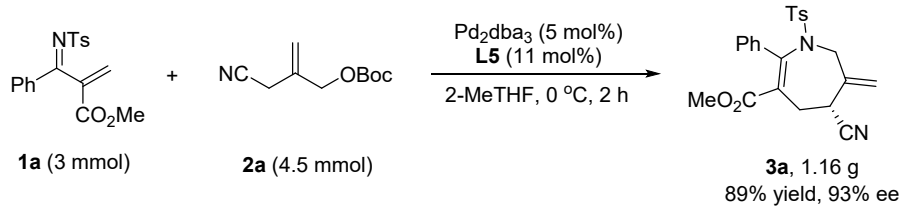


Methyl (*R*)-5-((diphenylmethylene)amino)-6-methylene-2-phenyl-1-tosyl-4,5,6,7-tetrahydro-1*H*-azepine-3-carboxylate (3r): Following the general procedure **A**, compound **3r** was obtained as a yellow solid in 68% yield (72 mg) and 87% *ee*;, R_f = 0.4 (petroleum ether/EtOAc/DCM = 12/1/1, v/v/v and tol:acetone=20:1,v/v); m.p.: 78-81 °C; **^{1}H NMR** (600 MHz, $CDCl_3$) δ 7.56 – 7.53 (m, 2H), 7.49 – 7.44 (m, 3H), 7.39 – 7.36 (m, 2H), 7.36 – 7.30 (m, 2H), 7.30 – 7.24 (m, 4H), 7.22 (d, *J* = 7.1 Hz, 2H), 7.14 (dd, *J* = 7.5, 1.9 Hz, 4H), 5.17 (s, 1H), 4.91 (s, 1H), 4.69 (br, 1H), 4.40 (br, 1H), 4.08 – 3.98 (m, 1H), 3.35 (s, 3H), 2.68 (dd, *J* = 13.4, 7.1 Hz, 1H), 2.44 (dd, *J* = 13.3, 3.1 Hz, 1H), 2.40 (s, 3H); **^{13}C NMR** (151 MHz, $CDCl_3$) δ 167.2, 147.4, 144. 7, 143.4, 134.0, 137.7, 136.4, 130.2, 129.4(2C), 128.9(3C), 128.6(4C), 128.6, 128.1(3C), 127.8(2C), 127.6(2C), 127.4(2C), 117.0, 62.1, 54.2, 51.7, 36.3, 21.7. **HRMS** (ESI-TOF) calcd for $C_{35}H_{33}N_2O_4S$ $[M+H]^+$: 577.2156, found: 577.2157. $[\alpha]_D^{20}$ = -59.3 (*c* = 0.4, CH_2Cl_2); **HPLC** (Chiralpak IC-H, *n*-hexane/*i*-propanol = 80/20, flow rate = 1.0 mL/min, λ = 254 nm) t_R=17.435 min (major), 19.757 min (minor).



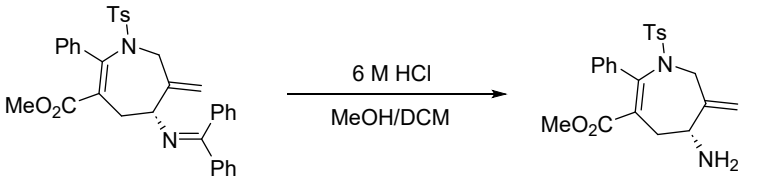
Methyl (*R*)-5-((diphenylmethylene)amino)-2-(furan-2-yl)-6-methylene-1-tosyl-4,5,6,7-tetrahydro-1H-azepine-3-carboxylate (3s): Following the general procedure **A**, compound **3s** was obtained as a colorless oil in 53% yield (60 mg) and 84% *ee*; R_f = 0.4 (petroleum ether/EtOAc/DCM = 12/1/1, v/v/v); **^{1}H NMR** (400 MHz, $CDCl_3$) δ 7.63 (d, *J* = 8.2 Hz, 2H), 7.58 – 7.52 (m, 2H), 7.49 – 7.43 (m, 3H), 7.43 – 7.33 (m, 2H), 7.27 (dd, *J* = 16.4, 8.2 Hz, 4H), 7.16 – 7.06 (m, 2H), 6.56 (dd, *J* = 3.4, 0.8 Hz, 1H), 6.45 (dd, *J* = 3.4, 1.9 Hz, 1H), 5.11 (s, 1H), 4.85 (s, 1H), 4.63 (d, *J* = 14.0 Hz, 1H), 4.38 (br, 1H), 3.92 (dd, *J* = 7.3, 2.6 Hz, 1H), 3.56 (s, 3H), 2.48 (dd, *J* = 13.6, 7.3 Hz, 1H), 2.42 (s, 3H), 2.15 (dd, *J* = 13.6, 2.6 Hz, 1H); **^{13}C NMR** (100 MHz, $CDCl_3$) δ 169.7, 167.2, 150.2, 144.5, 143.7, 143.4, 139.4, 137.8, 136.4, 136.0, 130.3, 129.6(2C), 128.6(4C), 128.6, 128.0(2C), 127.6(2C), 127.6(2C), 127.3, 116.8, 112.5, 111.7, 61.8, 53.5, 51.9, 36.2, 21.7. **HRMS** (ESI-TOF) calcd for $C_{33}H_{31}N_2O_5S$ $[M+H]^+$: 567.1948, found: 567.1979. $[\alpha]_D^{20}$ = -113.1 (*c* = 0.6, CH_2Cl_2); **HPLC** (Chiralpak IA, *n*-hexane/*i*-propanol = 80/20, flow rate = 0.9 mL/min, λ = 254 nm) t_R=7.970 min (major), 19.937 min (minor).

3 Gram-scale preparation of compound 3a



1a (3 mmol) **2a** (4.5 mmol) **3a**, 1.16 g
89% yield, 93% ee

To a flame-dried and N_2-purged round-bottom flask was added ligand **L5** (162 mg, 0.33 mmol, 11 mol%), and $Pd_2(dba)_3$ (138 mg, 0.15 mmol, 5 mol%) and anhydrous 2-Me-THF (30.0 mL). The resulting solution was stirred for 0.5 h at room temperature. Then the reaction tube was moved to 0 ℃. After 5 minutes, *α,β*-unsaturated imine **1a** (3 mmol, 1.0 equiv) and trimethylenemethane（TMM）donor **2a** (4.5 mmol, 1.5 equiv) was added sequentially. The resulting solution was stirred vigorously at 0 ℃. Once starting material was consumed (monitored by TLC), the mixture was concentrated and purified by column chromatography (PE/EA/DCM = 6:1:1, v/v/v) to give the desired product **3a** as a light yellow solid (1.16 g, 89%, 93% ee).



3r, 87% ee **4**, 80% yield, 88% ee

To a solution of **3r** (27.8 mg, 0.05 mmol, 87% ee) in DCM (1 mL) and MeOH (1 mL) was added 6M HCl (20 eq.) at 0 °C, the resulting solution was stirred for 2 h at room temperature. Once starting material was consumed (monitored by TLC), the sodium bicarbonate saturated solution was added at 0 °C to adjust pH > 8. Then the mixture extracted with EA (3 times). The organic phase was concentrated and residue was purified by column chromatography (EA, R_f = 0.1) to give the desired product **4** as a yellow oil (16 mg, 80% yield, 88% ee). **^{1}H NMR** (400 MHz, $CDCl_3$) δ 7.32 – 7.24 (m, 3H), 7.22 – 7.17 (m, 2H), 7.15 – 7.08 (m, 4H), 5.21 – 5.14 (m, 2H), 4.52 (d, *J* = 13.9 Hz, 1H), 4.26 (d, *J* = 13.9 Hz, 1H), 3.66 – 3.57 (m, 1H), 3.42 (s, 3H), 2.68 (dd, *J* = 14.0, 3.6 Hz, 1H), 2.53 (dd, *J* = 13.9, 8.1 Hz, 1H), 2.38 (s, 3H), 1.97 (br, 2H). **^{13}C NMR** (100 MHz, $CDCl_3$) δ 169.6, 147.2, 143.4, 137.4, 136.9, 129.3(2C), 128.9, 128.8(2C), 127.7(2C), 127.67, 127.2(2C), 115.6, 53.5, 51.9, 51.6, 37.0, 21.5. **HRMS** (ESI-TOF) calcd for $C_{22}H_{24}N_2O_4S$ $[M+H]^+$: 413.1530, found: 413.1526. $[\alpha]_D^{20}$ = -100.8 (*c* = 0.1, CH_2Cl_2); **HPLC** (Chiralpak IF, *n*-hexane/*i*-propanol = 70/30, flow rate = 0.7 mL/min, λ = 254 nm) t_R=27.238 min (major), 35.031 min (minor).

4 The X-Ray crystal structure

The crystal of enantiopure **3a** was obtained through slow vapor diffusion of *n*-hexane into the ethyl acetate solution of **3a**. The structure and absolute configuration (*R*) of **3a** were then determined by X-ray crystallographic analysis (**Figure S1**).

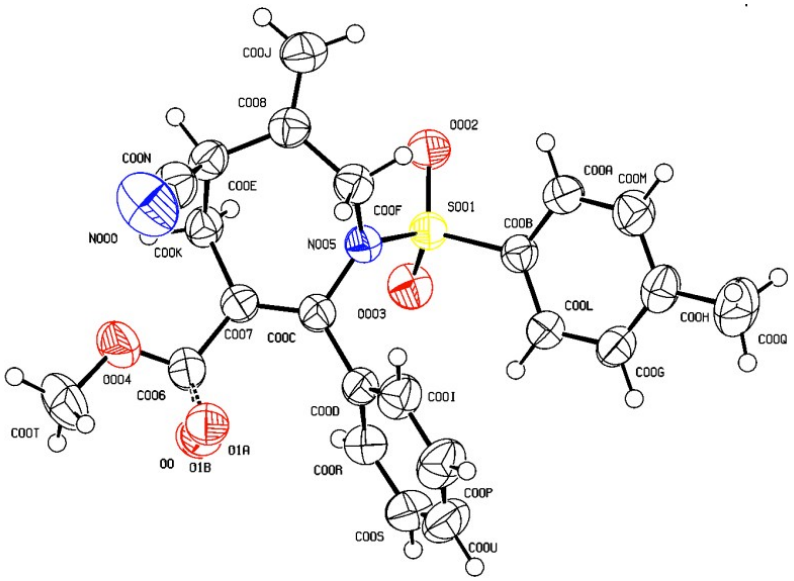


Fig S1. The X-ray structure of (*R*)-**3a** with thermal ellipsoids at the 30% probability level (CCDC 2322002)

Table S1. Crystal data and structure refinement for 2023042501_0m.

Identification code	data_2023042501_0m	
Empirical formula	C23 H22 N2 O4 S	
Formula weight	494.04	
Temperature	120(2) K	
Wavelength	1.54178 Å	
Crystal system	monoclinic	
Space group	P 1 21 1	
Unit cell dimensions	a = 6.4786(6) Å	a = 90°.
	b = 13.3933(12) Å	b = 101.591(3)°.
	c = 12.7182(12) Å	g = 90°.
Volume	1081.05(17) $Å^3$	
Z	2	
Density (calculated)	1.298 Mg/m^3	
Absorption coefficient	1.594 mm^{-1}	
F(000)	444	

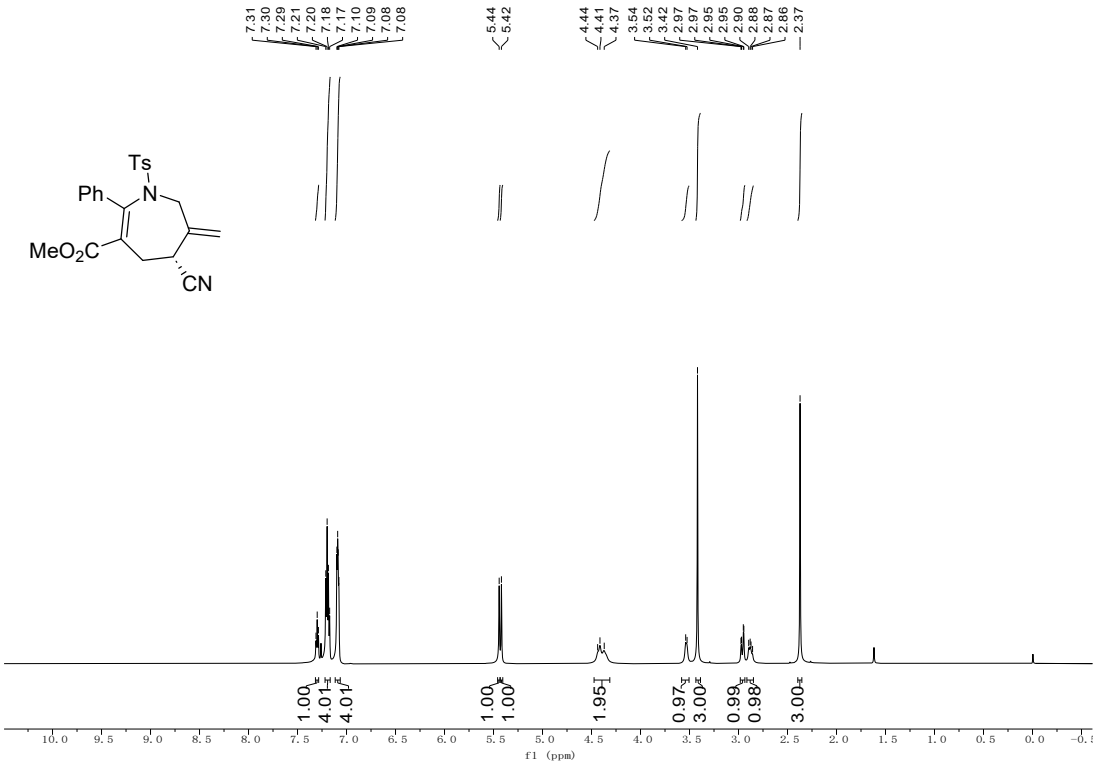
Crystal size	0.260 x 0.250 x 0.23 mm^3
Theta range for data collection	3.547 to 68.492°.
Index ranges	-7<=h<=7, -14<=k<=16, -15<=l<=14
Reflections collected	14460
Independent reflections	3873 [R(int) = 0.0337]
Completeness to theta = 67.679°	99.5 %
Absorption correction	multi-scan
Max. and min. transmission	0.7531 and 0.6189
Refinement method	Full-matrix least-squares on F^2
Data / restraints / parameters	3873 / 25 / 291
Goodness-of-fit on F^2	1.107
Final R indices [I>2sigma(I)]	R1 = 0.0295, wR2 = 0.0839
R indices (all data)	R1 = 0.0301, wR2 = 0.0849
Extinction coefficient	0.041(6)
Largest diff. peak and hole	0.278 and -0.420 $e.Å^{-3}$

5 References

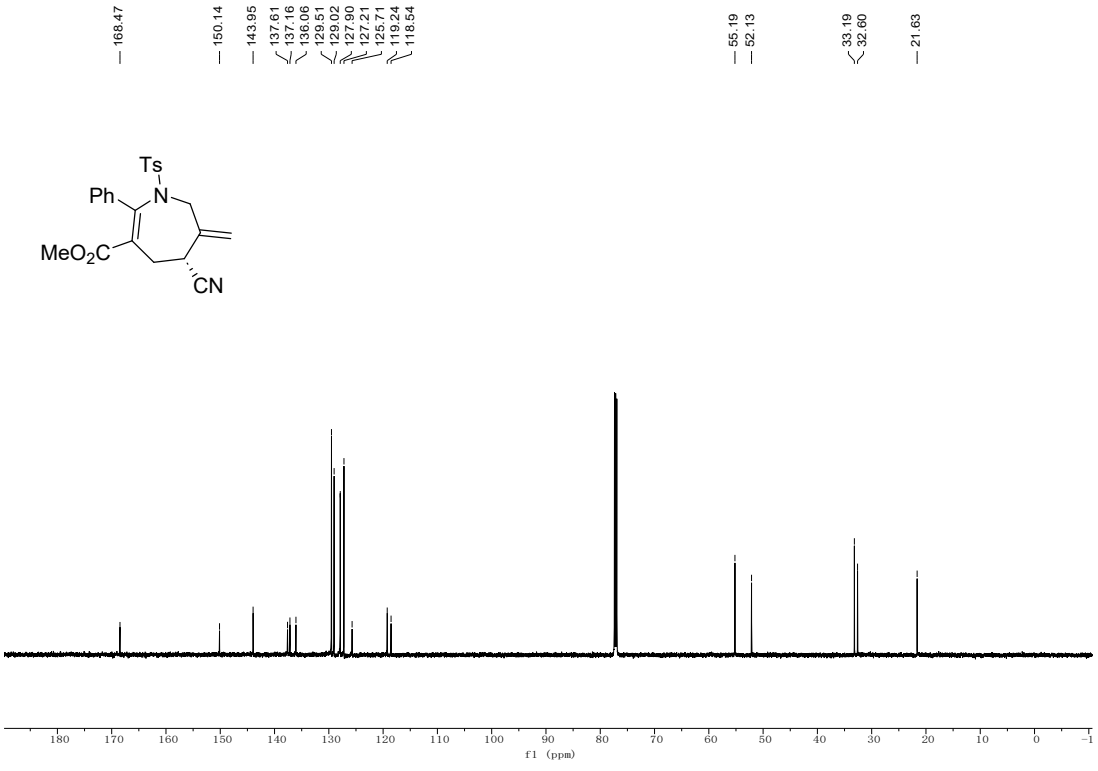
1. H. Liu, Q. Zhang, L. Wang and X. Tong, PPh_3-catalyzed reactions of alkyl propiolates with N-tosylimines: A facile synthesis of alkyl 2-[aryl(tosylimino)methyl]acrylate and an insight into the reaction mechanism, *Chem. Eur. J.*, 2010, **16**, 1968–1972.
2. B. M. Trost and G. Mata, Enantioselective palladium-catalyzed [3+2] cycloaddition of trimethylenemethane and fluorinated ketones, *Angew. Chem., Int. Ed.,* 2018, **57**, 12333–12337.

6 ^{1}H NMR and ^{13}C NMR spectra

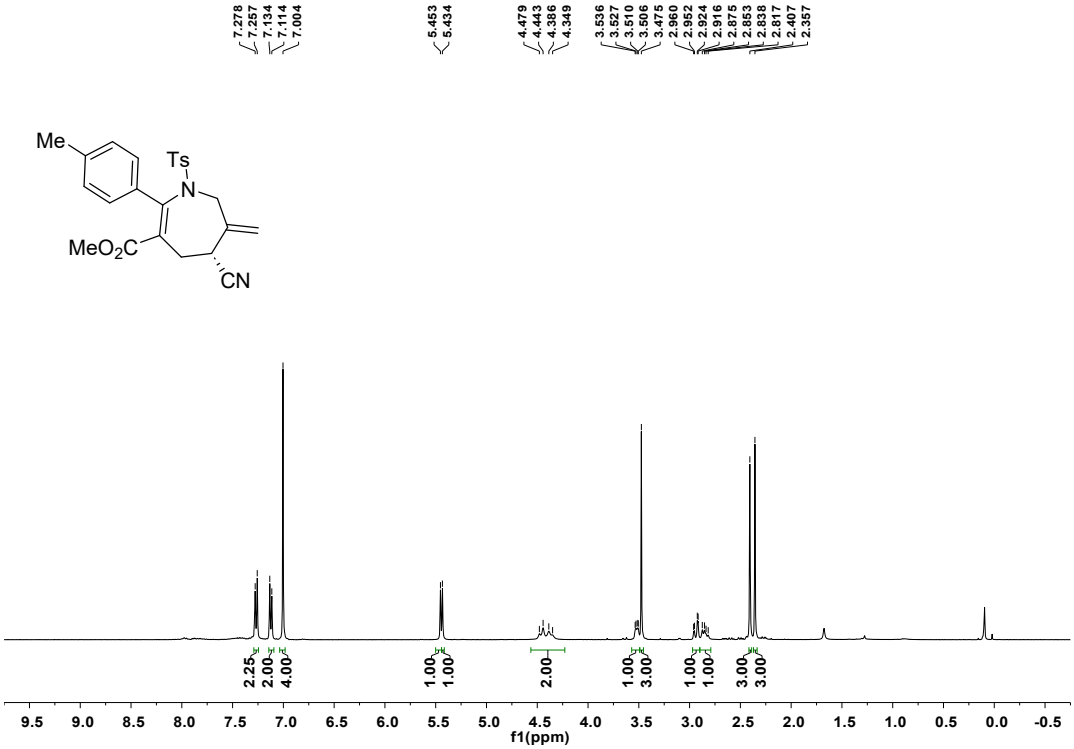
^{1}H NMR of **3a** in $CDCl_3$ (600 MHz)



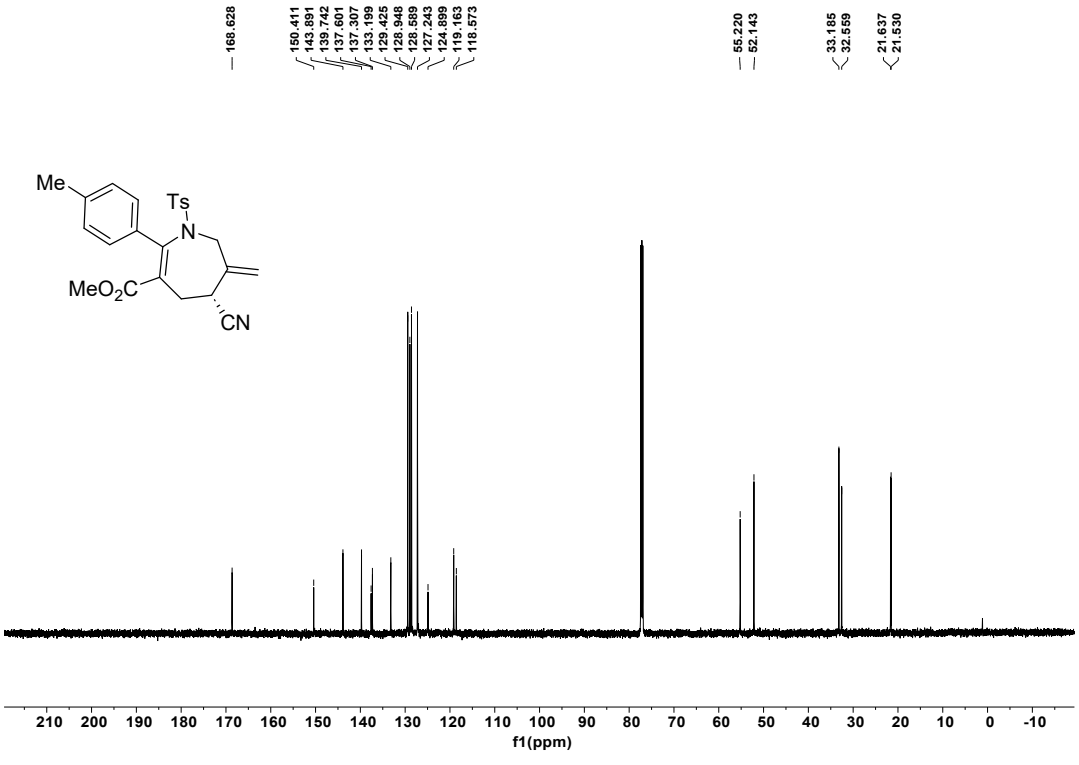
^{13}C NMR of **3a** in $CDCl_3$ (150 MHz)



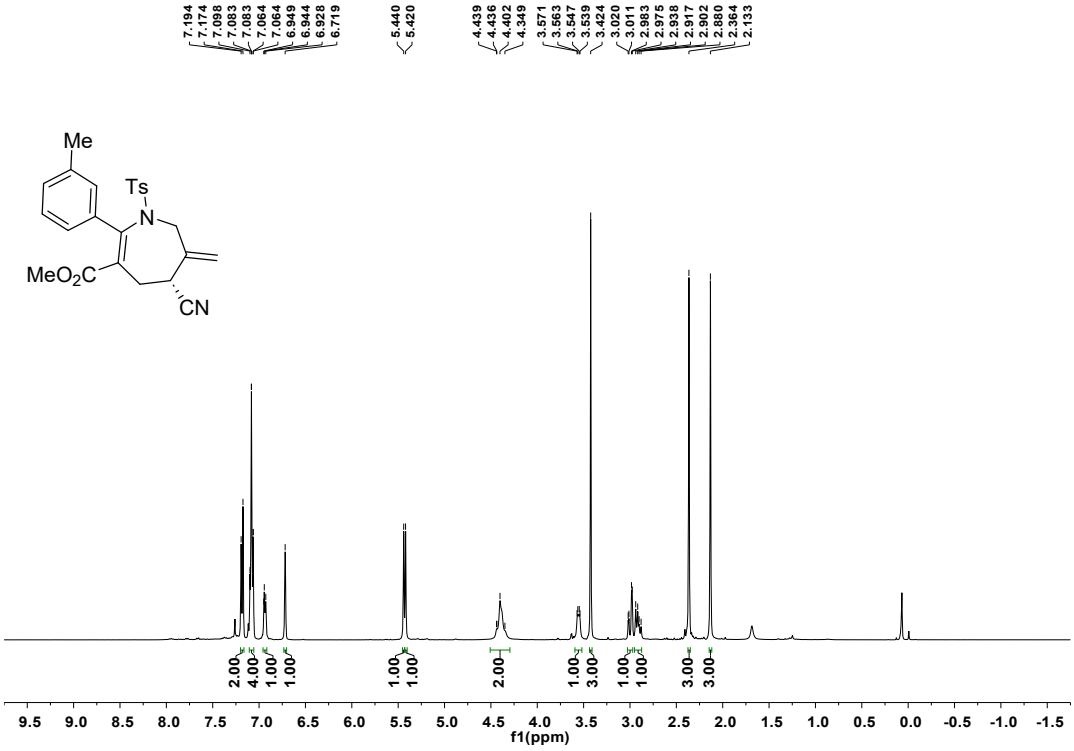
^{1}H NMR of **3b** in $CDCl_3$ (600 MHz)



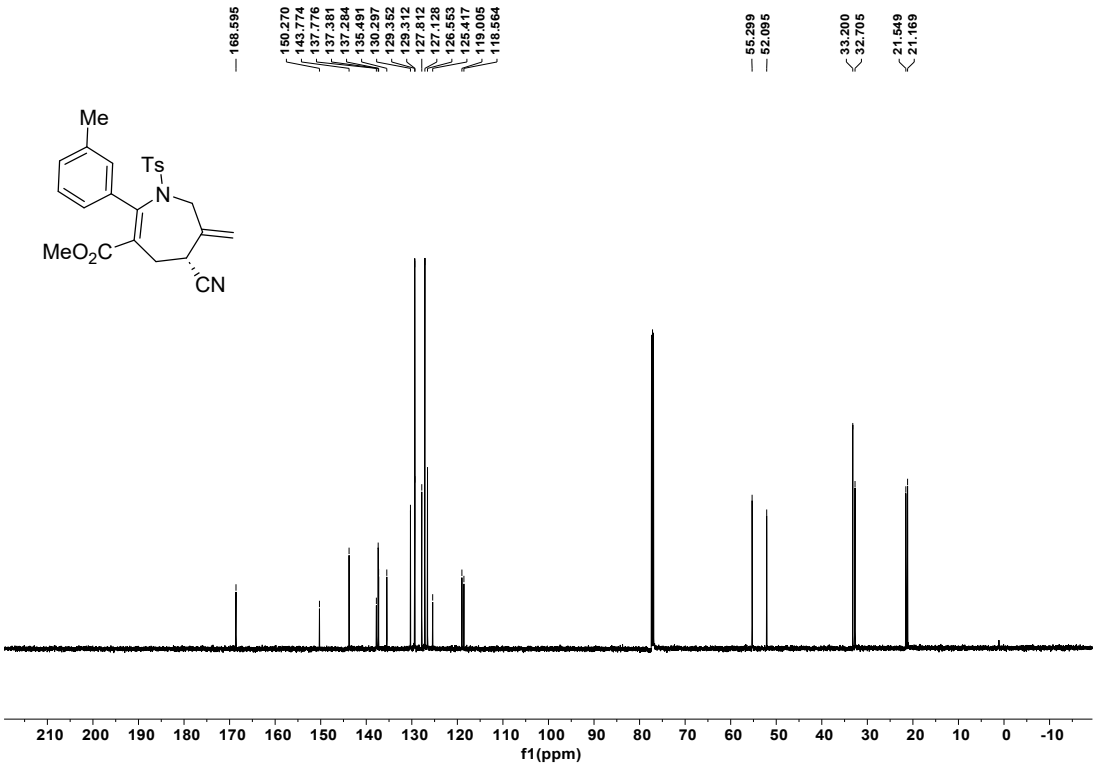
^{13}C NMR of **3b** in $CDCl_3$ (150 MHz)



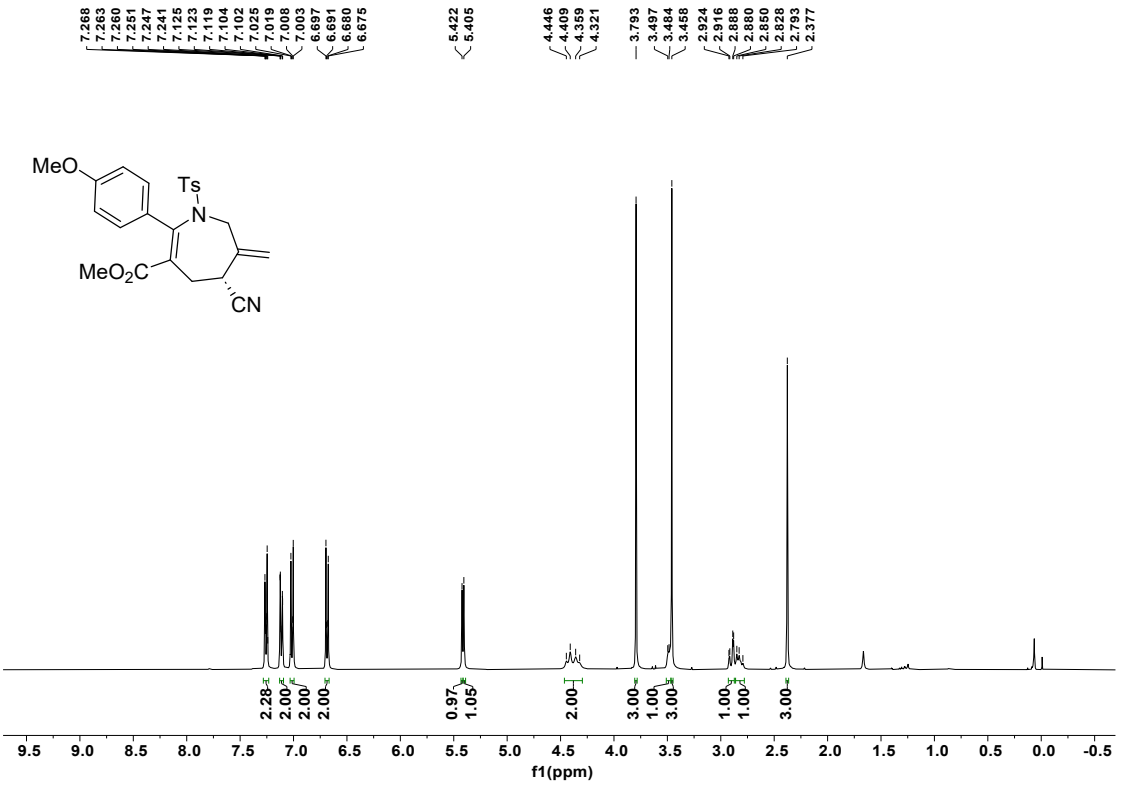
^{1}H NMR of **3c** in $CDCl_3$ (600 MHz)



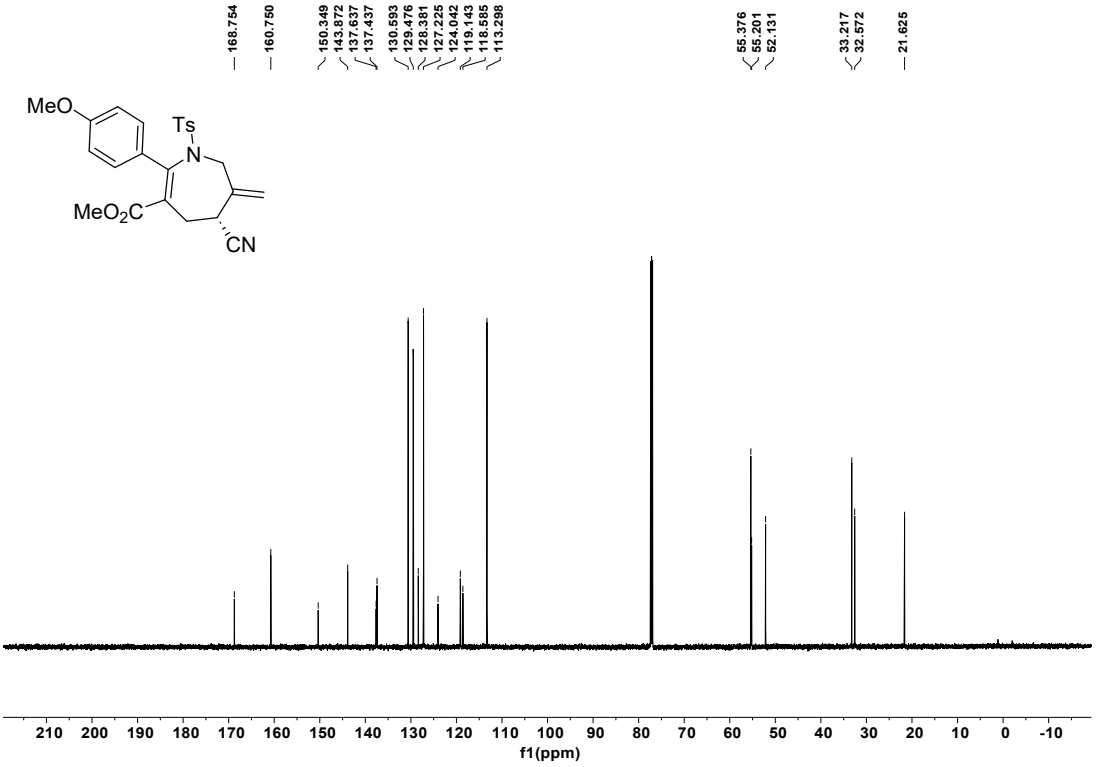
^{13}C NMR of **3c** in $CDCl_3$ (150 MHz)



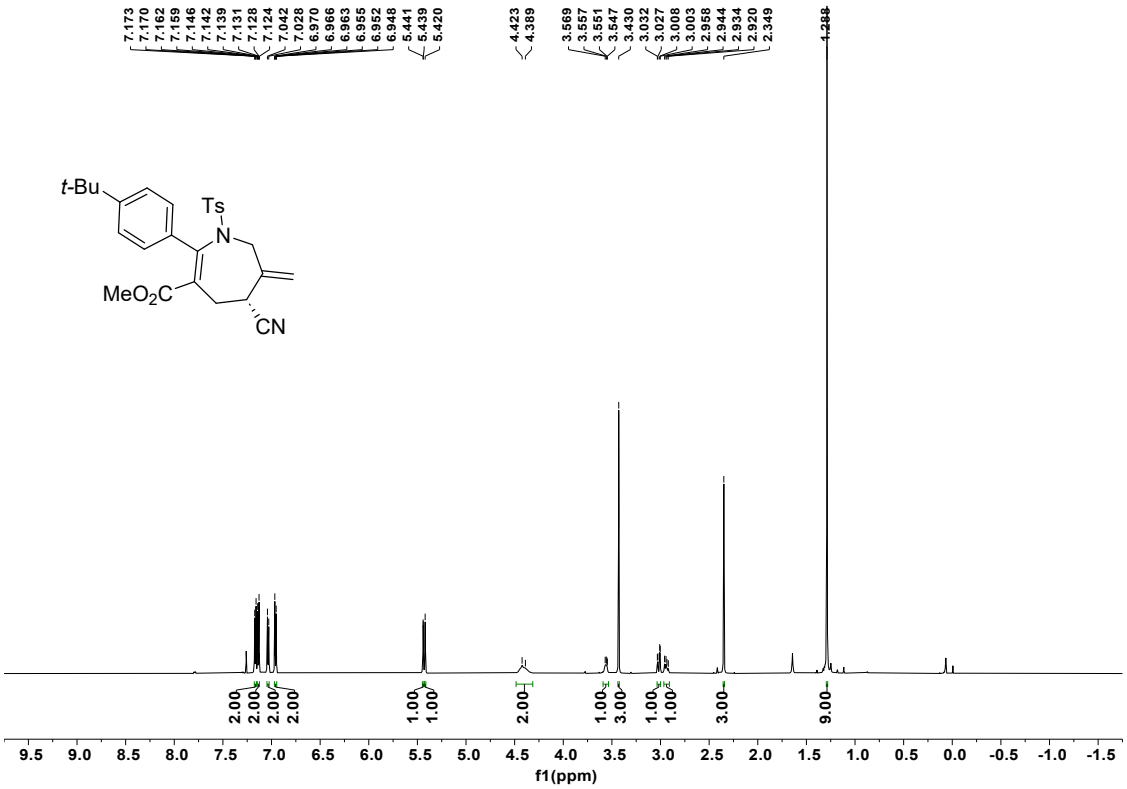
^{1}H NMR of **3d** in $CDCl_3$ (600 MHz)



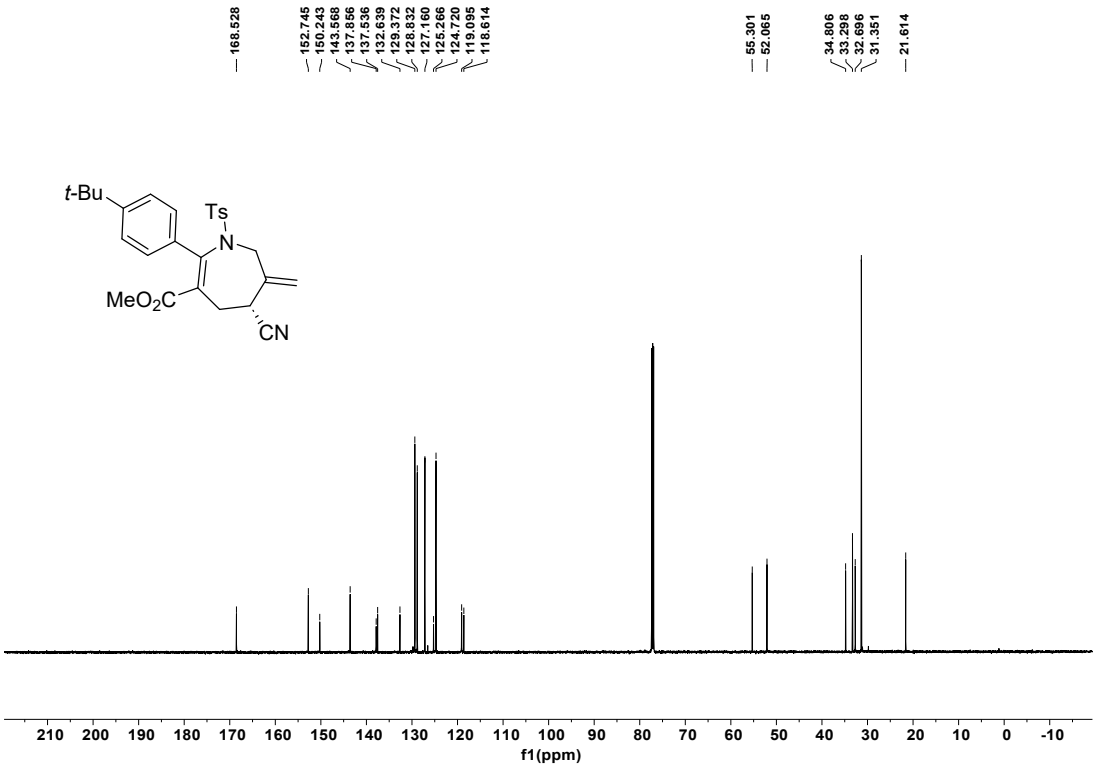
^{13}C NMR of **3d** in $CDCl_3$ (150 MHz)



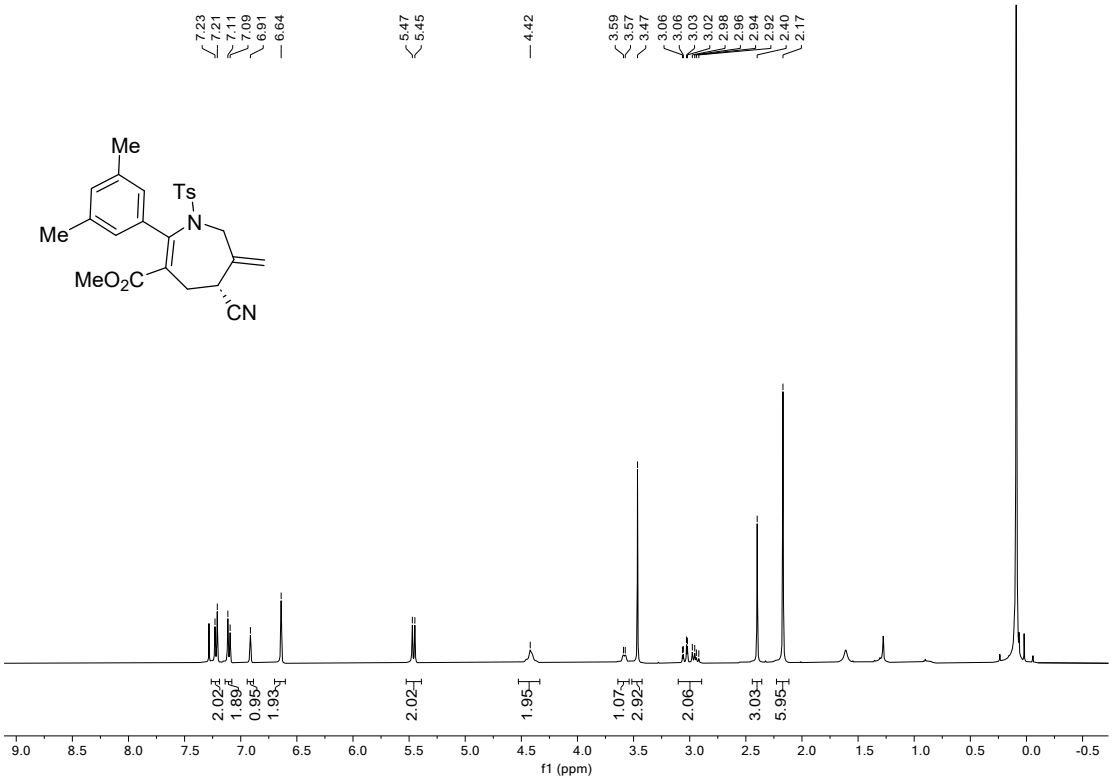
^{1}H NMR of **3e** in $CDCl_3$ (600 MHz)



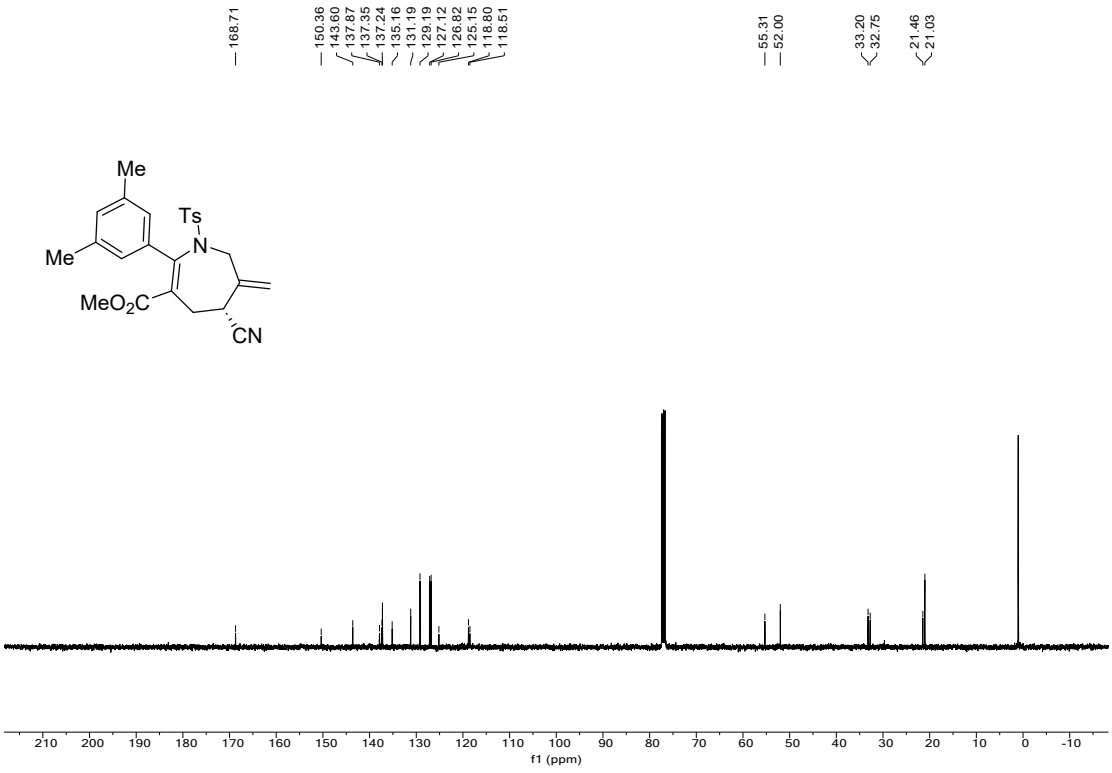
^{13}C NMR of **3e** in $CDCl_3$ (150 MHz)



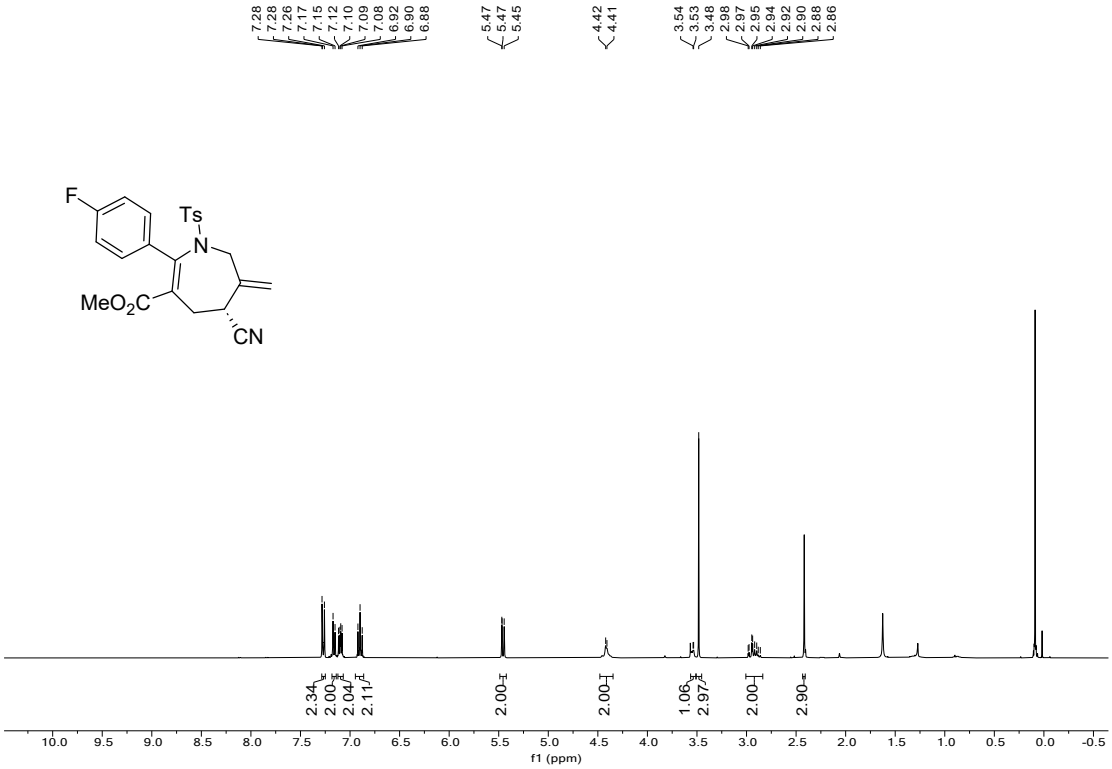
^{1}H NMR of **3f** in $CDCl_3$ (600 MHz)



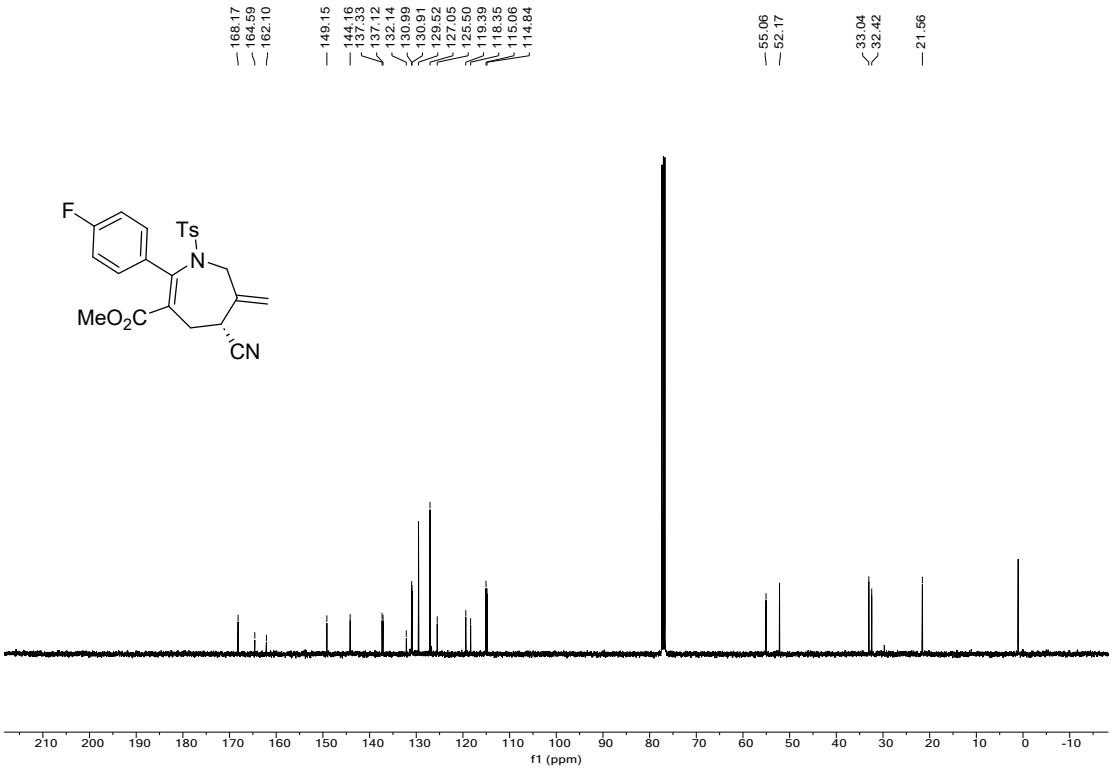
^{13}C NMR of **3f** in $CDCl_3$ (150 MHz)



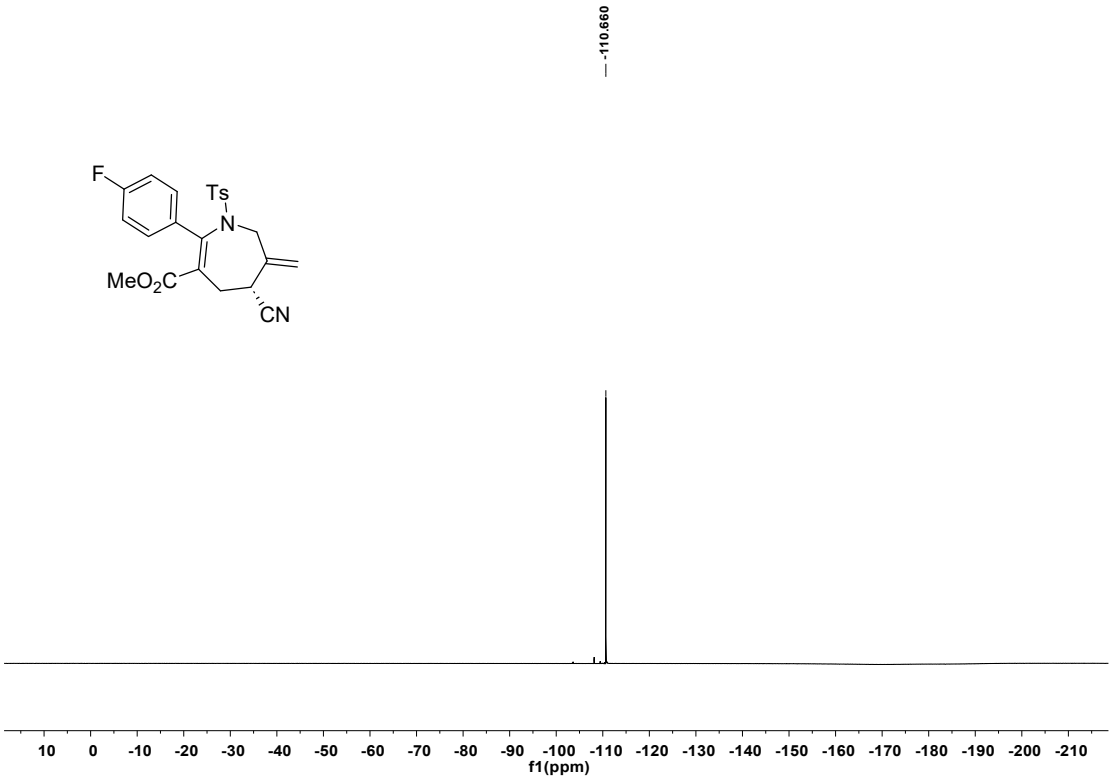
^{1}H NMR of **3g** in $CDCl_3$ (600 MHz)



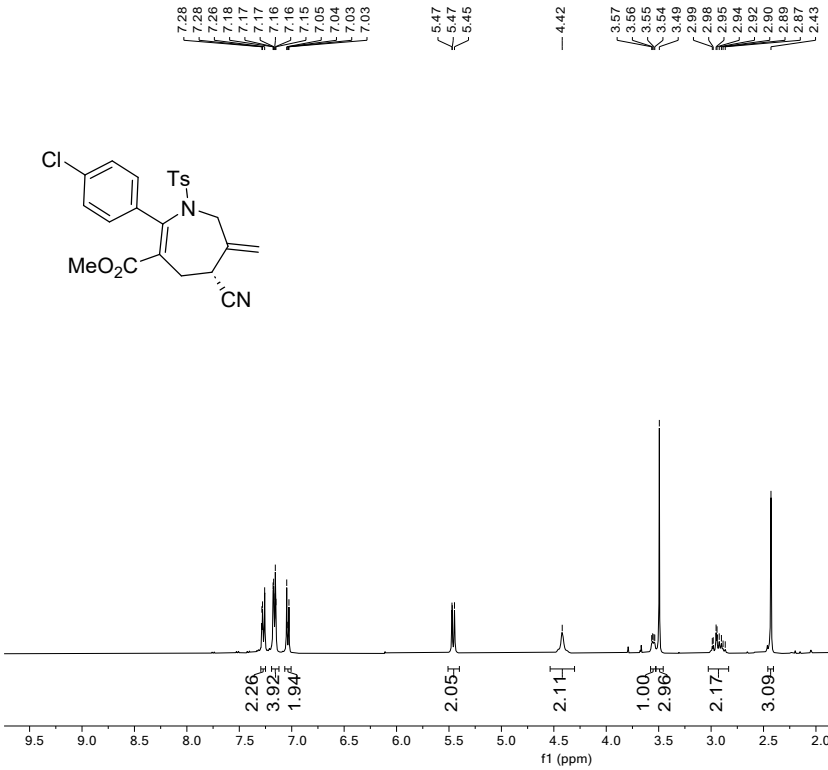
^{13}C NMR of **3g** in $CDCl_3$ (150 MHz)



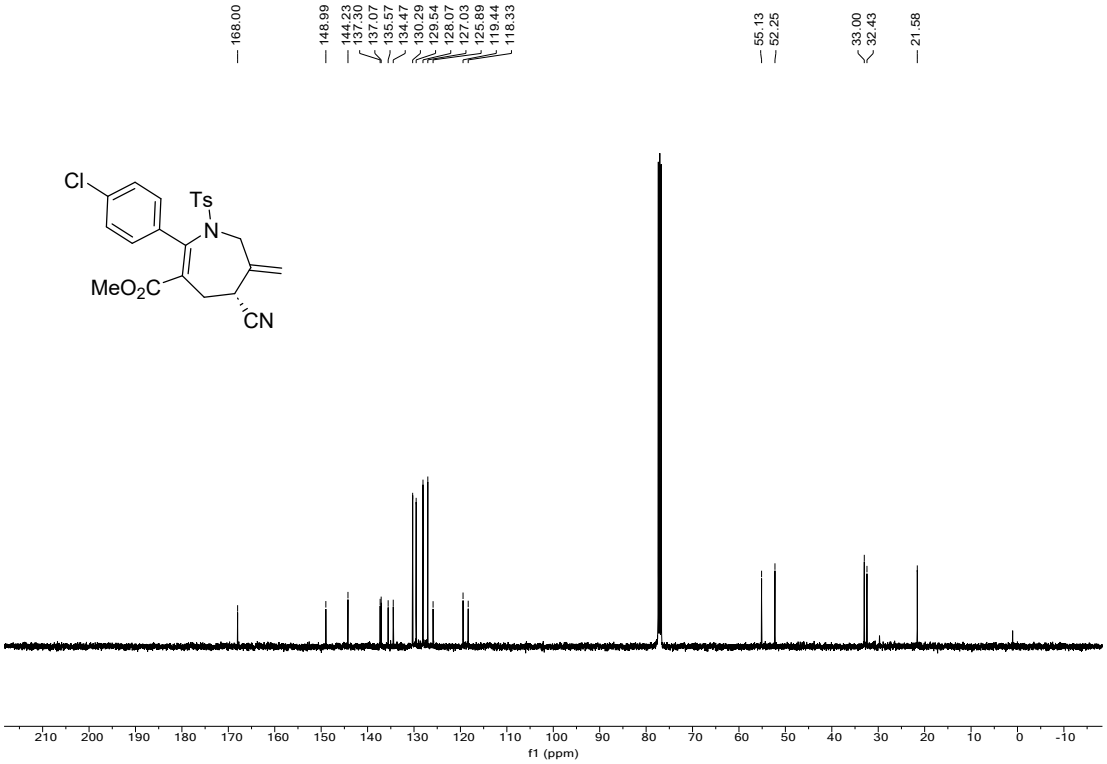
^{19}F NMR of **3g** in $CDCl_3$ (565 MHz)



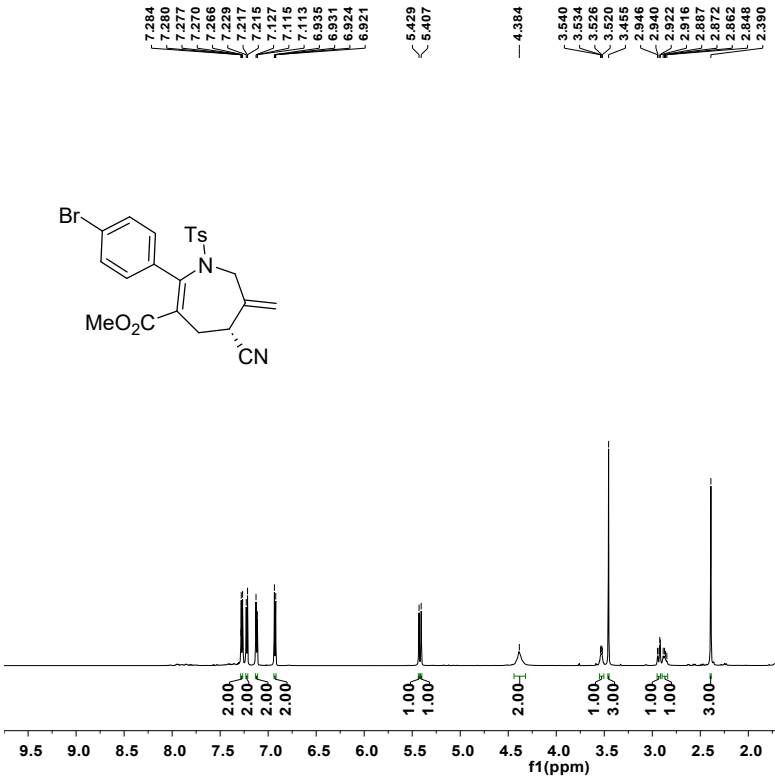
^{1}H NMR of **3h** in $CDCl_3$ (400 MHz)



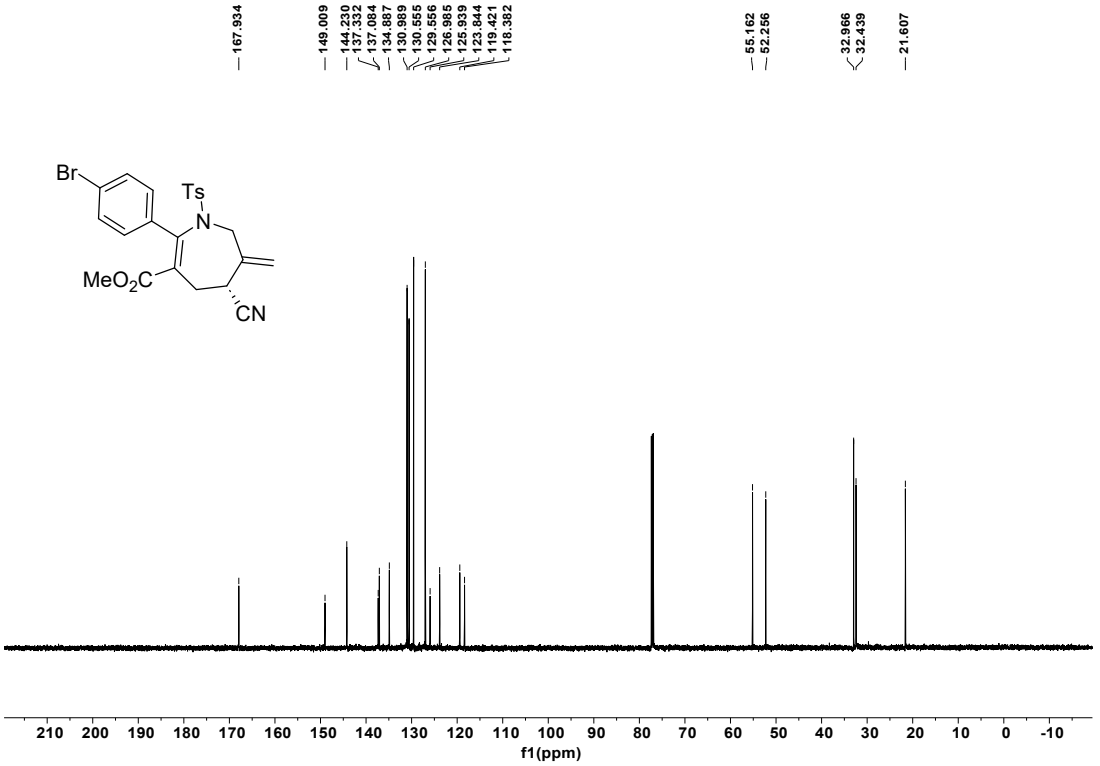
^{1}H NMR of **3h** in $CDCl_3$ (100 MHz)



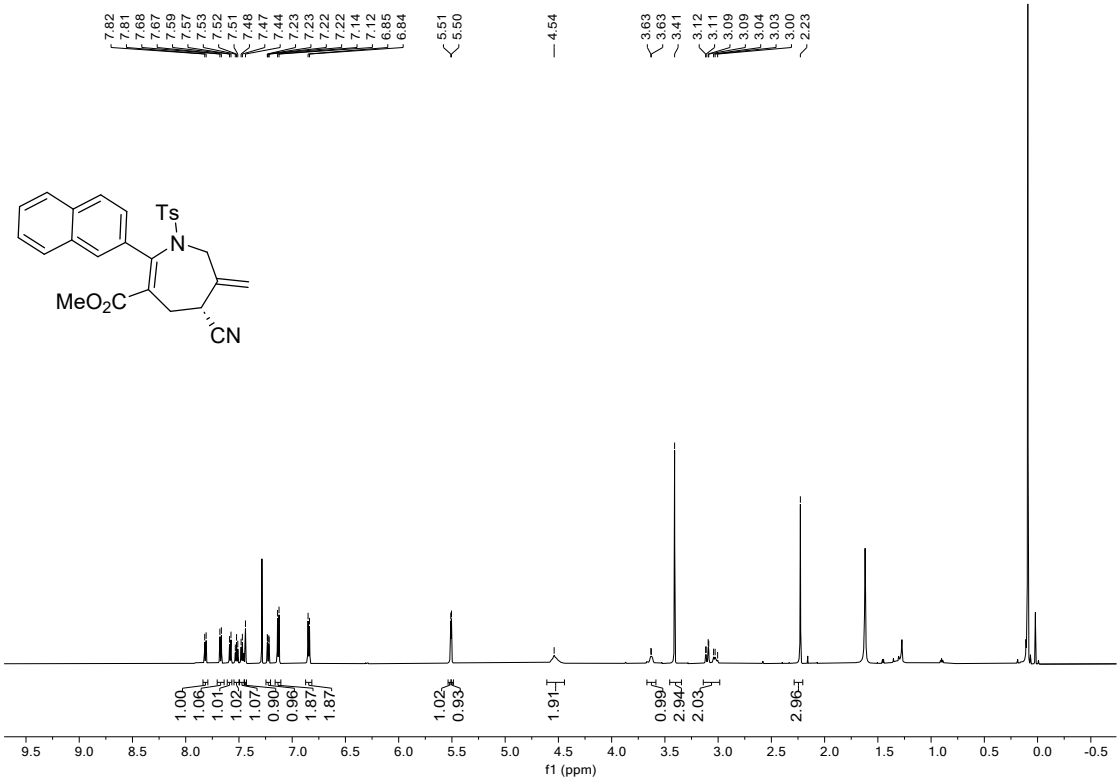
^{1}H NMR of **3i** in $CDCl_3$ (600 MHz)



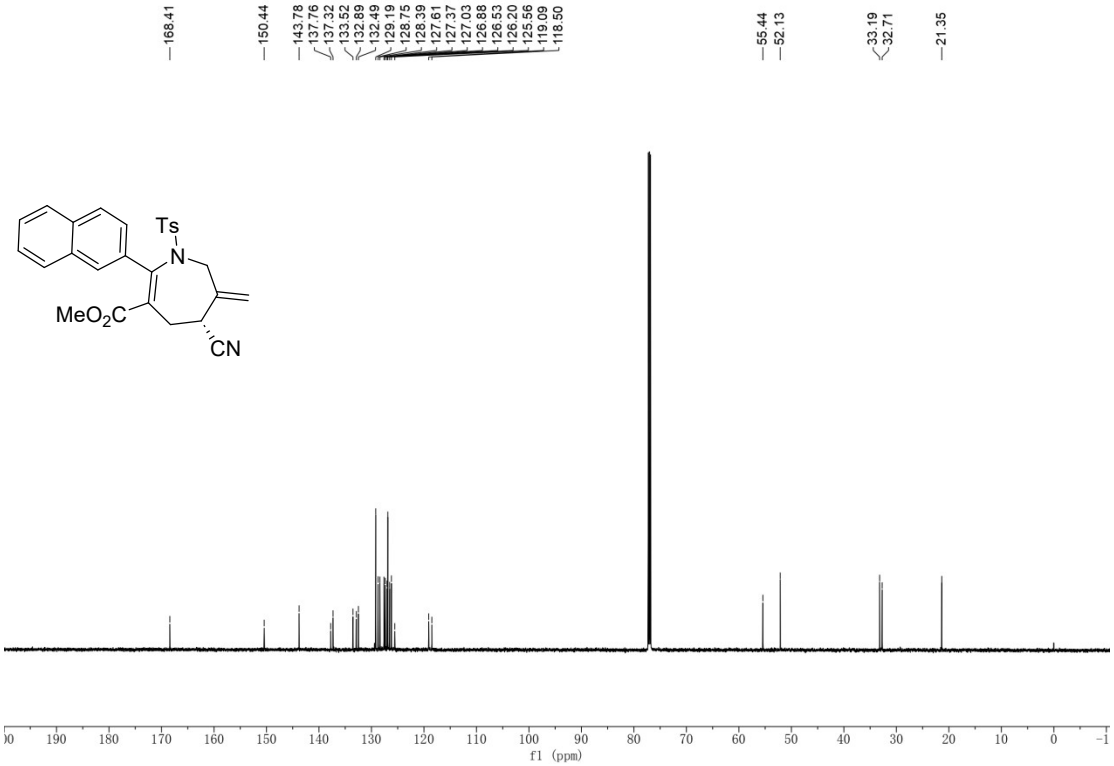
^{13}C NMR of **3i** in $CDCl_3$ (150 MHz)



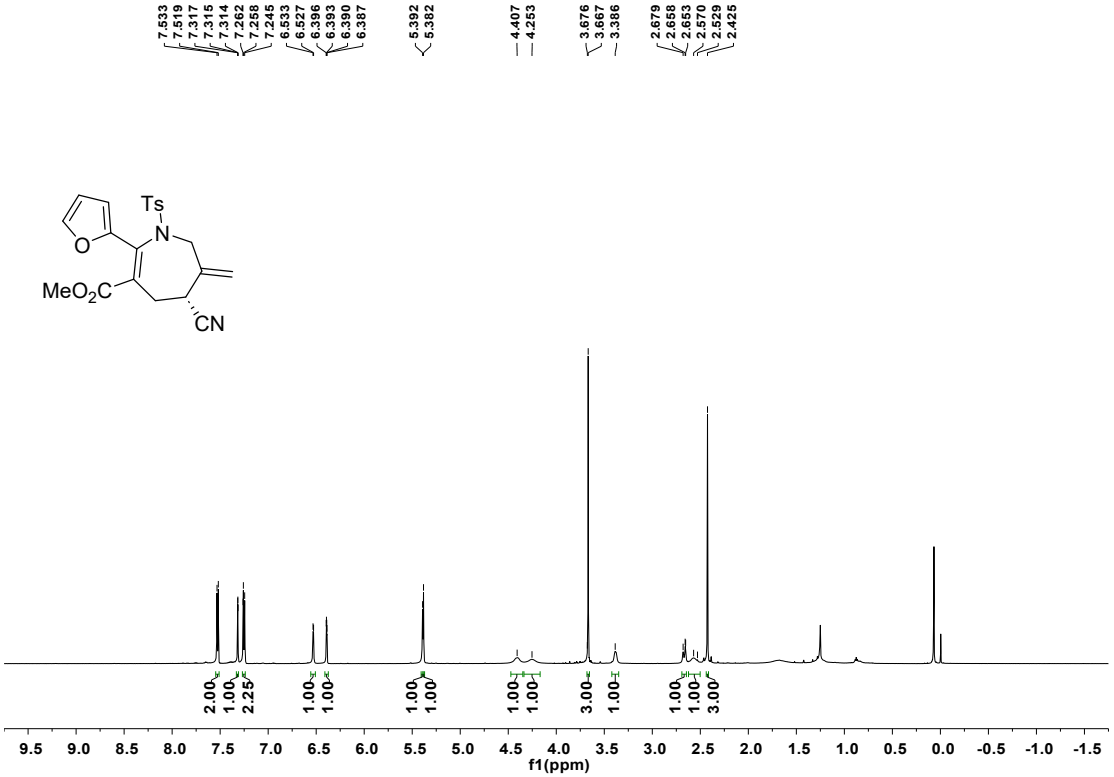
^{1}H NMR of **3j** in $CDCl_3$ (600 MHz)



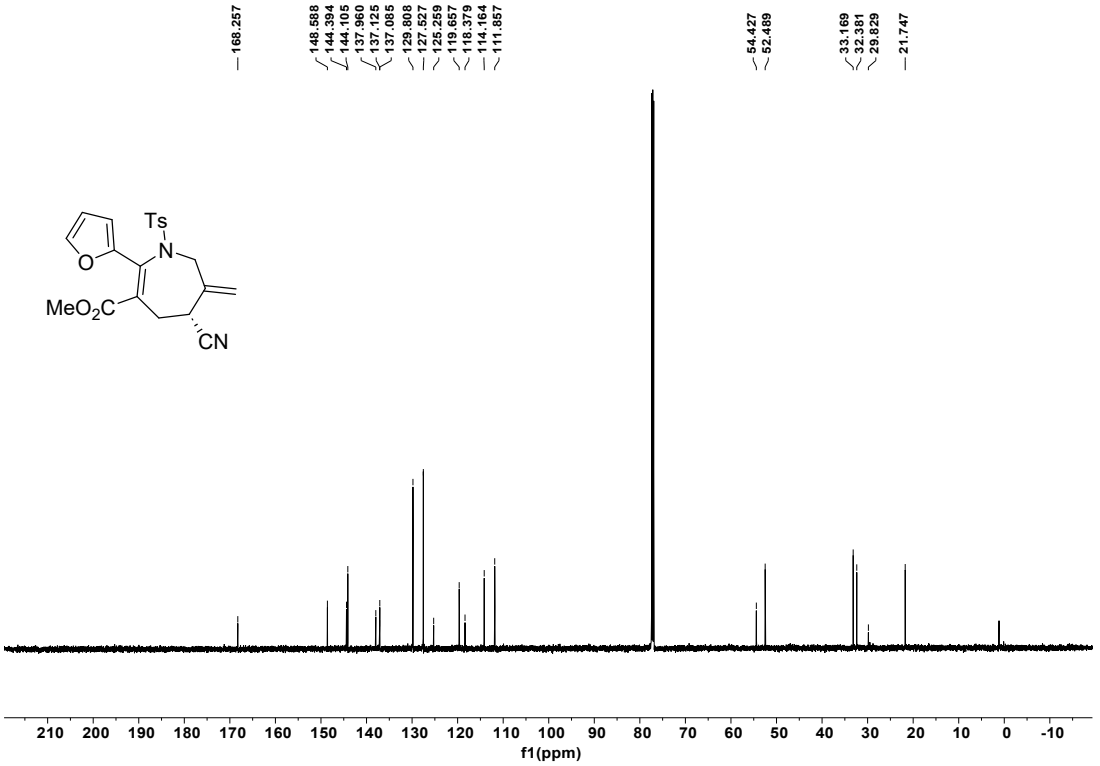
^{13}C NMR of **3j** in $CDCl_3$ (150 MHz)



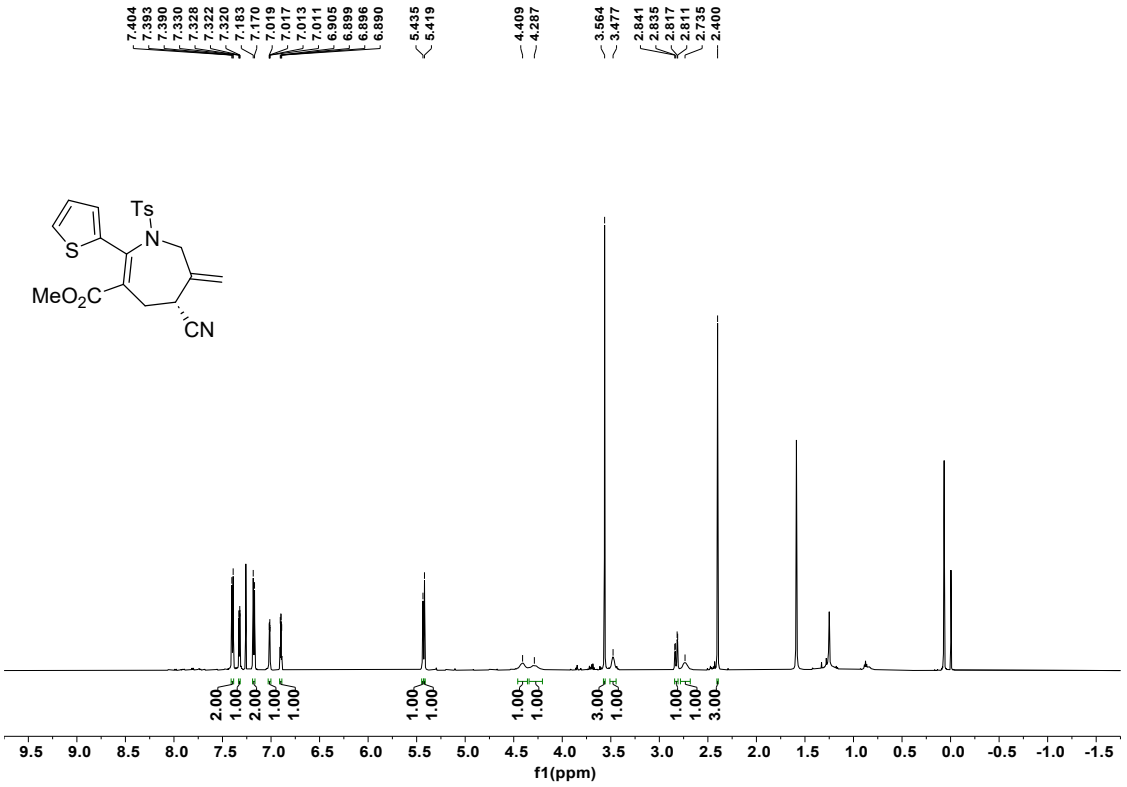
^{1}H NMR of **3k** in $CDCl_3$ (600 MHz)



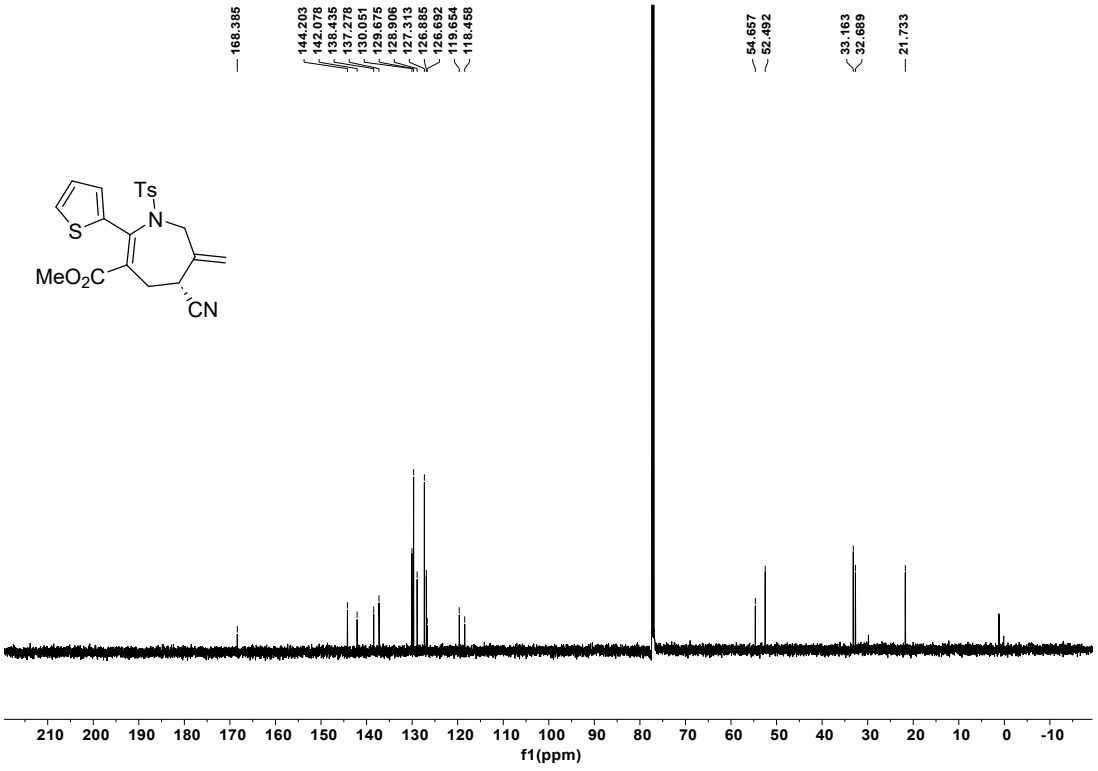
^{13}C NMR of **3k** in $CDCl_3$ (150 MHz)



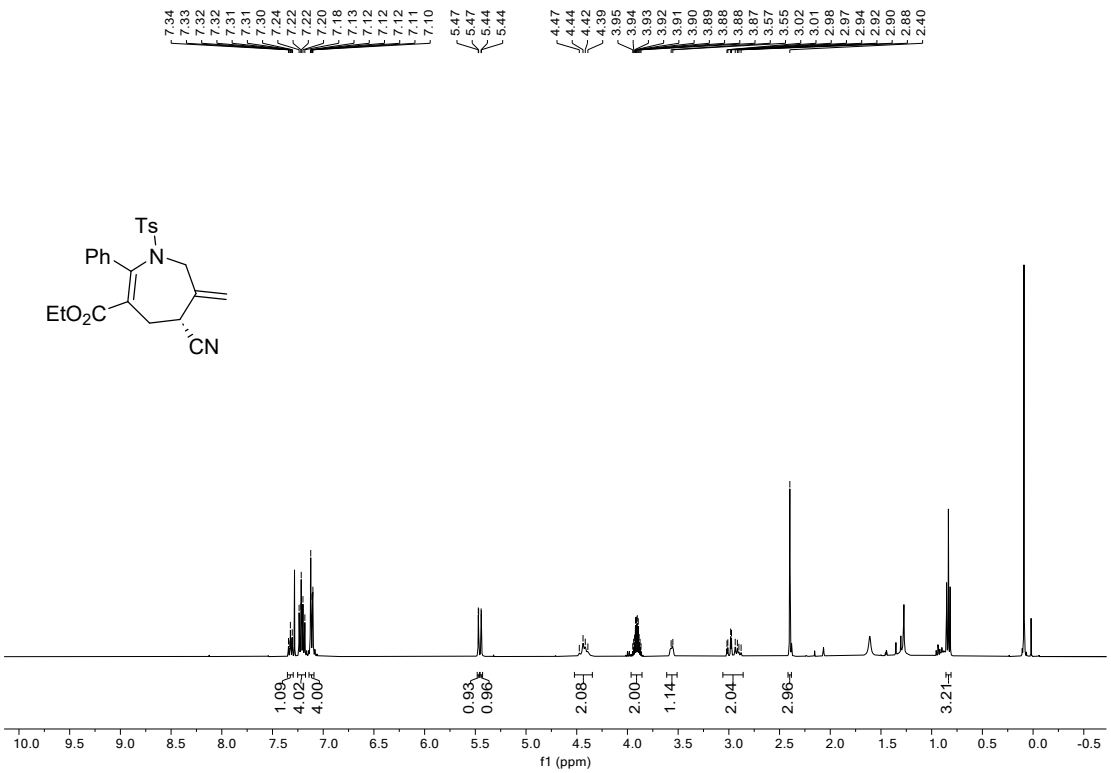
^{1}H NMR of **3l** in $CDCl_3$ (600 MHz)



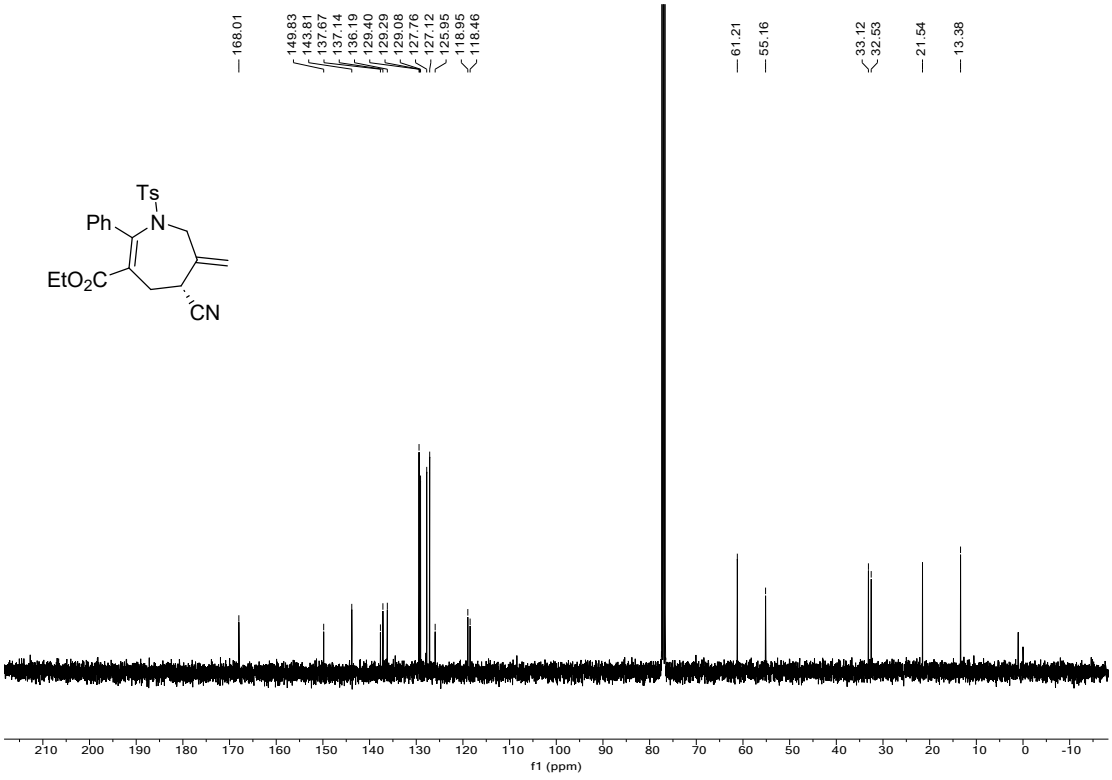
^{13}C NMR of **3l** in $CDCl_3$ (150 MHz)



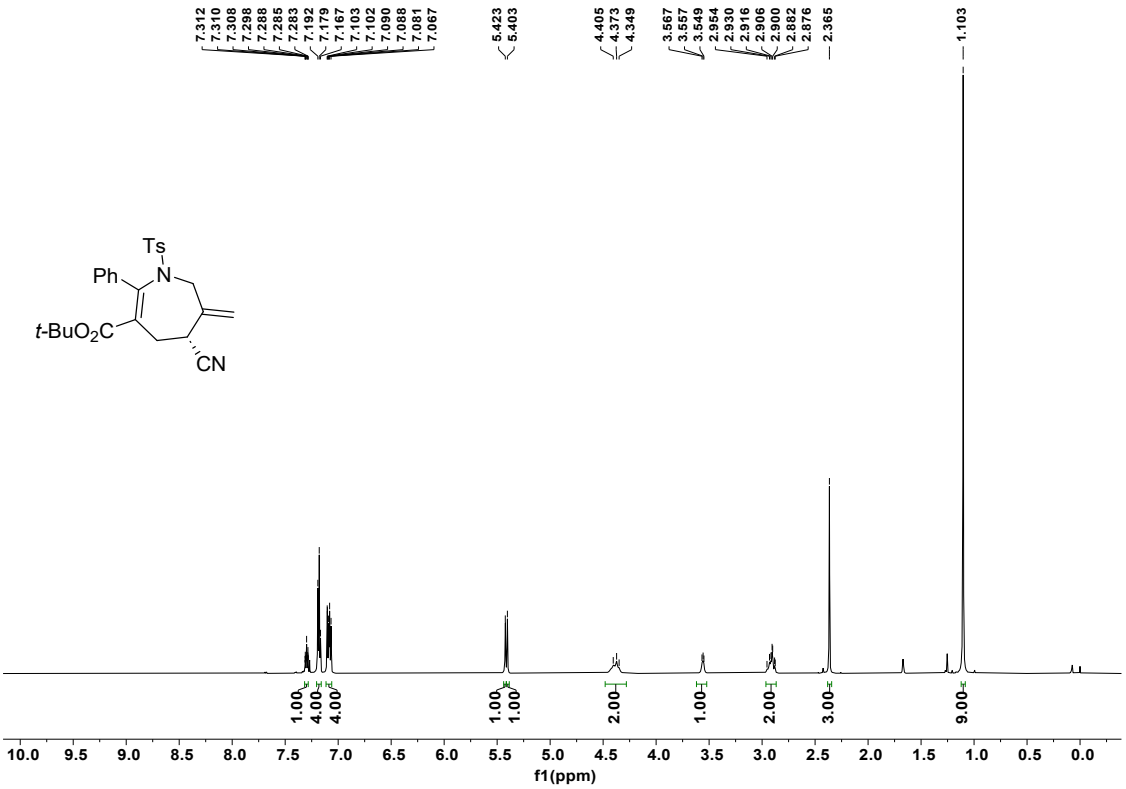
^{1}H NMR of **3m** in $CDCl_3$ (600 MHz)



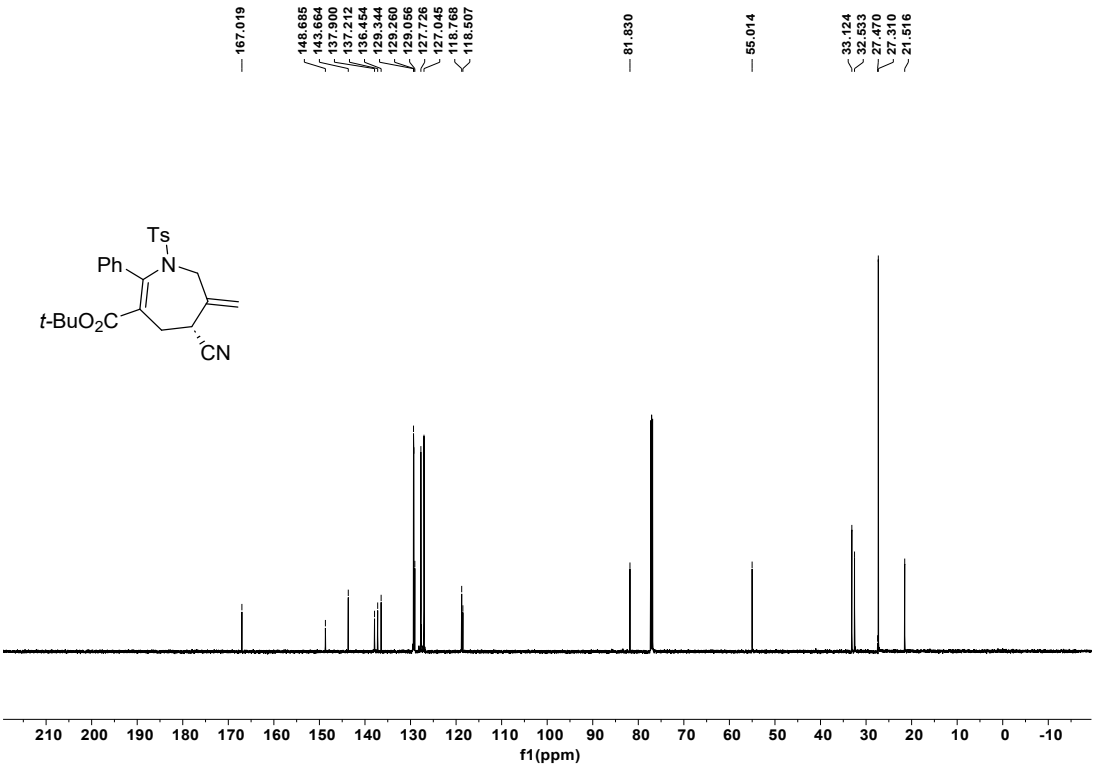
^{13}C NMR of **3m** in $CDCl_3$ (150 MHz)



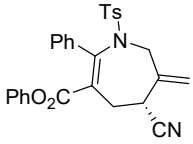
^{1}H NMR of **3n** in $CDCl_3$ (600 MHz)

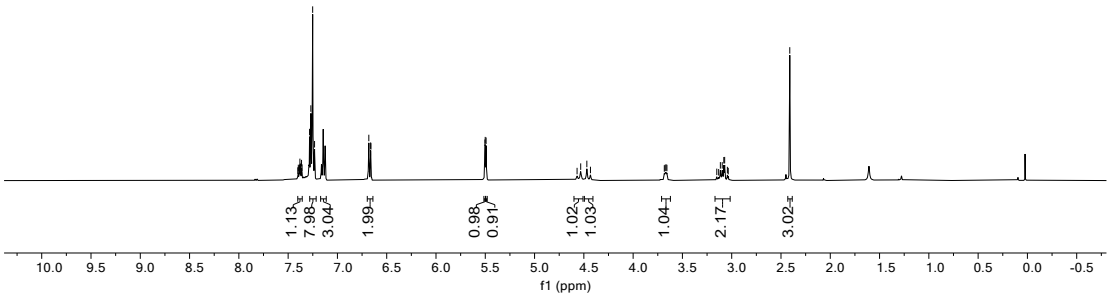


^{13}C NMR of **3n** in $CDCl_3$ (150 MHz)

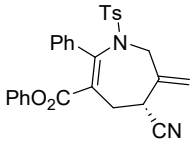


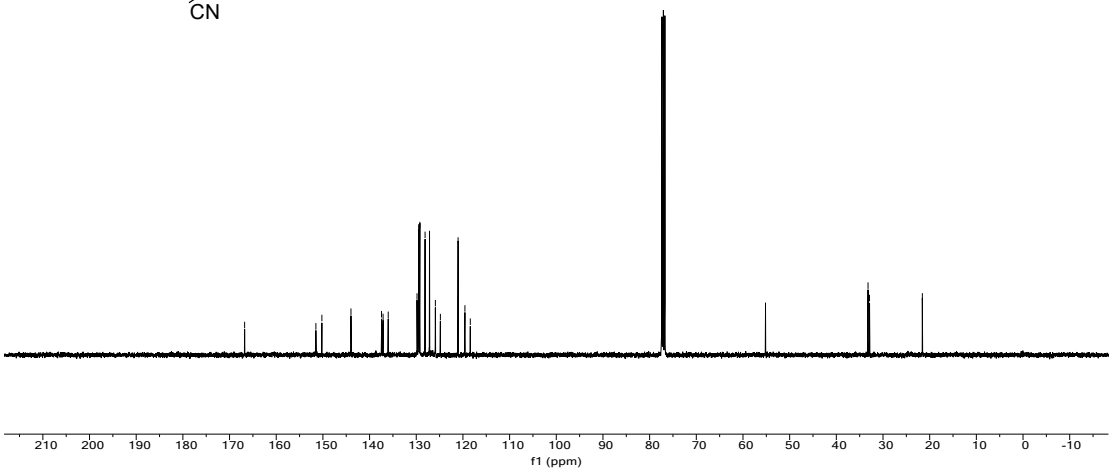
^{1}H NMR of **3o** in $CDCl_3$ (400 MHz)



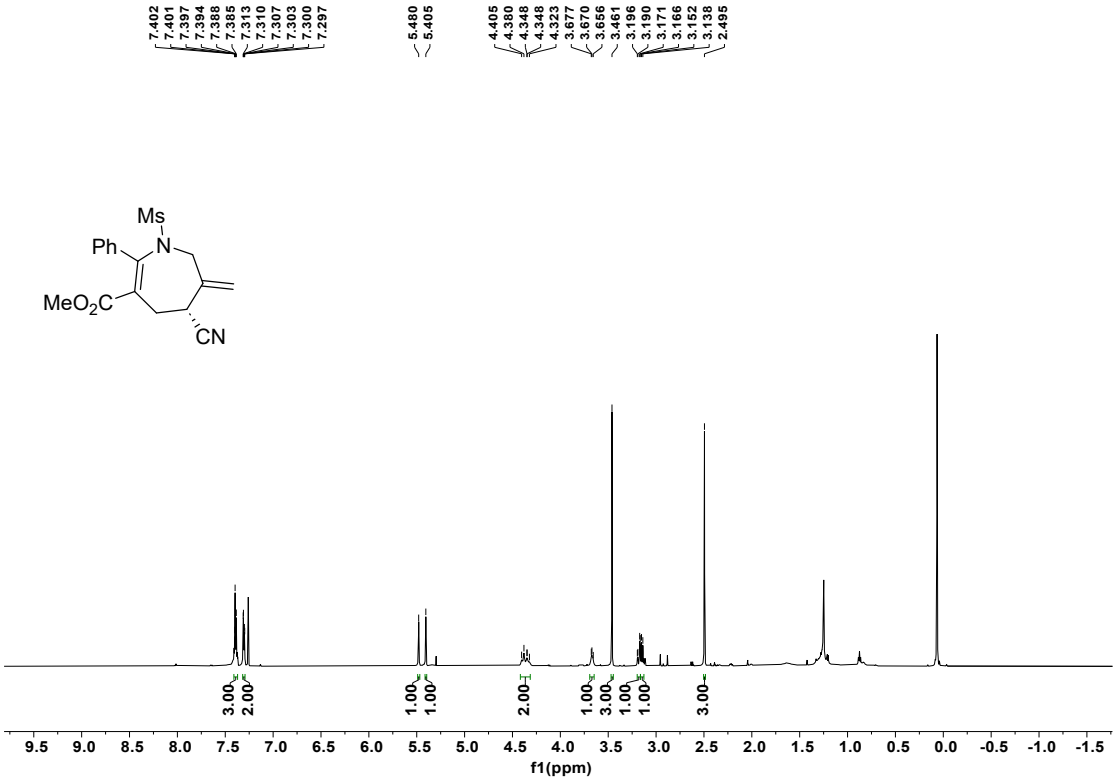


^{13}C NMR of **3o** in $CDCl_3$ (100 MHz)\

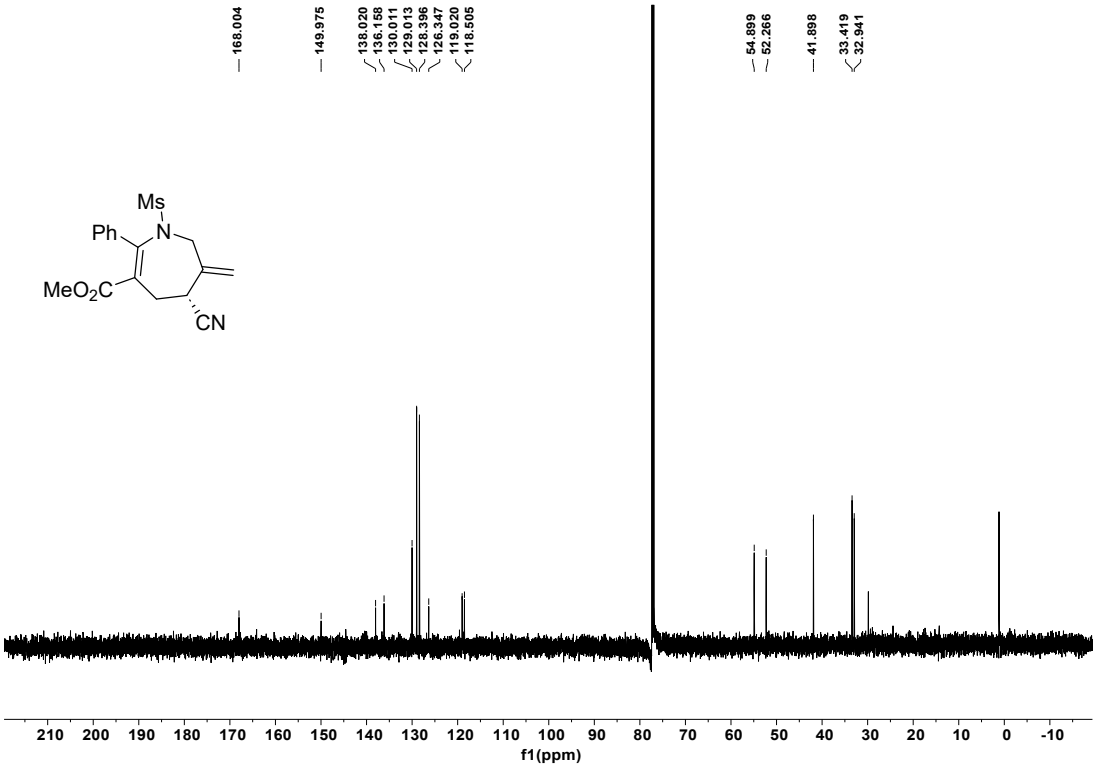




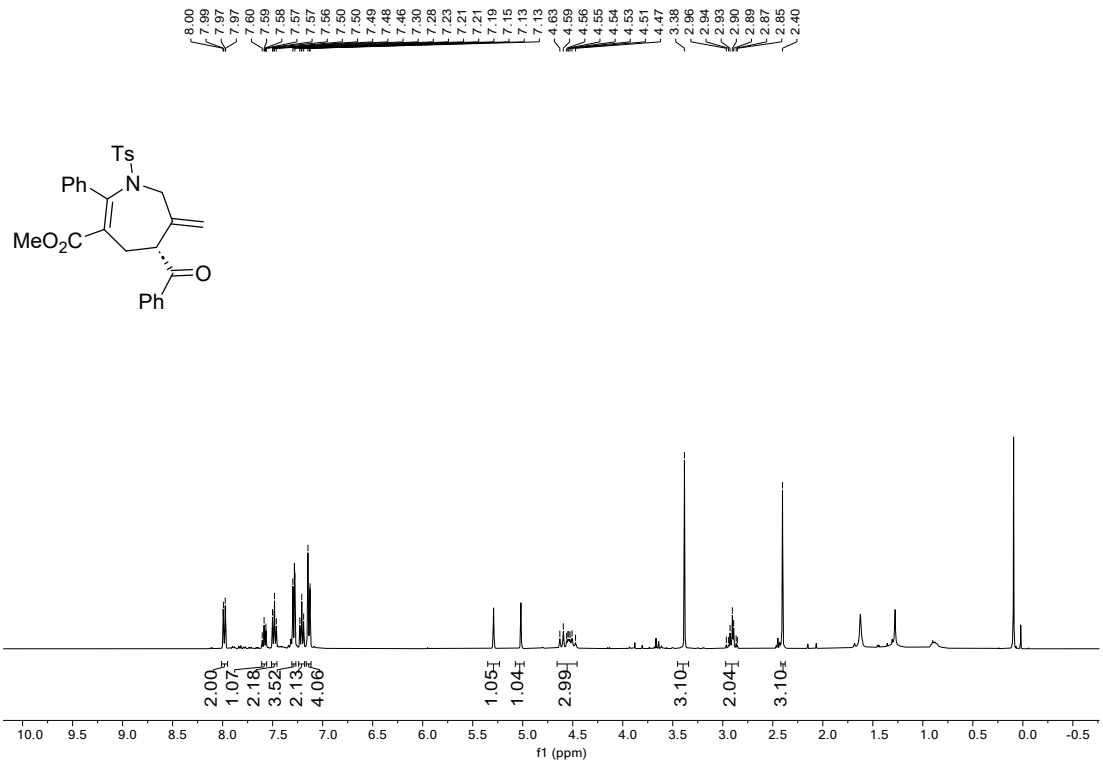
^{1}H NMR of **3p** in $CDCl_3$ (600 MHz)



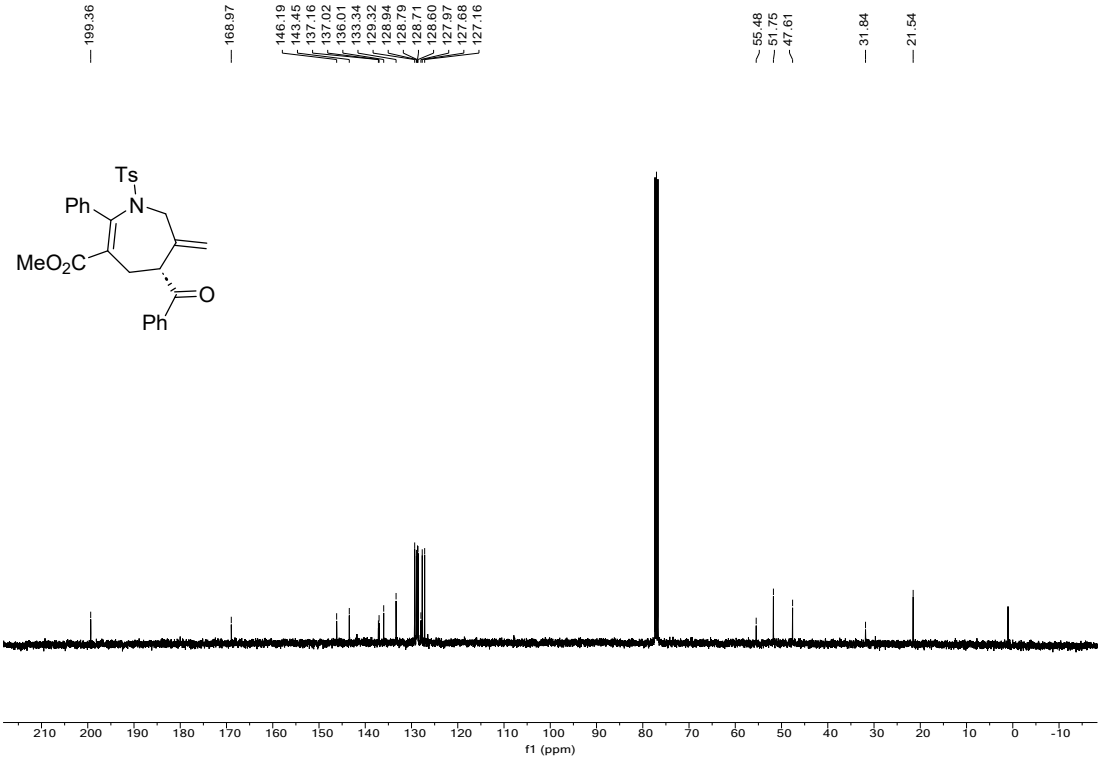
^{13}C NMR of **3p** in $CDCl_3$ (150 MHz)



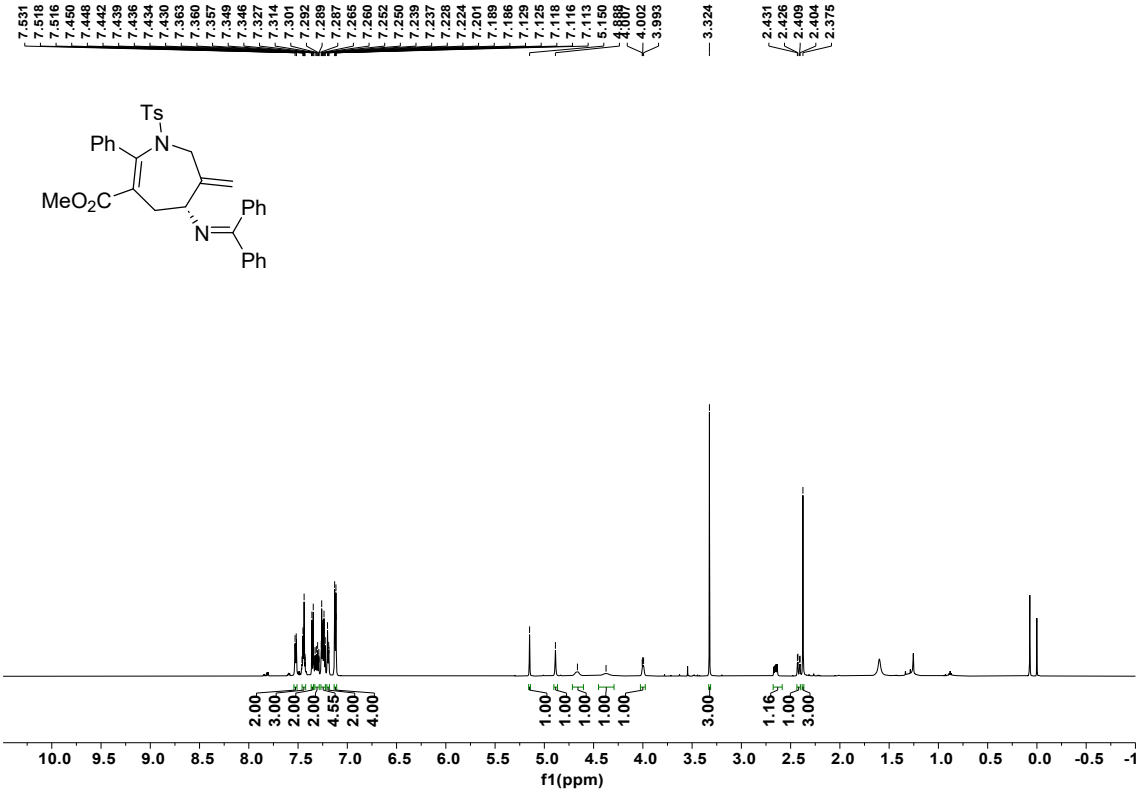
^{1}H NMR of **3q** in $CDCl_3$ (400 MHz)



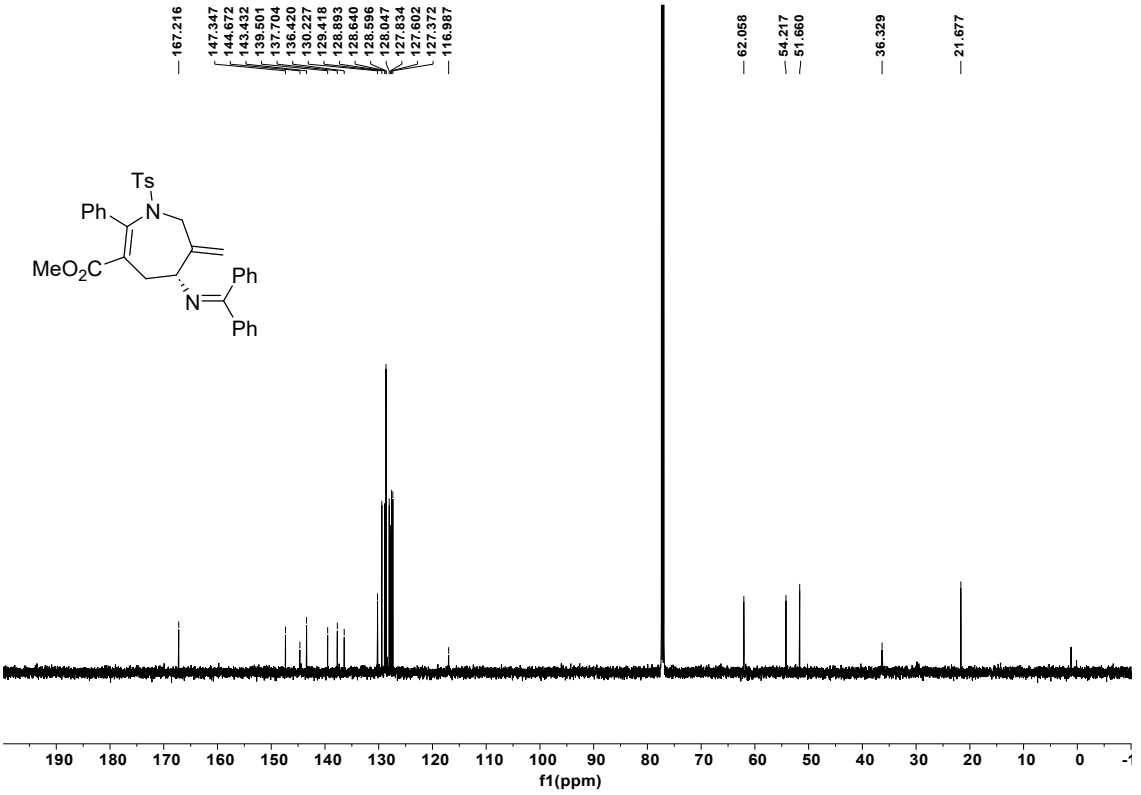
^{13}C NMR of **3q** in $CDCl_3$ (150 MHz)



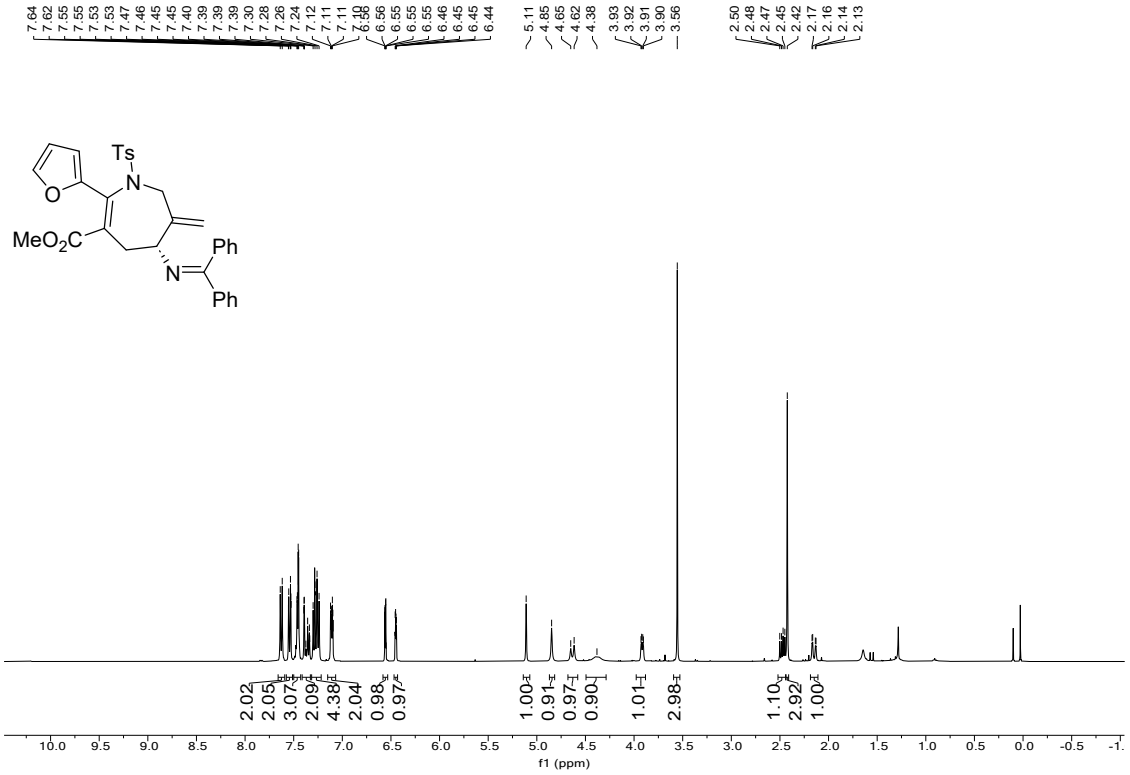
^{1}H NMR of **3r** in $CDCl_3$ (600 MHz)



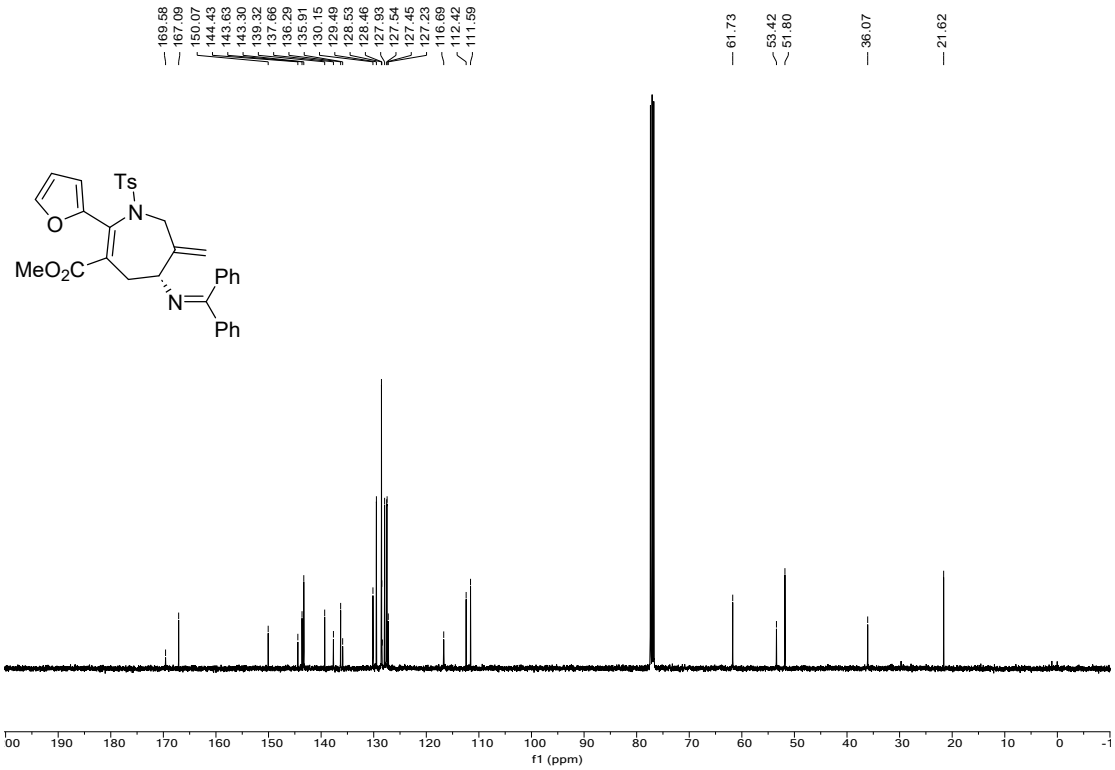
^{13}C NMR of **3r** in $CDCl_3$ (150 MHz)



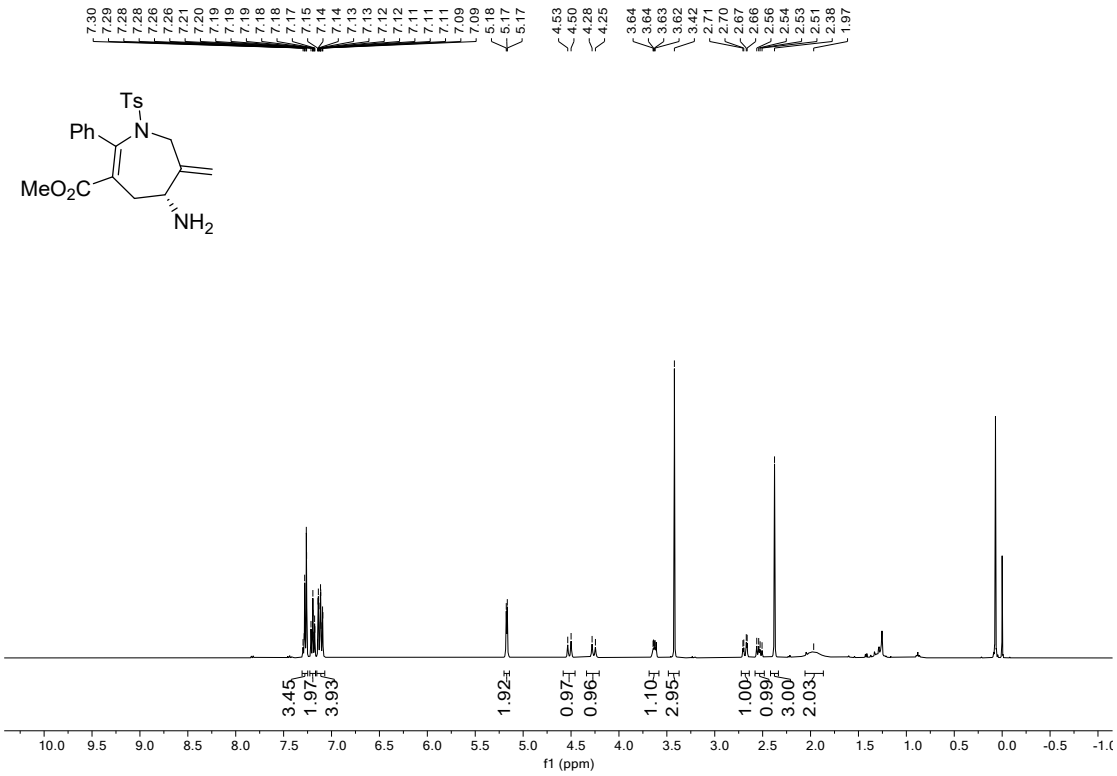
^{1}H NMR of **3s** in $CDCl_3$ (400 MHz)



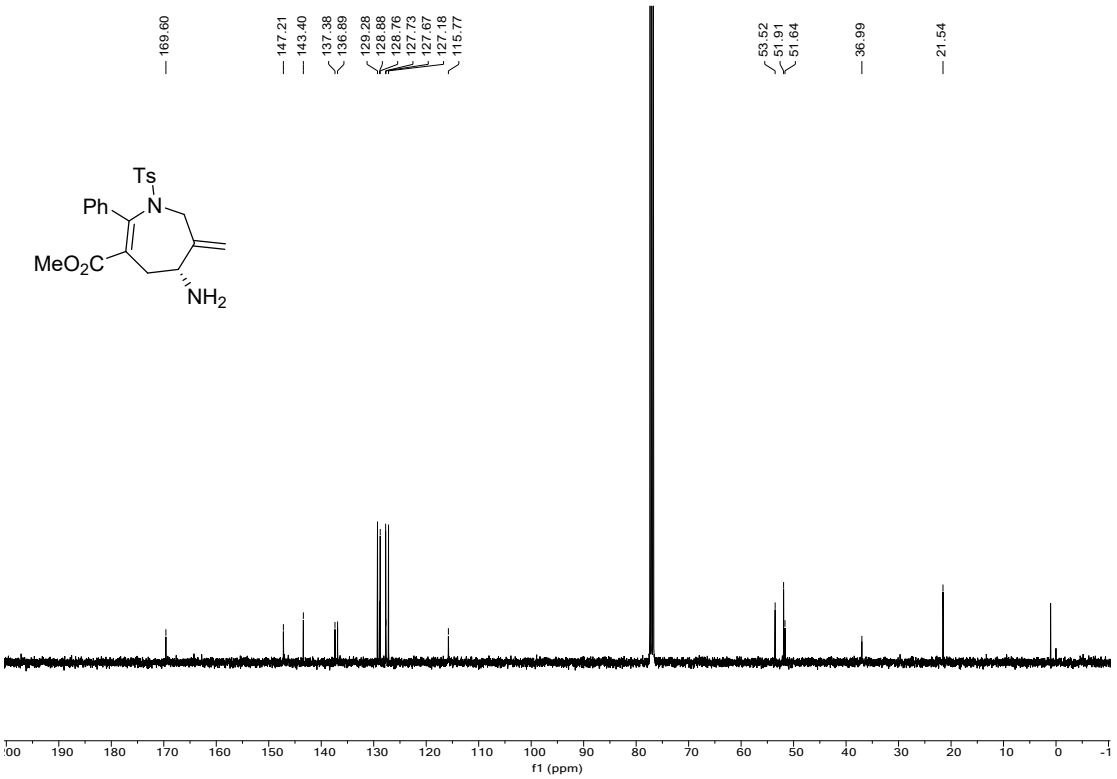
^{13}C NMR of **3s** in $CDCl_3$ (100 MHz)



^{1}H NMR of **4** in $CDCl_3$ (400 MHz)

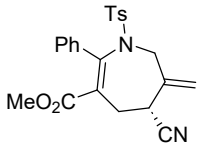


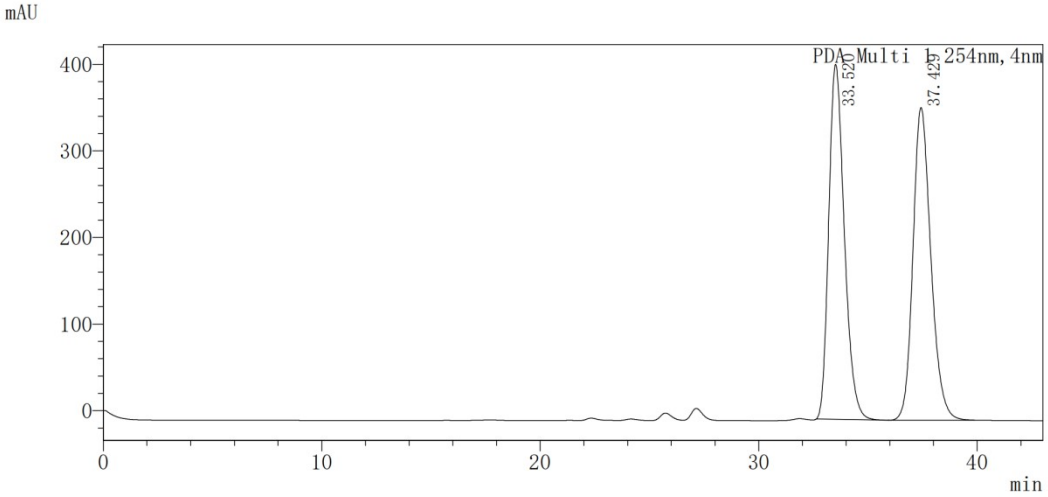
^{13}C NMR of **4** in $CDCl_3$ (100 MHz)



7 HPLC chromatograms

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

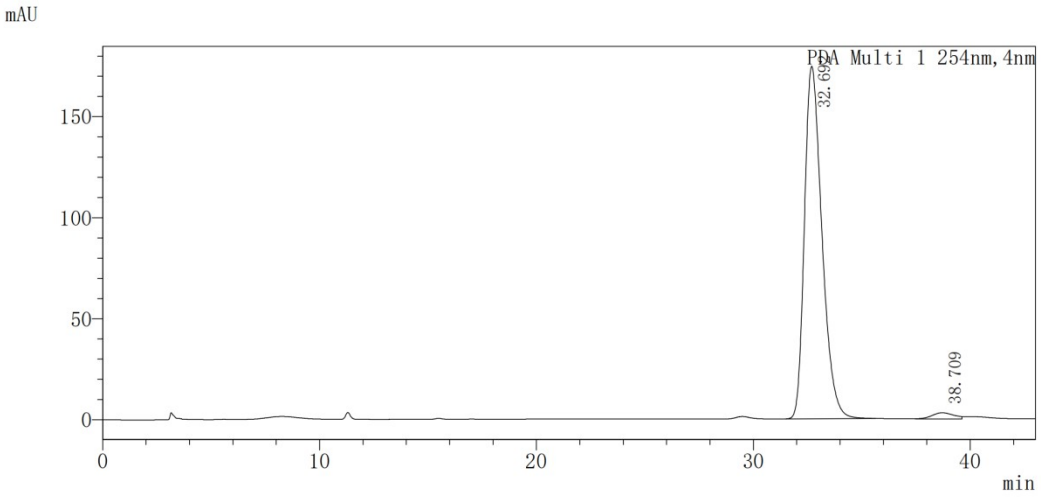




〈Peak table〉

PDA Ch1 254nm

Peak	Area	Height	Area%	Ren.time
1	20305396	409660	49.681	33.520
2	20565792	361224	50.319	37.429
Total	40871188	770884	100.000	

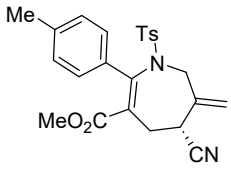


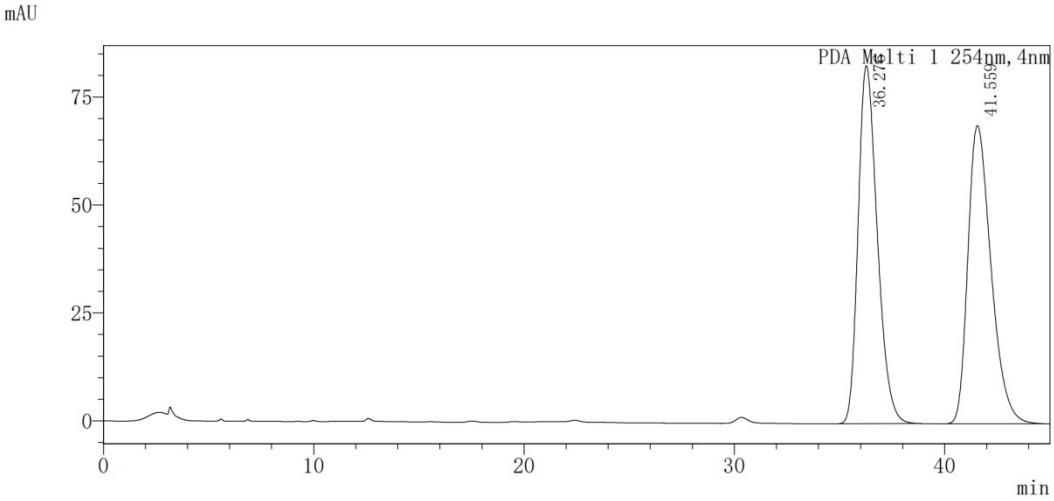
〈Peak table〉

PDA Ch1 254nm

Peak	Area	Height	Area%	Ren.time
1	9776892	174503	97.907	32.692
2	209003	3025	2.093	38.709
Total	9985895	177528	100.000	

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

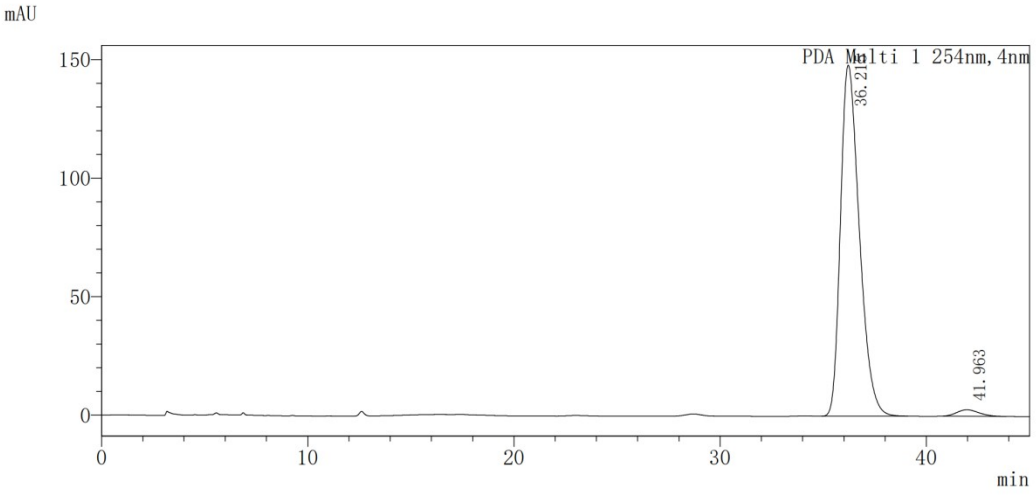




〈Peak table〉

PDA Ch1 254nm

Peak	Area	Height	Area%	Ren.time
1	5261274	82908	49.883	36.276
2	5285965	69048	50.117	41.559
Total	10547238	151955	100.000	

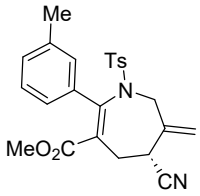


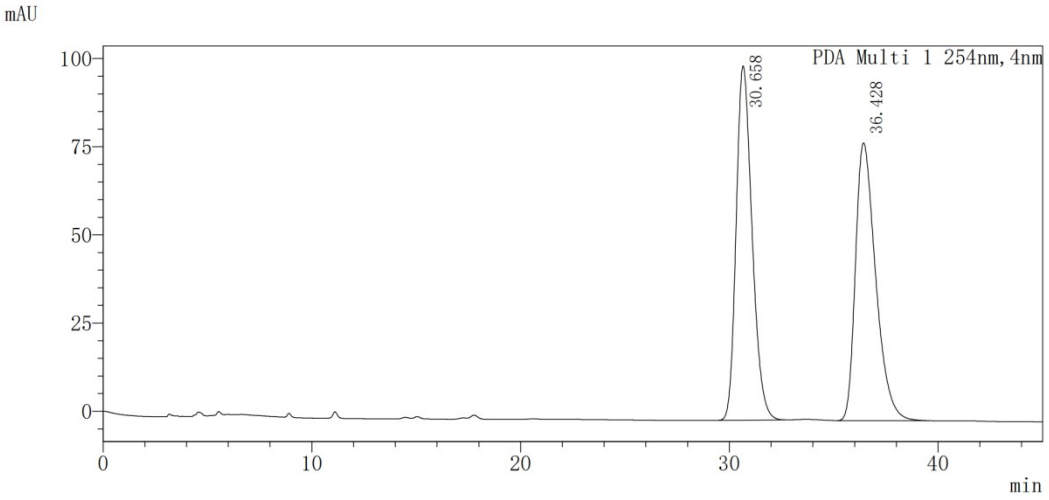
〈Peak table〉

PDA Ch1 254nm

Peak	Area	Height	Area%	Ren.time
1	9425823	148110	97.905	36.215
2	201660	2719	2.095	41.963
Total	9627483	150830	100.000	

HPLC chromatogram of compound **3c** (97% *ee*)

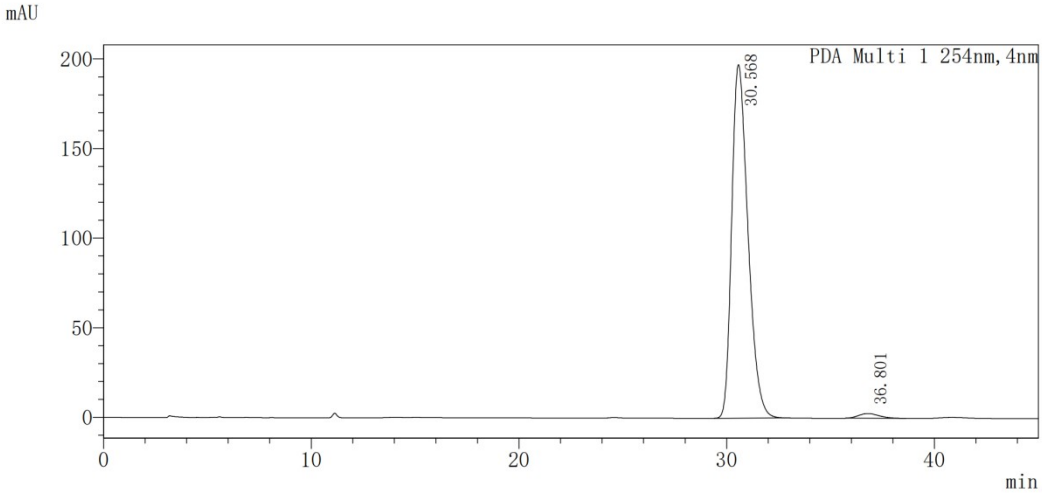




<Peak table>

PDA Ch1 254nm

Peak	Area	Height	Area%	Ren.time
1	5322845	100454	50.102	30.658
2	5301241	78749	49.898	36.428
Total	10624086	179204	100.000	

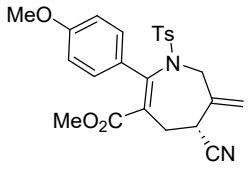


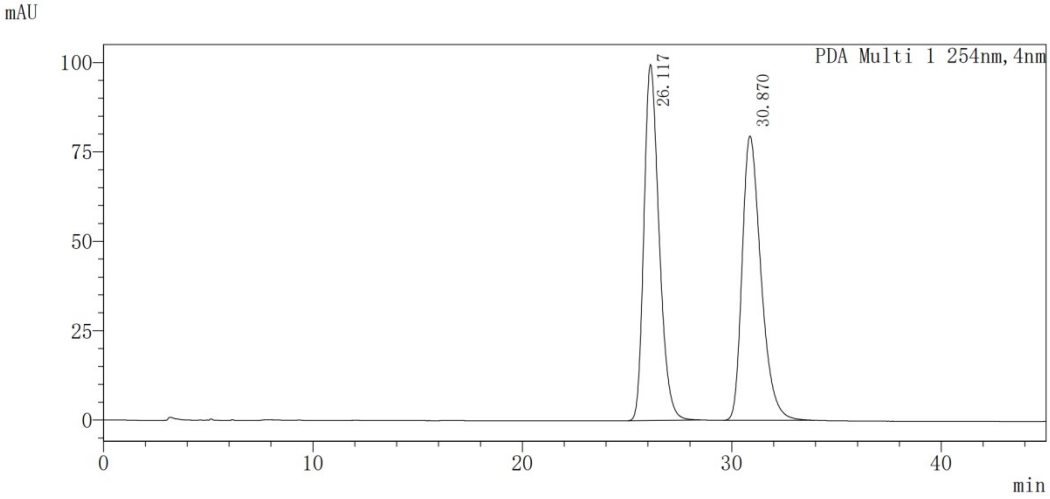
<Peak table>

PDA Ch1 254nm

Peak	Area	Height	Area%	Ren.time
1	10725630	197284	98.349	30.568
2	180077	2620	1.651	36.801
Total	10905707	199904	100.000	

HPLC chromatogram of compound **3d** (95% *ee*)

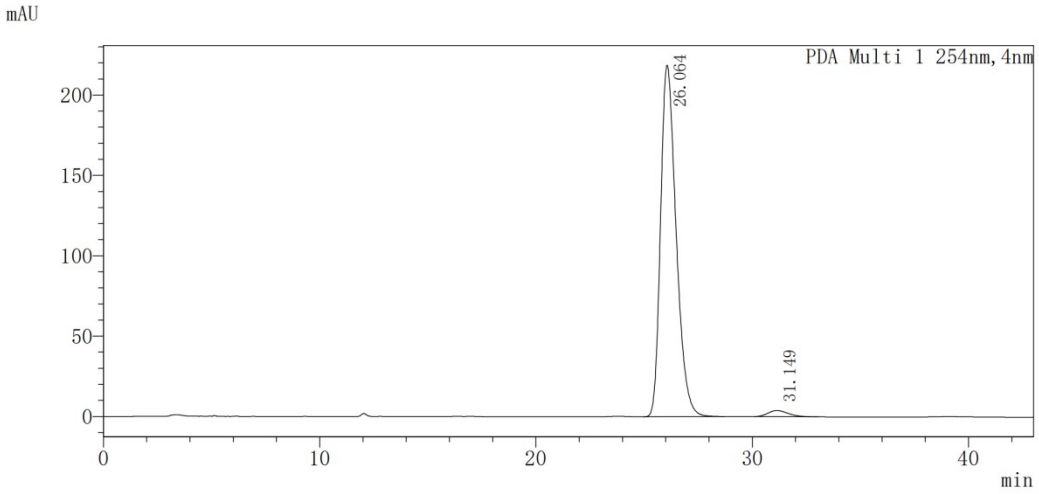




<Peak table>

PDA Ch1 254nm

Peak	Area	Height	Area%	Ren.time
1	5004196	99542	50.145	26.117
2	4975273	79511	49.855	30.870
Total	9979468	179053	100.000	

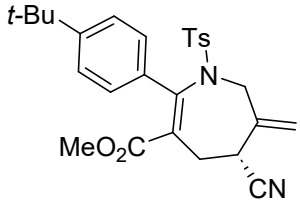


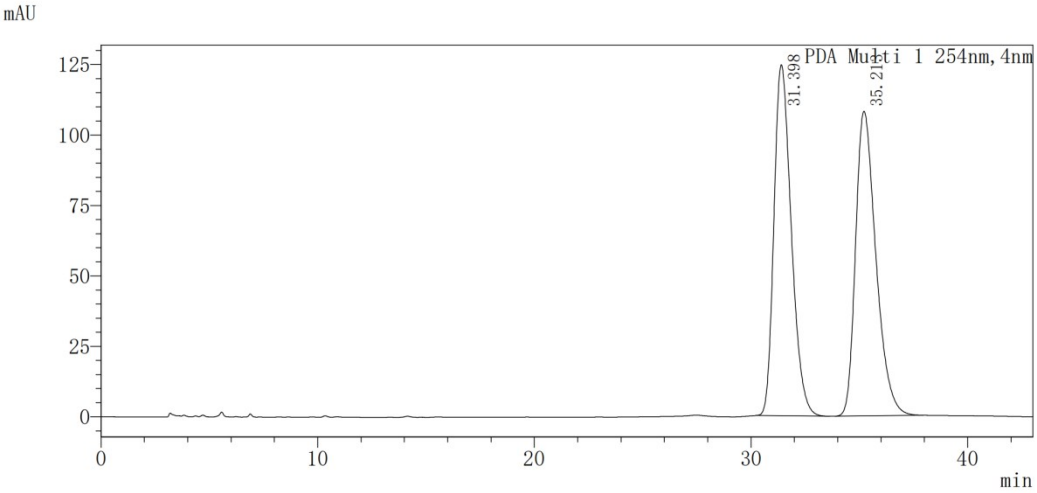
<Peak table>

PDA Ch1 254nm

Peak	Area	Height	Area%	Ren.time
1	10941202	218741	97.753	26.064
2	251500	3843	2.247	31.149
Total	11192702	222585	100.000	

HPLC chromatogram of compound **3e** (97% *ee*)

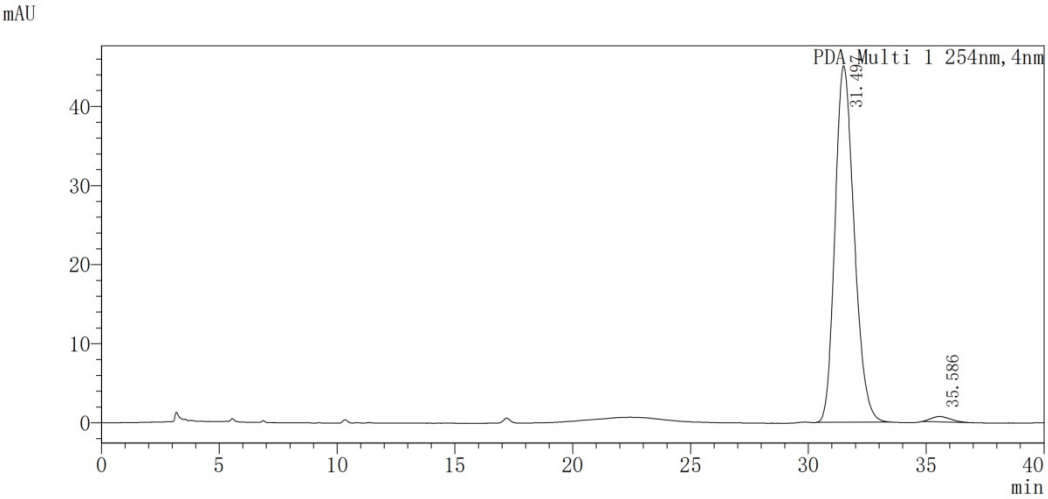




<Peak table>

PDA Ch1 254nm

Peak	Area	Height	Area%	Ren.time
1	6924689	124554	49.516	31.398
2	7060013	108103	50.484	35.213
Total	13984702	232657	100.000	

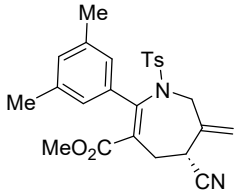


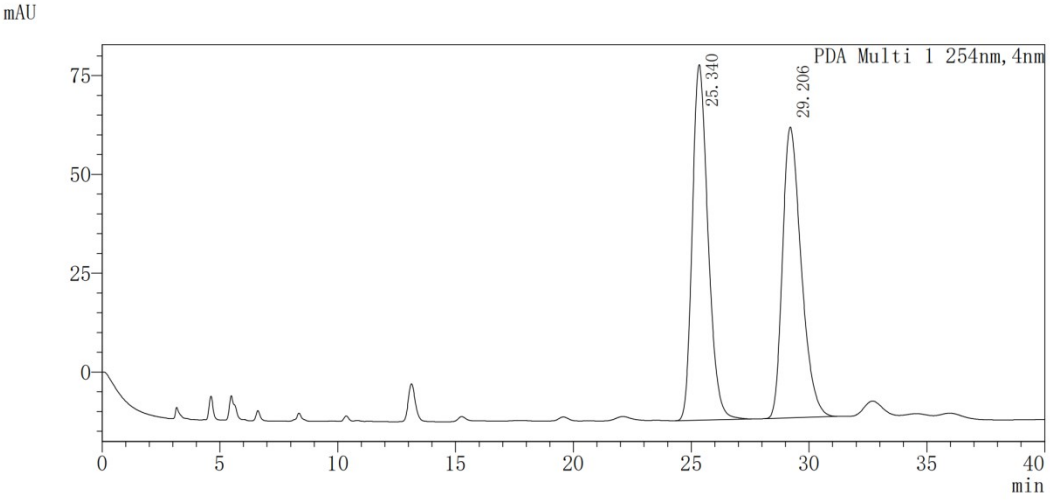
<Peak table>

PDA Ch1 254nm

Peak	Area	Height	Area%	Ren.time
1	2550812	45080	98.499	31.497
2	38875	676	1.501	35.586
Total	2589687	45755	100.000	

HPLC chromatogram of compound **3f** (97% *ee*)

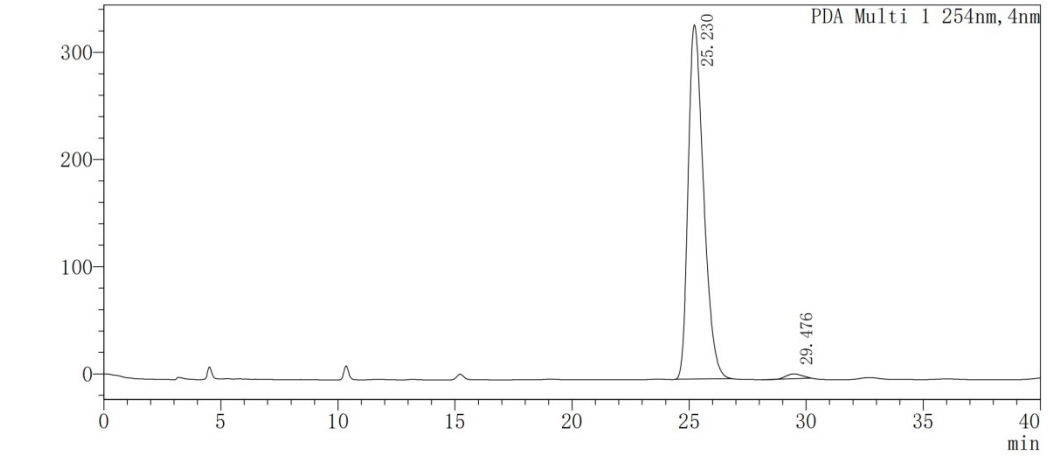




<Peak table>

PDA Ch1 254nm

Peak	Area	Height	Area%	Ren.time
1	4168386	89947	50.665	25.340
2	4059007	73560	49.335	29.206
Total	8227393	163507	100.000	

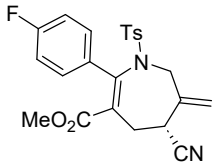


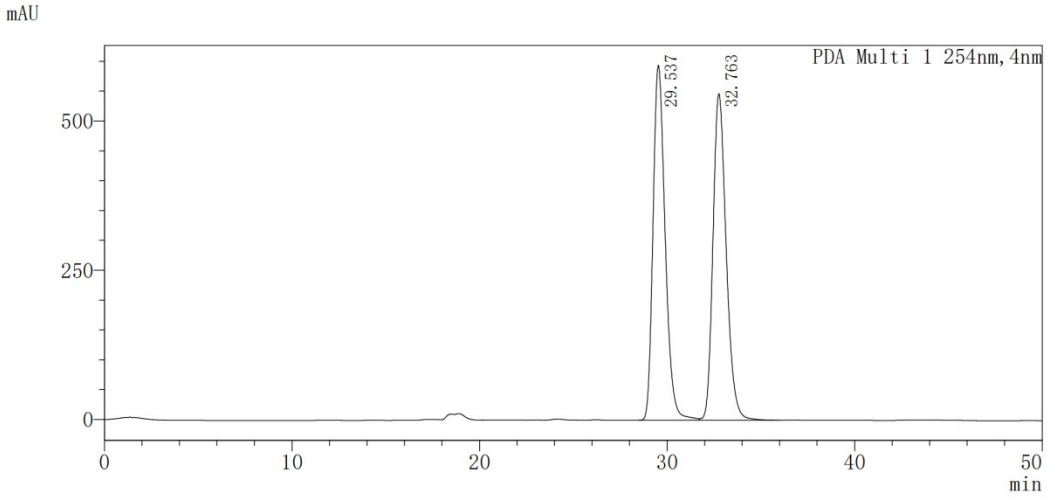
<Peak table>

PDA Ch1 254nm

Peak	Area	Height	Area%	Ren.time
1	15125816	330444	98.742	25.230
2	192743	4283	1.258	29.476
Total	15318559	334727	100.000	

HPLC chromatogram of compound **3g** (95% *ee*)

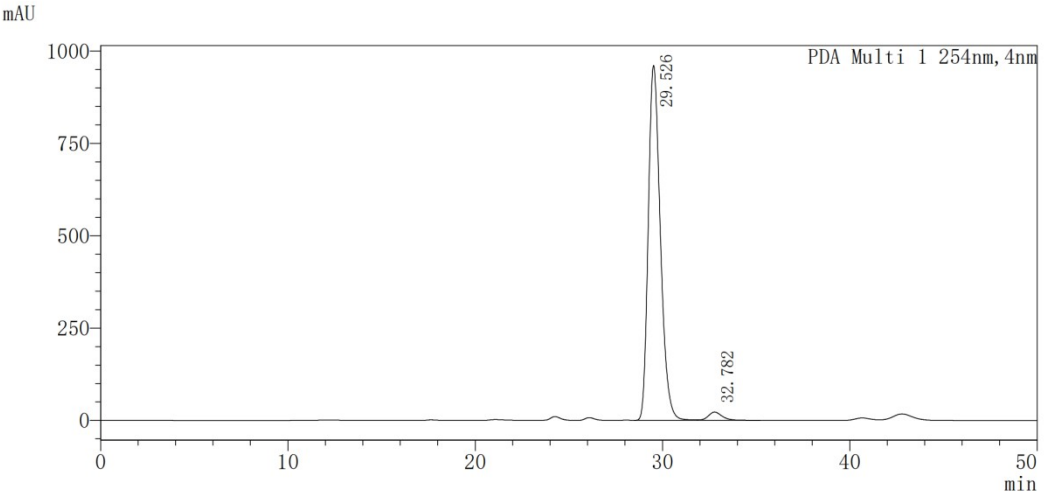




〈Peak table〉

PDA Ch1 254nm

Peak	Area	Height	Area%	Ren.time
1	26787712	594406	49.939	29.537
2	26853414	546997	50.061	32.763
Total	53641127	1141403	100.000	

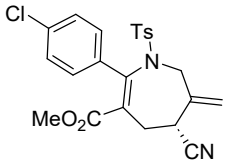


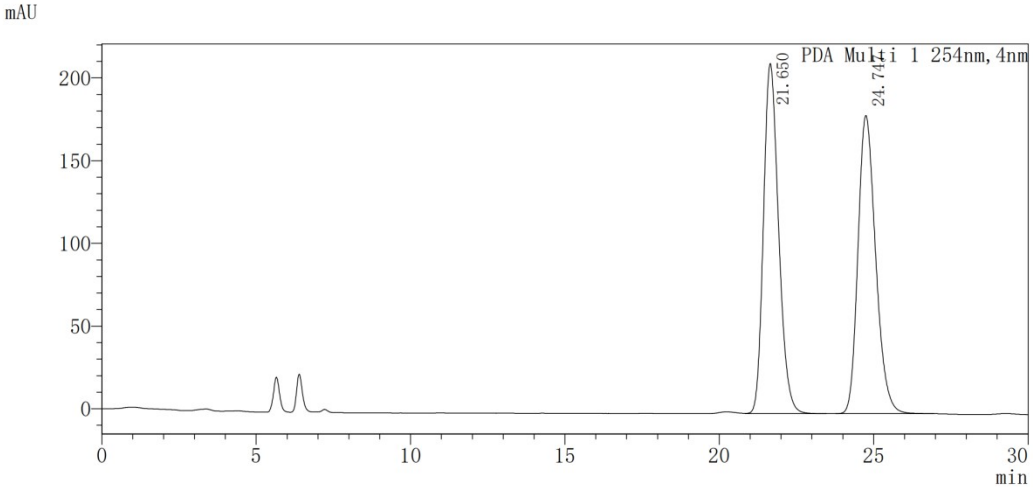
〈Peak table〉

PDA Ch1 254nm

Peak	Area	Height	Area%	Ren.time
1	43110545	961119	97.375	29.526
2	1162067	22328	2.625	32.782
Total	44272612	983447	100.000	

HPLC chromatogram of compound **3h** (89% *ee*)

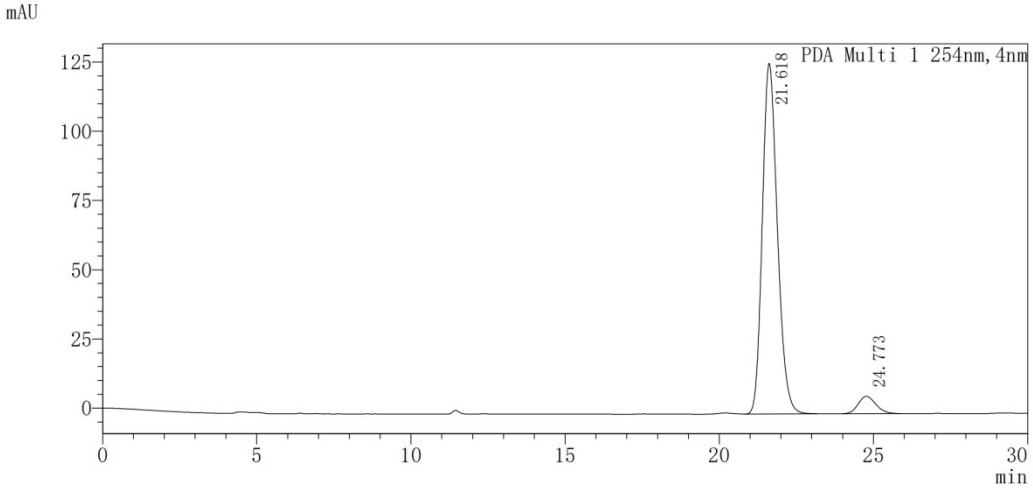




<Peak table>

PDA Ch1 254nm

Peak	Area	Height	Area%	Ren.time
1	7215265	211670	50.108	21.650
2	7184163	180325	49.892	24.747
Total	14399428	391995	100.000	

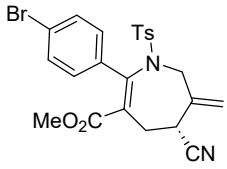


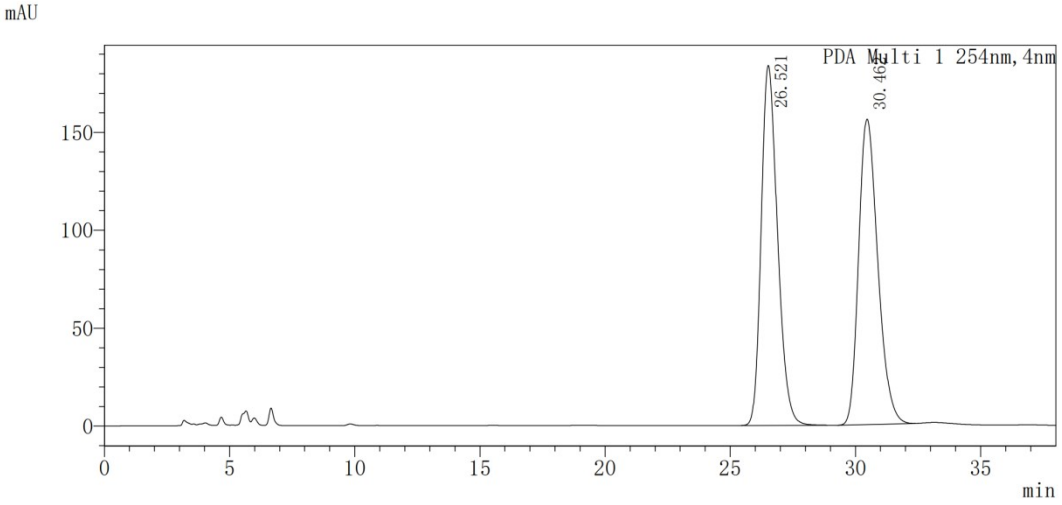
<Peak table>

PDA Ch1 254nm

Peak	Area	Height	Area%	Ren.time
1	4296878	126615	94.517	21.618
2	249289	6242	5.483	24.773
Total	4546167	132857	100.000	

HPLC chromatogram of compound **3i** (90% *ee*)

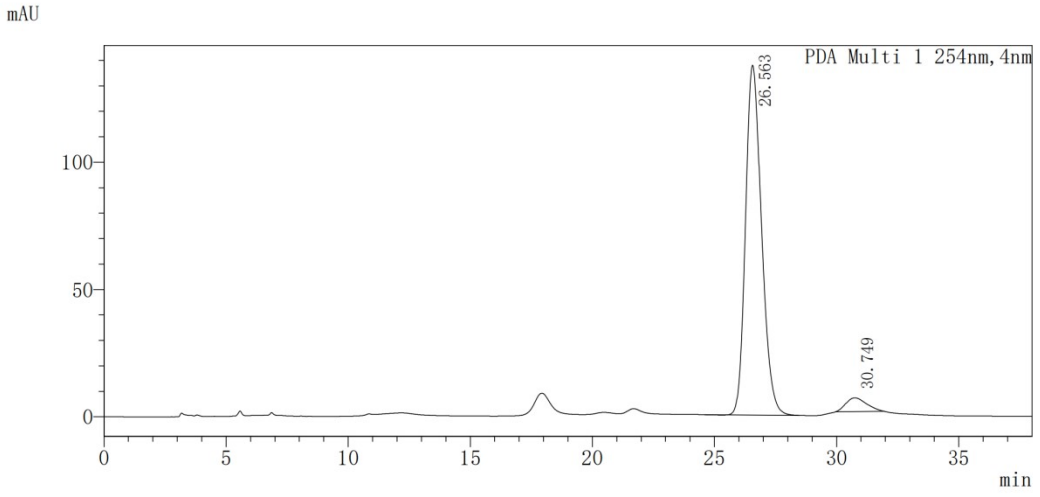




<Peak table>

PDA Ch1 254nm

Peak	Area	Height	Area%	Ren.time
1	8353108	183994	50.133	26.521
2	8308848	156094	49.867	30.462
Total	16661956	340088	100.000	

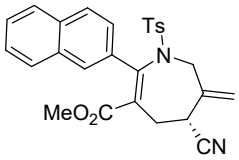


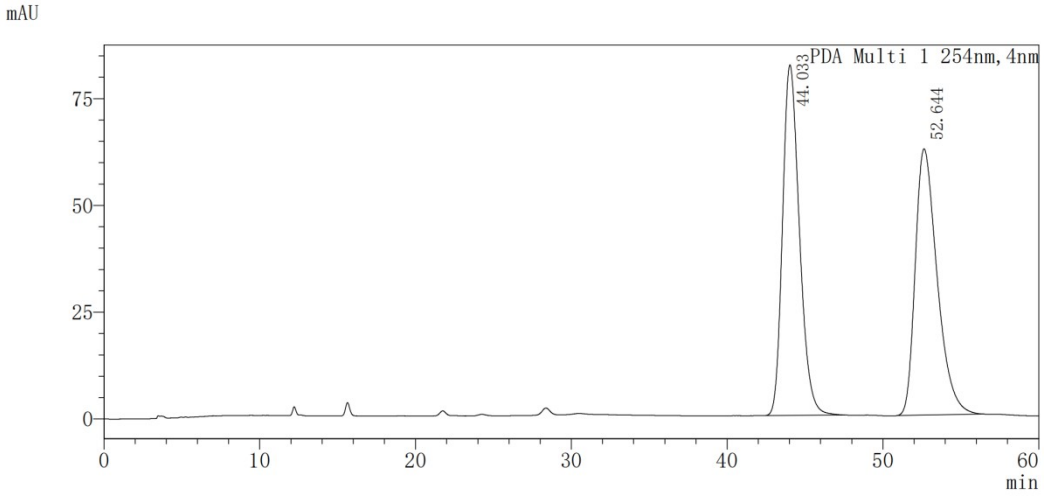
<Peak table>

PDA Ch1 254nm

Peak	Area	Height	Area%	Ren.time
1	6287914	137437	95.169	26.563
2	319201	5413	4.831	30.749
Total	6607115	142850	100.000	

HPLC chromatogram of compound **3j** (91%*ee*)

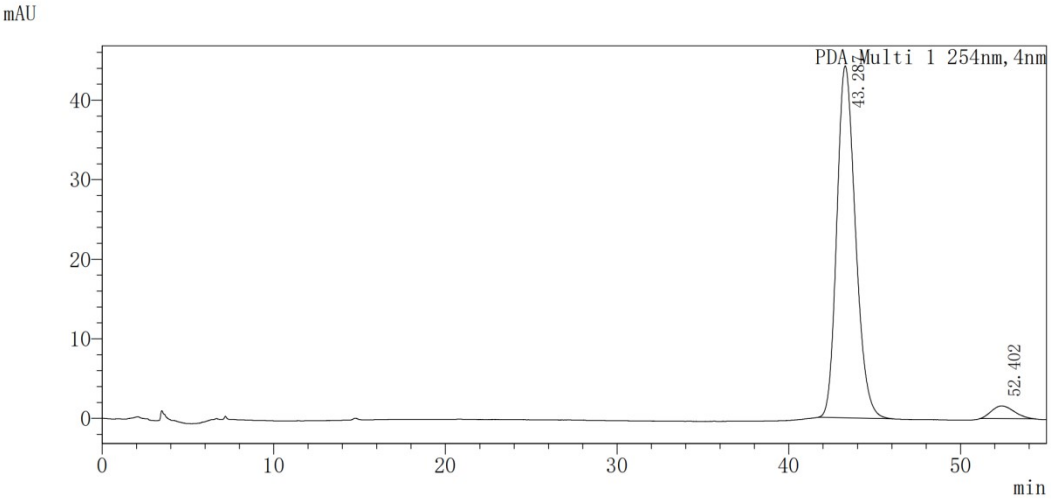




<Peak table>

PDA Ch1 254nm

Peak	Area	Height	Area%	Ren.time
1	6175804	82052	50.295	44.033
2	6103423	62357	49.705	52.644
Total	12279226	144409	100.000	

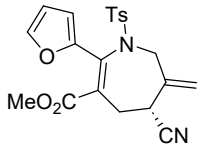


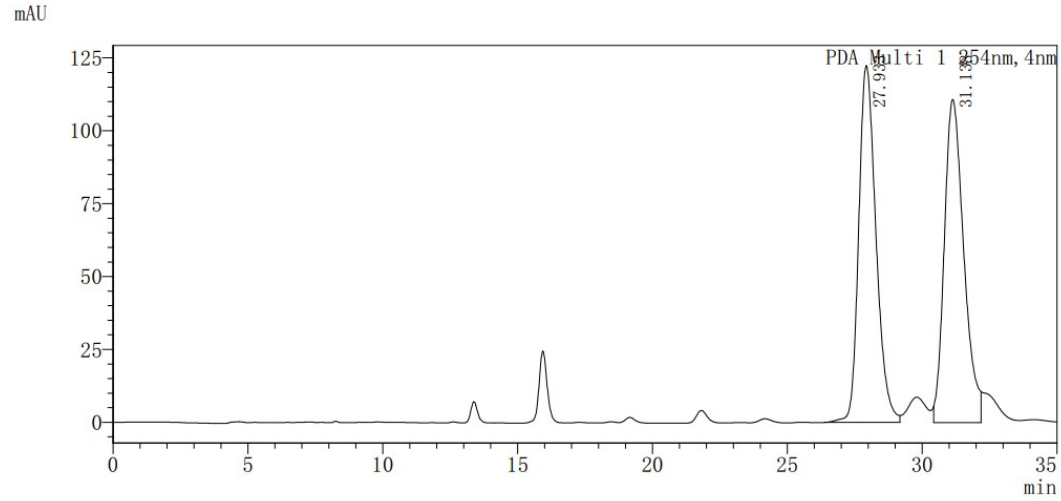
<Peak table>

PDA Ch1 254nm

Peak	Area	Height	Area%	Ren.time
1	3336416	44236	95.730	43.287
2	148807	1609	4.270	52.402
Total	3485223	45845	100.000	

HPLC chromatogram of compound **3k** (93% *ee*)

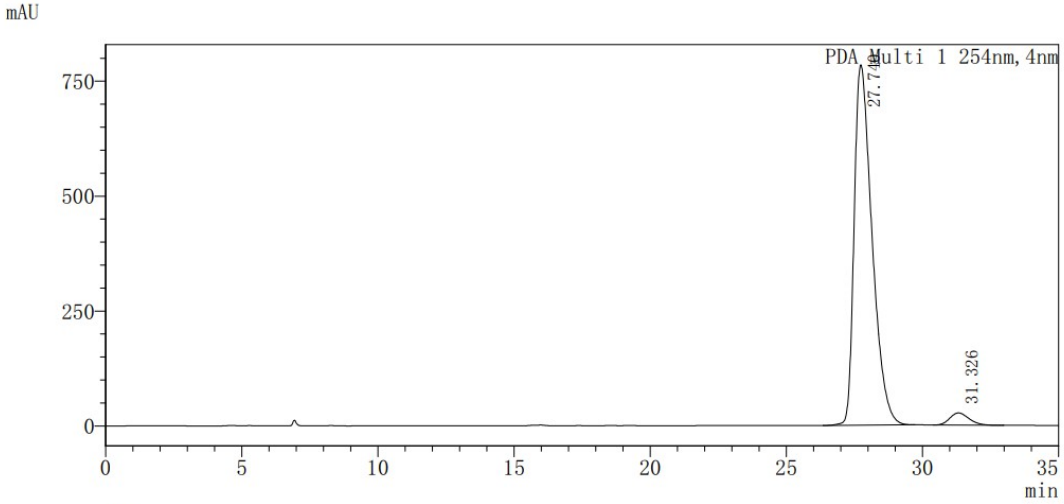




<Peak table>

PDA Ch1 254nm

Peak	Area	Height	Area%	Ren.time
1	5452786	122446	49.493	27.933
2	5564440	110818	50.507	31.138
Total	11017225	233264	100.000	

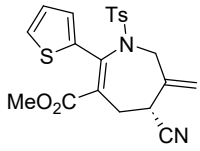


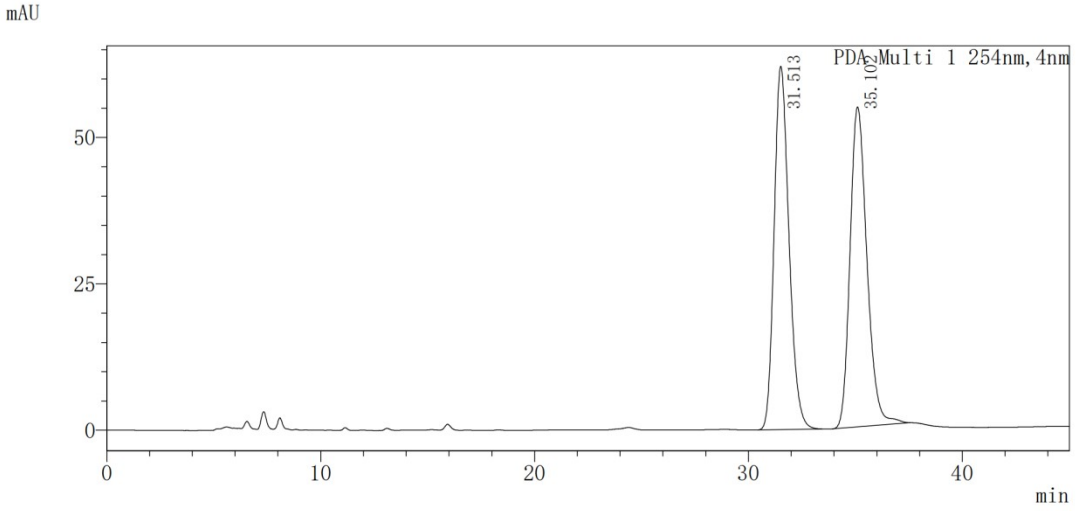
<Peak table>

PDA Ch1 254nm

Peak	Area	Height	Area%	Ren.time
1	35789367	784140	96.449	27.740
2	1317756	26671	3.551	31.326
Total	37107124	810811	100.000	

HPLC chromatogram of compound **3l** (88% *ee*)

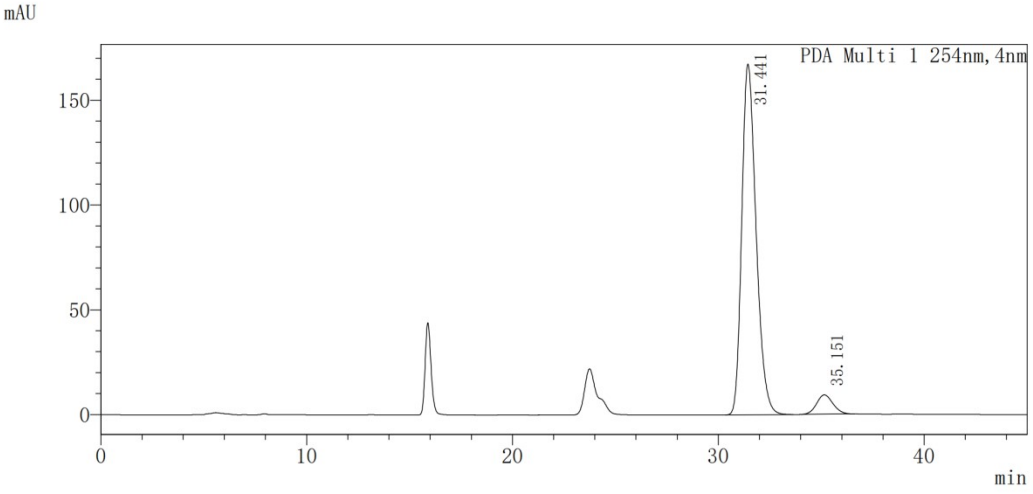




<Peak table>

PDA Ch1 254nm

Peak	Area	Height	Area%	Ren.time
1	2991616	62059	49.900	31.513
2	3003574	54669	50.100	35.102
Total	5995191	116728	100.000	

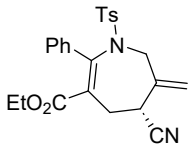


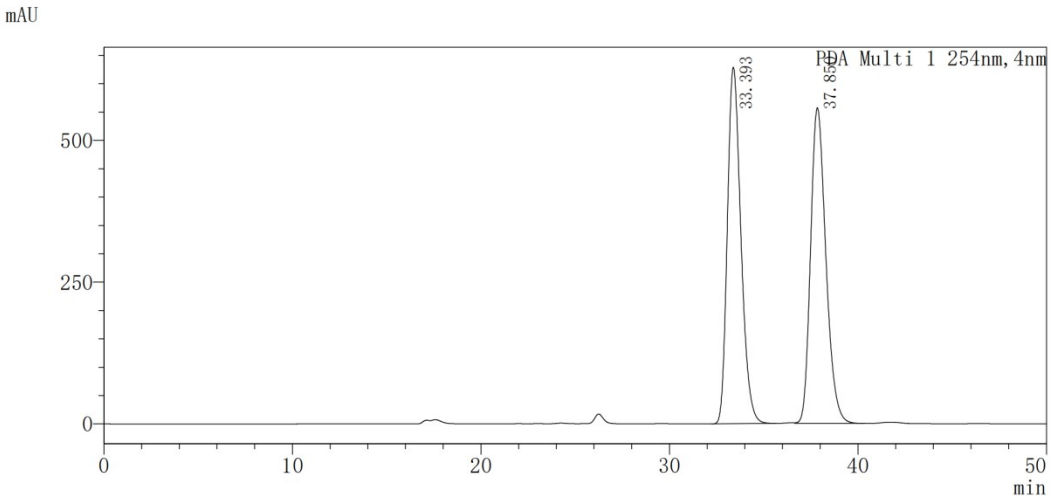
<Peak table>

PDA Ch1 254nm

Peak	Area	Height	Area%	Ren.time
1	8076394	167325	94.039	31.441
2	511925	9225	5.961	35.151
Total	8588319	176551	100.000	

HPLC chromatogram of compound **3m** (95% *ee*)

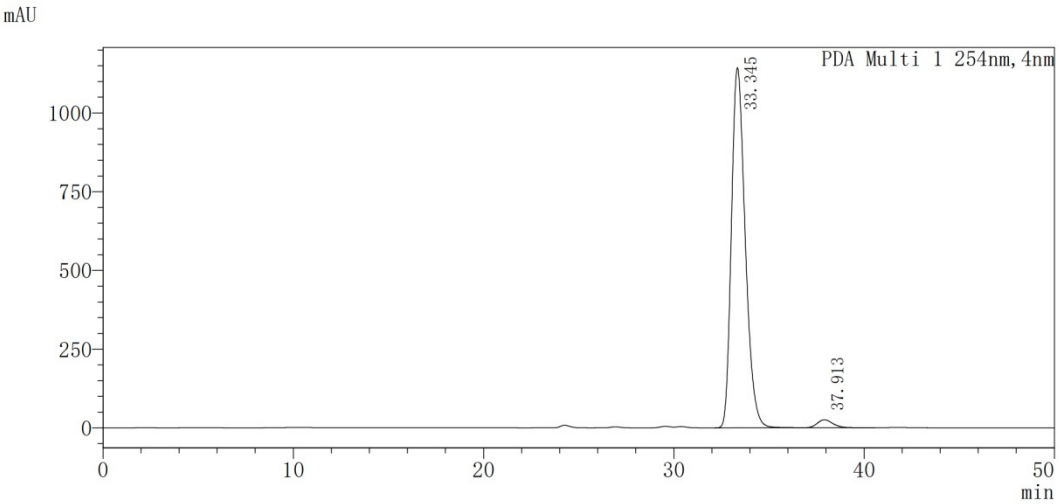




<Peak table>

PDA Ch1 254nm

Peak	Area	Height	Area%	Ren.time
1	31408042	628691	50.032	33.393
2	31367967	556576	49.968	37.850
Total	62776010	1185266	100.000	

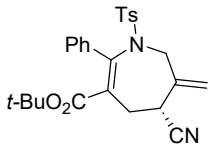


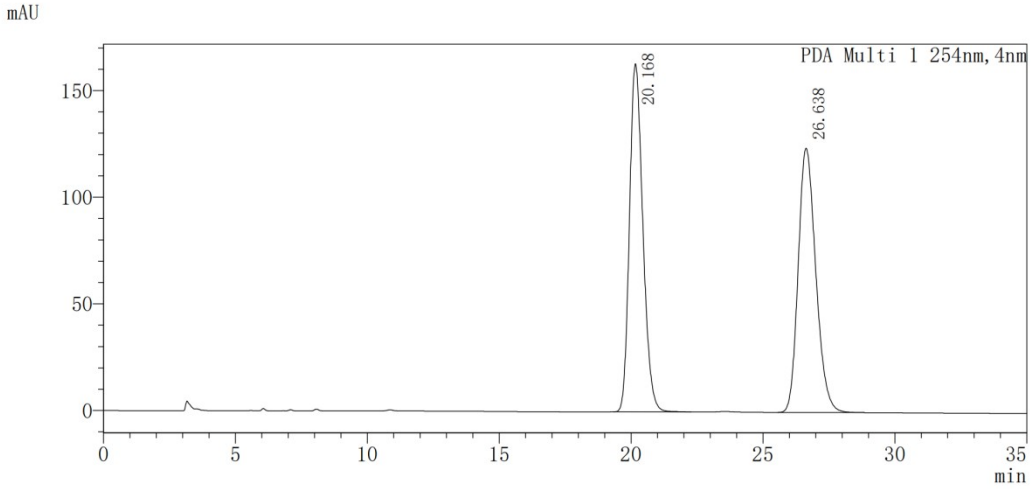
<Peak table>

PDA Ch1 254nm

Peak	Area	Height	Area%	Ren.time
1	57801643	1143850	97.455	33.345
2	1509389	25586	2.545	37.913
Total	59311032	1169436	100.000	

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

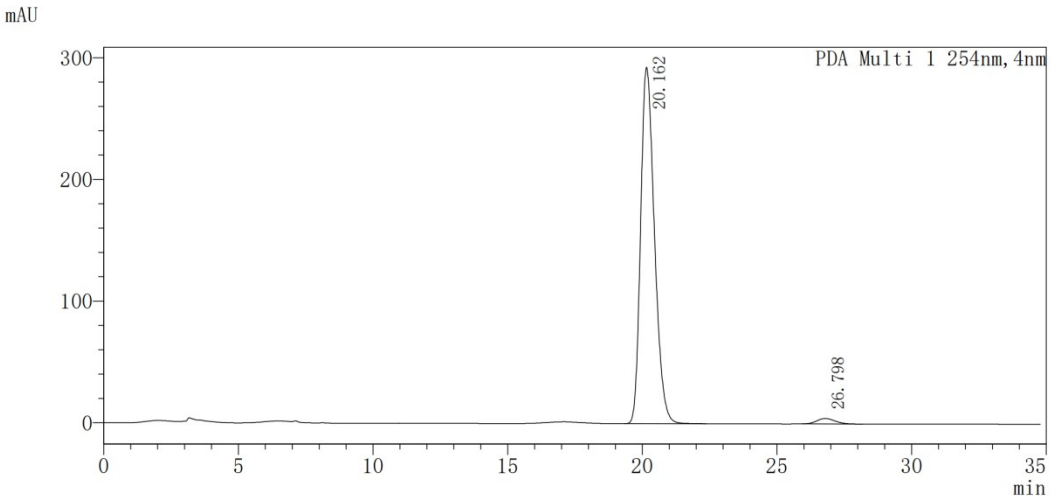




〈Peak table〉

PDA Ch1 254nm

Peak	Area	Height	Area%	Ren.time
1	5767264	163230	50.052	20.168
2	5755194	123928	49.948	26.638
Total	11522457	287158	100.000	

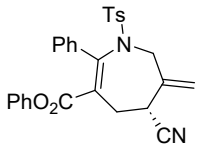


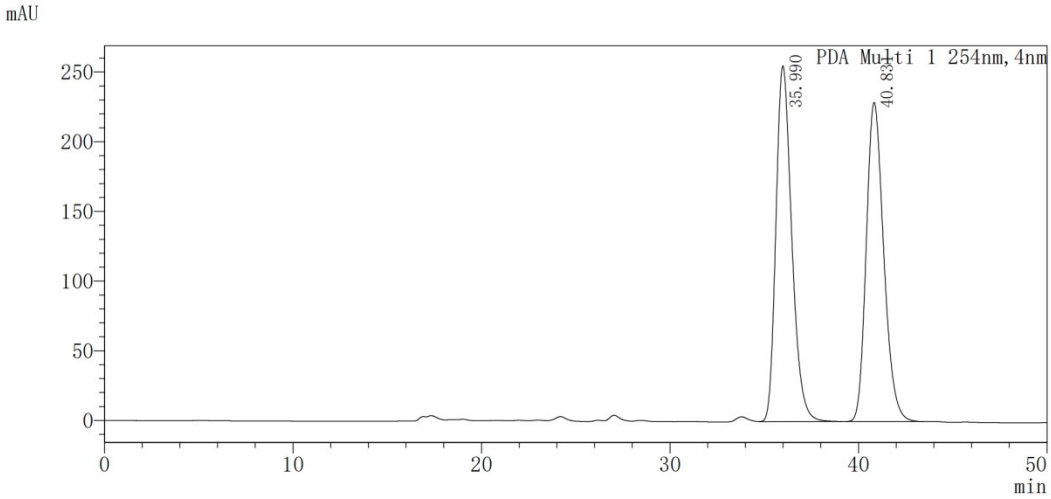
〈Peak table〉

PDA Ch1 254nm

Peak	Area	Height	Area%	Ren.time
1	10442458	292770	98.032	20.162
2	209647	4508	1.968	26.798
Total	10652105	297277	100.000	

HPLC chromatogram of compound **3o** (93% *ee*)

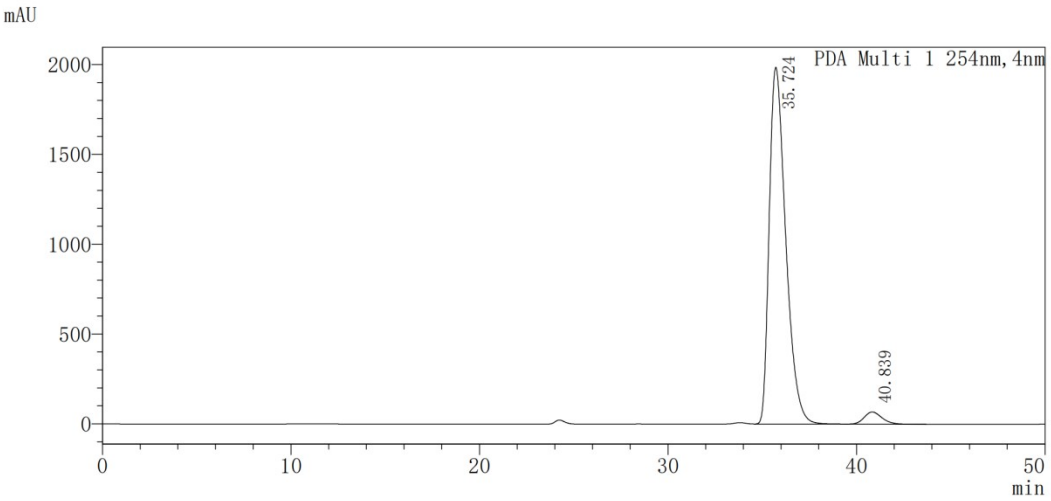




<Peak table>

PDA Ch1 254nm

Peak	Area	Height	Area%	Ren.time
1	14911720	255465	50.257	35.990
2	14759444	229040	49.743	40.831
Total	29671164	484505	100.000	

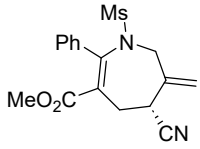


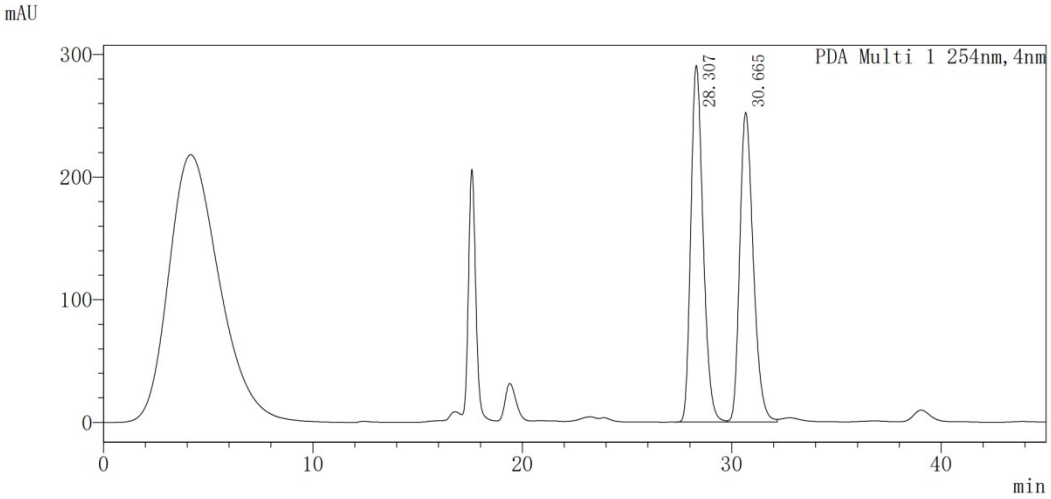
<Peak table>

PDA Ch1 254nm

Peak	Area	Height	Area%	Ren.time
1	121050572	1986875	96.397	35.724
2	4524054	68157	3.603	40.839
Total	125574626	2055032	100.000	

HPLC chromatogram of compound **3p** (93% *ee*)

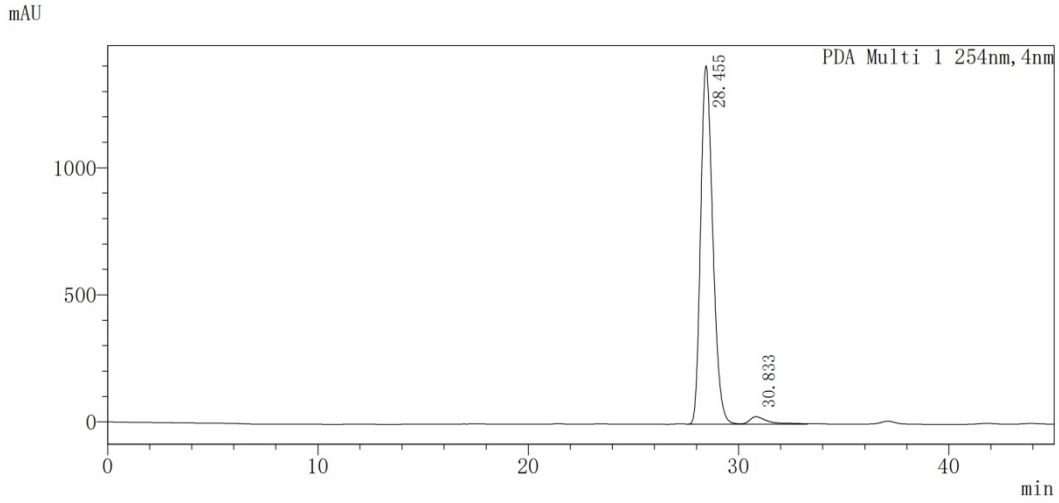




<Peak table>

PDA Ch1 254nm

Peak	Area	Height	Area%	Ren.time
1	11832624	290916	51.056	28.307
2	11343265	252553	48.944	30.665
Total	23175889	543469	100.000	

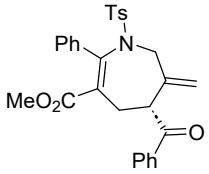


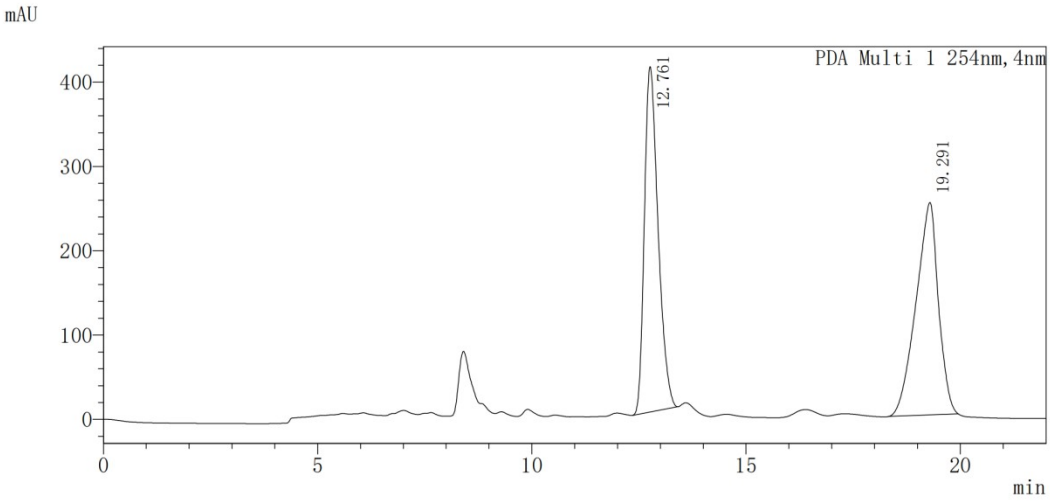
<Peak table>

PDA Ch1 254nm

Peak	Area	Height	Area%	Ren.time
1	56592594	1411355	96.724	28.455
2	1916861	30084	3.276	30.833
Total	58509455	1441439	100.000	

HPLC chromatogram of compound **3q** (87% ee)

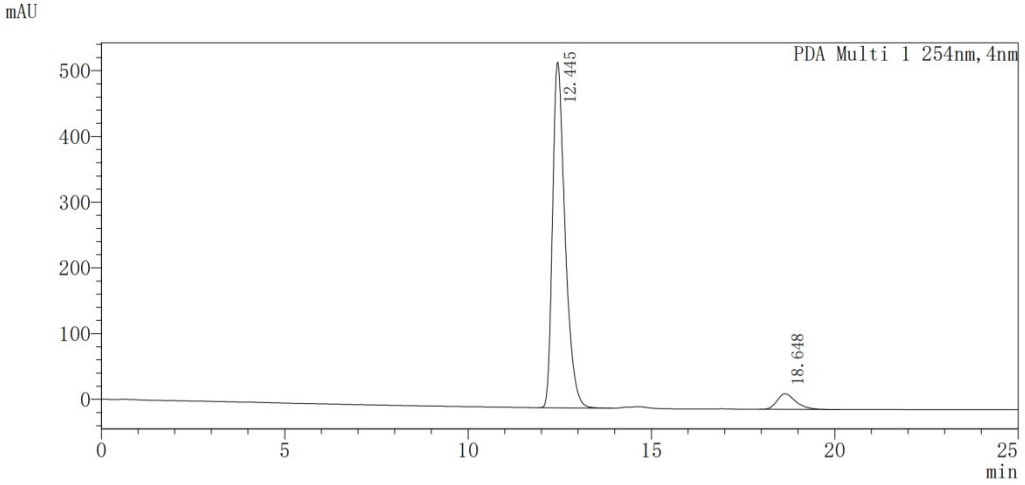




<Peak table>

PDA Ch1 254nm

Peak	Area	Height	Area%	Ren.time
1	9109607	409499	49.885	12.761
2	9151476	251812	50.115	19.291
Total	18261084	661311	100.000	

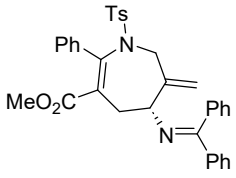


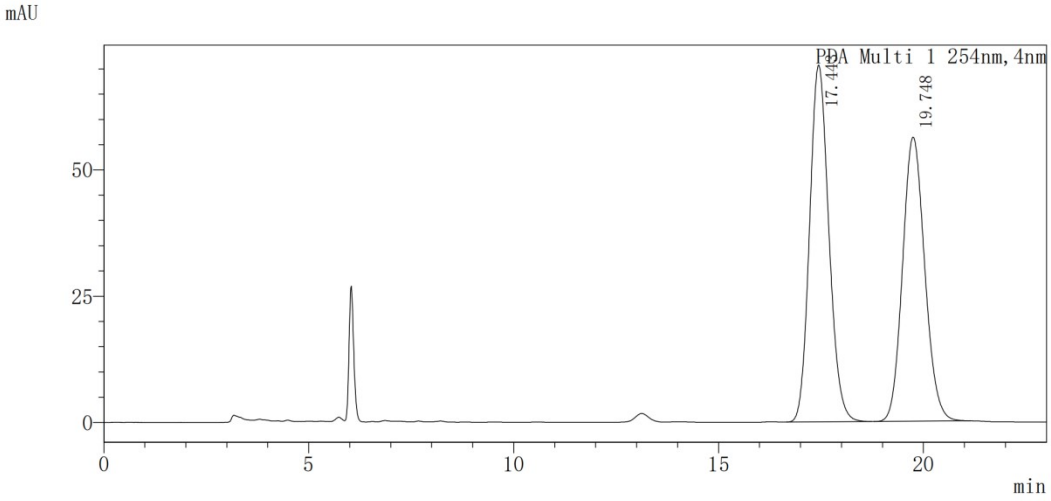
<Peak table>

PDA Ch1 254nm

Peak	Area	Height	Area%	Ren.time
1	12527993	525711	93.666	12.445
2	847125	23840	6.334	18.648
Total	13375117	549551	100.000	

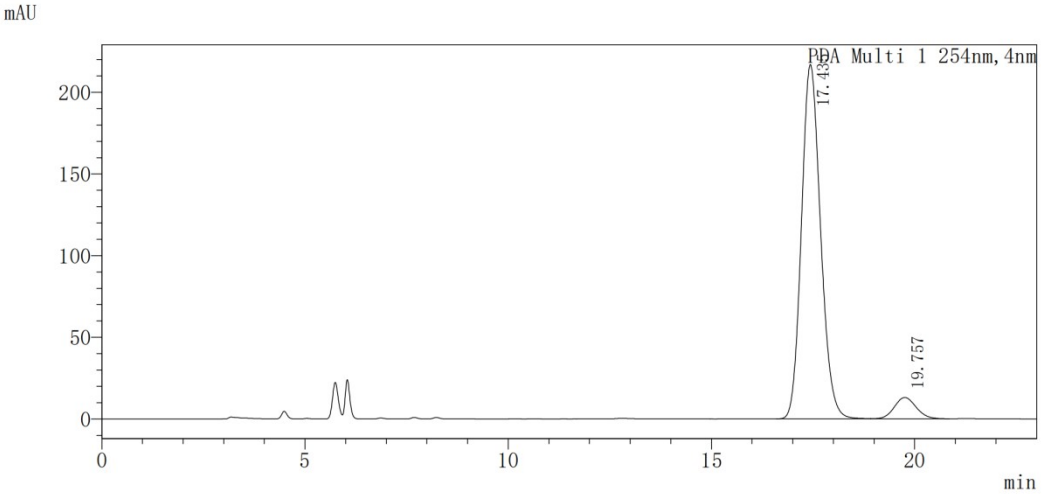
HPLC chromatogram of compound **3r** (87% *ee*)





<Peak table>
PDA Ch1 254nm

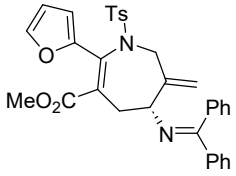
Peak	Area	Height	Area%	Ren.time
1	2312183	70643	52.203	17.443
2	2117003	56249	47.797	19.748
Total	4429185	126892	100.000	

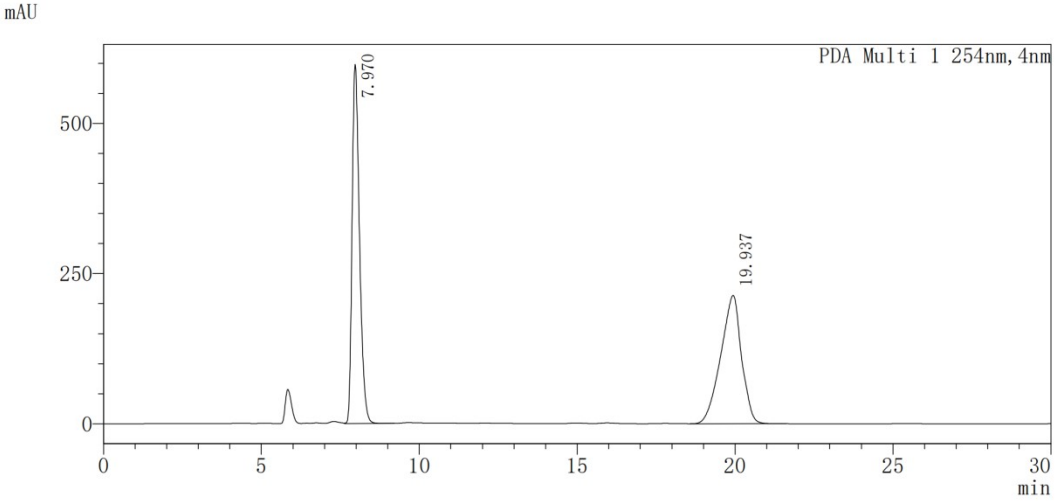


<Peak table>
PDA Ch1 254nm

Peak	Area	Height	Area%	Ren.time
1	7102925	216857	93.564	17.435
2	488601	13053	6.436	19.757
Total	7591527	229910	100.000	

HPLC chromatogram of compound **3s** (84% *ee*)

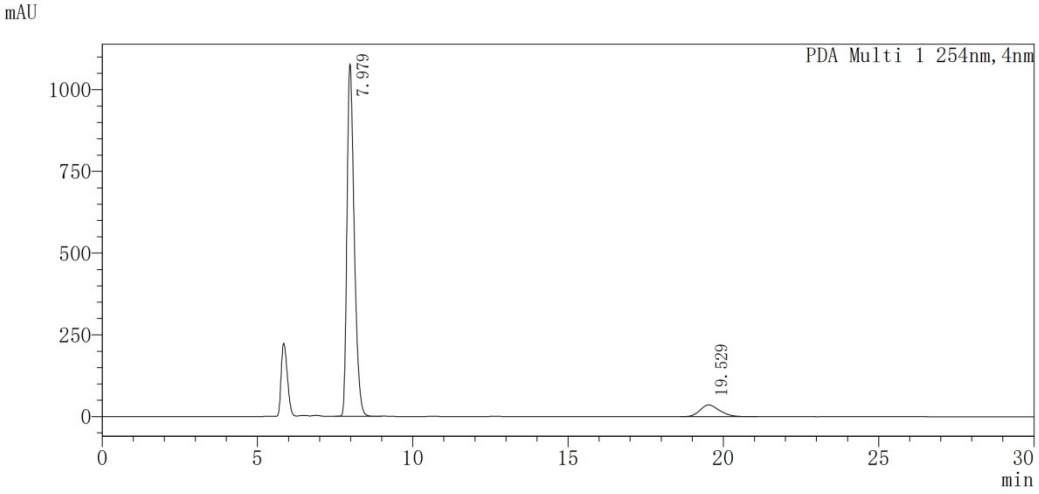




<Peak table>

PDA Ch1 254nm

Peak	Area	Height	Area%	Ren.time
1	9720461	597797	49.835	7.970
2	9784982	213692	50.165	19.937
Total	19505443	811489	100.000	

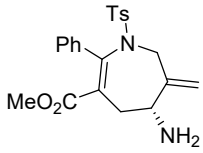


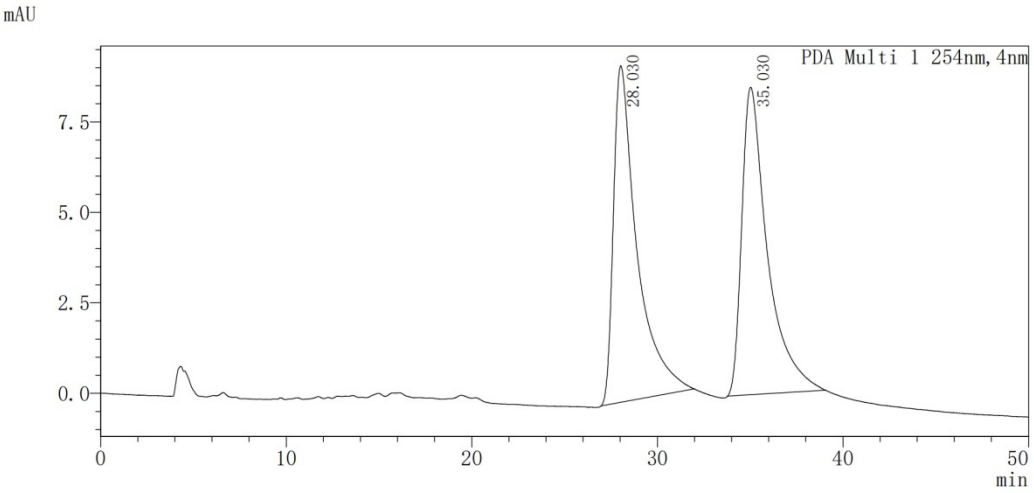
<Peak table>

PDA Ch1 254nm

Peak	Area	Height	Area%	Ren.time
1	17502582	1078114	91.871	7.979
2	1548610	35698	8.129	19.529
Total	19051192	1113812	100.000	

HPLC chromatogram of compound **4** (88% *ee*)

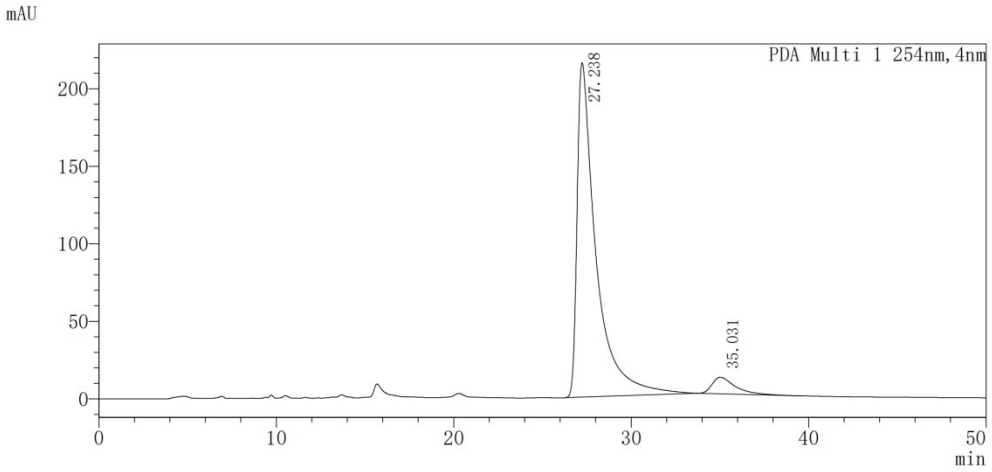




<Peak table>

PDA Ch1 254nm

Peak	Area	Height	Area%	Ren.time
1	818749	9299	49.987	28.030
2	819184	8499	50.013	35.030
Total	1637934	17798	100.000	



<Peak table>

PDA Ch1 254nm

Peak	Area	Height	Area%	Ren.time
1	15999562	215743	94.190	27.238
2	986991	10793	5.810	35.031
Total	16986552	226537	100.000	