Electronic Supplementary Information

Chiral squaramide-catalyzed asymmetric dearomative tandem annulation reaction through kinetic resolution of MBH alcohols: highly enantioselective synthesis of three-dimensional heterocyclic compounds

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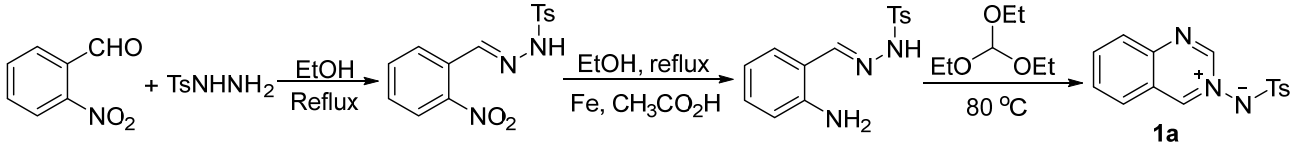
General Information

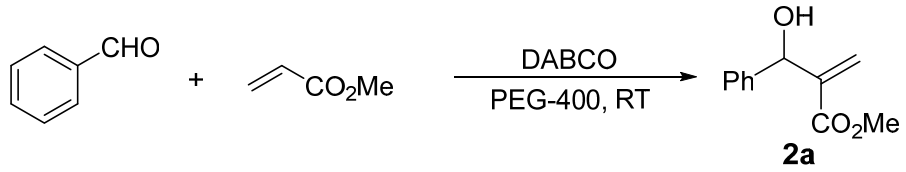
All reactions were performed under N_2 atmospheres in oven-dried glassware with magnetic stirring. Unless otherwise stated, all reagents were purchased from commercial suppliers and used without further purification. All solvents were purified and dried according to standard methods prior to use. Organic solutions were concentrated under reduced pressure on a rotary evaporator or an oil pump. Reactions were monitored through thin layer chromatography (TLC) on silica gel–precoated glass plates. Chromatograms were visualized by fluorescence quenching with UV light at 254 nm. Flash column chromatography was performed using Qingdao Haiyang flash silica gel (200–300 mesh). Infrared spectra were recorded using a Bruker Optics TENSOR 27 instrument. ^{1}H and ^{13}C NMR spectra were recorded in $CDCl_3$ or DMSO-d_6 using a 300 MHz NMR instrument (referenced internally to Me_4Si). ^{1}H NMR data are reported as follows: chemical shift, multiplicity (s = singlet; d = doublet; q = quartet; m = multiplet; br = broad), coupling constant (Hz), and integral. Data for ^{13}C NMR spectra are reported in terms of chemical shift. Optical rotation was obtained on an Autopol VI automatic polarimeter. Accurate mass measurements were performed using an Agilent instrument with the ESI-MS technique. Melting points were determined on a Stuard SMP3 melting point apparatus. X-ray crystallographic data were collected using a MM007HF Saturn724+. HPLC analysis was performed on Agilent 1100 or 1200 series, UV detection monitored at 254 or 220 nm, using Chiralpak OD-H column, Chiralpak IA column with hexane and *i*-PrOH as the eluent.

General Procedure for Preparation of N-Iminoquinazolinium Ylides[1]



N-iminoquinazolinium ylides were prepared by the reported procedure.

General Procedure for Preparation of Morita-Baylis-Hillman Adducts[2]



The Morita-Baylis-Hillman adducts (MBH adducts) were prepared according to the literature.

General Procedure for Squaramide-Catalyzed Asymmetric Tandem Annulation Reaction

Under a nitrogen atmosphere, at –20 °C, to a mixture of N-iminoquinazolinium ylides **1** (0.1 mmol, 1.0 equiv) and catalyst **C5** (0.02 mmol, 20 mol%) in DCM (2 mL) was added MBH adducts **2** (0.25 mmol, 2.5 equiv) via a syringe. Then the reaction solution was vigorously stirred at -20 ° C and monitored by TLC. After the reaction was complete, the mixture was directly purified by column chromatography on silica gel (petroleum ether/EtOAc as the eluent) to furnish the corresponding product. Notably, strict anhydrous condition is very important.

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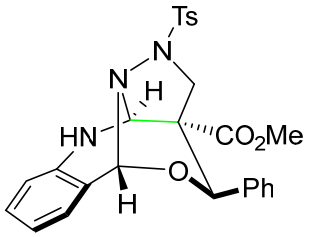
[1] (a) Wang, T.; Luo, J.; Gu, C.; Li, R.; Tang, X.; Yu, D.; Li, J. CN 103172575A. (b) Wang, T.; Shao, A.-L.; Feng, H.-Y.; Yang, S.-W.; Gao, M.; Tian, J.; Lei, A.-W. *Tetrahedron.* **2015**, *71,* 4473–4477.

[2] (a) Feng, J.; Lu, X.; Kong, A.; Han, X. *Tetrahedron* **2007**, *63*, 6035–6041.

Characterization Data for Chiral Squaramide-Catalyzed Tandem Annulation Reaction Products 3

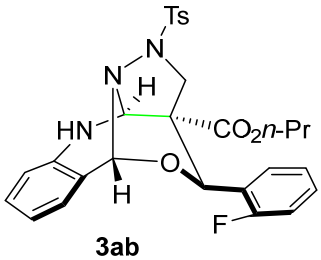
Methyl (3*S*,3a*S*,9*R*,10*S*,12*R*)-12-phenyl-1-tosyl-1,2,4,9-tetrahydro-9,3-(epoxymethano)pyrazolo [5,1-*b*]quinazoline-3(3a*H*)-carboxylate (3aa)



3aa

Prepared according to the general procedure as described above in 90% yield. $[\alpha]^{20}_{D}$= –41.9 (*c*= 0.96, CH_2Cl_2); white solid. mp = 183 – 184 °C; ^{1}H NMR (300 MHz, $CDCl_3$) δ 7.94 – 7.79 (m, 2H), 7.38 – 7.22 (m, 7H), 7.22 – 7.12 (m, 1H), 7.04 (dd, *J* = 7.6, 1.5 Hz, 1H), 6.77 – 6.58 (m, 2H), 5.36 (s, 1H), 5.19 (s, 1H), 4.85 (d, *J* = 4.9 Hz, 1H), 4.08 – 3.96 (m, 2H), 3.78 (d, *J* = 11.2 Hz, 1H), 3.52 (s, 3H), 2.42 (s, 3H); ^{13}C NMR (75 MHz, $CDCl_3$) δ 169.2, 144.2, 140.3, 136.6, 132.7, 130.2, 129.3, 128.4, 128.0, 127.8, 126.5, 117.8, 117.0, 112.2, 86.8, 70.9, 70.8, 58.7, 51.8, 47.0, 21.3; HRMS (ESI) calcd for $C_{26}H_{25}N_3O_5SH^+$ $[M+H]^+$ 492.1588, found 492.1582; HPLC analysis: 91% ee (OD, isopropanol/hexane = 15:85, 1.0 mL/min, UV: 254 nm), 11.52 min (minor), 18.49 min (major).

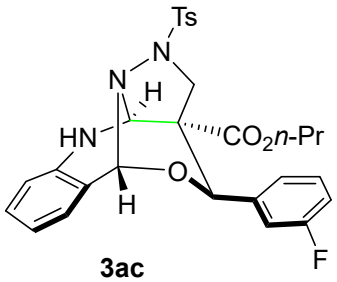
Propyl (3*S*,3a*S*,9*R*,10*S*,12*R*)-12-(2-fluorophenyl)-1-tosyl-1,2,4,9-tetrahydro-9,3-(epoxymethano) pyrazolo[5,1-*b*]quinazoline-3(3a*H*)-carboxylate (3ab)



3ab

Prepared according to the general procedure as described above in 98% yield. $[\alpha]^{20}_{D}$= –35.2 (*c*= 0.85, CH_2Cl_2); mp = 169 – 171 °C; ^{1}H NMR (300 MHz, $CDCl_3$) δ 7.99 – 7.79 (m, 2H), 7.75 – 7.70 (m, 1H), 7.42 – 7.15 (m, 5H), 7.08 –7.04 (m, *J* = 7.5, 1H), 6.97 – 6.90 (m, 1H), 6.80 – 6.65 (m, 2H), 5.47 (s, 1H), 5.38 (s, 1H), 4.88 (d, *J* = 4.4 Hz, 1H), 4.11 – 4.02 (m, 2H), 4.02 – 3.80 (m, 2H), 3.55 (d, *J* = 11.2 Hz, 1H), 2.48 (s, 3H), 1.47 – 1.39 (m, 2H), 0.72 (t, *J* = 7.4 Hz, 3H); ^{13}C NMR (75 MHz, $CDCl_3$) δ 169.1, 159.1 (d, *J* = 246.3 Hz), 144.2, 140.5, 132.5, 130.3, 129.4 (d, *J* = 4.8 Hz), 129.3, 128.4 (d, *J* = 3.7 Hz), 128.4, 128.3, 124.4, 124.3, 123.9 (d, *J* = 3.3 Hz), 117.7, 116.7, 114.2 (d, *J* = 21.5 Hz), 112.1, 87.0, 70.2, 66.8, 65.1 (d, *J* = 3.1 Hz), 57.3, 47.4, 21.3, 21.0, 9.8; HRMS (ESI) calcd for $C_{28}H_{28}FN_3O_5SH^+$ $[M+H]^+$ 538.1806, found 538.1804. HPLC analysis: 93% ee (OD, isopropanol/hexane = 15:85, 1.0 mL/min, UV: 254 nm), t_R = 9.51 min (minor), 12.10 min (major).

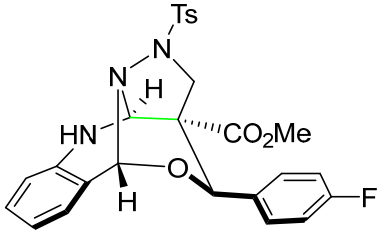
Propyl (3*S*,3a*S*,9*R*,10*S*,12*R*)-12-(3-fluorophenyl)-1-tosyl-1,2,4,9-tetrahydro-9,3-(epoxymethano) pyrazolo[5,1-*b*]quinazoline-3(3a*H*)-carboxylate (3ac)



3ac

Prepared according to the general procedure as described above in 86% yield. $[\alpha]^{20}_{D}$= –32.2 (*c*= 0.66, CH_2Cl_2); white solid. mp = 170 – 175 °C; ^{1}H NMR (300 MHz, $CDCl_3$) δ 7.91 (d, *J* = 8.3 Hz, 2H), 7.44 – 7.17 (m, 5H), 7.19 – 7.05 (m, 3H), 7.05 – 6.93 (m, 1H), 6.85 – 6.65 (m, 2H), 5.37 (s, 1H), 5.19 (s, 1H), 4.75 (d, *J* = 4.8 Hz, 1H), 4.09 – 3.83 (m, 4H), 3.83 – 3.72 (m, 1H), 2.47 (s, 3H), 1.58 – 1.38 (m, 2H), 0.75 (t, *J* = 7.4 Hz, 3H); ^{13}C NMR (75 MHz, $CDCl_3$) δ 168.9, 162.2 (d, *J* = 246.3 Hz), 144.2, 140.2, 139.2 (d, *J* = 7.1 Hz), 132.6, 130.3, 129.4 (d, *J* = 8.1 Hz), 129.3, 128.4, 122.3 (d, *J* = 2.8 Hz), 118.0, 116.9, 114.8 (d, J = 20.9 Hz), 113.9 (d, *J* = 22.7 Hz), 112.2, 86.8, 70.8, 70.4 (d, *J* = 2.0 Hz), 66.7, 58.5, 46.9, 21.3, 21.2, 9.7; HRMS (ESI) calcd for $C_{28}H_{28}FN_3O_5SH^+$ $[M+H]^+$ 538.1806, found 538.1804; HPLC analysis: 90% ee (OD, isopropanol/hexane = 10:90, 1.0 mL/min, UV: 254 nm), t_R = 13.05 min (minor), 17.02 min (major).

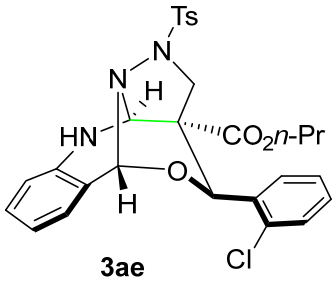
Methyl (3*S*,3a*S*,9*R*,10*S*,12*R*)-12-(4-fluorophenyl)-1-tosyl-1,2,4,9-tetrahydro-9,3-(epoxymethano) pyrazolo[5,1-*b*]quinazoline-3(3a*H*)-carboxylate (3ad)



3ad

Prepared according to the general procedure as described above in 94% yield. $[\alpha]^{20}_{D}$= + 38.8 (*c*= 0.92, CH_2Cl_2); white solid. mp = 177 – 180 °C; ^{1}H NMR (300 MHz, $CDCl_3$) δ 7.97 – 7.74 (m, 2H), 7.36 – 7.25 (m, 4H), 7.22 – 7.18 (m, 1H), 7.08 – 6.89 (m, 3H), 6.82 – 6.58 (m, 2H), 5.32 (s, 1H), 5.16 (s, 1H), 4.71 (d, *J* = 5.0 Hz, 1H), 4.04 (d, *J* = 4.9 Hz, 1H), 3.99 – 3.68 (m, 2H), 3.54 (s, 3H), 2.44 (s, 3H); ^{13}C NMR (75 MHz, $CDCl_3$) δ 169.2, 162.2 (d, *J* = 247.3 Hz), 144.2, 140.1, 132.5 (d, *J* = 3.3 Hz), 132.4, 130.2, 129.3, 128.4 (d, *J* = 1.8 Hz), 128.3, 118.0, 117.0, 114.7 (d, *J* = 21.4 Hz), 112.2, 86.7, 70.8, 70.2, 58.7, 51.8, 46.8, 21.3; HRMS (ESI) calcd for $C_{26}H_{24}FN_3O_5SH^+$ $[M+H]^+$ 510.1493, found 510.1489; HPLC analysis: 90% ee (OD, isopropanol/hexane = 10:90, 1.0 mL/min, UV: 254 nm), t_R = 21.79 min (minor), 36.84 min (major).

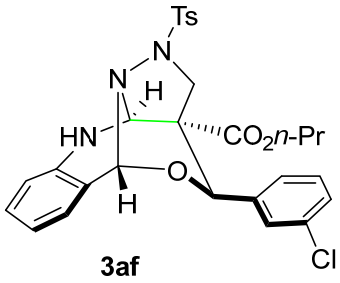
Propyl (3*S*,3a*S*,9*R*,10*S*,12*R*)-12-(2-chlorophenyl)-1-tosyl-1,2,4,9-tetrahydro-9,3-(epoxymethano) pyrazolo[5,1-*b*]quinazoline-3(3a*H*)-carboxylate (3ae)



3ae

Prepared according to the general procedure as described above in 98% yield. $[\alpha]^{20}_{D}$= –32.9 (*c*= 0.86, CH_2Cl_2); white solid. mp = 151 – 155 °C; ^{1}H NMR (300 MHz, $CDCl_3$) δ 7.97 – 7.86 (m, 2H), 7.83 – 7.68 (m, 1H), 7.44 – 7.31 (m, 3H), 7.28 – 7.17 (m, 3H), 7.07 – 7.03 (m, 1H), 6.76 – 6.70 (m, 2H), 5.62 (s, 1H), 5.36 (s, 1H), 4.91 (d, *J* = 4.6 Hz, 1H), 4.28 – 4.05 (m, 2H), 4.03 – 3.90 (m, 1H), 3.90 – 3.74 (m, 1H), 3.48 (d, *J* = 11.2 Hz, 1H), 2.48 (s, 3H), 1.42 – 1.28 (m, 2H), 0.64 (t, *J* = 7.4 Hz, 3H); ^{13}C NMR (75 MHz, $CDCl_3$) δ 169.4, 144.3, 140.7, 134.8, 132.6, 132.5, 130.4, 129.4, 128.9, 128.7, 128.6, 128.3, 126.6, 117.6, 116.7, 111.9, 87.2, 70.4, 67.4, 67.0, 56.7, 47.5, 21.3, 20.9, 9.7; HRMS (ESI) calcd for $C_{28}H_{28}ClN_3O_5SH^+$ $[M+H]^+$ 554.1511, found 554.1509; HPLC analysis: 88% ee (OD, isopropanol/hexane = 15:85, 1.0 mL/min, UV: 254 nm), t_R = 14.52 min (minor), 19.79 min (major).

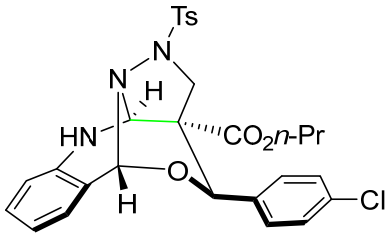
Propyl (3*S*,3a*S*,9*R*,10*S*,12*R*)-12-(3-chlorophenyl)-1-tosyl-1,2,4,9-tetrahydro-9,3-(epoxymethano) pyrazolo[5,1-*b*]quinazoline-3(3a*H*)-carboxylate (3af)



3af

Prepared according to the general procedure as described above in 85% yield. $[\alpha]^{20}_{D}$= –36.7 (*c*= 0.67, CH_2Cl_2); white solid. mp = 157 – 159 °C; ^{1}H NMR (300 MHz, $CDCl_3$) δ 7.96 – 7.83 (m, 2H), 7.39 – 7.31 (m, 3H), 7.31 – 7.19 (m, 4H), 7.07 (dd, *J* = 7.6, 1.5 Hz, 1H), 6.83 – 6.61 (m, 2H), 5.37 (s, 1H), 5.17 (s, 1H), 4.76 (d, *J* = 4.8 Hz, 1H), 4.06 – 3.85 (m, 4H), 3.82 – 3.72 (m, 1H), 2.47 (s, 3H), 1.57 – 1.40 (m, 2H), 0.75 (t, *J* = 7.4 Hz, 2H); ^{13}C NMR (75 MHz, $CDCl_3$) δ 168.9, 144.2, 140.2, 138.7, 130.3, 129.3, 129.1, 128.5, 128.4, 128.1, 126.9, 124.8, 118.0, 116.9, 112.2, 86.8, 70.8, 70.4, 66.7, 58.5, 46.9, 21.3, 21.2, 9.8; HRMS (ESI) calcd for $C_{28}H_{28}ClN_3O_5SH^+$ $[M+H]^+$ 554.1511, found 554.1509; HPLC analysis: 91% ee (OD, isopropanol/hexane = 10:90, 1.0 mL/min, UV: 254 nm), t_R = 13.21 min (minor), 16.90 min (major).

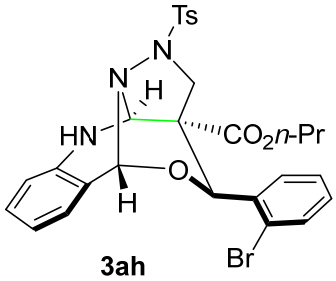
Propyl (3*S*,3a*S*,9*R*,10*S*,12*R*)-12-(2-chlorophenyl)-1-tosyl-1,2,4,9-tetrahydro-9,3-(epoxymethano) pyrazolo[5,1-*b*]quinazoline-3(3a*H*)-carboxylate (3ag)



3ag

Prepared according to the general procedure as described above in 82% yield. $[\alpha]^{20}_{D}$= –23.1 (*c*= 0.67, CH_2Cl_2); white solid. mp = 172 – 174 °C; ^{1}H NMR (300 MHz, $CDCl_3$) δ 8.01 – 7.80 (m, 2H), 7.43 – 7.31 (m, 2H), 7.30 (s, 4H), 7.28 – 7.20 (m , 1H), 7.12 – 7.06 (m, 1H), 6.81 – 6.66 (m, 2H), 5.37 (s, 1H), 5.18 (s, 1H), 4.72 (d, *J* = 4.9 Hz, 1H), 4.05 – 3.81 (m, 4H), 3.77 (d, *J* = 11.1 Hz, 1H), 2.47 (s, 3H), 1.60 – 1.39 (m, 2H), 0.76 (t, *J* = 7.4 Hz, 3H); ^{13}C NMR (75 MHz, $CDCl_3$) δ 168.8, 144.2, 140.2, 135.2, 133.8, 132.6, 130.3, 129.3, 128.4, 128.2, 127.9, 118.0, 117.0, 112.2, 86.8, 70.9, 70.3, 66.6, 58.5, 46.9, 21.3, 21.2, 9.7; HRMS (ESI) calcd for $C_{28}H_{28}ClN_3O_5SH^+$ $[M+H]^+$ 554.1511, found 554.1508; HPLC analysis: 92%ee (OD, alcohol/hexane = 10:90, 1.0 mL/min, UV: 254 nm), t_R = 13.61 min (minor), 18.42 min (major).

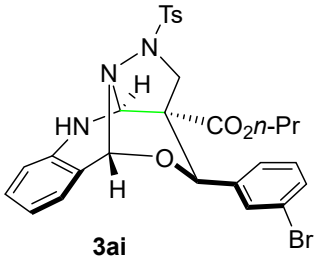
Propyl (3*S*,3a*S*,9*R*,10*S*,12*R*)-12-(2-bromophenyl)-1-tosyl-1,2,4,9-tetrahydro-9,3-(epoxymethano) pyrazolo[5,1-*b*]quinazoline-3(3a*H*)-carboxylate (3ah)



3ah

Prepared according to the general procedure as described above in 98% yield. $[\alpha]^{20}_{D}$= –32.9 (*c*= 0.92, CH_2Cl_2); white solid. mp = 143 – 146 °C; ^{1}H NMR (300 MHz, $CDCl_3$) δ 8.01 – 7.82 (m, 2H), 7.72 (dd, *J* = 7.9, 1.7 Hz, 1H), 7.51 – 7.31 (m, 4H), 7.25 –7.17 (m, 2H), 7.06 (dd, *J* = 7.6, 1.4 Hz, 1H), 6.83 – 6.62 (m, 2H), 5.60 (s, 1H), 5.35 (s, 1H), 4.88 (d, *J* = 4.7 Hz, 1H), 4.25 – 4.08 (m, 2H), 4.02 – 3.78 (m, 2H), 3.51 (d, *J* = 11.2 Hz, 1H), 2.48 (s, 3H), 1.42 – 1.29 (m, 2H), 0.63 (t, *J* = 7.4 Hz, 3H); ^{13}C NMR (75 MHz, $CDCl_3$) δ 169.4, 144.3, 140.7, 136.3, 132.6, 132.0, 130.4, 129.4, 129.3, 128.9, 128.5, 128.4, 127.1, 123.2, 117.6, 116.7, 111.9, 87.2, 70.5, 69.5, 67.1, 56.7, 47.7, 21.3, 20.9, 9.7; HRMS (ESI) calcd for $C_{28}H_{28}BrN_3O_5SH^+$ $[M+H]^+$ 598.1006, found 598.1003. HPLC analysis: 84% ee (OD, isopropanol/hexane = 10:90, 1.0 mL/min, UV: 254 nm), t_R = 15.89 min (minor), 22.34 min (major).

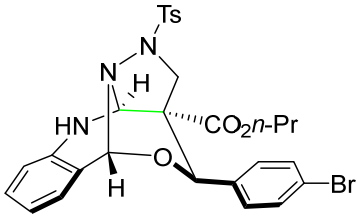
Propyl (3*S*,3a*S*,9*R*,10*S*,12*R*)-12-(3-bromophenyl)-1-tosyl-1,2,4,9-tetrahydro-9,3-(epoxymethano) pyrazolo[5,1-*b*]quinazoline-3(3a*H*)-carboxylate (3ai)



3ai

Prepared according to the general procedure as described above in 84% yield. $[\alpha]^{20}_{D}$= –39.7 (*c*= 0.69, CH_2Cl_2); white solid. mp = 152 – 154 °C; ^{1}H NMR (300 MHz, $CDCl_3$) δ 7.90 (d, *J* = 8.3 Hz, 2H), 7.52 – 7.38 (m, 2H), 7.40 – 7.27 (m, 3H), 7.28 – 7.13 (m, 2H), 7.07 (dd, *J* = 7.5, 1.5 Hz, 1H), 6.86 – 6.66 (m, 2H), 5.36 (s, 1H), 5.16 (s, 1H), 4.75 (d, *J* = 4.8 Hz, 1H), 4.11 – 3.82 (m, 4H), 3.77 (d, *J* = 11.3 Hz, 1H), 2.47 (s, 3H), 1.53 – 1.45 (m, 2H), 0.76 (t, *J* = 7.4 Hz, 3H); ^{13}C NMR (75 MHz, $CDCl_3$) δ 168.8, 144.2, 140.2, 138.9, 132.6, 131.0, 130.3, 129.7, 129.4, 129.3, 128.4, 128.4, 125.3, 121.9, 118.0, 116.9, 112.2, 86.8, 70.8, 70.3, 66.8, 58.5, 46.9, 21.3, 21.2, 9.7; HRMS (ESI) calcd for $C_{28}H_{28}BrN_3O_5SH^+$ $[M+H]^+$ 598.1006, found 598.1005; HPLC analysis: 92% ee (CHIRALPAK OD-H, isopropanol/hexane = 15:85, 1.0 mL/min, UV: 254 nm), t_R = 13.66 min (minor), 17.63 min (major).

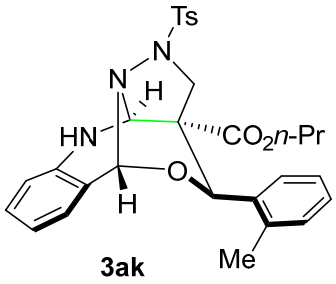
Propyl (3*S*,3a*S*,9*R*,10*S*,12*R*)-12-(4-bromophenyl)-1-tosyl-1,2,4,9-tetrahydro-9,3-(epoxymethano) pyrazolo[5,1-*b*]quinazoline-3(3a*H*)-carboxylate (3aj)



3aj

Prepared according to the general procedure as described above in 83% yield. $[\alpha]^{20}_{D}$= –22.5 (*c*= 0.71, CH_2Cl_2); white solid. mp = 170 – 173 °C; ^{1}H NMR (300 MHz, $CDCl_3$) δ 8.06 – 7.82 (m, 2H), 7.52 – 7.41 (m, 2H), 7.39 – 7.29 (m, 2H), 7.29 – 7.18 (m, 3H), 7.08 (dd, *J* = 7.6, 1.5 Hz, 1H), 6.85 – 6.63 (m, 2H), 5.37 (s, 1H), 5.16 (s, 1H), 4.73 (d, *J* = 4.9 Hz, 1H), 4.07 – 3.80 (m, 4H), 3.77 (d, *J* = 11.3 Hz, 1H), 2.47 (s, 3H), 1.52 – 1.45 (m, 2H), 0.76 (t, *J* = 7.4 Hz, 3H); ^{13}C NMR (75 MHz, $CDCl_3$) δ 168.7, 144.2, 140.1, 135.7, 132.5, 130.9, 130.3, 129.3, 128.5, 128.4, 122.0, 118.0, 117.0, 112.2, 86.8, 70.9, 70.3, 66.7, 58.4, 46.9, 21.3, 21.2, 9.7; HRMS (ESI) calcd for $C_{28}H_{28}BrN_3NaO_5S^+$ $[M+H]^+$ 620.0831, found 620.0825; HPLC analysis: 91% ee (CHIRALPAK OD-H, isopropanol/hexane = 10:90, 1.0 mL/min, UV: 254 nm), t_R = 14.09 min (minor), 19.03 min (major).

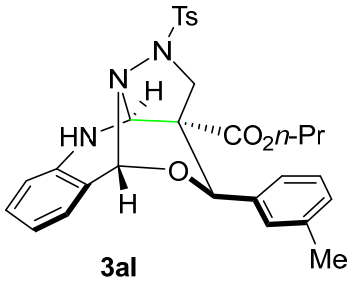
Propyl (3*S*,3a*S*,9*R*,10*S*,12*R*)-12-(*o*-tolyl)-1-tosyl-1,2,4,9-tetrahydro-9,3-(epoxymethano) pyrazolo[5,1-*b*]quinazoline-3(3a*H*)-carboxylate (3ak)



3ak

Prepared according to the general procedure as described above in 85% yield. $[\alpha]^{20}_D$= –35.1 (*c*= 0.84, CH_2Cl_2); white solid. mp = 148 – 151 °C; ^{1}H NMR (300 MHz, $CDCl_3$) δ 7.99 – 7.83 (m, 2H), 7.42 (dd, *J* = 7.0, 2.2 Hz, 1H), 7.34 (d, *J* = 8.1 Hz, 2H), 7.28 – 7.15 (m, 3H), 7.15 – 7.00 (m, 2H), 6.82 – 6.65 (m, 2H), 5.41 (s, 1H), 5.29 (s, 1H), 4.77 (d, *J* = 5.1 Hz, 1H), 4.37 (d, *J* = 11.0 Hz, 1H), 4.14 (d, *J* = 5.1 Hz, 1H), 4.03 – 3.77 (m, 3H), 2.47 (s, 3H), 1.97 (s, 3H), 1.41 – 1.31 (m, 2H), 0.64 (t, *J* = 7.4 Hz, 3H); ^{13}C NMR (75 MHz, $CDCl_3$) δ 169.8, 144.1, 140.7, 136.3, 134.6, 132.9, 130.4, 130.2, 129.3, 128.5, 128.4, 127.8, 126.0, 125.5, 117.9, 117.0, 112.0, 87.0, 71.8, 66.9, 66.7, 57.3, 48.4, 21.3, 21.1, 18.5, 9.6; HRMS (ESI) calcd for $C_{29}H_{31}N_3O_5SH^+$ $[M+H]^+$ 534.2057, found 534.2057; HPLC analysis: 89% ee (OD-H, isopropanol/hexane = 10:90, 1.0 mL/min, UV: 254 nm), t_R = 15.07 min (minor), 18.47 min (major).

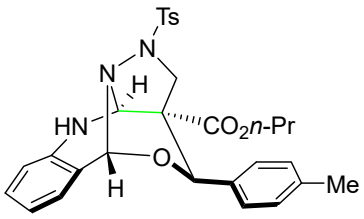
Propyl (3*S*,3a*S*,9*R*,10*S*,12*R*)-12-(*m*-tolyl)-1-tosyl-1,2,4,9-tetrahydro-9,3-(epoxymethano) pyrazolo[5,1-*b*]quinazoline-3(3a*H*)-carboxylate (3al)



3al

Prepared according to the general procedure as described above in 97% yield. $[\alpha]^{20}_D$= –37.7 (*c*= 0.75, CH_2Cl_2); white solid. mp = 163 – 167 °C; ^{1}H NMR (300 MHz, $CDCl_3$) δ 8.04 – 7.84 (m, 2H), 7.40 – 7.29 (m, 2H), 7.27 – 7.14 (m, 3H), 7.14 – 7.01 (m, 3H), 6.85 – 6.59 (m, 2H), 5.38 (s, 1H), 5.16 (s, 1H), 4.75 (d, *J* = 4.7 Hz, 1H), 4.08 (d, J = 11.2 Hz, 1H), 4.01 (d, *J* = 4.6 Hz, 1H), 3.88 (dt, *J* = 8.1, 6.6 Hz, 2H), 3.76 (d, *J* = 11.2 Hz, 1H), 2.47 (s, 3H), 2.34 (s, 3H), 1.45 (qd, *J* = 6.8, 2.8 Hz, 2H), 0.73 (t, *J* = 7.4 Hz, 3H); ^{13}C NMR (75 MHz, $CDCl_3$) δ 169.1, 144.2, 140.3, 137.5, 136.5, 132.7, 130.2, 129.3, 128.7, 128.4, 127.7, 127.2, 123.7, 117.9, 117.1, 112.2, 86.8, 70.9, 70.7, 66.5, 58.6, 47.0, 21.3, 21.1, 21.0, 9.7; HRMS (ESI) calcd for $C_{29}H_{31}N_3O_5SH^+$ $[M+H]^+$ 534.2057, found 534.2054; HPLC analysis: 91% ee (CHIRALPAK OD-H, isopropanol/hexane = 10:90, 1.0 mL/min, UV: 254 nm), t_R = 11.21 min (minor), 16.74 min (major).

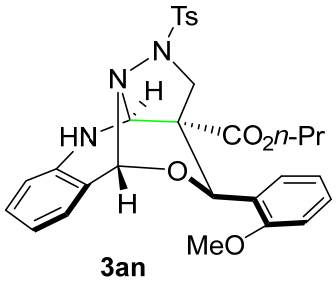
Propyl (3*S*,3a*S*,9*R*,10*S*,12*R*)-12-(*p*-tolyl)-1-tosyl-1,2,4,9-tetrahydro-9,3-(epoxymethano) pyrazolo[5,1-*b*]quinazoline-3(3a*H*)-carboxylate (3am)



3am

Prepared according to the general procedure as described above in 93% yield. $[\alpha]^{20}_{D}$= –35.2 (*c*= 0.72, CH_2Cl_2); white solid. mp = 177 – 180 °C; ^{1}H NMR (300 MHz, $CDCl_3$) δ 8.03 – 7.71 (m, 2H), 7.34 (d, *J* = 8.0 Hz, 2H), 7.27 – 7.17 (m, 3H), 7.16 – 7.02 (m, 3H), 6.82 – 6.66 (m, 2H), 5.37 (s, 1H), 5.17 (s, 1H), 4.75 (d, *J* = 4.7 Hz, 1H), 4.06 (d, *J* = 11.2 Hz, 1H), 4.00 (d, *J* = 4.7 Hz, 1H), 3.97 – 3.80 (m, 2H), 3.76 (d, *J* = 11.2 Hz, 1H), 2.47 (s, 3H), 2.32 (s, 3H), 1.57 – 1.34 (m, 2H), 0.73 (t, *J* = 7.4 Hz, 3H); ^{13}C NMR (75 MHz, $CDCl_3$) δ 169.1, 144.1, 140.3, 137.7, 133.6, 132.7, 130.1, 129.3, 128.5, 128.4, 126.5, 117.9, 117.2, 112.2, 86.7, 70.8, 70.7, 66.5, 58.6, 47.0, 21.3, 21.2, 20.7, 9.7; HRMS (ESI) calcd for $C_{29}H_{31}N_3O_5SH^+$ $[M+H]^+$ 534.2057, found 534.2056; HPLC analysis: 92% ee (OD-H, isopropanol/hexane = 10:90, 1.0 mL/min, UV: 254 nm), t_R = 12.42 min (minor), 17.75 min (major).

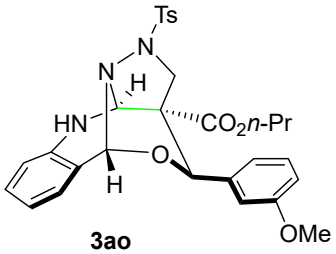
Propyl (3*S*,3a*S*,9*R*,10*S*,12*R*)-12-(2-methoxyphenyl)-1-tosyl-1,2,4,9-tetrahydro-9,3-(epoxymethano)pyrazolo[5,1-*b*]quinazoline-3(3a*H*)-carboxylate (3an)



3an

Prepared according to the general procedure as described above in 98% yield. $[\alpha]^{20}_{D}$= –44.7 (*c*= 0.78, CH_2Cl_2); white solid. mp = 169 – 171 °C; ^{1}H NMR (300 MHz, $CDCl_3$) δ 7.96 – 7.81 (m, 2H), 7.66 (dd, *J* = 7.7, 1.7 Hz, 1H), 7.39 – 7.30 (m, 2H), 7.30 – 7.16 (m, 2H), 7.10 – 7.00 (m, 2H), 6.79 – 6.61 (m, 3H), 5.51 (s, 1H), 5.34 (s, 1H), 4.95 (d, *J* = 4.3 Hz, 1H), 4.10 (d, *J* = 3.5 Hz, 1H), 4.05 (d, *J* = 11.0 Hz, 1H), 4.00 – 3.86 (m, 1H), 3.75 – 3.56 (m, 4H), 3.44 (d, *J* = 11.1 Hz, 1H), 2.47 (s, 3H), 1.42 – 1.31 (m, 2H), 0.67 (t, *J* = 7.4 Hz, 3H); ^{13}C NMR (75 MHz, $CDCl_3$) δ 169.7, 155.5, 144.1, 140.8, 132.8, 130.1, 129.3, 128.6, 128.4, 128.3, 127.6, 125.4, 120.3, 117.2, 117.1, 111.9, 108.8, 86.8, 70.0, 66.2, 65.4, 56.7, 54.5, 47.5, 21.3, 21.0, 9.8; HRMS (ESI) calcd for $C_{29}H_{31}N_3O_6SH^+$ $[M+H]^+$ 550.2006, found 550.2004; HPLC analysis: 86% ee (CHIRALPAK OD-H, isopropanol/hexane = 10:90, 1.0 mL/min, UV: 254 nm), t_R = 18.04 min (minor), 36.03 min (major).

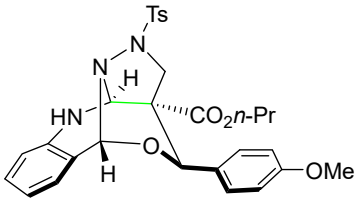
Propyl (3*S*,3a*S*,9*R*,10*S*,12*R*)-12-(3-methoxyphenyl)-1-tosyl-1,2,4,9-tetrahydro-9,3-(epoxymethano)pyrazolo[5,1-*b*]quinazoline-3(3a*H*)-carboxylate (3ao)



3ao

Prepared according to the general procedure as described above in 95% yield. $[\alpha]^{20}_{D}$= –36.7 (*c*= 0.55, CH_2Cl_2); white solid. mp = 150 – 152 °C; ^{1}H NMR (300 MHz, $CDCl_3$) δ 7.96 – 7.83 (m, 2H), 7.45 – 7.31 (m, 2H), 7.27 – 7.18 (m, 2H), 7.08 (dd, *J* = 7.6, 1.5 Hz, 1H), 6.96 – 6.87 (m, 2H), 6.86 – 6.80 (m, 1H), 6.79 – 6.66 (m, 2H), 5.38 (s, 1H), 5.17 (s, 1H), 4.75 (d, *J* = 4.7 Hz, 1H), 4.06 (d, *J* = 11.2 Hz, 1H), 4.00 (d, *J* = 4.6 Hz, 1H), 3.96 – 3.83 (m, 2H), 3.80 (s, 3H), 3.76 (d, *J* = 11.3 Hz, 1H), 2.47 (s, 3H), 1.46 (qd, *J* = 6.7, 1.8 Hz, 2H), 0.74 (t, *J* = 7.4 Hz, 3H); ^{13}C NMR (75 MHz, $CDCl_3$) δ 169.0, 159.2, 144.1, 140.3, 138.1, 132.7, 130.2, 129.3, 128.8, 128.5, 128.4, 118.9, 117.9, 113.6, 112.3, 112.2, 86.8, 70.8, 70.7, 66.5, 58.6, 54.9, 47.0, 21.3, 21.2, 9.8; HRMS (ESI) calcd for $C_{29}H_{31}N_3O_6SH^+$ $[M+H]^+$ 550.2006, found 550.2005; HPLC analysis: 95% ee (CHIRALPAK OD-H, isopropanol/hexane = 10:90, 1.0 mL/min, UV: 254 nm), t_R = 16.49 min (minor), 25.44 min (major).

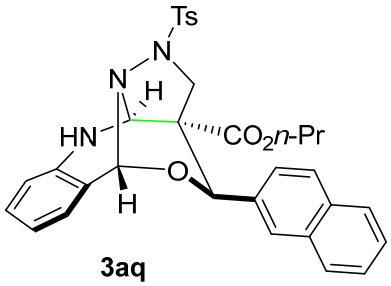
Propyl (3*S*,3a*S*,9*R*,10*S*,12*R*)-12-(4-methoxyphenyl)-1-tosyl-1,2,4,9-tetrahydro-9,3-(epoxymethano)pyrazolo[5,1-*b*]quinazoline-3(3a*H*)-carboxylate (3ap)



3ap

Prepared according to the general procedure as described above in 80% yield. $[\alpha]^{20}_{D}$= –29.5 (*c*= 0.90, CH_2Cl_2); white solid. mp = 173 – 175 °C; ^{1}H NMR (300 MHz, $CDCl_3$) δ 7.99 – 7.75 (m, 2H), 7.34 (d, *J* = 8.0 Hz, 2H), 7.30 – 7.18 (m, 3H), 7.08 (dd, *J* = 7.5, 1.5 Hz, 1H), 6.92 – 6.80 (m, 2H), 6.82 – 6.66 (m, 2H), 5.37 (s, 1H), 5.16 (s, 1H), 4.71 (d, *J* = 4.8 Hz, 1H), 4.04 (d, *J* = 11.2 Hz, 1H), 3.98 (d, *J* = 4.7 Hz, 1H), 3.96 – 3.83 (m, 2H), 3.80 (s, 4H), 2.47 (s, 3H), 1.47 (qd, *J* = 6.7, 1.6 Hz, 2H), 0.75 (t, *J* = 7.4 Hz, 3H); ^{13}C NMR (75 MHz, $CDCl_3$) δ 169.0, 159.2, 144.1, 140.3, 132.7, 130.1, 129.3, 128.7, 128.5, 128.4, 127.9, 117.9, 117.2, 113.2, 112.2, 86.8, 70.8, 70.5, 66.5, 58.7, 54.9, 47.0, 21.3, 21.2, 9.8; HRMS (ESI) calcd for $C_{29}H_{31}N_3O_6SH^+$ $[M+H]^+$ 550.2006, found 550.2003; HPLC analysis: 94% ee (CHIRALPAK OD-H, isopropanol/hexane = 10:90, 1.0 mL/min, UV: 254 nm), t_R = 19.63 min (minor), 29.70 min (major).

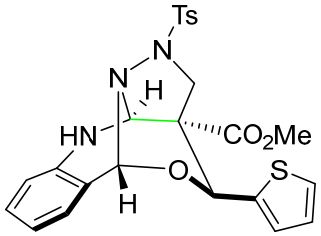
Propyl (3*S*,3a*S*,9*R*,10*S*,12*R*)-12-(naphthalen-2-yl)-1-tosyl-1,2,4,9-tetrahydro-9,3-(epoxymethano)pyrazolo[5,1-*b*]quinazoline-3(3a*H*)-carboxylate (3aq)



3aq

Prepared according to the general procedure as described above in 95% yield. $[\alpha]^{20}_{D}$= –52.7 (*c*= 0.98, CH_2Cl_2); white solid. mp = 177 – 180 °C; ^{1}H NMR (300 MHz, $CDCl_3$) δ 7.96 – 7.70 (m, 6H), 7.54 – 7.42 (m, 2H), 7.36 – 7.30 (m, 3H), 7.25 – 7.18 (m, 1H), 7.08 (dd, *J* = 7.5, 1.5 Hz, 1H), 6.80 – 6.67 (m, 2H), 5.43 (s, 1H), 5.35 (s, 1H), 4.80 (d, *J* = 4.8 Hz, 1H), 4.11 – 4.03 (m, 2H), 3.77 (d, *J* = 11.3 Hz, 1H), 3.49 (s, 3H), 2.44 (s, 3H); ^{13}C NMR (75 MHz, $CDCl_3$) δ 169.4, 144.2, 140.3, 134.1, 132.8, 132.7, 130.2, 129.3, 128.4, 127.8, 127.4, 127.2, 125.9, 124.2, 117.9, 117.1, 112.2, 86.8, 70.9, 70.8, 58.8, 51.8, 47.0, 21.3; HRMS (ESI) calcd for $C_{30}H_{27}N_3O_5SH^+$ $[M+H]^+$ 542.1744, found 542.1739; HPLC analysis: 82% ee (CHIRALPAK OD-H, isopropanol/hexane = 10:90, 1.0 mL/min, UV: 254 nm), t_R = 8.67 min (minor), 14.13 min (major).

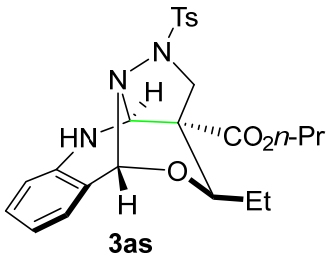
Methyl (3*S*,3a*S*,9*R*,10*S*,12*R*)-12-(thiophen-2-yl)-1-tosyl-1,2,4,9-tetrahydro-9,3-(epoxymethano) pyrazolo[5,1-*b*]quinazoline-3(3a*H*)-carboxylate (3ar)



3ar

Prepared according to the general procedure as described above in 96% yield. $[\alpha]^{20}_{D}$= –24.8 (*c*= 0.96, CH_2Cl_2); white solid. mp = 198 – 200 °C; ^{1}H NMR (300 MHz, $CDCl_3$) δ 7.97 – 7.81 (m, 2H), 7.41 – 7.16 (m, 4H), 7.05 (dd, *J* = 7.6, 1.5 Hz, 1H), 6.98 – 6.87 (m, 2H), 6.80 – 6.60 (m, 2H), 5.45 (s, 1H), 5.29 (s, 1H), 4.60 (d, *J* = 5.4 Hz, 1H), 4.17 – 3.92 (m, 3H), 3.63 (s, 3H), 2.44 (s, 3H); ^{13}C NMR (75 MHz, $CDCl_3$) δ 168.9, 144.1, 140.0, 139.1, 132.8, 130.3, 129.3, 128.5, 128.4, 126.1, 125.2, 125.1, 118.2, 116.9, 112.4, 86.9, 71.3, 68.1, 59.2, 52.0, 48.0, 21.3.; HRMS (ESI) calcd for $C_{24}H_{23}N_3O_5S_2H^+$ $[M+H]^+$ 498.1152, found 498.1146; HPLC analysis: 94% ee (CHIRALPAK OD-H, isopropanol/hexane = 10:90, 1.0 mL/min, UV: 254 nm), t_R = 27.27 min (minor), 52.01 min (major).

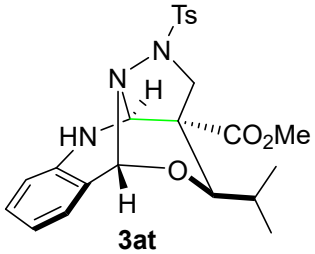
Propyl (3*S*,3a*S*,9*R*,10*S*,12*R*)-12-ethyl-1-tosyl-1,2,4,9-tetrahydro-9,3-(epoxymethano) pyrazolo[5,1-*b*]quinazoline-3(3a*H*)-carboxylate (3as)



3as

Prepared according to the general procedure as described above in 61% yield. $[\alpha]^{20}_{D}$= –13.7 (*c*= 0.57, CH_2Cl_2); white solid, mp = 167 – 172 °C; ^{1}H NMR (300 MHz, $CDCl_3$) δ 8.00 – 7.83 (m, 2H), 7.36 – 7.30 (m, 2H), 7.22 – 7.17 (m, 1H), 7.04 (dd, *J* = 7.6, 1.5 Hz, 1H), 6.78 – 6.76 (m, 1H), 6.62 (dd, *J* = 8.0, 1.1 Hz, 1H), 5.14 (s, 1H), 4.50 (d, *J* = 5.3 Hz, 1H), 4.08 (td, *J* = 6.6, 1.6 Hz, 2H), 4.00 – 3.82 (m, 4H), 2.46 (s, 3H), 1.70 – 1.63 (m, 2H), 1.57 – 1.37 (m, 2H), 0.96 (t, *J* = 7.4 Hz, 3H), 0.84 (t, *J* = 7.3 Hz, 3H); ^{13}C NMR (75 MHz, $CDCl_3$) δ 169.4, 144.0, 140.4, 132.9, 129.9, 129.2, 117.9, 117.6, 112.1, 86.2, 71.3, 69.9, 66.6, 57.8, 48.2, 24.0, 21.4, 21.3, 10.0, 9.6; HRMS (ESI) calcd for $C_{24}H_{29}N_3O_5SH^+$ $[M+H]^+$ 472.1901, found 472.1898; HPLC analysis: -36% ee (CHIRALPAK OD-H, isopropanol/hexane = 10:90, 1.0 mL/min, UV: 254 nm), t_R = 8.90 min (major), 10.58 min (minor).

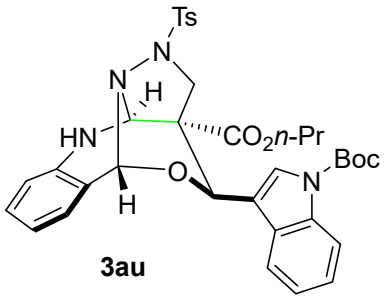
Methyl (3*S*,3a*S*,9*R*,10*S*,12*R*)-12-isopropyl-1-tosyl-1,2,4,9-tetrahydro-9,3-(epoxymethano) pyrazolo[5,1-*b*]quinazoline-3(3a*H*)-carboxylate (3at)



3at

Prepared according to the general procedure as described above in 55% yield. $[\alpha]^{20}_{D}$= –14.2 (*c*= 0.68, CH_2Cl_2); white solid. mp = 128 – 130 °C; ^{1}H NMR (300 MHz, $CDCl_3$) δ 7.94 – 7.74 (m, 2H), 7.34 – 7.27 (m, 2H), 7.18 – 7.14 (m, 1H), 6.98 (dd, *J* = 7.6, 1.5 Hz, 1H), 6.70 (td, *J* = 7.4, 1.1 Hz, 1H), 6.63 – 6.55 (m, 1H), 5.10 (s, 1H), 4.56 (d, *J* = 4.8 Hz, 1H), 4.05 – 3.93 (m, 2H), 3.89 (d, *J* = 4.6 Hz, 1H), 3.75 (d, *J* = 6.5 Hz, 1H), 3.69 (s, 3H), 2.42 (s, 3H), 1.81 – 1.70 (m, 1H), 0.89 (d, *J* = 6.7 Hz, 3H), 0.70 (d, *J* = 6.8 Hz, 3H); ^{13}C NMR (75 MHz, $CDCl_3$) δ 170.4, 144.0, 140.4, 132.9, 129.8, 129.2, 128.4, 128.2, 117.7, 117.5, 111.9, 86.3, 73.0, 71.5, 57.1, 51.9, 48.0, 30.3, 21.3, 19.3, 18.1; HRMS (ESI) calcd for $C_{23}H_{27}N_3O_5SH^+$ $[M+H]^+$ 458.1744, found 458.1739; HPLC analysis: 46% ee (CHIRALPAK OD-H, isopropanol/hexane = 10:90, 1.0 mL/min, UV: 254 nm), t_R = 6.66 min (minor), 7.63 min (major).

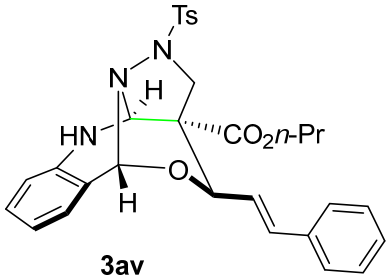
Propyl (3*S*,3a*S*,9*R*,10*S*,12*R*)-12-(1-(*tert*-butoxycarbonyl)-1*H*-indol-3-yl)-1-tosyl-1,2,4,9-tetrahydro-9,3-(epoxymethano)pyrazolo[5,1-*b*]quinazoline-3(3a*H*)-carboxylate (3au)



3au

Prepared according to the general procedure as described above in 79% yield. $[\alpha]^{20}_D$= –34.6 (*c*= 0.77, CH_2Cl_2); white solid. mp = 179 – 180 °C; ^{1}H NMR (300 MHz, $CDCl_3$) δ 8.14 (d, *J* = 8.3 Hz, 1H), 8.00 – 7.85 (m, 2H), 7.64 (s, 1H), 7.43 (dt, *J* = 7.7, 1.0 Hz, 1H), 7.40 – 7.24 (m, 4H), 7.24 – 7.05 (m, 2H), 6.85 – 6.70 (m, 2H), 5.47 (s, 1H), 5.39 (s, 1H), 4.81 (d, *J* = 4.8 Hz, 1H), 4.19 (d, *J* = 11.1 Hz, 1H), 4.07 (d, *J* = 4.8 Hz, 1H), 3.97 – 3.72 (m, 2H), 3.69 – 3.48 (m, 1H), 2.48 (s, 3H), 1.71 (s, 9H), 1.24 (q, *J* = 7.1 Hz, 2H), 0.57 (t, *J* = 7.4 Hz, 3H); ^{13}C NMR (75 MHz, $CDCl_3$) δ 169.2, 149.0, 144.2, 140.4, 134.9, 132.7, 130.3, 129.3, 128.5, 128.4, 128.1, 124.3, 123.7, 122.2, 119.3, 118.0, 116.9, 116.8, 114.8, 112.2, 86.8, 83.7, 70.8, 66.7, 65.9, 57.9, 27.8, 21.3, 20.9, 9.4; HRMS (ESI) calcd for $C_{35}H_{38}N_4O_7SH^+$ $[M+H]^+$ 659.2534, found 659.2530; HPLC analysis: 80% ee (OD-H, isopropanol/hexane = 10:90, 1.0 mL/min, UV: 254 nm), t_R = 14.84 min (minor), 20.82 min (major).

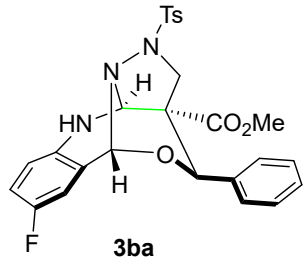
Propyl (3*S*,3a*S*,9*R*,10*S*,12*R*)-12-((E)-styryl)-1-tosyl-1,2,4,9-tetrahydro-9,3-(epoxymethano) pyrazolo[5,1-*b*]quinazoline-3(3a*H*)-carboxylate (3av)



3av

Prepared according to the general procedure as described above in 29% yield. $[\alpha]^{20}_D$= –45.7 (*c*= 0.28, CH_2Cl_2); white solid. mp = 169 – 171 °C; ^{1}H NMR (300 MHz, $CDCl_3$) δ 7.99 – 7.85 (m, 2H), 7.46 – 7.18 (m, 9H), 7.11 (dd, *J* = 7.6, 1.5 Hz, 1H), 6.87 – 6.59 (m, 3H), 6.13 (dd, *J* = 15.9, 5.5 Hz, 1H), 5.32 (s, 1H), 4.77 (dd, *J* = 5.5, 1.4 Hz, 1H), 4.56 (d, *J* = 5.6 Hz, 1H), 4.07 (td, *J* = 6.6, 1.7 Hz, 2H), 4.04 – 3.91 (m, 3H), 2.47 (s, 3H), 1.62 (q, *J* = 7.0 Hz, 2H), 0.91 (t, *J* = 7.4 Hz, 3H); ^{13}C NMR (75 MHz, $CDCl_3$) δ 168.9, 144.1, 140.1, 135.9, 133.5, 132.8, 130.1, 129.3, 128.5, 128.4, 128.2, 127.6, 126.2, 123.3, 118.2, 117.4, 112.4, 86.4, 71.4, 68.8, 66.7, 48.5, 21.5, 21.3, 10.0; HRMS (ESI) calcd for $C_{30}H_{31}N_3O_5SH^+$ $[M+H]^+$ 546.2057, found 546.2052; HPLC analysis: 83% ee (OD-H, isopropanol/hexane = 10:90, 1.0 mL/min, UV: 254 nm), t_R = 17.89 min (minor), 40.24 min (major).

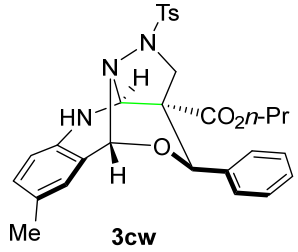
Methyl (3*S*,3a*S*,9*R*,10*S*,12*R*)-7-fluoro-12-phenyl-1-tosyl-1,2,4,9-tetrahydro-9,3-(epoxymethano) pyrazolo[5,1-*b*]quinazoline-3(3a*H*)-carboxylate (3ba)



3ba

Prepared according to the general procedure as described above in 96% yield. $[\alpha]^{20}_{D}$= –36.5 (*c*= 0.94, CH_2Cl_2); white solid. mp = 184 – 186 °C; ^{1}H NMR (300 MHz, $CDCl_3$) δ 8.03 – 7.72 (m, 2H), 7.37 – 7.26 (m, 7H), 6.95 – 6.90 (m, 1H), 6.77 (dd, *J* = 8.2, 2.8 Hz, 1H), 6.62 (dd, *J* = 8.8, 4.3 Hz, 1H), 5.25 (s, 1H), 5.16 (s, 1H), 4.67 (d, *J* = 4.9 Hz, 1H), 4.06 (d, *J* = 4.8 Hz, 1H), 3.87 (dd, *J* = 63.4, 11.3 Hz, 2H), 3.52 (s, 3H), 2.44 (s, 3H); ^{13}C NMR (75 MHz, $CDCl_3$) δ 169.2, 155.3 (d, *J* = 238.0 Hz), 144.3, 136.4, 136.3, 132.7, 129.3, 128.4, 128.1, 127.9, 126.5, 117.9 (d, *J* = 6.9 Hz), 117.2 (d, *J* = 22.9 Hz), 114.6 (d, *J* = 23.0 Hz), 113.4 (d, *J* = 7.6 Hz), 86.0, 70.9, 70.8, 58.6, 51.8, 46.8, 21.3; HRMS (ESI) calcd for $C_{26}H_{24}FN_3O_5SH^+$ $[M+H]^+$ 510.1493, found 510.1489; HPLC analysis: 89% ee (CHIRALPAK OD-H, isopropanol/hexane = 10:90, 1.0 mL/min, UV: 254 nm), t_R = 21.28 min (minor), 36.32 min (major).

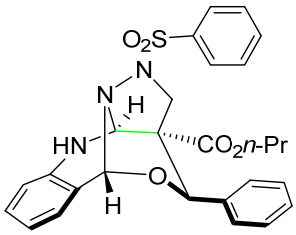
Propyl (3*S*,3a*S*,9*R*,10*S*,12*R*)-7-methyl-12-phenyl-1-tosyl-1,2,4,9-tetrahydro-9,3-(epoxymethano) pyrazolo[5,1-*b*]quinazoline-3(3a*H*)-carboxylate (3cw)



3cw

Prepared according to the general procedure as described above in 85% yield. $[\alpha]^{20}_{D}$= –27.7 (*c*= 0.82, CH_2Cl_2); white solid. mp = 161 – 163 °C; ^{1}H NMR (300 MHz, $CDCl_3$) δ 7.98 – 7.75 (m, 2H), 7.45 – 7.18 (m, 8H), 7.14 – 6.96 (m, 1H), 6.89 (d, *J* = 2.0 Hz, 1H), 6.63 (d, *J* = 8.1 Hz, 1H), 5.34 (s, 1H), 5.20 (s, 1H), 4.62 (d, *J* = 4.7 Hz, 1H), 4.12 – 4.01 (m, 1H), 3.98 (d, *J* = 4.7 Hz, 1H), 3.96 – 3.80 (m, 2H), 3.75 (d, *J* = 11.2 Hz, 1H), 2.47 (s, 3H), 2.23 (s, 3H), 1.56 – 1.36 (m, 2H), 0.72 (t, *J* = 7.4 Hz, 3H); ^{13}C NMR (75 MHz, $CDCl_3$) δ 169.0, 144.1, 137.9, 136.6, 132.7, 130.9, 129.3, 128.7, 128.4, 128.0, 127.9, 127.8, 126.7, 117.1, 112.3, 86.8, 71.0, 70.8, 66.4, 46.9, 21.3, 21.1, 19.9, 9.7; HRMS (ESI) calcd for $C_{29}H_{31}N_3O_5SH^+$ $[M+H]^+$ 534.2057, found 534.2056; HPLC analysis: 96% ee (CHIRALPAK OD-H, isopropanol/hexane = 10:90, 1.0 mL/min, UV: 254 nm), t_R = 14.39 min (minor), 25.29 min (major).

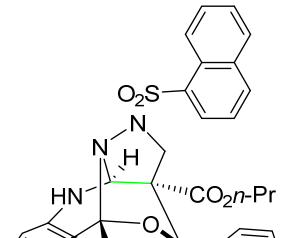
Propyl (3*S*,3a*S*,9*R*,10*S*,12*R*)-12-phenyl-1-(phenylsulfonyl)-1,2,4,9-tetrahydro-9,3-(epoxymethano)pyrazolo[5,1-*b*]quinazoline-3(3a*H*)-carboxylate (3dw)



3dw

Prepared according to the general procedure as described above in 83% yield. $[\alpha]^{20}_{D}$= –36.4 (*c*= 0.80, CH_2Cl_2); white solid. mp = 163 – 165 °C; ^{1}H NMR (300 MHz, $CDCl_3$) δ 8.13 – 7.96 (m, 2H), 7.75 – 7.62 (m, 1H), 7.61 – 7.50 (m, 2H), 7.40 – 7.27 (m, 5H), 7.24 (td, *J* = 7.7, 1.5 Hz, 1H), 7.07 (dd, *J* = 7.6, 1.5 Hz, 1H), 6.83 – 6.64 (m, 2H), 5.37 (s, 1H), 5.21 (s, 1H), 4.76 (d, *J* = 4.7 Hz, 1H), 4.12 – 3.99 (m, 2H), 3.98 – 3.82 (m, 2H), 3.78 (d, *J* = 11.2 Hz, 1H), 1.45 (qd, *J* = 6.8, 1.9 Hz, 2H), 0.73 (t, *J* = 7.4 Hz, 3H); ^{13}C NMR (75 MHz, $CDCl_3$) δ 169.0, 140.3, 136.5, 135.7, 133.2, 130.2, 128.6, 128.5, 128.4, 128.0, 127.8, 126.6, 117.9, 117.1, 112.2, 86.7, 70.9, 66.5, 58.6, 46.9, 21.1, 9.8; HRMS (ESI) calcd for $C_{27}H_{27}N_3O_5SH^+$ $[M+H]^+$ 506.1744, found 506.1741. HPLC analysis: 94% ee (CHIRALPAK OD-H, isopropanol/hexane = 10:90, 1.0 mL/min, UV: 254 nm), t_R = 6.43 min (minor), 7.80 min (major).

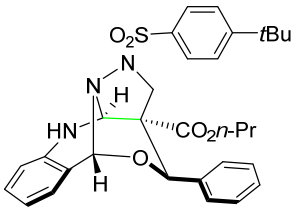
Propyl (3*S*,3a*S*,9*R*,10*S*,12*R*)-1-(naphthalen-1-ylsulfonyl)-12-phenyl-1,2,4,9-tetrahydro-9,3-(epoxymethano)pyrazolo[5,1-*b*]quinazoline-3(3a*H*)-carboxylate (3ew)



3ew

Prepared according to the general procedure as described above in 96% yield. $[\alpha]^{20}_{D}$= +13.3 (*c*= 0.70, CH_2Cl_2); white solid. mp = 123 – 124 °C; ^{1}H NMR (300 MHz, $CDCl_3$) δ 9.02 (dd, *J* = 8.7, 1.1 Hz, 1H), 8.40 (dd, *J* = 7.4, 1.3 Hz, 1H), 8.14 (d, *J* = 8.2 Hz, 1H), 7.99 (dd, *J* = 8.4, 1.1 Hz, 1H), 7.83 – 7.77 (m, 1H), 7.71 – 7.65 (m, 1H), 7.56 (dd, *J* = 8.2, 7.4 Hz, 1H), 7.41 – 7.31 (m, 5H), 7.18 – 7.16 (m, *J* = 8.1, 7.3, 1.5 Hz, 1H), 6.79 (dd, *J* = 7.6, 1.5 Hz, 1H), 6.75 – 6.57 (m, 2H), 5.20 (s, 1H), 4.96 – 4.79 (m, 2H), 4.65 (d, *J* = 4.8 Hz, 1H), 4.13 (d, *J* = 3.2 Hz, 2H), 3.93 – 3.90 (m, 2H), 1.47 – 1.43 (m, 2H), 0.72 (t, *J* = 7.4 Hz, 3H); ^{13}C NMR (75 MHz, $CDCl_3$) δ 169.1, 140.4, 136.6, 134.9, 133.8, 131.6, 131.4, 130.1, 128.7, 128.4, 128.1, 128.0, 127.8, 126.6, 126.5, 125.1, 123.8, 117.6, 116.9, 112.2, 86.2, 71.3, 70.9, 66.5, 58.3, 45.5, 21.1, 9.8; HRMS (ESI) calcd for $C_{31}H_{29}N_3O_5SH^+$ $[M+H]^+$ 556.1901, found 556.1903; HPLC analysis: 91% ee (CHIRALPAK OD-H, isopropanol/hexane = 10:90, 1.0 mL/min, UV: 254 nm), t_R = 17.71 min (minor), 33.12 min (major).

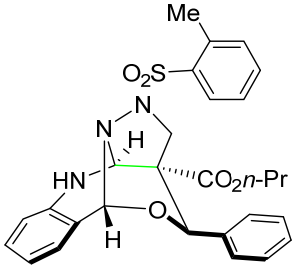
Propyl (3*S*,3a*S*,9*R*,10*S*,12*R*)-1-((4-(tert-butyl)phenyl)sulfonyl)-12-phenyl-1,2,4,9-tetrahydro-9,3-(epoxymethano)pyrazolo[5,1-*b*]quinazoline-3(3a*H*)-carboxylate (3fw)



3fw

Prepared according to the general procedure as described above in 95% yield. $[\alpha]^{20}_D$= –41.7 (*c*= 0.72, CH_2Cl_2); white solid. mp = 164 – 166 °C; ^{1}H NMR (300 MHz, $CDCl_3$) δ8.04 – 7.90 (m, 2H), 7.66 – 7.50 (m, 2H), 7.38 – 7.30 (m, 5H), 7.23 (td, *J* = 7.7, 1.5 Hz, 1H), 7.06 (dd, *J* = 7.4, 1.5 Hz, 1H), 6.82 – 6.64 (m, 2H), 5.36 (s, 1H), 5.22 (s, 1H), 4.81 (d, *J* = 4.7 Hz, 1H), 4.18 – 4.02 (m, 2H), 3.99 – 3.76 (m, 3H), 1.38 (s, 12H), 0.72 (t, *J* = 7.4 Hz, 3H); ^{13}C NMR (75 MHz, $CDCl_3$) δ 169.0, 157.1, 140.3, 136.6, 132.8, 130.2, 128.4, 128.3, 128.0, 127.8, 126.7, 125.7, 117.9, 117.1, 112.2, 86.7, 70.9, 66.5, 58.5, 46.7, 34.9, 30.7, 21.1, 9.8; HRMS (ESI) calcd for $C_{31}H_{35}N_3O_5SH^+$ $[M+H]^+$ 562.2370, found 562.2369; HPLC analysis: 93% ee (CHIRALPAK OD-H, isopropanol /hexane = 10:90, 1.0 mL/min, UV: 254 nm), t_R = 11.11 min (minor), 12.84 min (major).

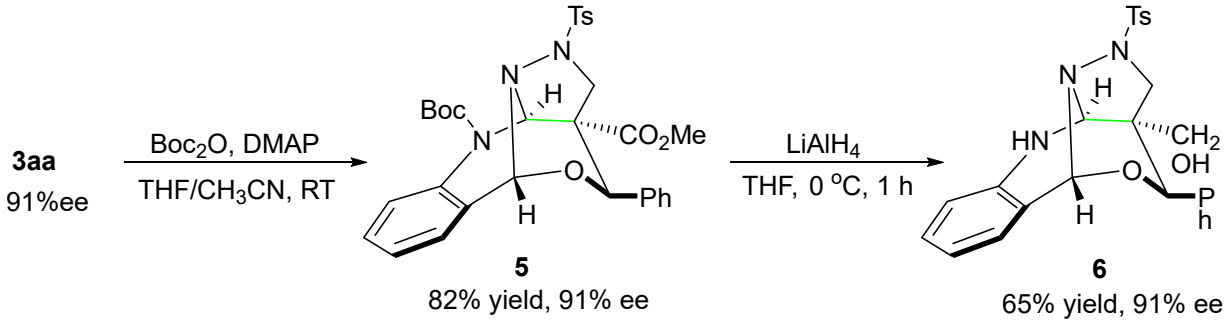
Propyl (3*S*,3a*S*,9*R*,10*S*,12*R*)-12-phenyl-1-(*o*-tolylsulfonyl)-1,2,4,9-tetrahydro-9,3-(epoxymethano)pyrazolo[5,1-*b*]quinazoline-3(3a*H*)-carboxylate (3gw)



3gw

Prepared according to the general procedure as described above in 98% yield. $[\alpha]^{20}_D$= –55.3 (*c*= 0.77, CH_2Cl_2); white solid. mp = 170 – 172 °C; ^{1}H NMR (300 MHz, $CDCl_3$) δ 8.08 (dd, *J* = 7.9, 1.4 Hz, 1H), 7.54 – 7.49 (m, 1H), 7.44 – 7.35 (m, 1H), 7.35 – 7.28 (m, 6H), 7.20 – 7.16 (m, 1H), 6.91 (dd, J = 7.6, 1.5 Hz, 1H), 6.76 – 6.61 (m, 2H), 5.22 (s, 1H), 4.95 (d, *J* = 2.8 Hz, 2H), 4.71 (d, *J* = 4.8 Hz, 1H), 4.04 (dd, *J* = 23.7, 12.5 Hz, 2H), 3.96 – 3.86 (m, 2H), 2.88 (s, 3H), 1.54 – 1.33 (m, 2H), 0.71 (t, *J* = 7.4 Hz, 3H); ^{13}C NMR (75 MHz, $CDCl_3$) δ 169.1, 140.4, 138.8, 136.6, 134.7, 133.3, 132.1, 130.9, 130.2, 128.2, 128.1, 128.0, 127.8, 126.5, 125.8, 117.6, 116.8, 112.3, 86.2, 71.3, 71.0, 66.6, 58.2, 45.4, 21.1, 20.3, 9.8; HRMS (ESI) calcd for $C_{28}H_{29}N_3O_5SH^+$ $[M+H]^+$ 520.1901, found 520.1889; HPLC analysis: 93% ee (CHIRALPAK OD-H, isopropanol/hexane = 10:90, 1.0 mL/min, UV: 254 nm), t_R = 11.77 min (minor), 21.52 min (major).

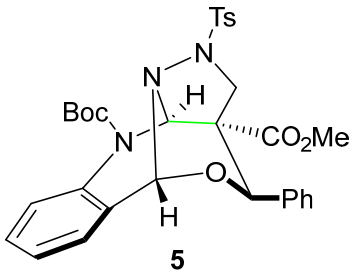
Transformations of the Product 3aa



Under a nitrogen atmosphere, the cycloaddition **3aa** (49.1 mg, 0.1 mmol) was dissolved in 0.5 mL CH_3CN and 0.5 mL of THF, then DMAP (2.4 mg, 0.02 mmol) and Boc_2O (65.4 mg, 0.3 mmol) was added, the mixture was stirred overnight. Once starting material was consumed (monitored by TLC), the mixture was concentrated to dryness. The residue was purified through flash column chromatography (EtOAc/PE) to afford the corresponding product **5** as a white solid, 82% yield, 91% ee.

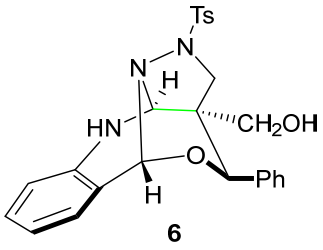
The product **5** (59.1 mg, 0.1 mmol) was dissolved in 1 ml of THF, then slowly added to $LiAlH_4$ (30.4 mg, 0.8 mmol) in 1ml of THF, the resulting mixture was stirred at 0 °C for 1 h. Once starting material was consumed (monitored by TLC), the mixture was concentrated to dryness. The residue was purified through flash column chromatography (25% EtOAc/PE) to afford the corresponding product **6** as a white solid, 65% yield, 91% ee.

4-(*tert*-butyl) 3-methyl (3*S*,3a*S*,9*R*,10*S*,12*R*)-12-phenyl-1-tosyl-1,2-dihydro-9,3-(epoxymethano) pyrazolo[5,1-*b*]quinazoline-3,4(3a*H*,9*H*)-dicarboxylate (5)



Prepared according to the general procedure as described above in 82% yield. It was purified by flash chromatography (20% EtOAc/PE) to afford a white solid. mp = 198 – 200 °C; $[\alpha]^{20}_D$= + 11.0 (*c* 0.48, CH_2Cl_2); ^{1}H NMR (300 MHz, $CDCl_3$) δ 8.51 (d, J = 8.7 Hz, 1H), 8.00 – 7.82 (m, 2H), 7.46 – 7.15 (m, 10H), 7.08 (dd, J = 7.4, 1.0 Hz, 1H), 5.55 (s, 1H), 5.03 (s, 1H), 4.66 (s, 1H), 4.13 (d, J = 11.0 Hz, 1H), 3.86 (d, J = 11.1 Hz, 1H), 3.57 (s, 3H), 2.43 (s, 3H), 1.37 (s, 9H); ^{13}C NMR (75 MHz, $CDCl_3$) δ 167.6, 151.3, 144.2, 136.1, 135.7, 132.1, 130.0, 129.6, 128.7, 128.5, 128.2, 127.9, 127.2, 122.9, 120.3, 118.1, 86.6, 83.0, 71.2, 69.8, 57.2, 51.8, 48.6, 27.4, 21.3; HRMS (ESI) calcd for $C_{31}H_{33}N_3O_7SNH^+$ $[M+H]^+$ 592.2112, found 592.2107; HPLC analysis: 91% ee (CHIRALPAK OD-H, isopropanol/hexane = 10:90, 1.0 mL/min, UV: 254 nm), t_R = 9.54 min (minor), 14.429 min (major).

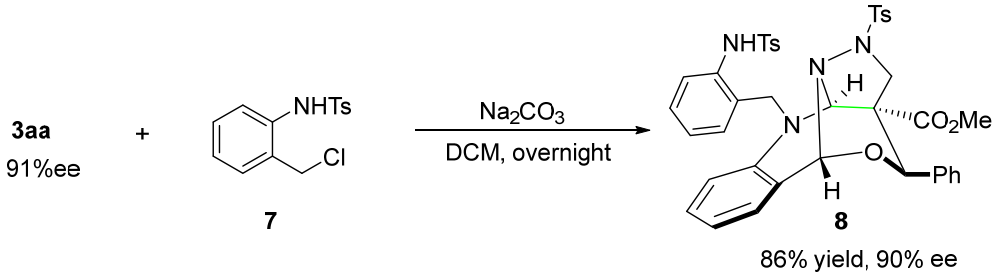
((3*R*,3a*S*,9*R*,10*S*,12*R*)-12-phenyl-1-tosyl-1,2,4,9-tetrahydro-9,3-(epoxymethano)pyrazolo[5,1-*b*]quinazolin-3(3a*H*)-yl)methanol (6)



6

Prepared according to the general procedure as described above in 65% yield. It was purified by flash chromatography (30% EtOAc/PE) to afford a white solid. mp = 228 – 229 °C; $[\alpha]^{20}_{D}$= -48.5 (*c*= 0.20, CH_2Cl_2); ^{1}H NMR (300 MHz, DMSO) δ 7.82 – 7.64 (m, 2H), 7.47 – 6.98 (m, 9H), 6.86 (d, J = 6.2 Hz, 1H), 6.70 – 6.47 (m, 2H), 5.33 (s, 1H), 4.59 (t, J = 5.3 Hz, 1H), 4.53 (s, 1H), 3.64 – 3.46 (m, 2H), 3.34 – 3.23 (m, 2H), 2.81 (dd, J = 11.5, 5.1 Hz, 1H), 2.39 (s, 3H); ^{13}C NMR (75 MHz, DMSO) δ 144.1, 142.7, 137.4, 132.7, 130.1, 129.8, 128.5, 128.4, 128.1, 127.9, 127.0, 117.6, 116.3, 112.6, 86.9, 71.9, 67.3 , 56.8, 51.3, 46.8, 21.2; HRMS (ESI) calcd for $C_{25}H_{25}N_3O_4SH^+$ $[M+H]^+$ 464.1639, found 464.1635; HPLC analysis: 91% ee (CHIRALPAK OD-H, isopropanol/hexane = 10:90, 1.0 mL/min, UV: 220 nm), t_R = 20.40 min (major), 26.09 min (minor).

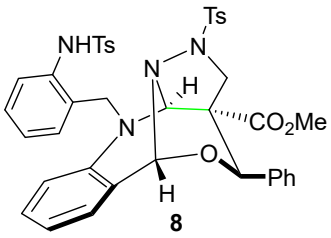
Transformations of the product 3aa



86% yield, 90% ee

The cycloaddition product **3aa** (49.1 mg, 0.1 mmol) was dissolved in 1 ml of DCM, to the solution was added aza-*o*-quinone methide precursor **7** (59.0 mg, 0.2 mmol) and Na_2CO_3 (31.8 mg, 0.3 mmol), the resulting mixture was stirred overnigh at rt. Once starting material was consumed (monitored by TLC), the mixture was concentrated to dryness. The residue was purified through flash column chromatography (40% EtOAc/PE) to afford the corresponding product **8** as a white solid, 86% yield, 90% ee.

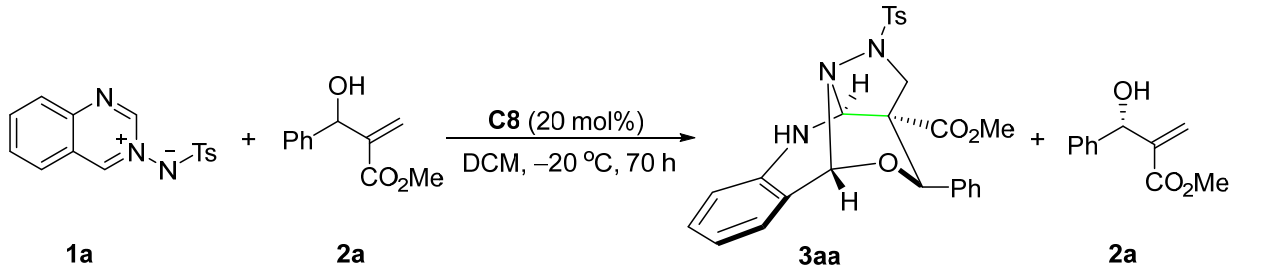
Methyl (3*S*,3a*S*,9*R*,10*S*,12*R*)-4-(2-((4-methylphenyl)sulfonamido)benzyl)-12-phenyl-1-tosyl-1,2,4,9-tetrahydro-9,3-(epoxymethano)pyrazolo[5,1-*b*]quinazoline-3(3a*H*)-carboxylate (8)



8

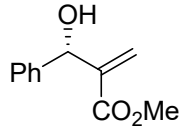
Prepared according to the general procedure as described above in 86% yield. It was purified by flash chromatography (25% EtOAc/PE) to afford a white solid. mp = 230 – 231 °C; $[\alpha]^{20}_D$= -104.1 (*c*= 0.59, CH_2Cl_2); ^{1}H NMR (300 MHz, $CDCl_3$) δ 7.82 (d, J = 8.2 Hz, 2H), 7.62 (d, J = 8.2 Hz, 2H), 7.42 – 7.25 (m, 8H), 7.22 – 7.02 (m, 7H), 6.79 – 6.64 (m, 2H), 6.56 – 6.30 (m, 2H), 5.42 (s, 1H), 5.22 (s, 1H), 4.95 (d, J = 18.1 Hz, 1H), 4.27 (d, J = 18.1 Hz, 1H), 4.07 (d, J = 11.2 Hz, 1H), 3.99 (s, 1H), 3.88 (d, J = 11.2 Hz, 1H), 3.62 (s, 3H), 2.45 (s, 3H), 2.26 (s, 3H); ^{13}C NMR (75 MHz, $CDCl_3$) δ 168.8, 143.9, 143.8, 141.2, 136.5, 135.9, 133.8, 133.4, 132.6, 130.3, 129.4, 129.3, 128.7, 128.3, 128.0, 127.8, 127.6, 127.4, 127.4, 127.2, 127.1, 127.0, 117.9, 117.8, 110.5, 87.0, 77.6, 70.5, 58.0, 52.0, 49.9, 47.7, 21.2, 21.1; HRMS (ESI) calcd for $C_{40}H_{38}N_4O_7S_2H^+$ $[M+H]^+$ 751.2255, found 751.2249; HPLC analysis: 90% ee (CHIRALPAK IC, isopropanol/hexane = 20:80, 1.0 mL/min, UV: 220 nm), t_R = 45.03 min (minor), 75.68 min (major).

Kinetic Resolution of 2a



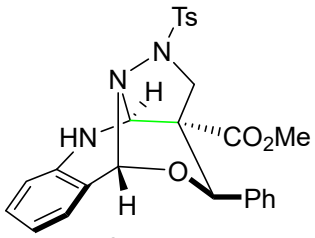
Under a nitrogen atmosphere, at –20 °C, to a mixture of N-iminoquinazolinium ylides **1** (0.1 mmol, 1.0 equiv) and catalyst **C8** (0.02 mmol, 20 mol %) in DCM (2 mL) was added MBH adducts **2** (0.1 mmol, 1.0 equiv) via a syringe. Then the reaction solution was vigorously stirred at –20 °C and monitored by TLC. After the reaction was complete, the mixture was directly purified by column chromatography on silica gel (petroleum ether/EtOAc as the eluent) to furnish the corresponding product (**2a**, 47% yield, 83% ee). Notably, strict anhydrous condition is very important.

Methyl (*S*)-2-(hydroxy(phenyl)methyl)acrylate

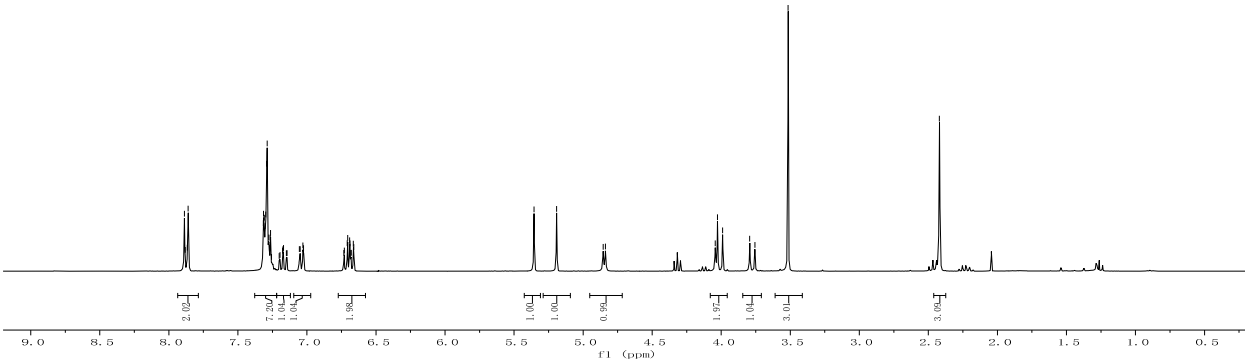


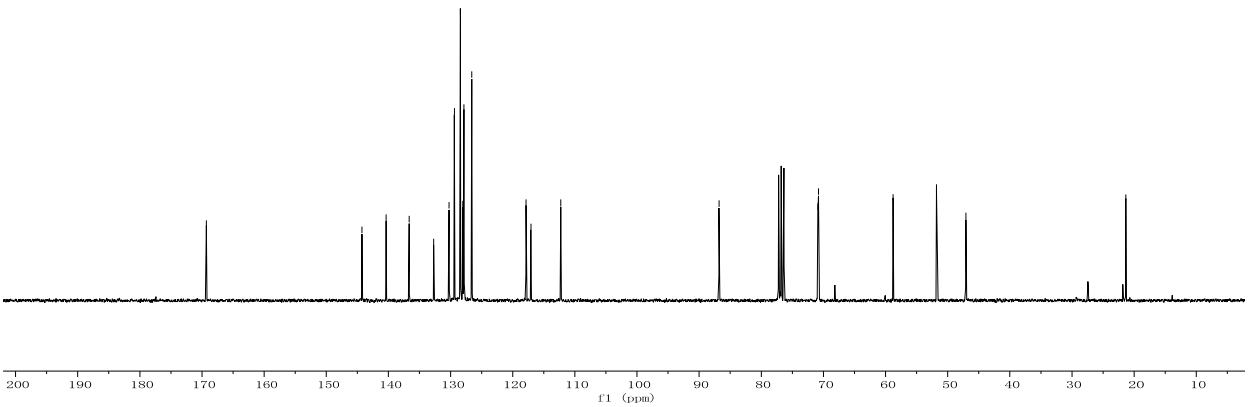
2a

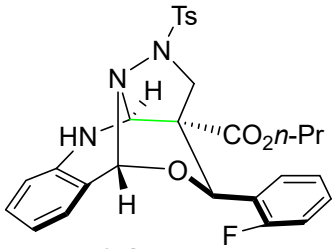
Prepared according to the general procedure as described above in 47% yield. $[\alpha]^{20}_D$= +20.0 (*c*= 0.50, CH_2Cl_2). The absolute configuration of **2a** was determined by the comparison of $[\alpha]^{20}_D$ with reported result. HPLC analysis: 83% ee (CHIRALPAK OD-H, isopropanol/hexane = 10:90, 1.0 mL/min, UV: 220 nm), t_R = 11.77 min (minor), 21.52 min (major).


Ts
N
N
H
HN
CO2Me
O
Ph
H

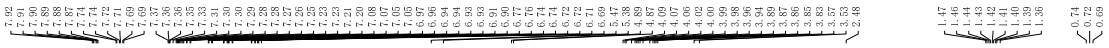
3aa

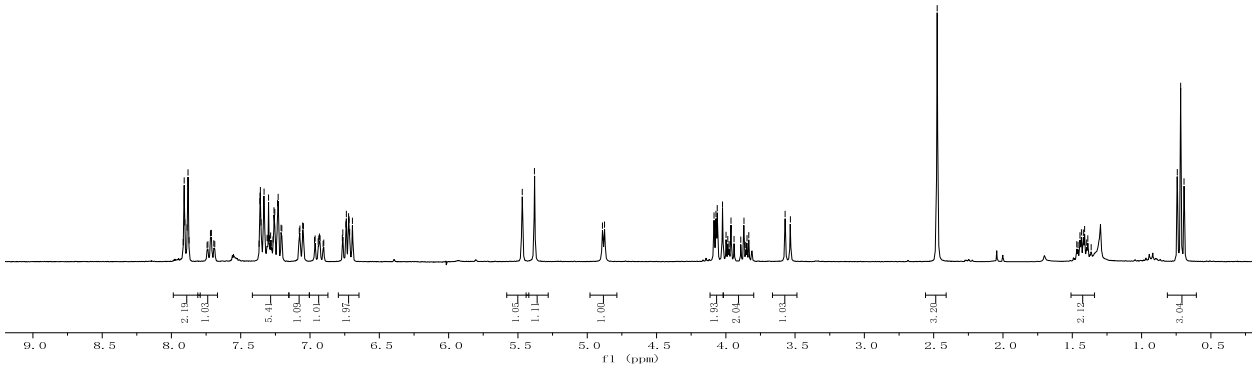

2.02
7.20
1.04
1.04
1.98
1.00
1.00
0.99
1.97
1.04
3.04
3.04
f1 (ppm)


f1 (ppm)


Ts
N
N
H
HN
CO_2n-Pr
O
H
F

3ab

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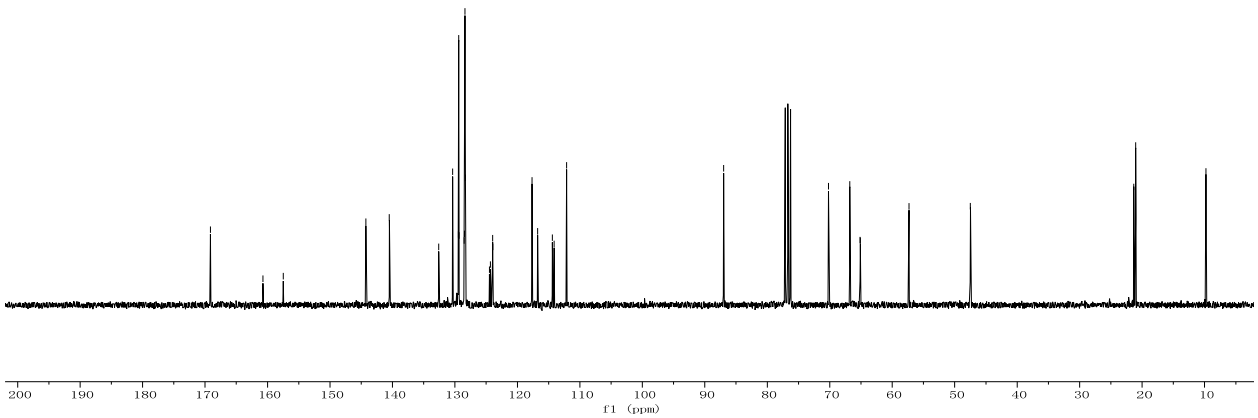
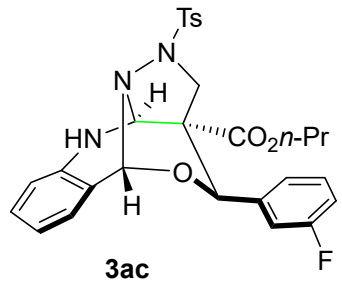
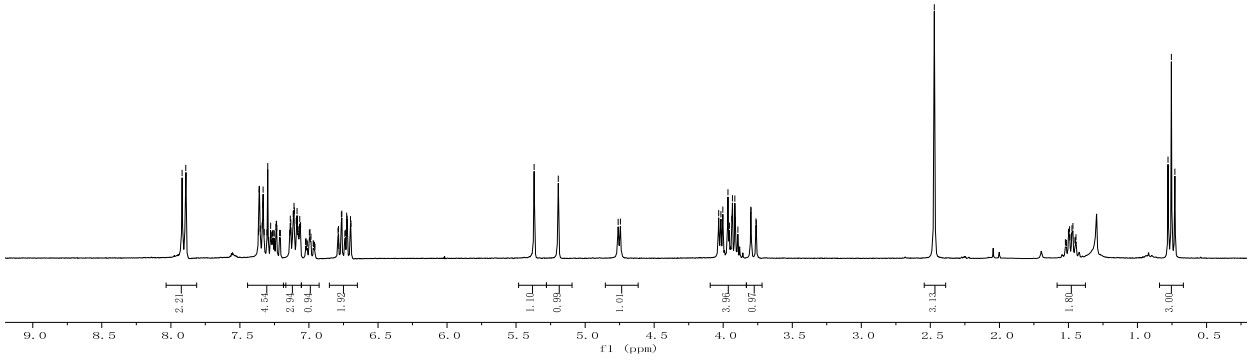
5.44
1.09
1.04
1.97
1.05
1.11
1.00
1.83
2.04
1.03
3.20
2.12
3.04
9.0
8.5
8.0
7.5
7.0
6.5
6.0
5.5
5.0
4.5
4.0
3.5
3.0
2.5
2.0
1.5
1.0
0.5
f1 (ppm)


169.13
160.74
157.47
144.26
140.50
132.59
130.38
129.45
129.39
129.34
128.52
128.47
128.40
128.33
124.48
124.31
123.97
123.93
117.67
116.77
114.40
114.11
112.13
87.00
70.21
66.80
65.14
65.10
57.32
47.49
21.33
21.03
9.78


200
190
180
170
160
150
140
130
120
110
100
90
80
70
60
50
40
30
20
10
f1 (ppm)


Ts
N
N
H
HN
CO2n-Pr
O
H
F

3ac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4.54
2.94
0.94
1.92
1.10
0.99
1.01
3.96
0.97
3.13
1.80
3.00
9.0
8.5
8.0
7.5
7.0
6.5
6.0
5.5
5.0
4.5
4.0
3.5
3.0
2.5
2.0
1.5
1.0
0.5
f1 (ppm)


168.89
163.90
160.64
144.26
140.20
139.27
139.18
132.64
130.34
129.41
129.37
129.31
126.45
122.34
122.30
118.05
116.98
115.02
114.74
114.69
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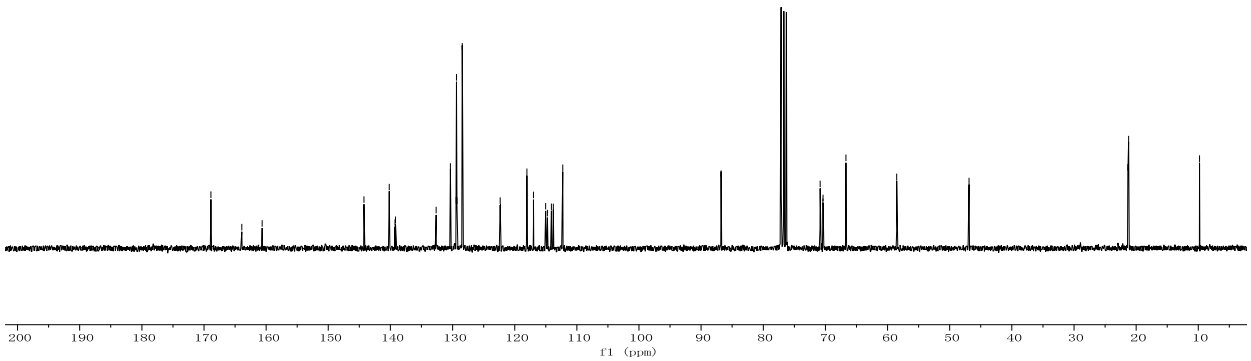
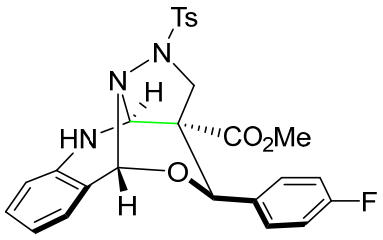
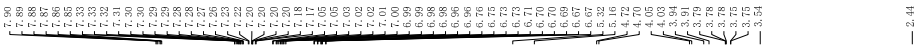
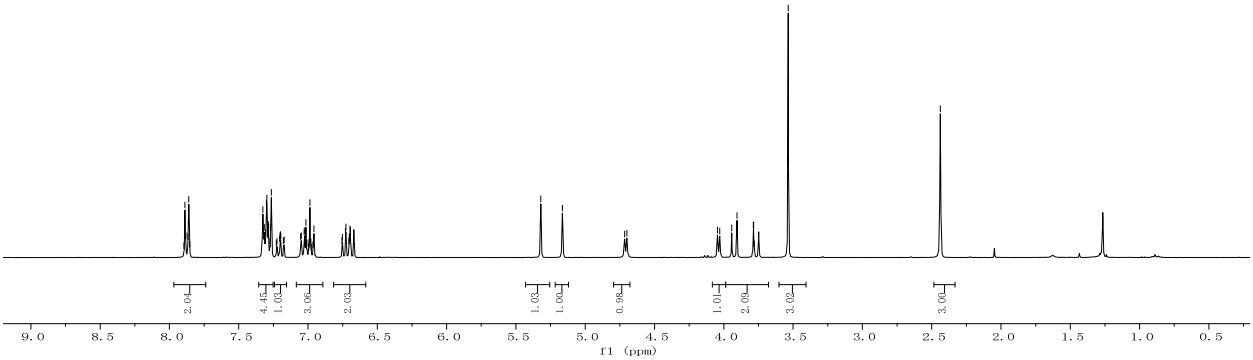
66.70
58.52
46.90
21.33
21.20
9.79


200
190
180
170
160
150
140
130
120
110
100
90
80
70
60
50
40
30
20
10
f1 (ppm)


Ts
N
N
H
HN
CO2Me
O
H
F

3ad




2.04
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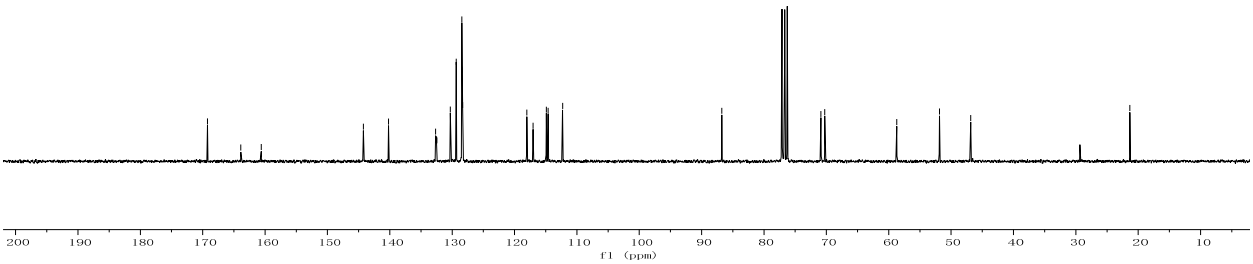
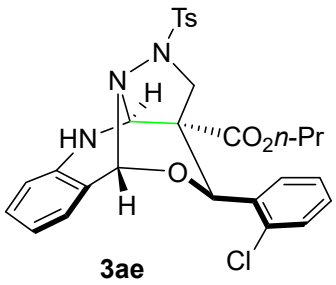
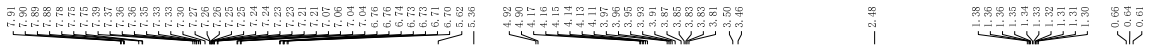
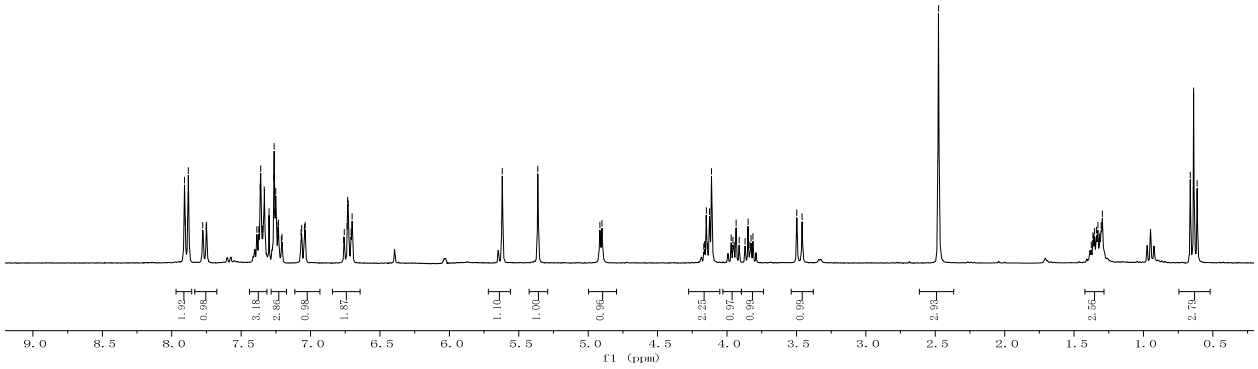
1.03
3.06
2.03
1.03
1.04
0.98
1.01
2.09
3.02
3.00
f1 (ppm)

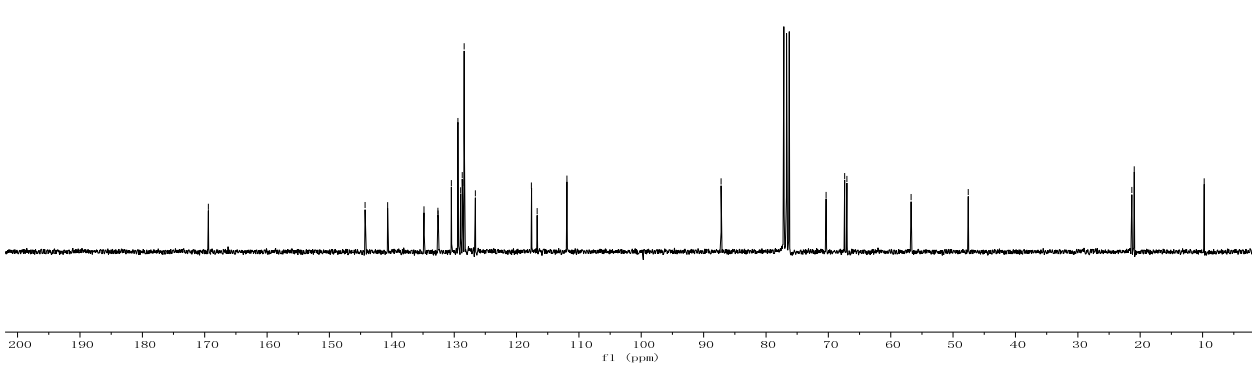

f1 (ppm)

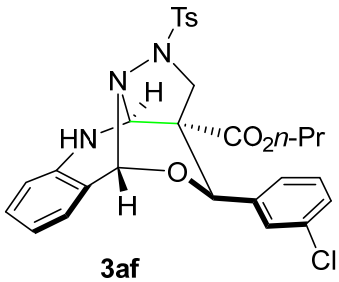


3ae









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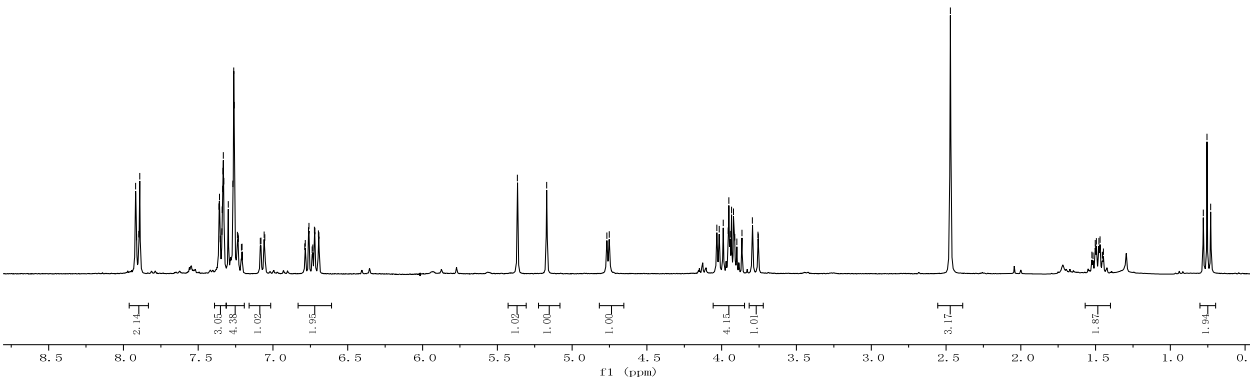

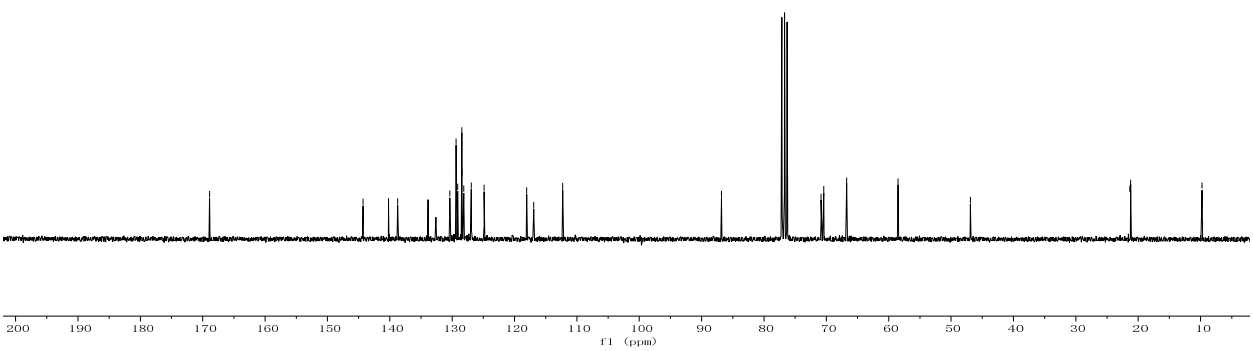

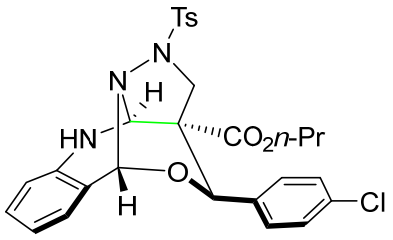

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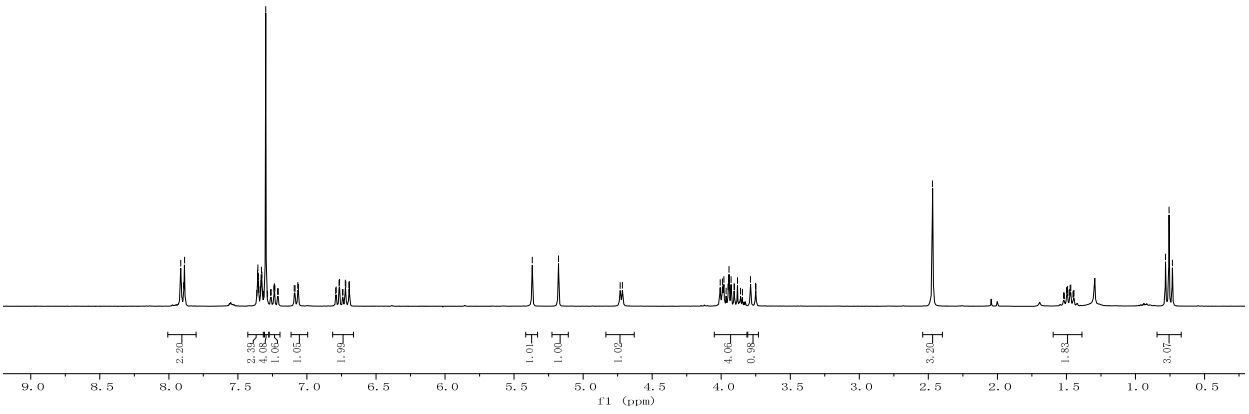
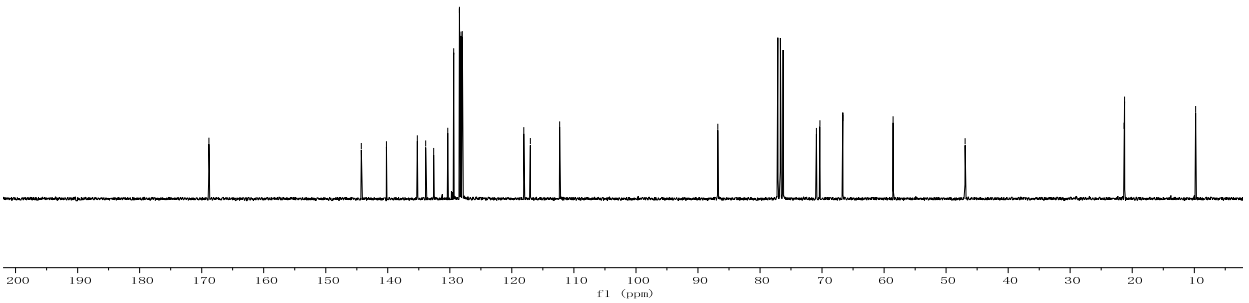
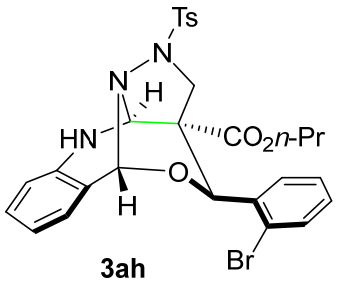
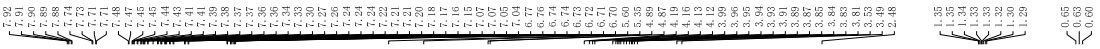
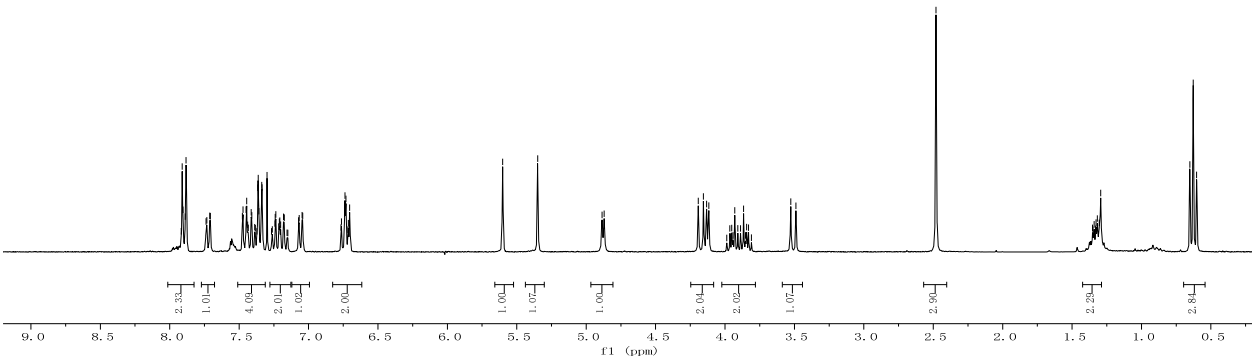


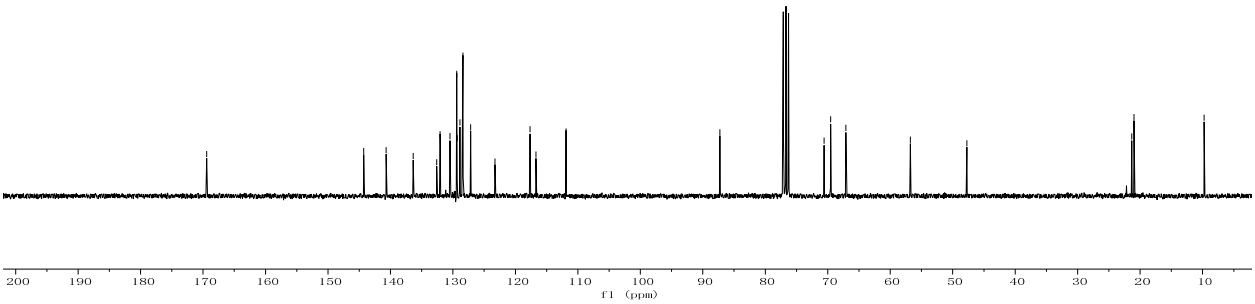


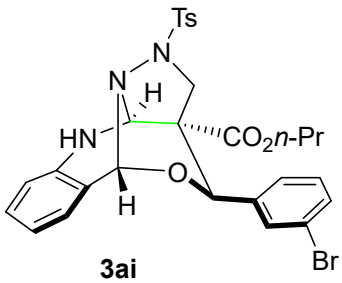

Ts
N
N
H
HN
CO2n-Pr
O
H
Br

3ah

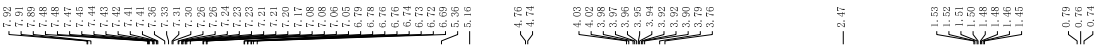


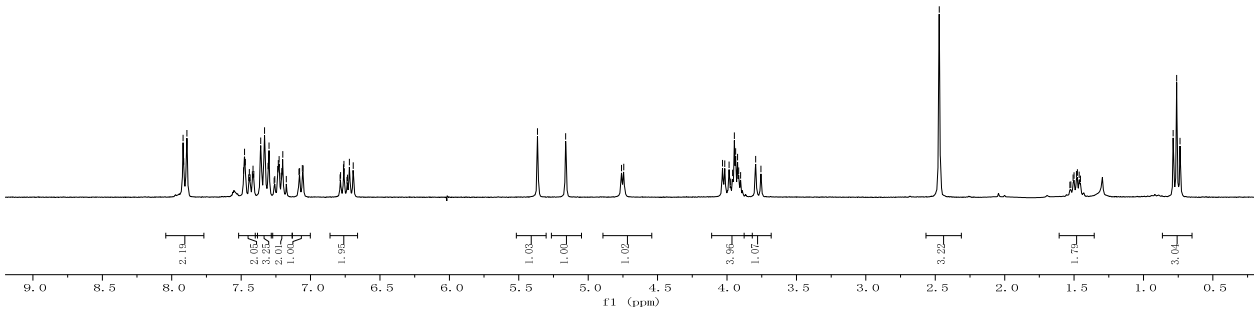

2.33
1.01
4.09
2.01
1.02
2.00
1.00
1.07
1.00
2.04
2.02
1.07
2.90
2.29
2.84
9.0
8.5
8.0
7.5
7.0
6.5
6.0
5.5
5.0
4.5
4.0
3.5
3.0
2.5
2.0
1.5
1.0
0.5
f1 (ppm)

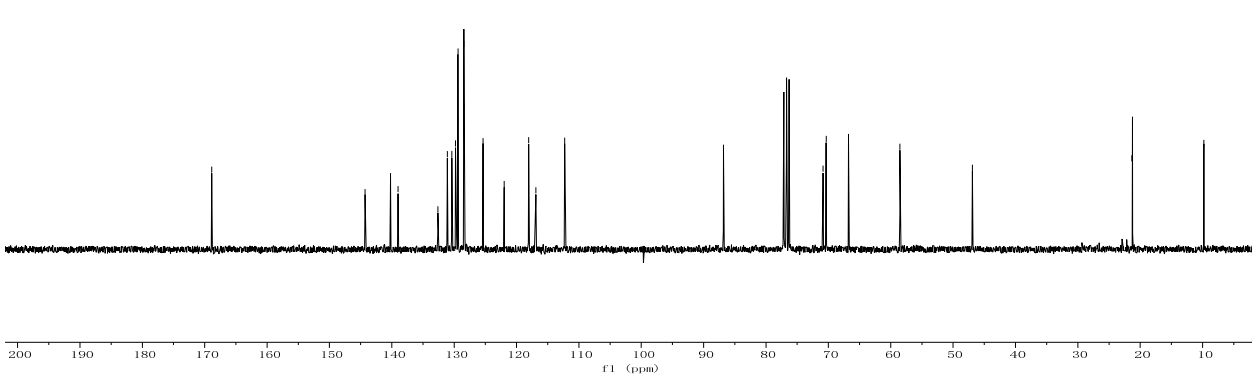

200
190
180
170
160
150
140
130
120
110
100
90
80
70
60
50
40
30
20
10
f1 (ppm)

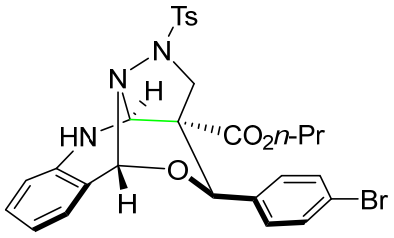


3ai









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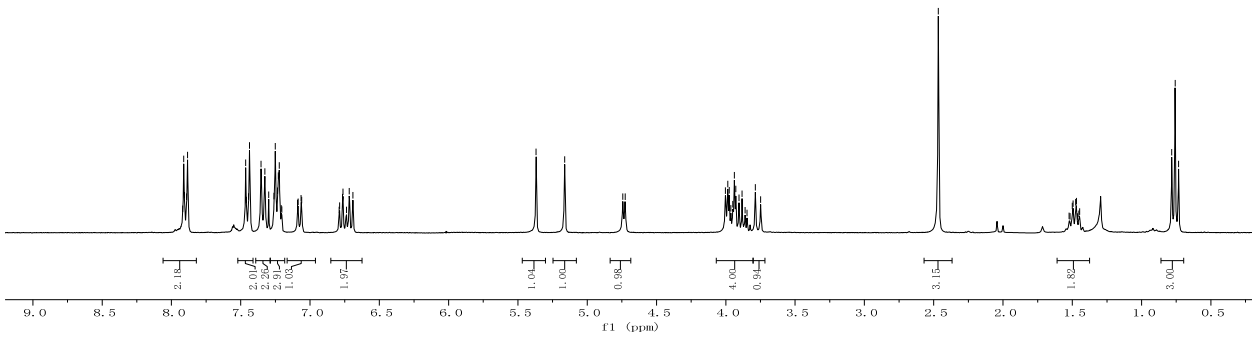
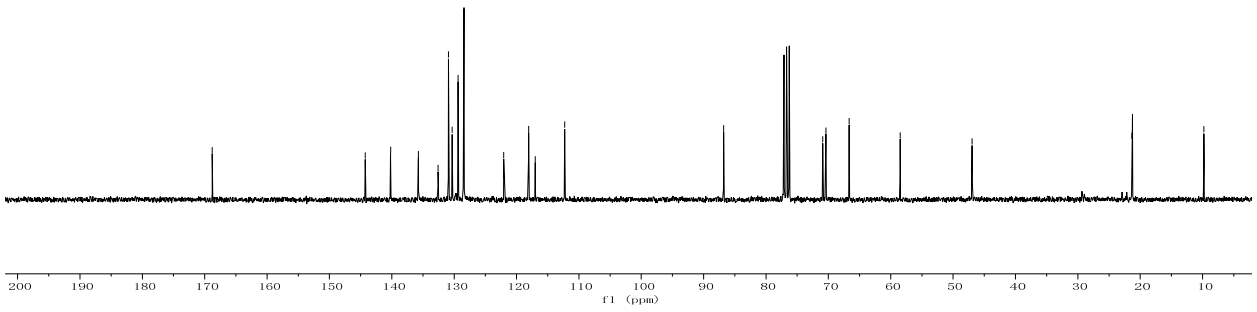
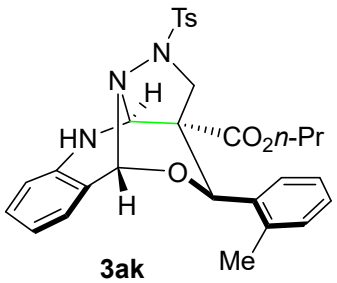
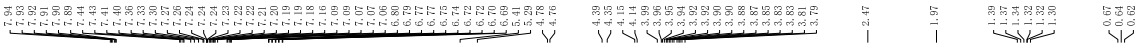
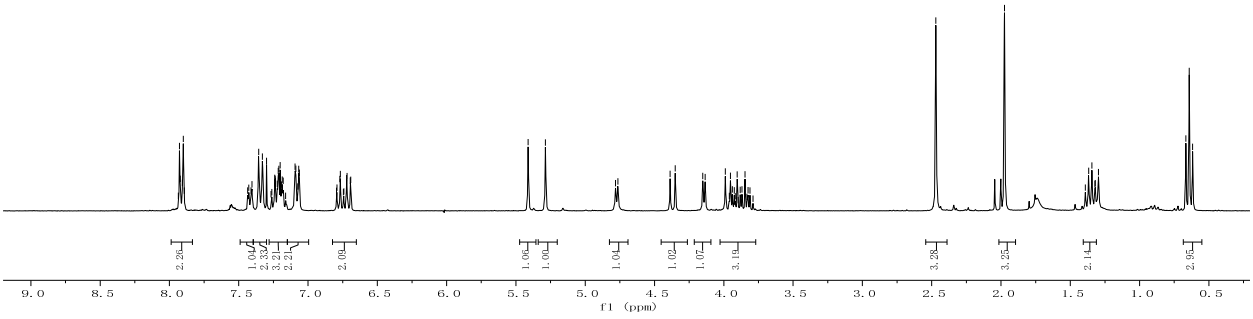




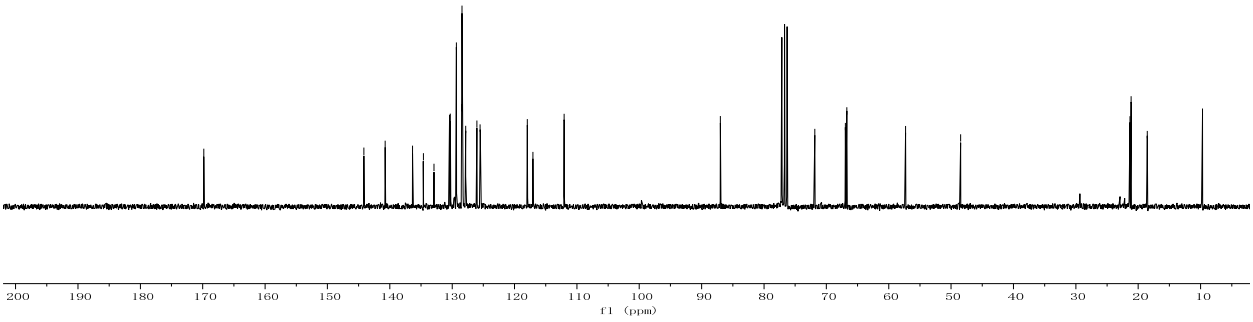

Ts
N
N
H
HN
CO2n-Pr
O
H
Me

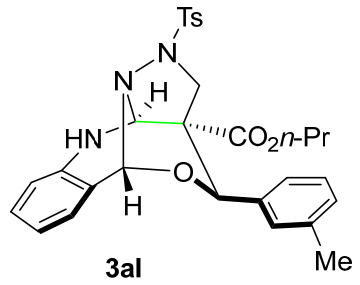
3ak



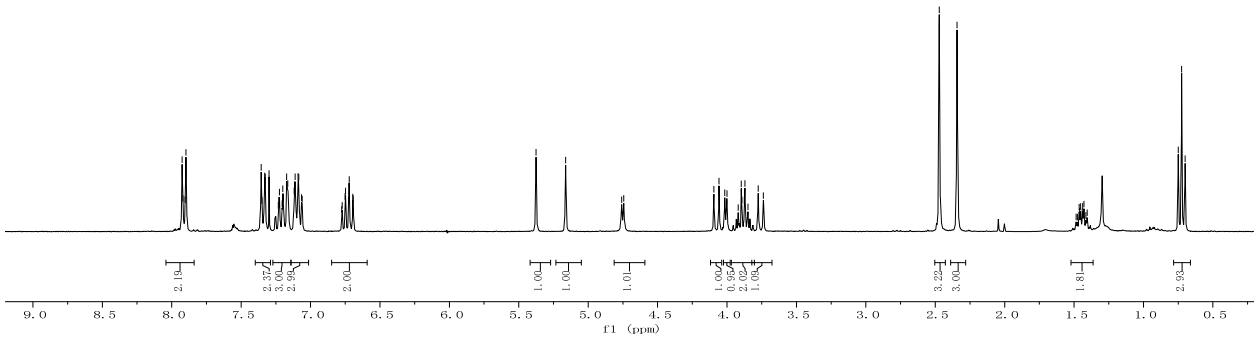

2.26
1.04
2.33
3.21
2.21
2.09
1.06
1.04
1.04
1.02
1.07
3.19
3.28
3.25
2.14
2.95
9.0
8.5
8.0
7.5
7.0
6.5
6.0
5.5
5.0
4.5
4.0
3.5
3.0
2.5
2.0
1.5
1.0
0.5
f1 (ppm)

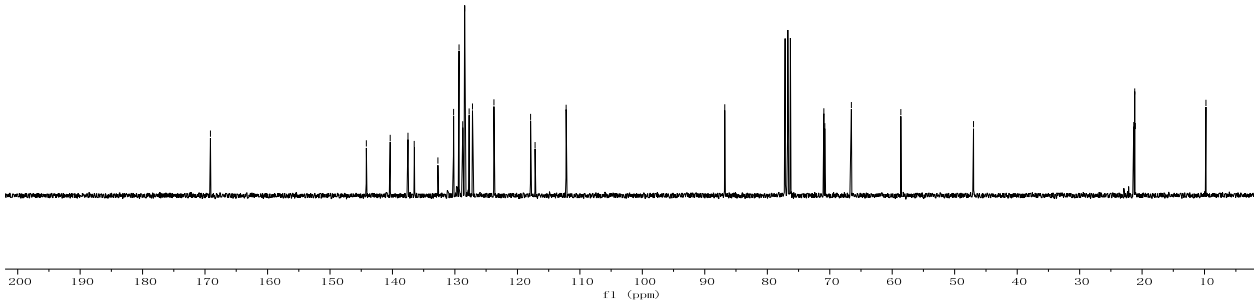

zhoulijie-13C4-34
13C NMR of 43-2-Me-MBH
169.82
144.16
140.74
136.37
134.62
132.93
130.43
130.29
129.33
128.48
128.43
127.84
126.05
125.51
117.04
111.04
112.05
87.00
71.85
66.96
66.72
57.31
48.48
21.32
21.13
18.55
9.69

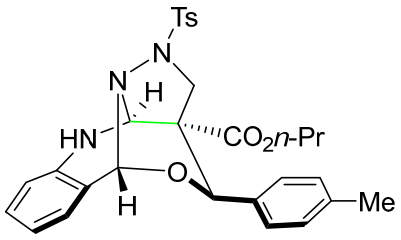

200
190
180
170
160
150
140
130
120
110
100
90
80
70
60
50
40
30
20
10
f1 (ppm)



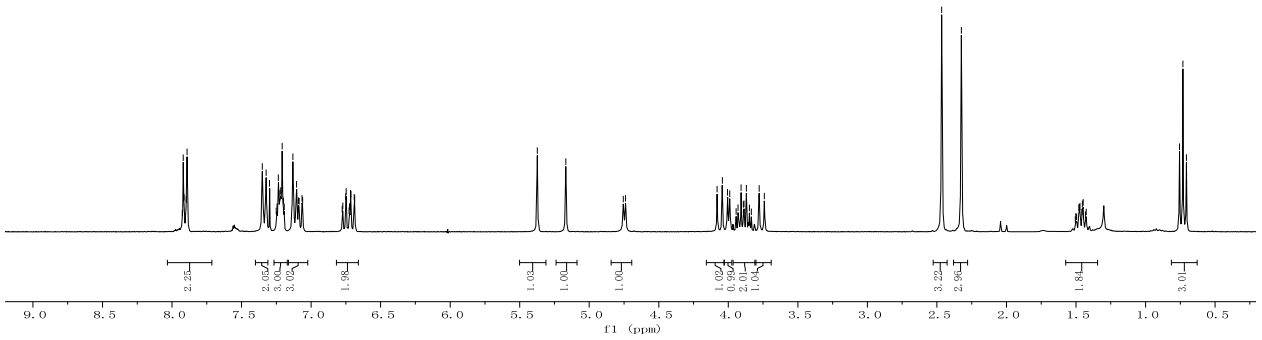
3al

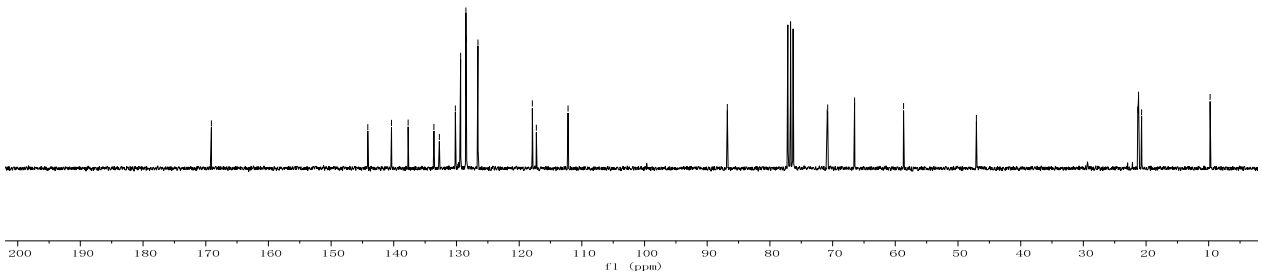


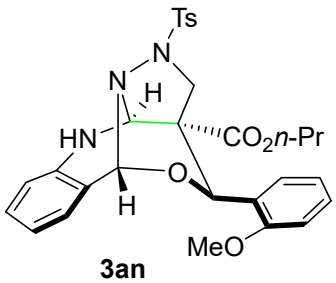




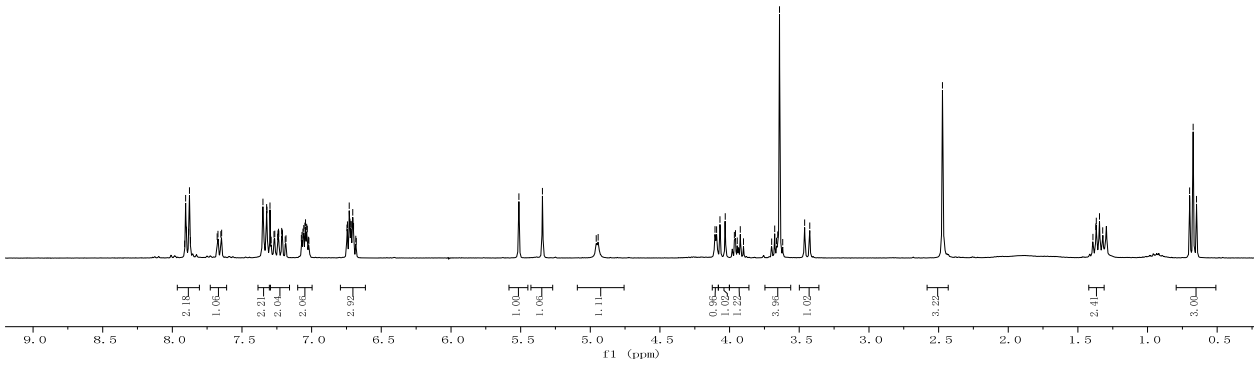
3am

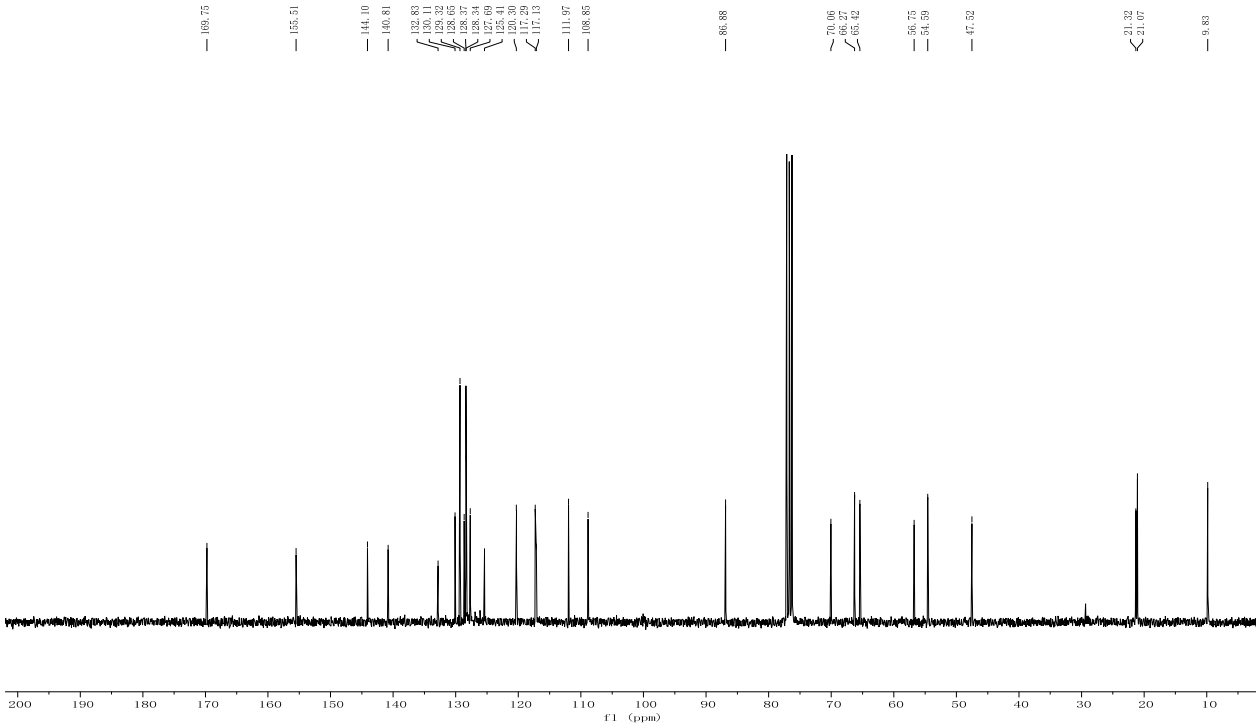


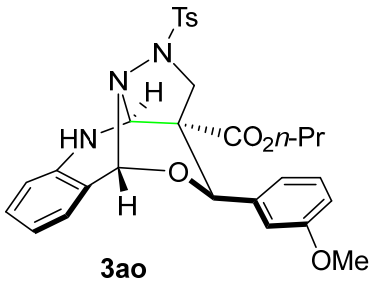



Ts
N
N
H
HN
CO2n-Pr
O
H
MeO

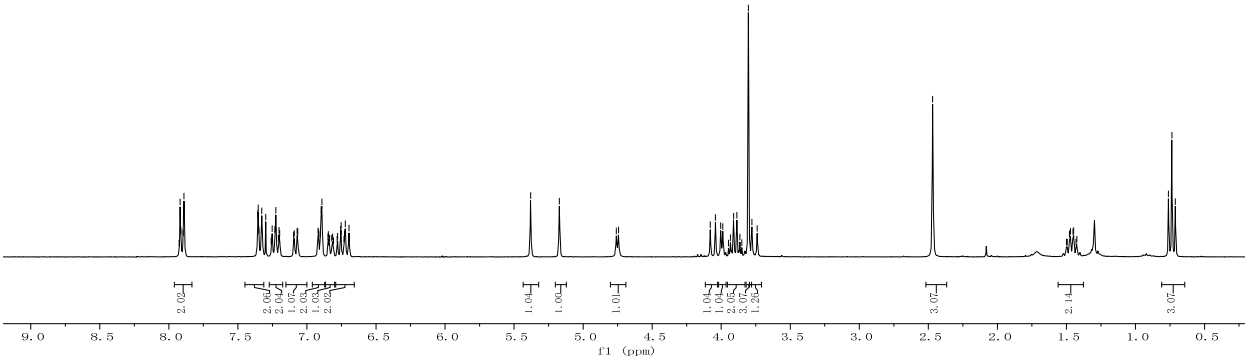
3an

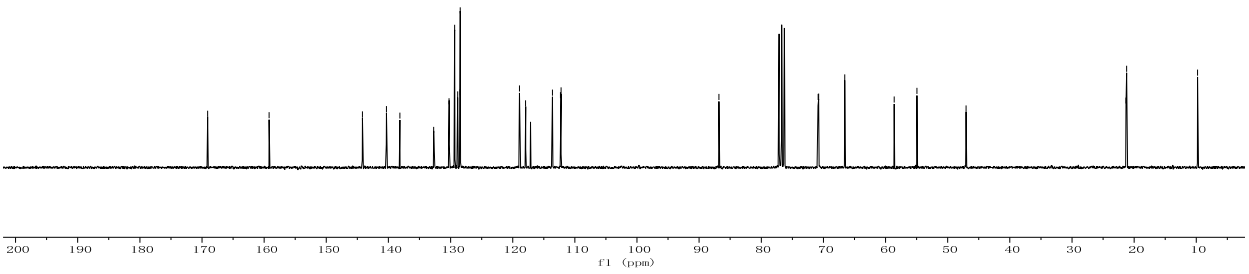

2.18
1.06
2.21
2.04
2.06
2.92
1.00
1.06
1.11
0.96
1.02
1.22
3.96
1.02
3.22
2.41
3.00
9.0
8.5
8.0
7.5
7.0
6.5
6.0
5.5
5.0
4.5
4.0
3.5
3.0
2.5
2.0
1.5
1.0
0.5
f1 (ppm)

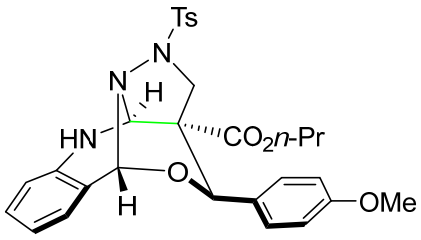

169.75
155.51
144.10
140.81
132.83
130.11
129.32
128.65
128.37
128.34
127.69
125.41
120.30
117.29
117.13
111.97
108.85
86.88
70.06
66.27
65.42
56.75
54.69
47.52
21.32
21.07
9.83
200
190
180
170
160
150
140
130
120
110
100
90
80
70
60
50
40
30
20
10
f1 (ppm)



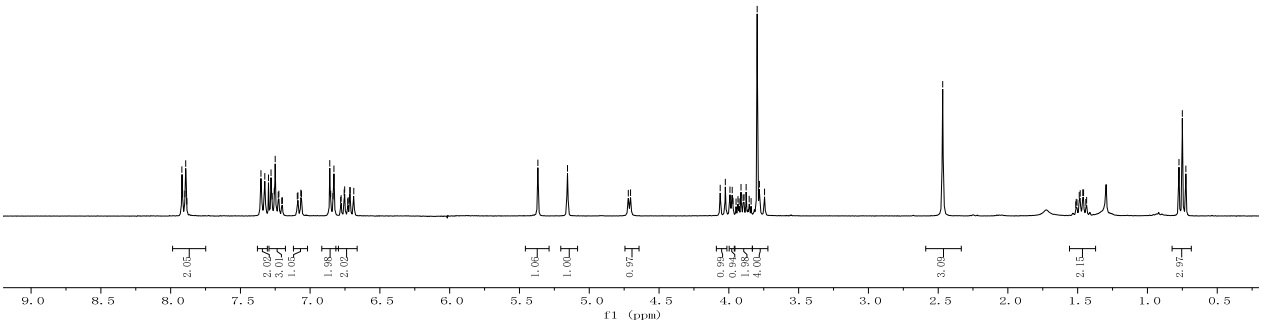
3ao

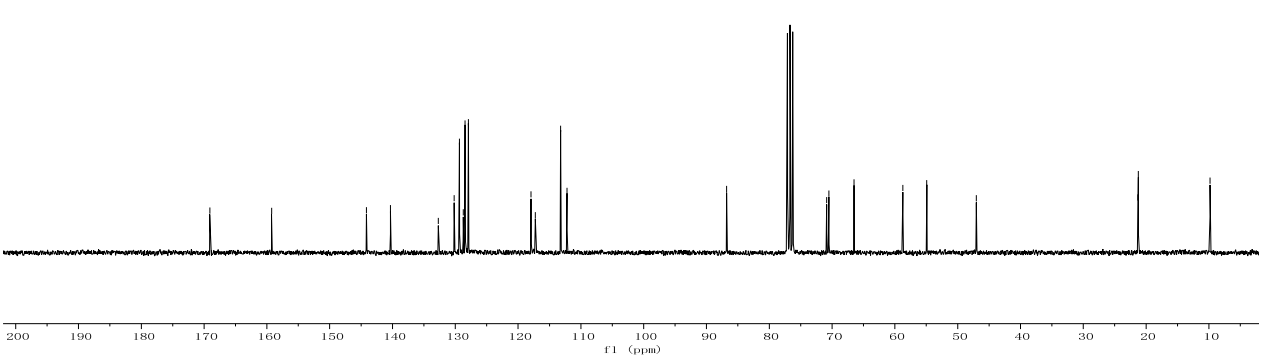


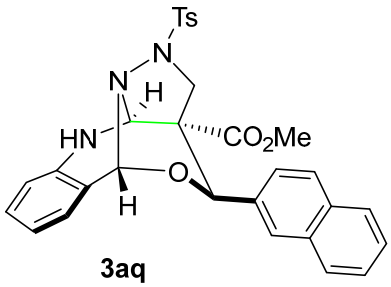




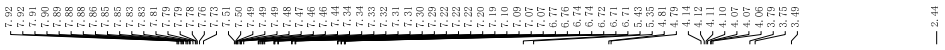
3ap

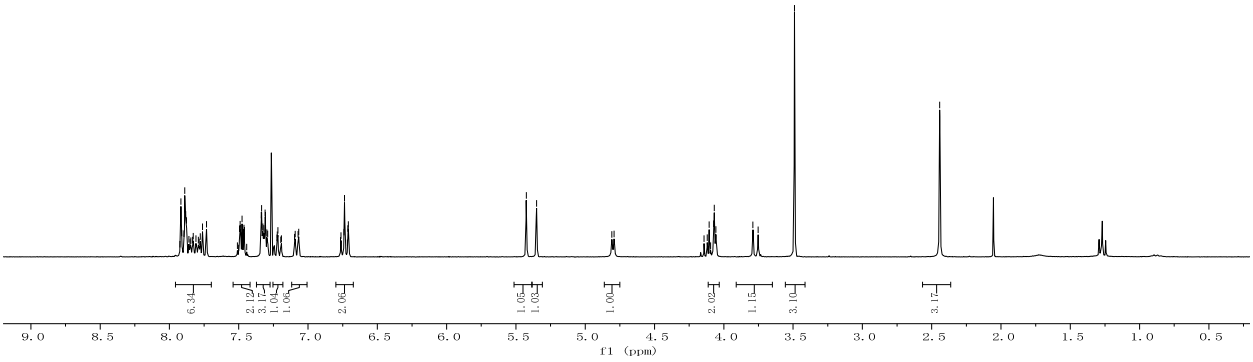


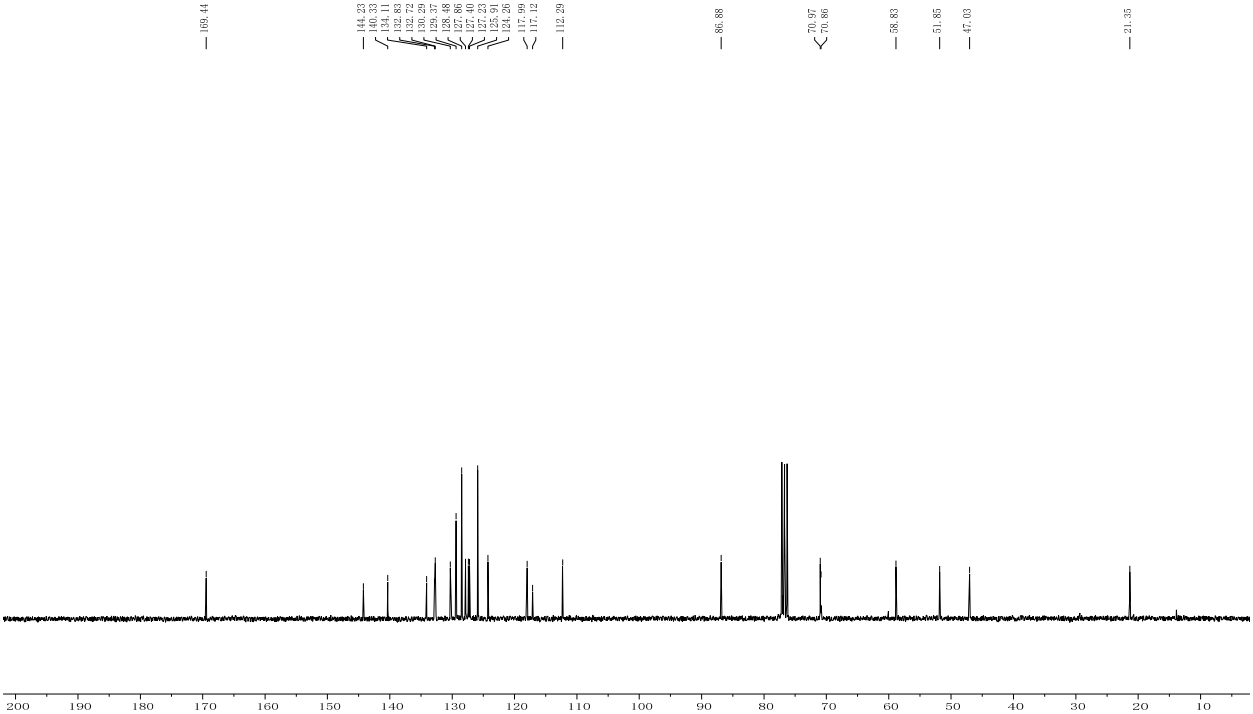


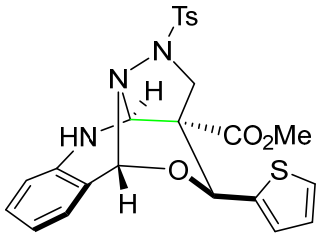

Ts
N
N
H
HN
CO2Me
O
H

3aq

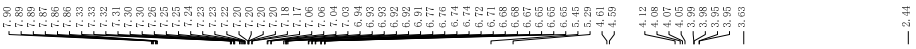


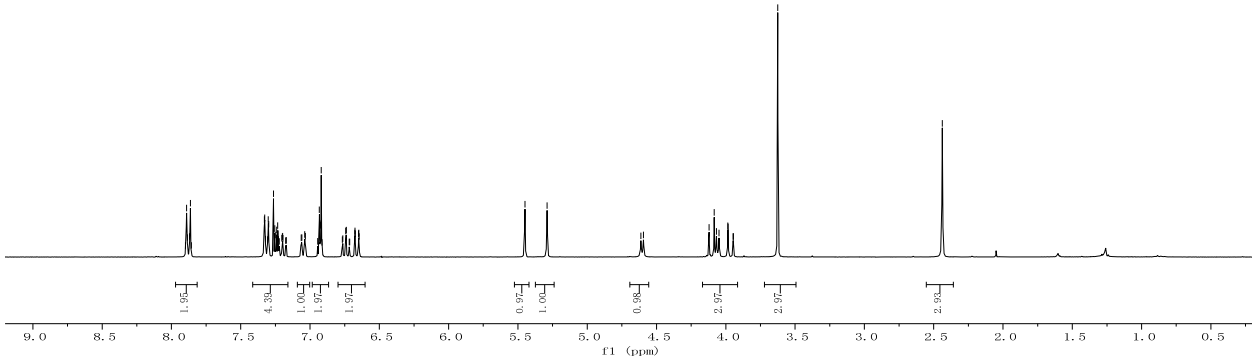

6.34
2.19
3.17
1.04
1.08
2.06
1.05
1.03
1.00
2.02
1.15
3.10
3.17
9.0
8.5
8.0
7.5
7.0
6.5
6.0
5.5
5.0
4.5
4.0
3.5
3.0
2.5
2.0
1.5
1.0
0.5
f1 (ppm)

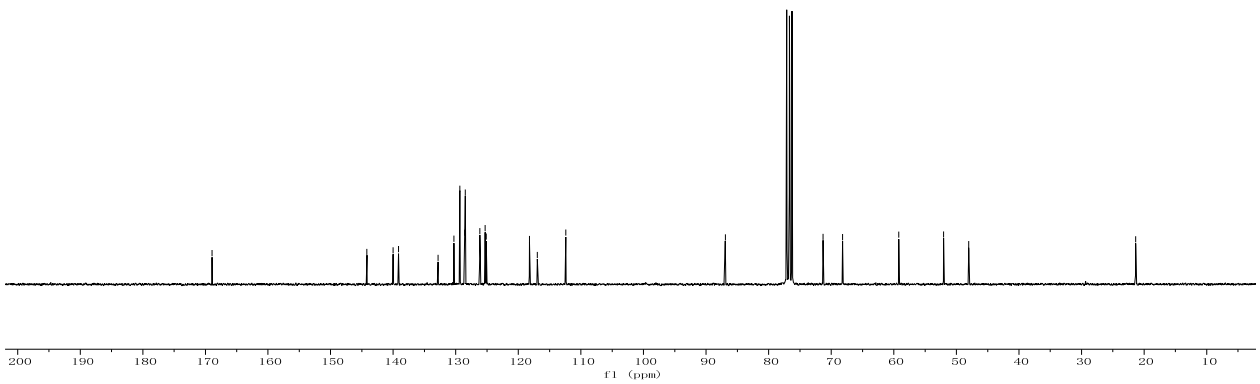

200
190
180
170
160
150
140
130
120
110
100
90
80
70
60
50
40
30
20
10
f1 (ppm)

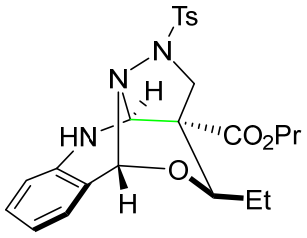

Ts
N
N
H
HN
CO2Me
O
S
H

3ar

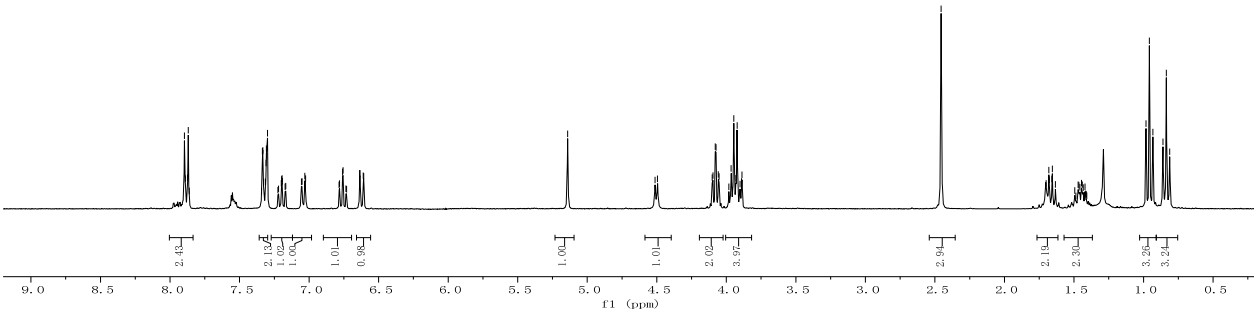


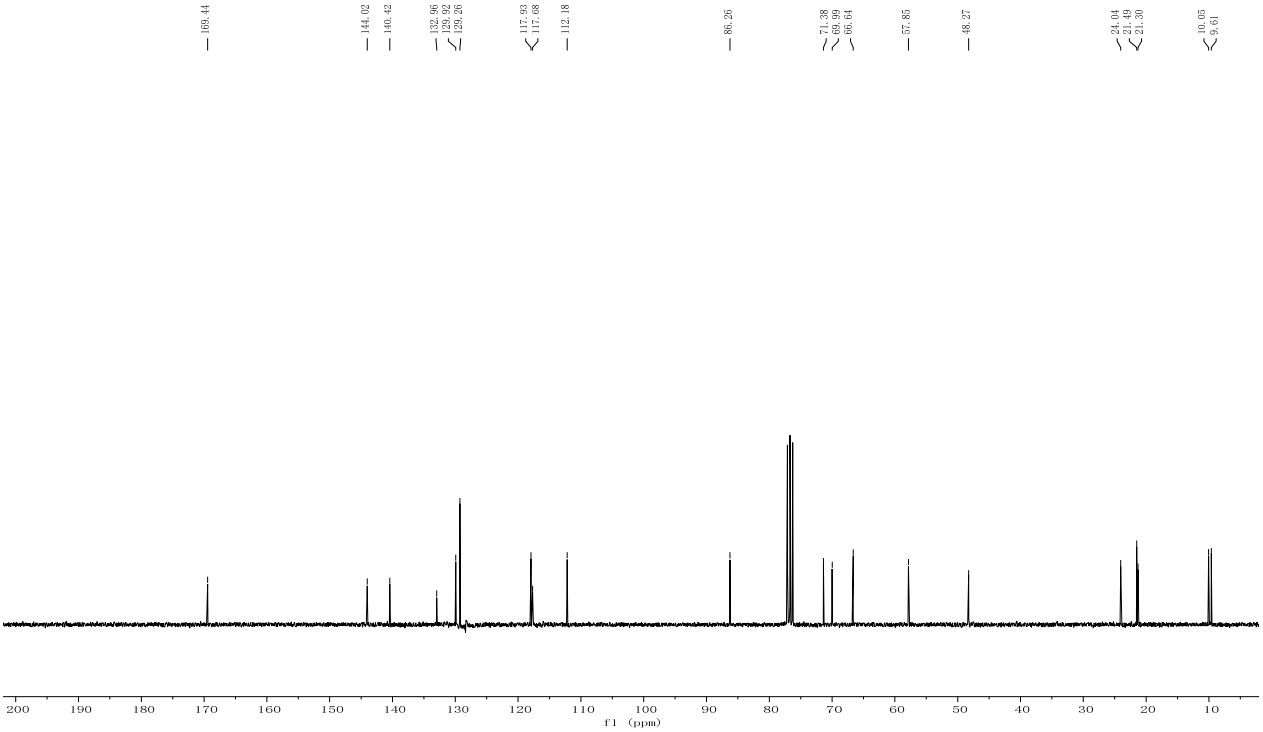

1.95
4.39
1.00
1.97
1.97
0.97
1.00
0.98
2.97
2.97
2.93
f1 (ppm)


f1 (ppm)


Ts
N
N
H
HN
CO2Pr
O
H
Et

3as


2.43
2.10
1.02
1.06
1.01
0.98
1.00
1.01
2.02
3.97
2.94
2.19
2.30
3.26
3.24
f1 (ppm)


169.44
144.02
140.42
132.96
129.52
129.26
117.93
117.68
112.18
86.26
71.38
68.99
66.64
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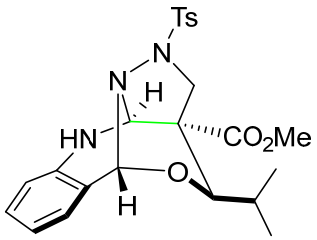
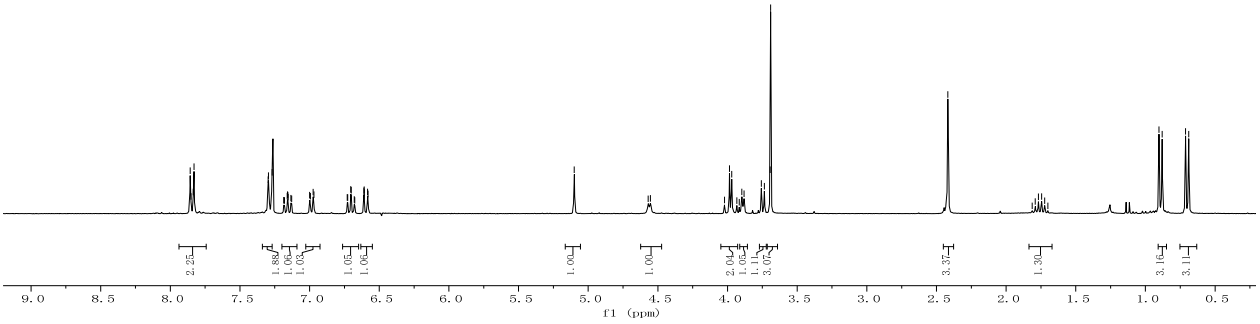
24.04
21.49
21.30
10.05
9.61
f1 (ppm)


Ts
N
N
H
HN
CO2Me
O
H

3at


7.86
7.85
7.84
7.83
7.30
7.27
7.19
7.18
7.16
7.16
7.15
7.15
7.13
7.00
6.99
6.97
6.73
6.70
6.70
6.68
6.68
6.61
6.61
6.61
6.58
6.58
5.10
4.57
4.55
4.02
3.99
3.97
3.93
3.92
3.90
3.88
3.76
3.74
3.69
3.69
2.42
1.81
1.79
1.77
1.75
1.72
1.70
0.90
0.88
0.71
0.69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1.89
1.06
1.03
1.05
1.06
1.00
1.00
2.04
1.05
1.12
3.05
3.37
1.30
3.16
3.11
9.0
8.5
8.0
7.5
7.0
6.5
6.0
5.5
5.0
4.5
4.0
3.5
3.0
2.5
2.0
1.5
1.0
0.5
f1 (ppm)


170.43
144.00
140.44
132.97
129.89
129.24
128.42
128.12
117.74
117.53
111.98
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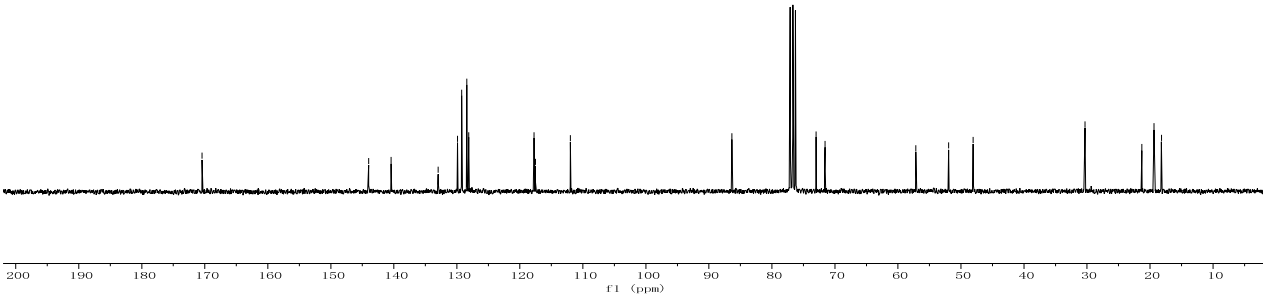
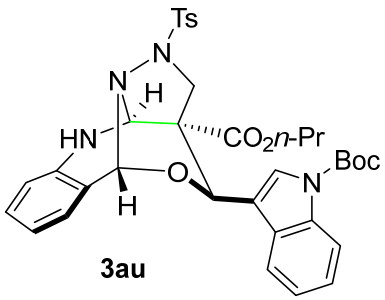
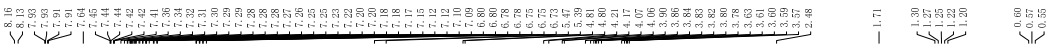
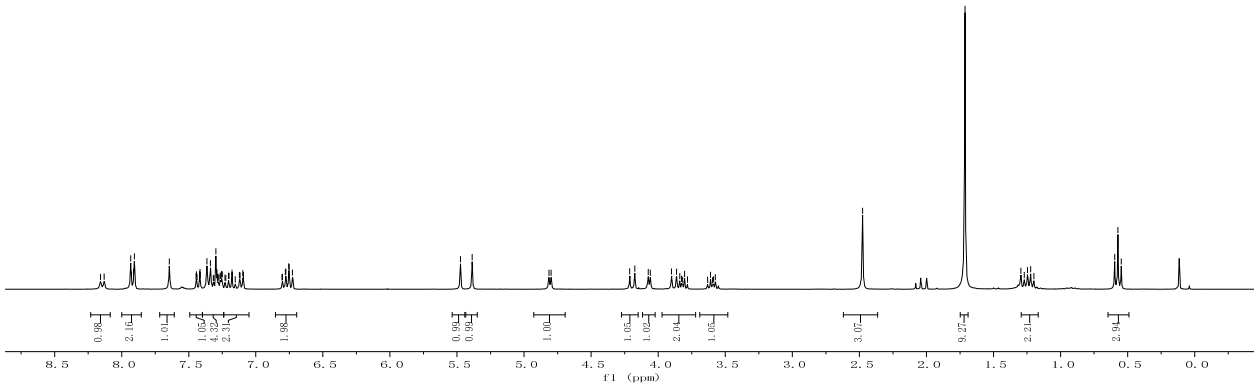
51.96
48.07
30.32
21.31
19.36
18.19

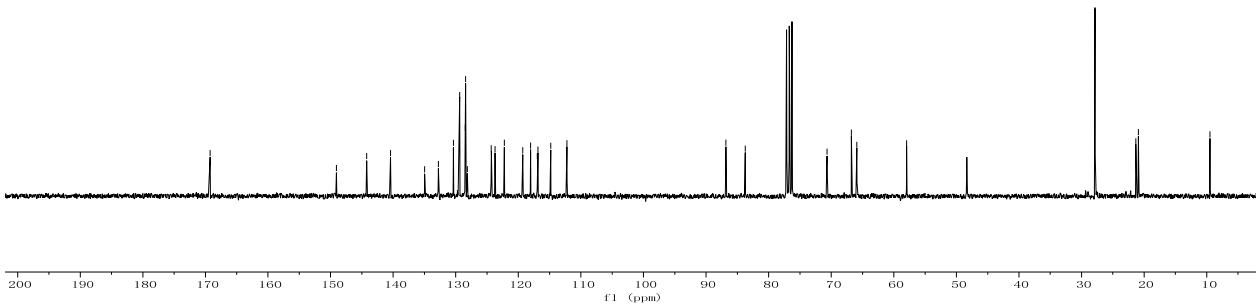

200
190
180
170
160
150
140
130
120
110
100
90
80
70
60
50
40
30
20
10
f1 (ppm)

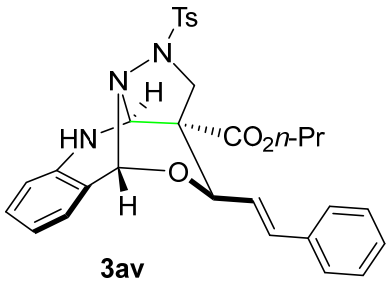


3au

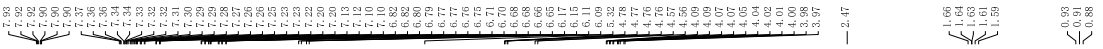


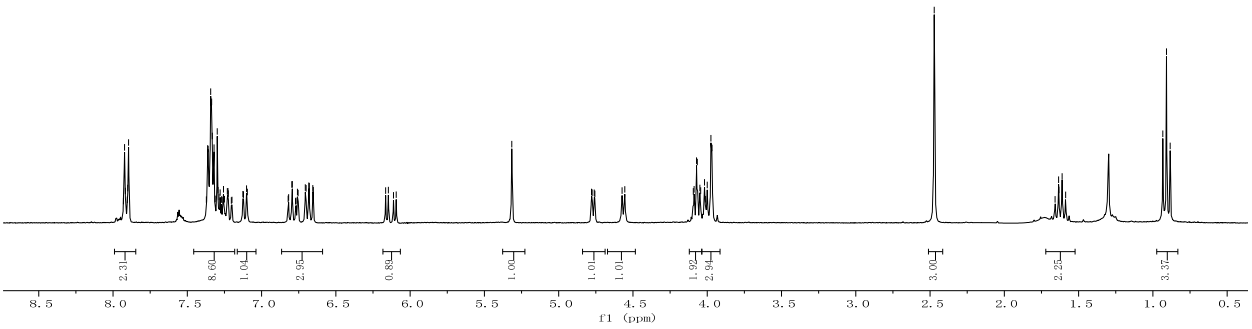


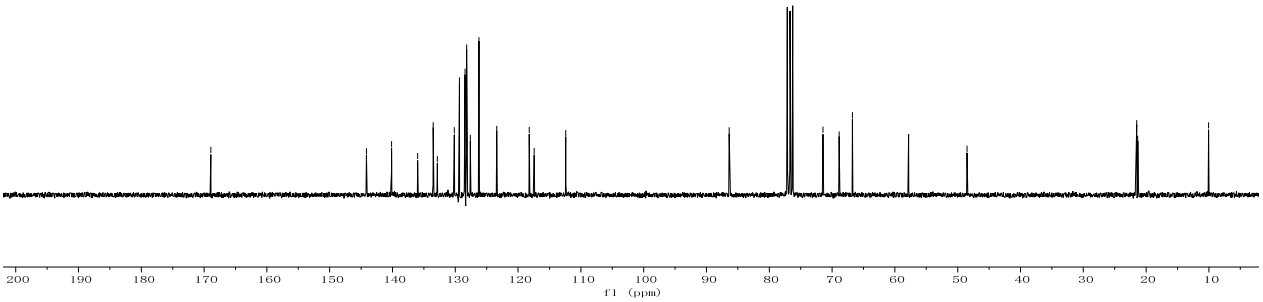


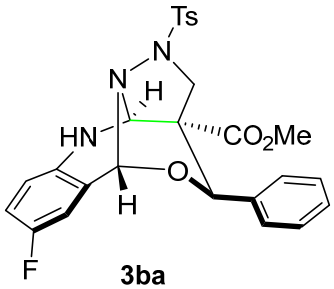


3av



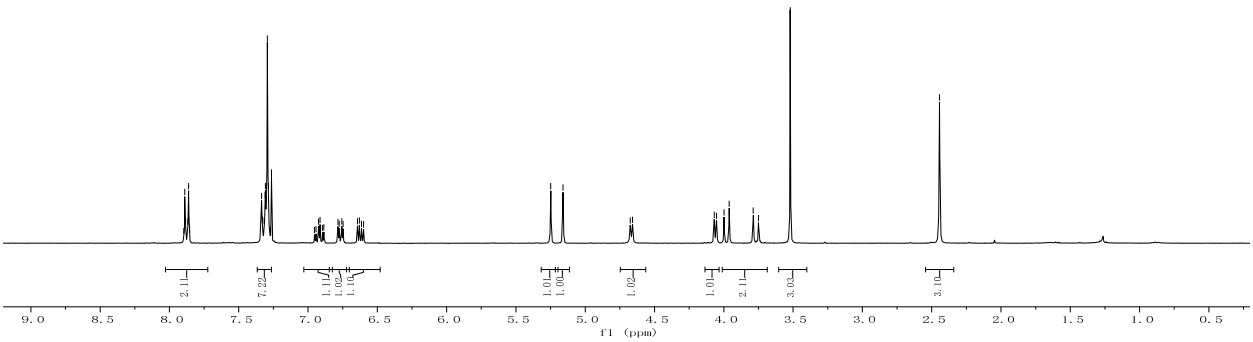


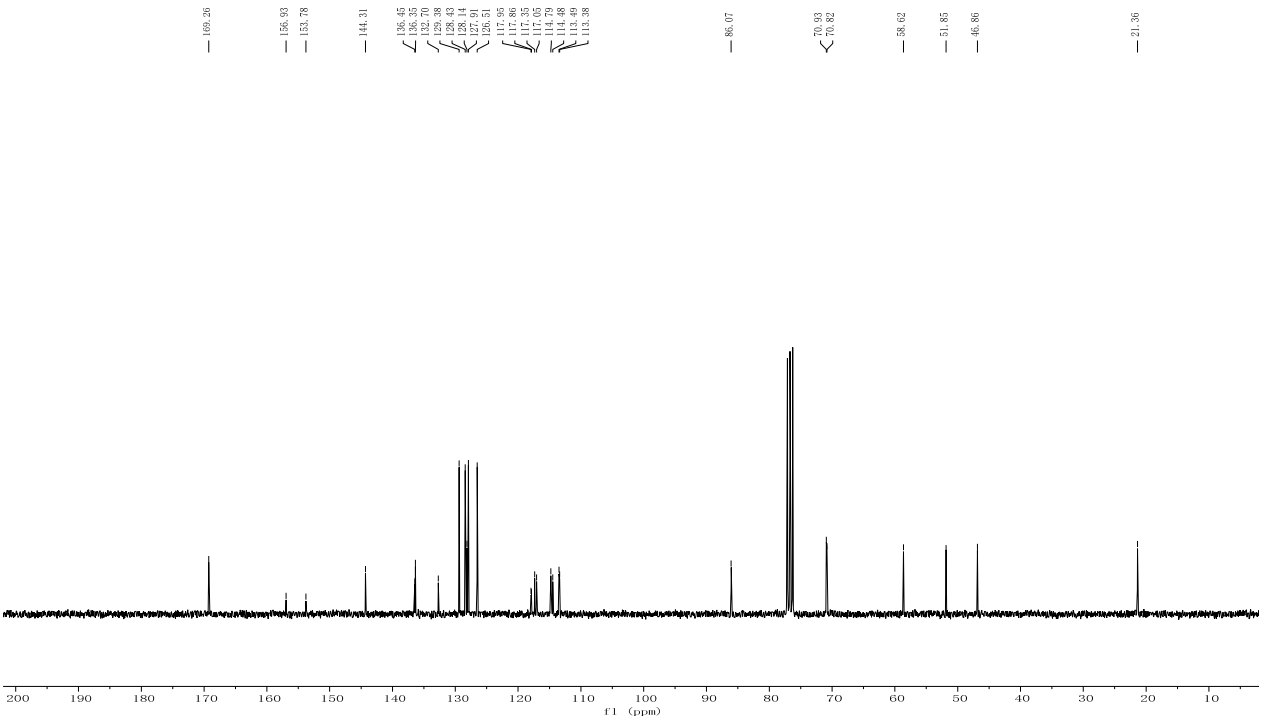


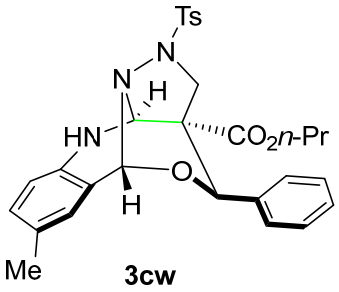

Ts
N
N
H
HN
CO2Me
O
H
F

3ba

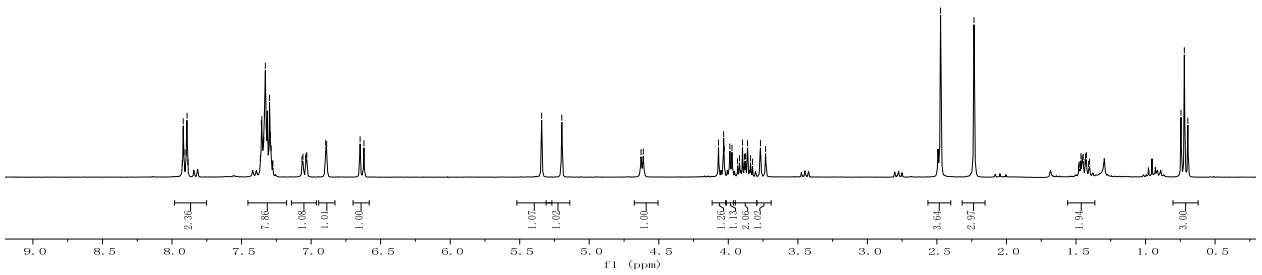

7.90
7.89
7.88
7.87
7.86
7.85
7.34
7.33
7.32
7.31
7.31
7.30
7.29
7.29
7.27
7.26
6.95
6.94
6.92
6.91
6.90
6.89
6.78
6.77
6.76
6.75
6.64
6.63
6.61
6.60
5.25
5.16
4.68
4.66
4.07
4.05
4.00
3.96
3.79
3.75
3.52
2.44

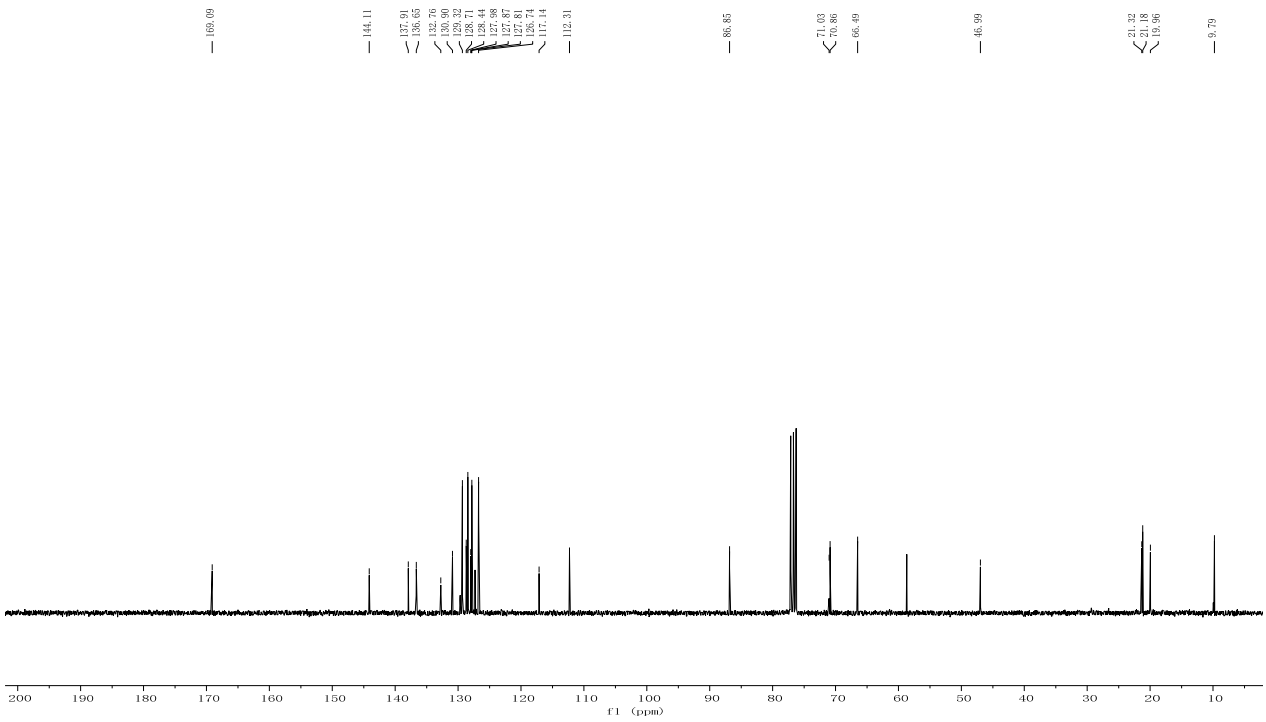

2.11
7.22
1.11
1.02
1.10
1.01
1.00
1.02
1.01
2.11
3.03
3.10
9.0
8.5
8.0
7.5
7.0
6.5
6.0
5.5
5.0
4.5
4.0
3.5
3.0
2.5
2.0
1.5
1.0
0.5
f1 (ppm)

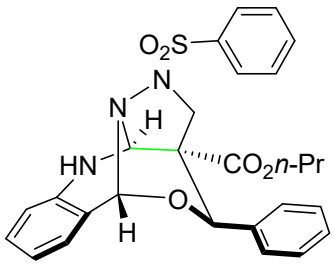

169.26
156.93
153.78
144.31
136.45
136.35
132.70
129.38
128.43
128.14
127.91
126.51
117.95
117.86
117.35
117.05
114.79
114.48
113.49
113.38
86.07
70.93
70.82
58.62
51.85
46.86
21.36
200
190
180
170
160
150
140
130
120
110
100
90
80
70
60
50
40
30
20
10
f1 (ppm)



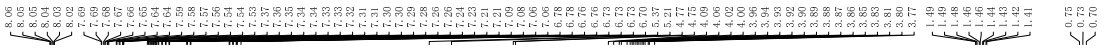
3cw

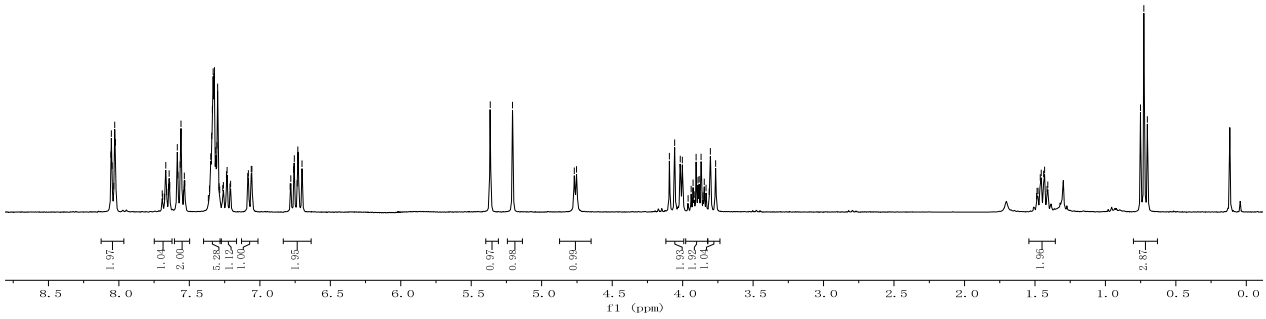





O2S
N
N
H
HN
CO2n-Pr
O
H

3dw

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1.92
1.06
1.96
2.87
f1 (ppm)


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140.30
136.57
135.72
133.24
130.28
129.09
128.46
128.43
128.05
127.86
126.68
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117.10
112.25
86.78
70.91
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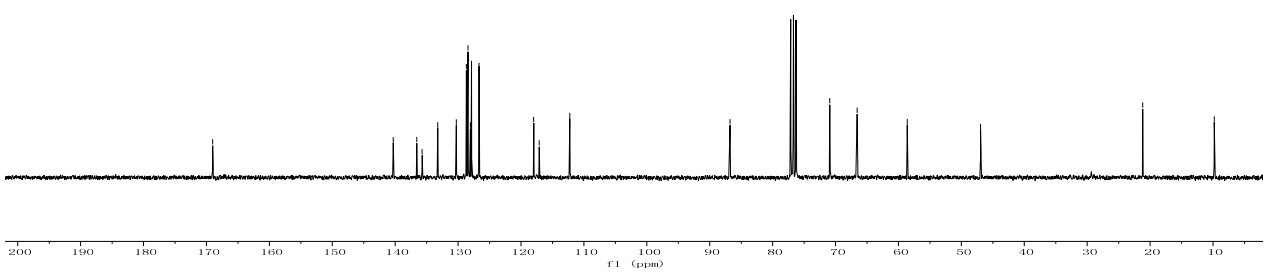
58.60
46.95
21.18
9.81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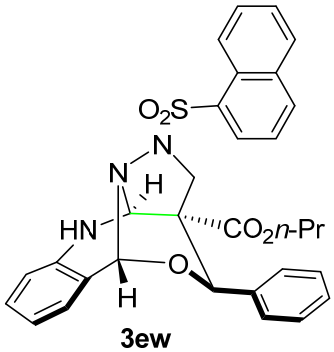
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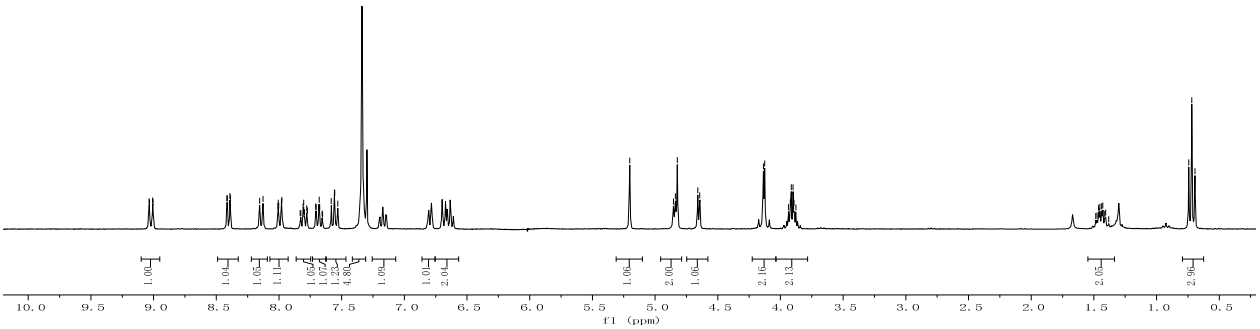
N
N
H
HN
CO2n-Pr
O
H

3ew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2.04
1.06
2.00
1.06
2.16
2.13
2.05
2.96
10.0
9.5
9.0
8.5
8.0
7.5
7.0
6.5
6.0
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3.0
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2.0
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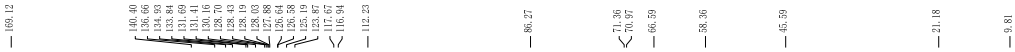
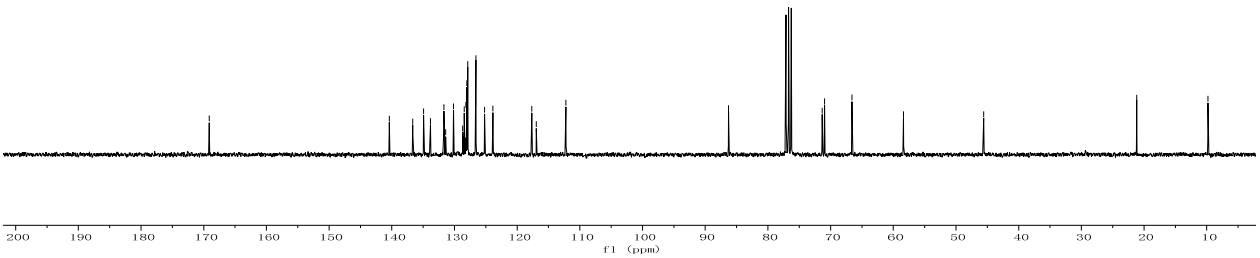
1.0
0.5
f1 (ppm)

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80
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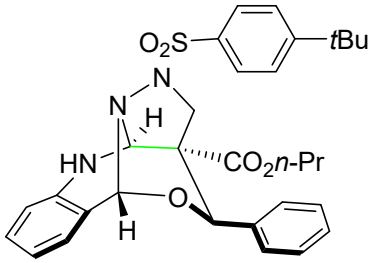
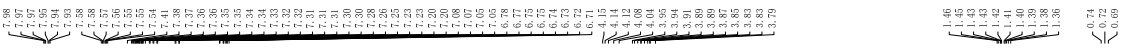
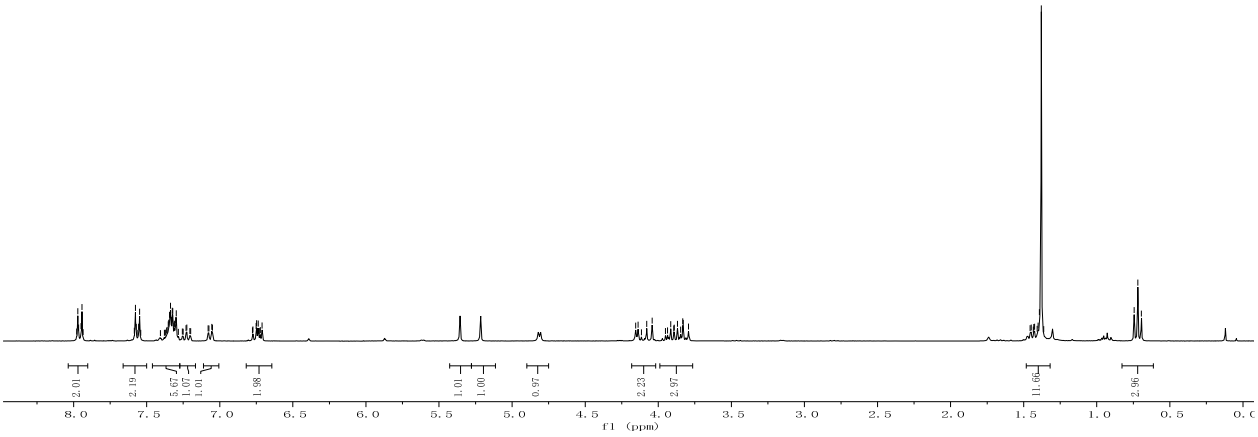
20
10
f1 (ppm)


O2S
tBu
N
N
H
HN
CO2n-Pr
O
H

3fw

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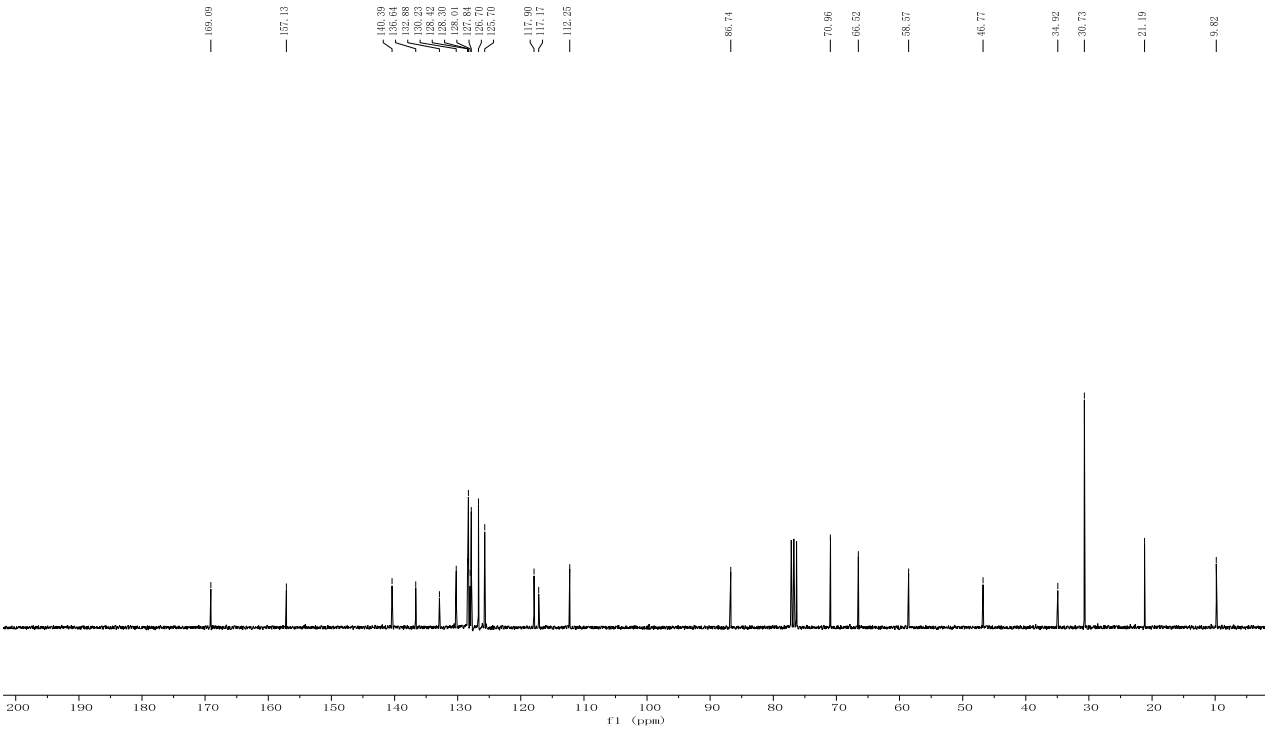
f1 (ppm)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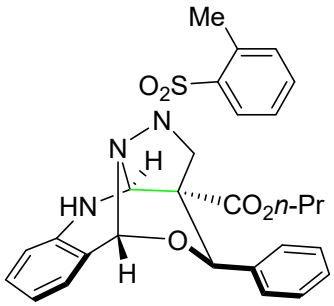
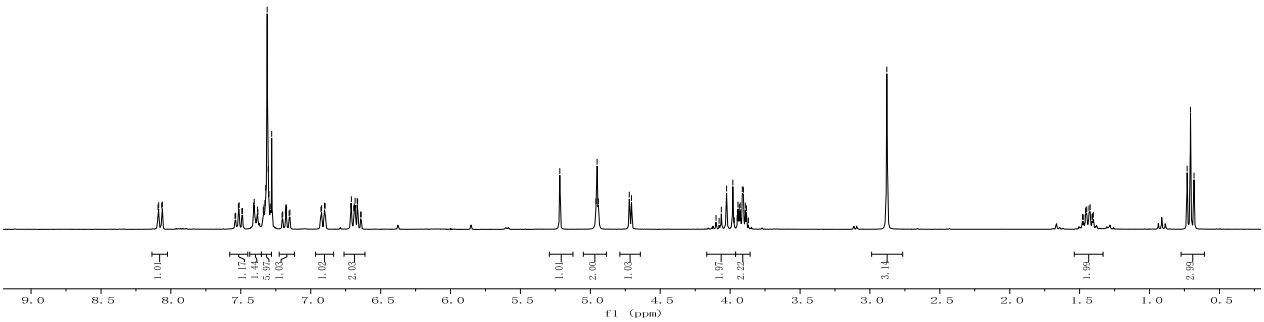
9.82
f1 (ppm)


Me
O2S
N
N
H
HN
CO2n-Pr
O
H

3gw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1.03
1.97
2.22
3.14
1.99
2.99
9.0
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8.0
7.5
7.0
6.5
6.0
5.5
5.0
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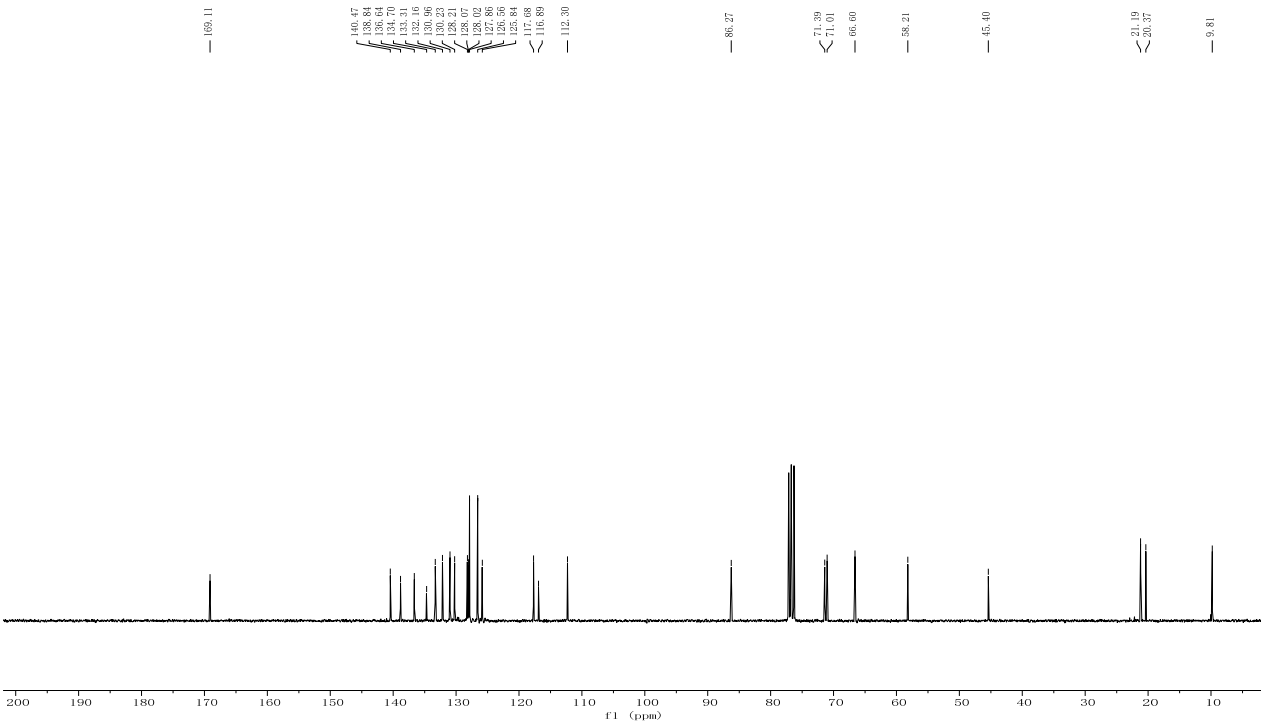
4.0
3.5
3.0
2.5
2.0
1.5
1.0
0.5
f1 (ppm)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125.84
117.68
116.89
112.30
86.27
71.39
71.01
66.60
58.21
45.40
21.19
20.37
9.81
200
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60
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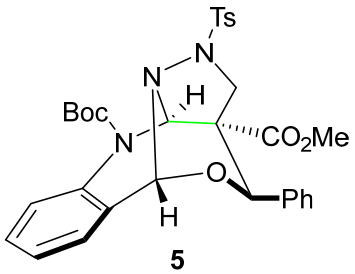
20
10
f1 (ppm)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N
N
H
Boc
N
CO2Me
O
Ph
H

5


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7.41
7.39
7.38
7.38
7.37
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7.35
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7.07
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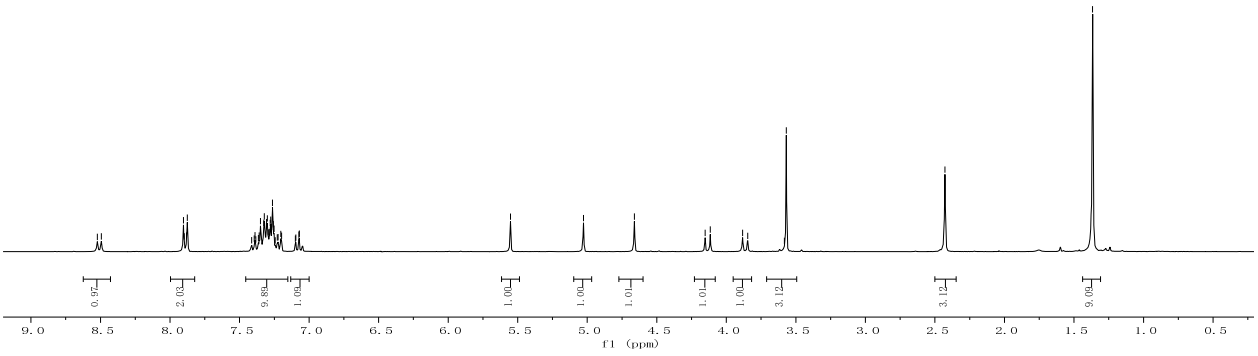
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1.01
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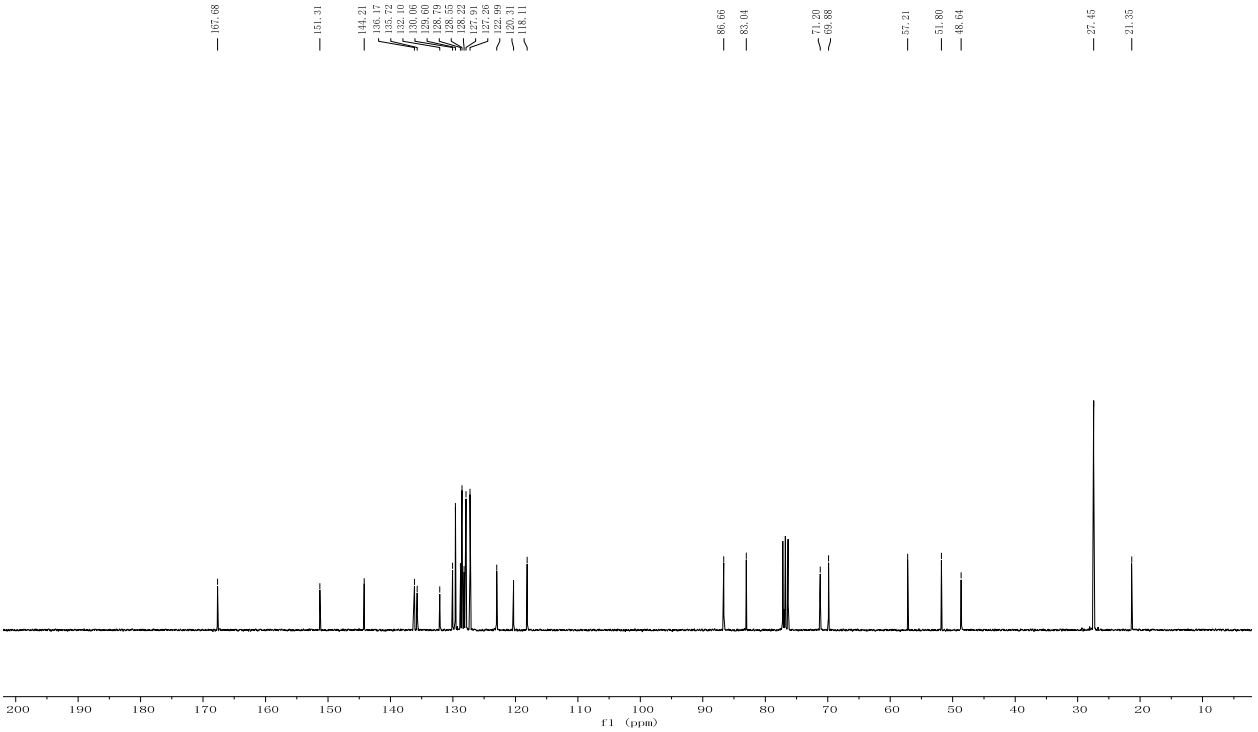
1.0
0.5
f1 (ppm)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120.31
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86.66
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71.20
69.88
57.21
51.80
48.64
27.45
21.35
200
190
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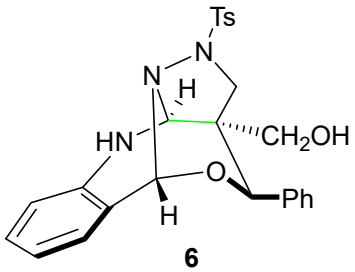
f1 (ppm)



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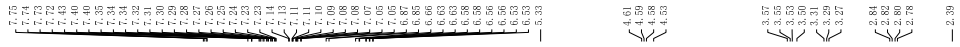

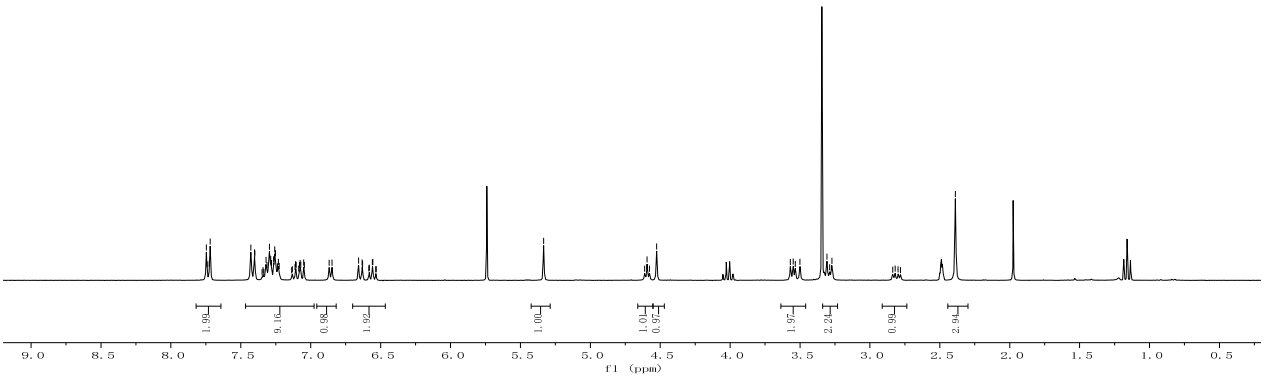

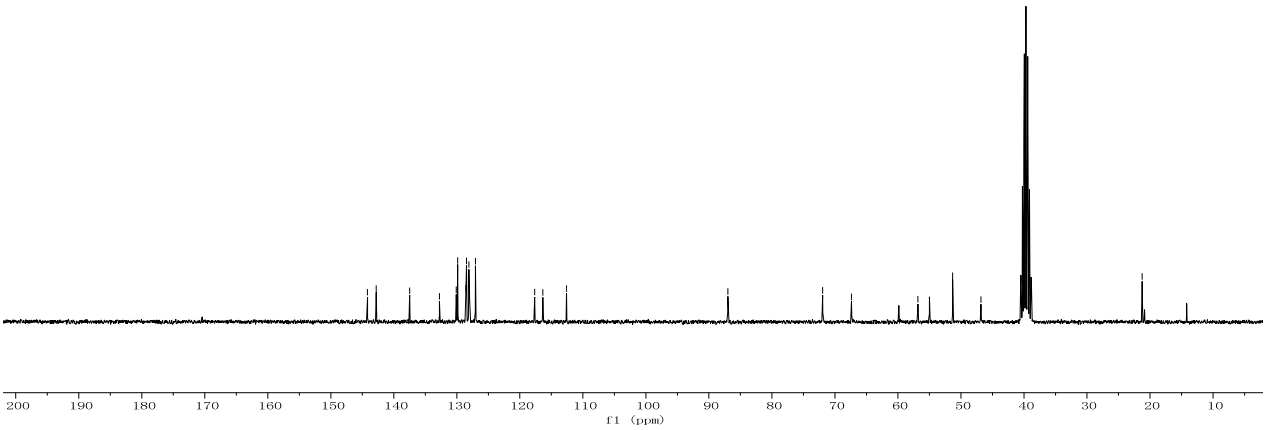

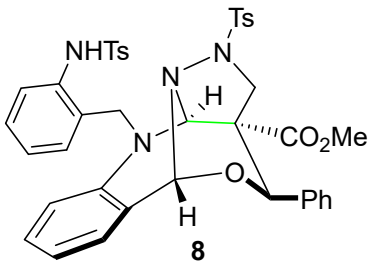

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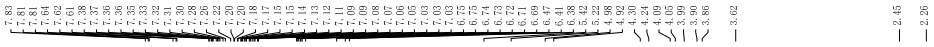
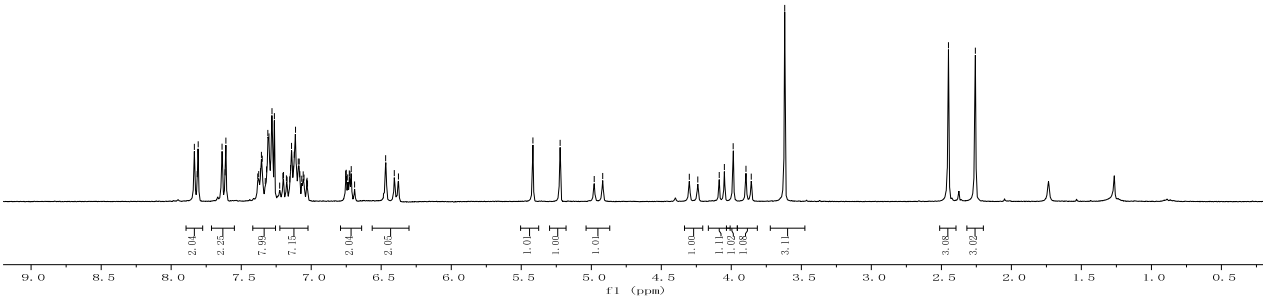
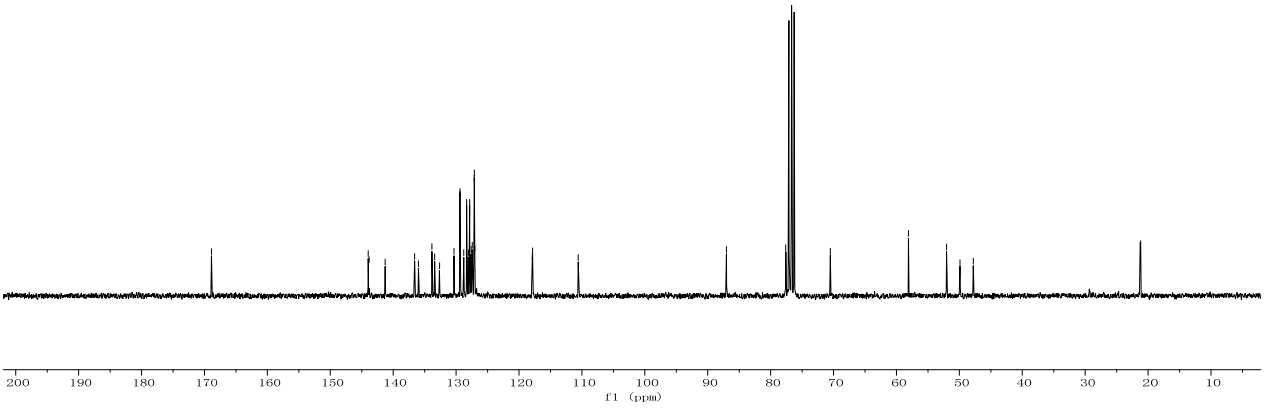
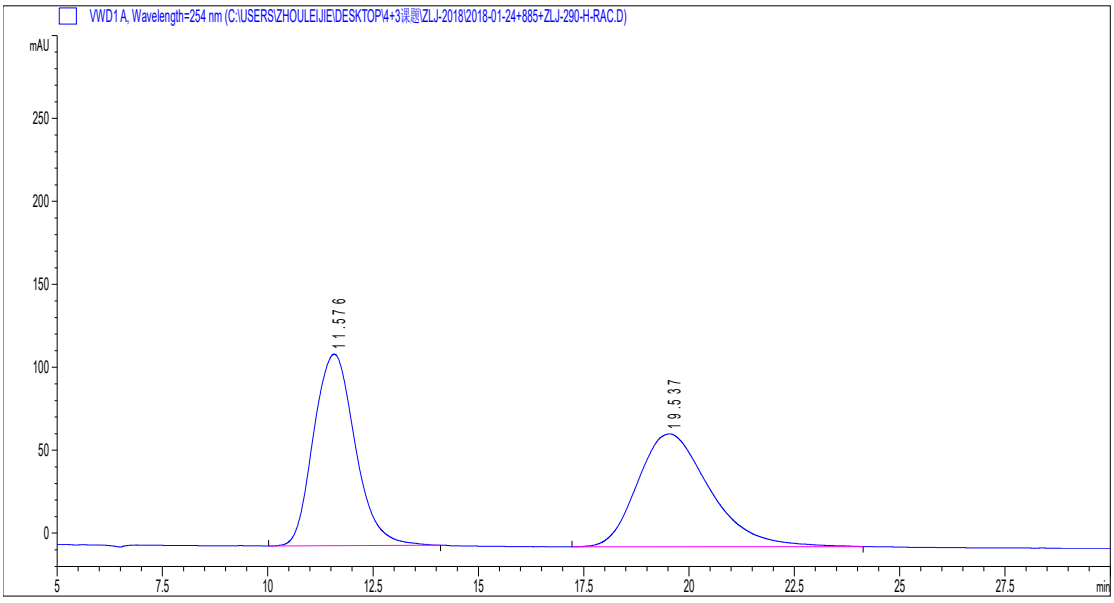




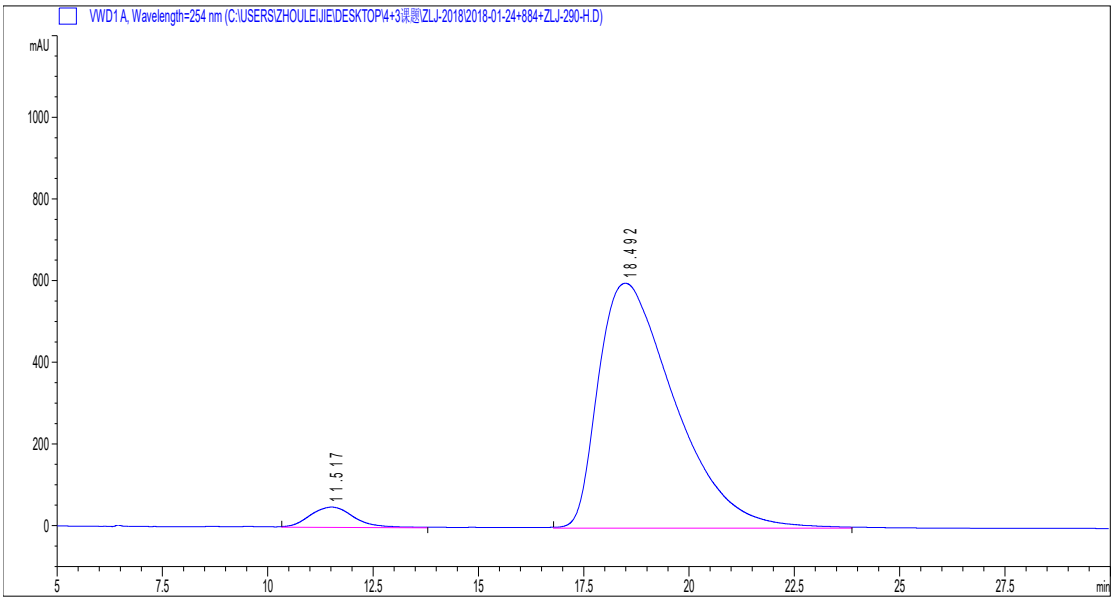


HPLC chromatogram of racemic 3aa



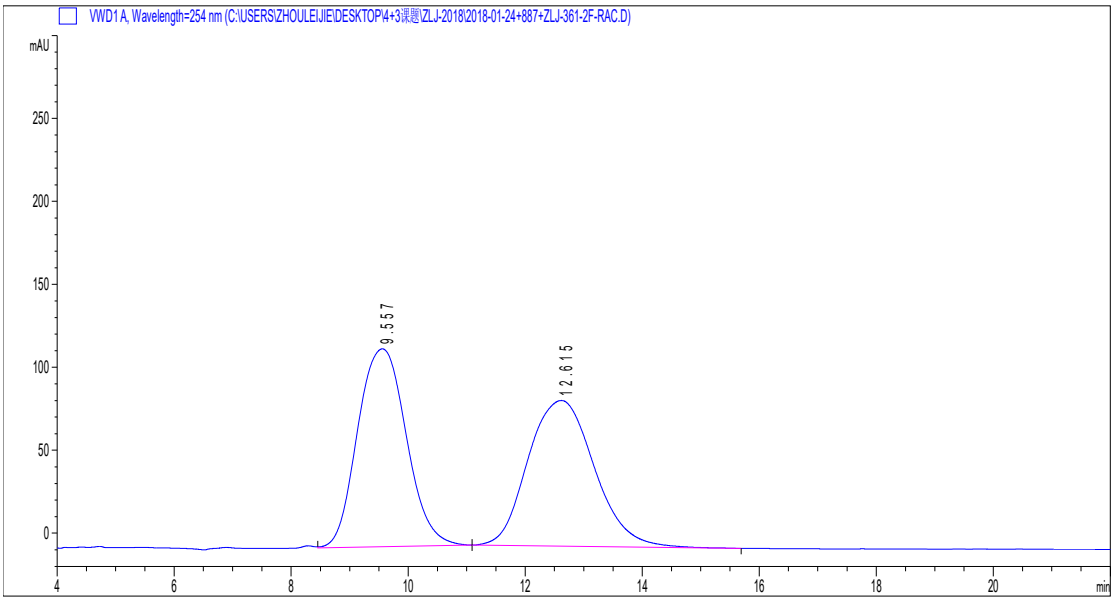
Peak #	RetTime [min]	Type	Width [min]	Area mAU *s	Height [mAU]	Area %
1	11.576	BB	1.0919	7907.02393	115.46571	49.4147
2	19.537	BB	1.7299	8094.33838	68.04297	50.5853

HPLC chromatogram of chiral 3aa



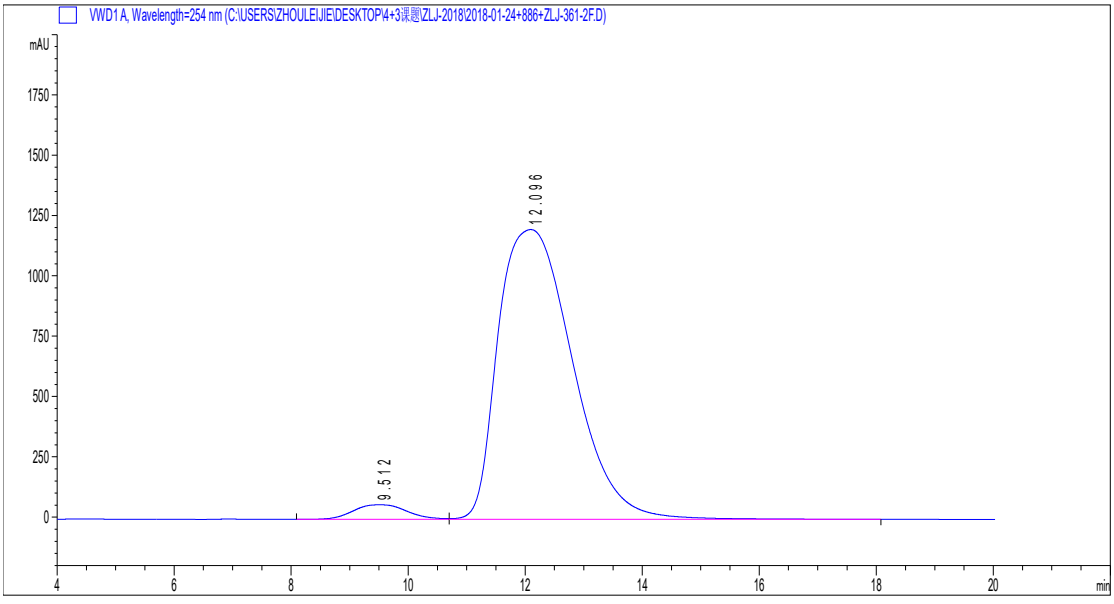
Peak #	RetTime [min]	Type	Width [min]	Area mAU *s	Height [mAU]	Area %
1	11.517	MM	1.2133	3605.95581	49.53336	4.5548
2	18.492	MM	2.0999	7.55618e4	599.73773	95.4452

HPLC chromatogram of racemic 3ab



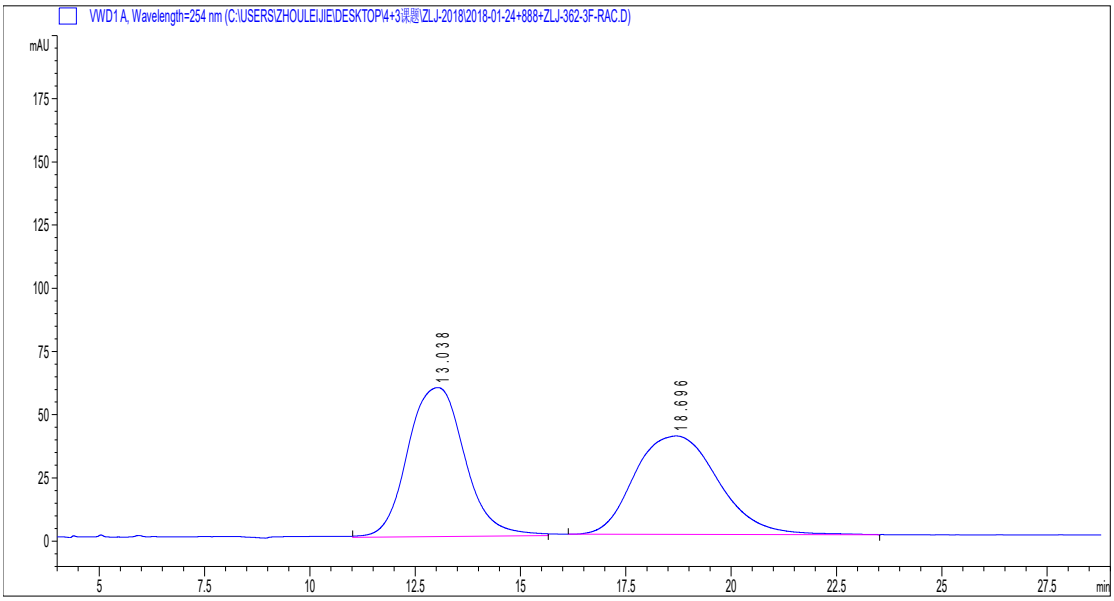
Peak #	RetTime [min]	Type	Width [min]	Area mAU *s	Height [mAU]	Area %
1	9.557	VB	0.9232	6889.84668	119.22799	49.8958
2	12.615	BB	1.2618	6918.61719	87.84875	50.1042

HPLC chromatogram of chiral 3ab



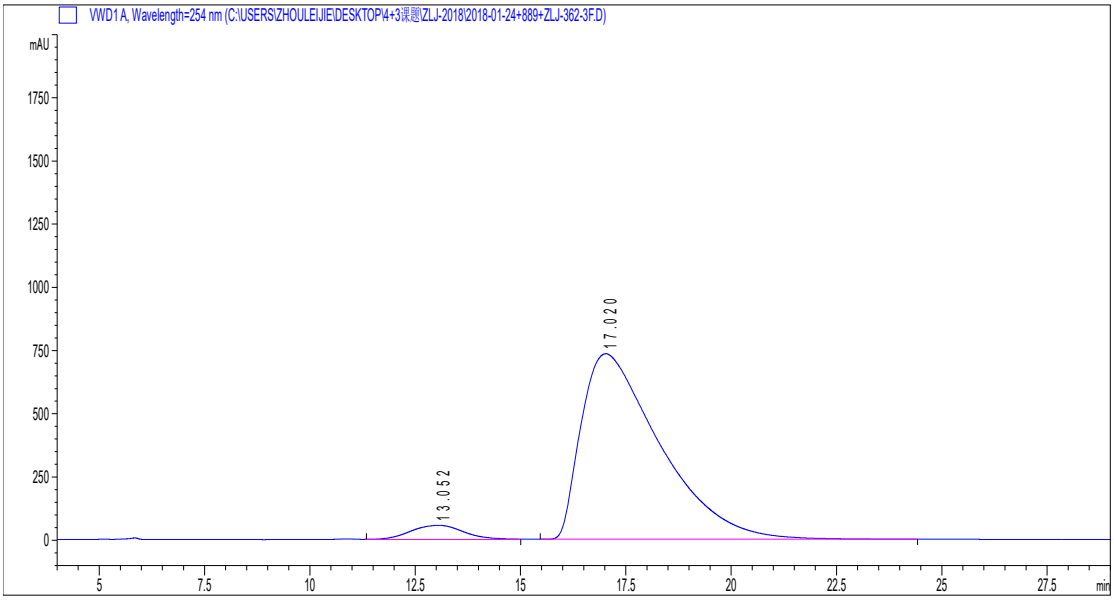
Peak #	RetTime [min]	Type	Width [min]	Area mAU *s	Height [mAU]	Area %
1	9.512	BV	1.0003	3832.02783	60.55790	3.4879
2	12.096	VB	1.4060	1.06035e5	1201.01648	96.5121

HPLC chromatogram of racemic 3ac



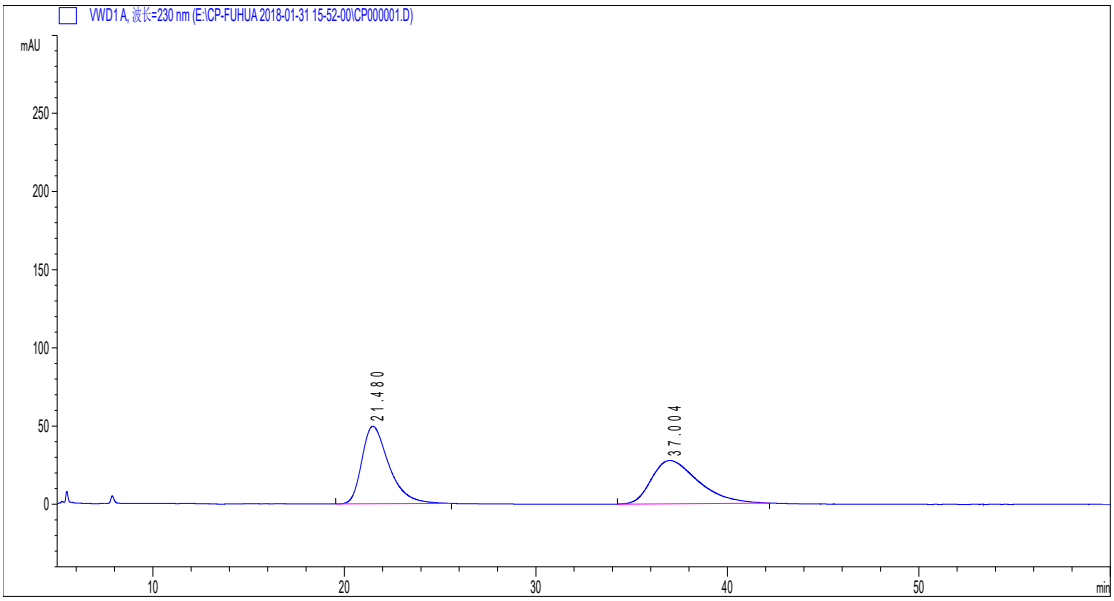
Peak #	RetTime [min]	Type	Width [min]	Area mAU *s	Height [mAU]	Area %
1	13.038	MM	1.5669	5542.35645	58.95221	50.7757
2	18.696	BB	1.8881	5373.02100	38.95719	49.2243

HPLC chromatogram of chiral 3ac



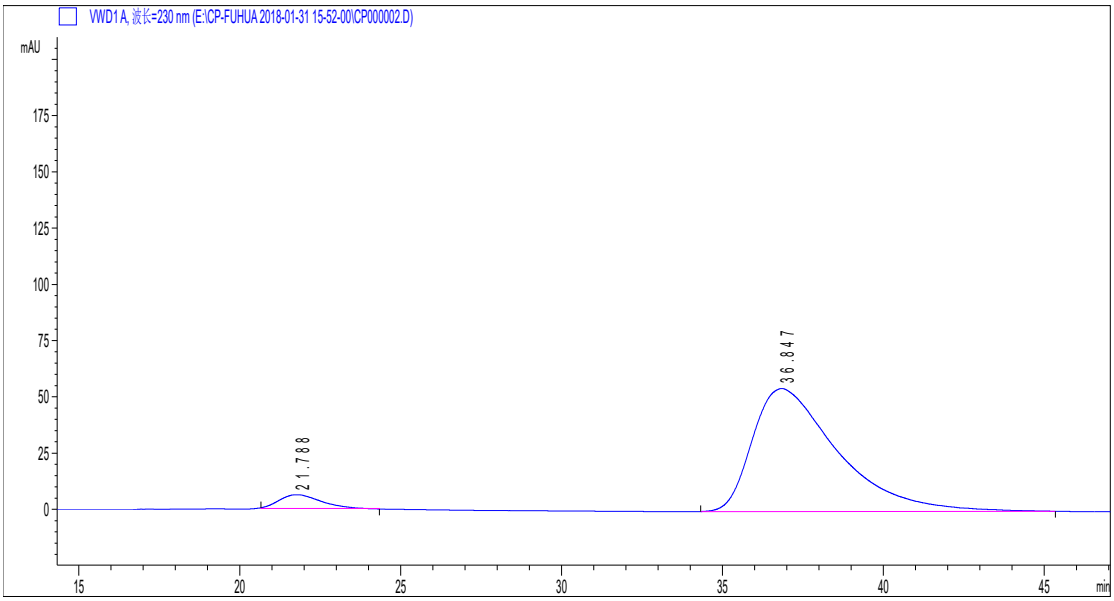
Peak #	RetTime [min]	Type	Width [min]	Area mAU *s	Height [mAU]	Area %
1	13.052	MM	1.4600	4848.01074	55.34131	4.8386
2	17.020	BB	1.9349	9.53464e4	733.81061	95.1614

HPLC chromatogram of racemic 3ad



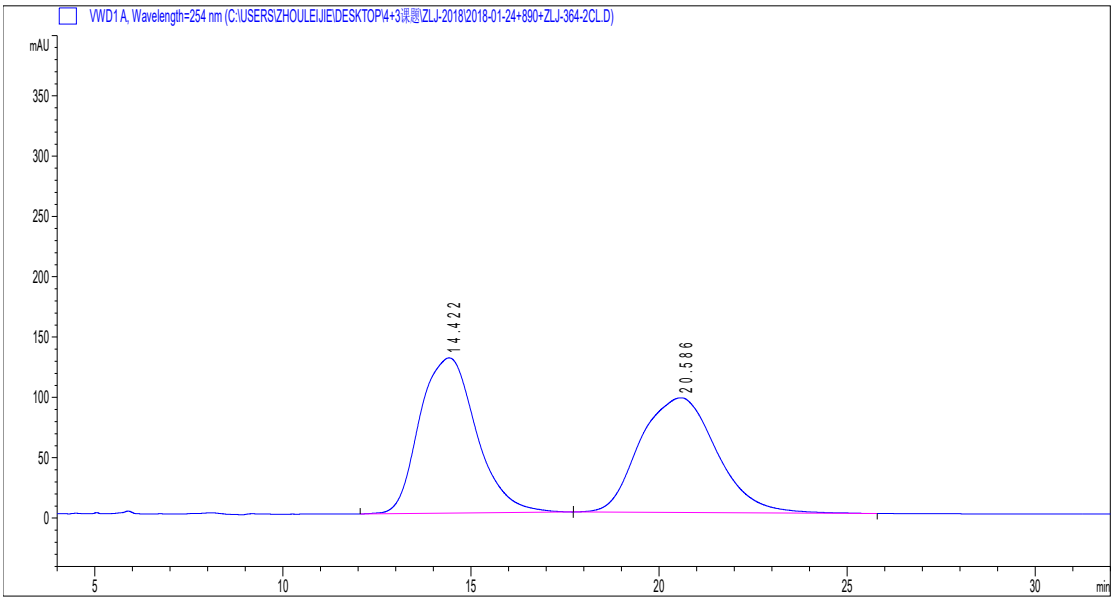
Peak #	RetTime [min]	Type	Width [min]	Area mAU *s	Height [mAU]	Area %
1	21.480	BB	1.4450	4885.16309	49.64736	50.9684
2	37.004	BB	2.1722	4699.53125	27.69119	49.0316

HPLC chromatogram of chiral 3ad



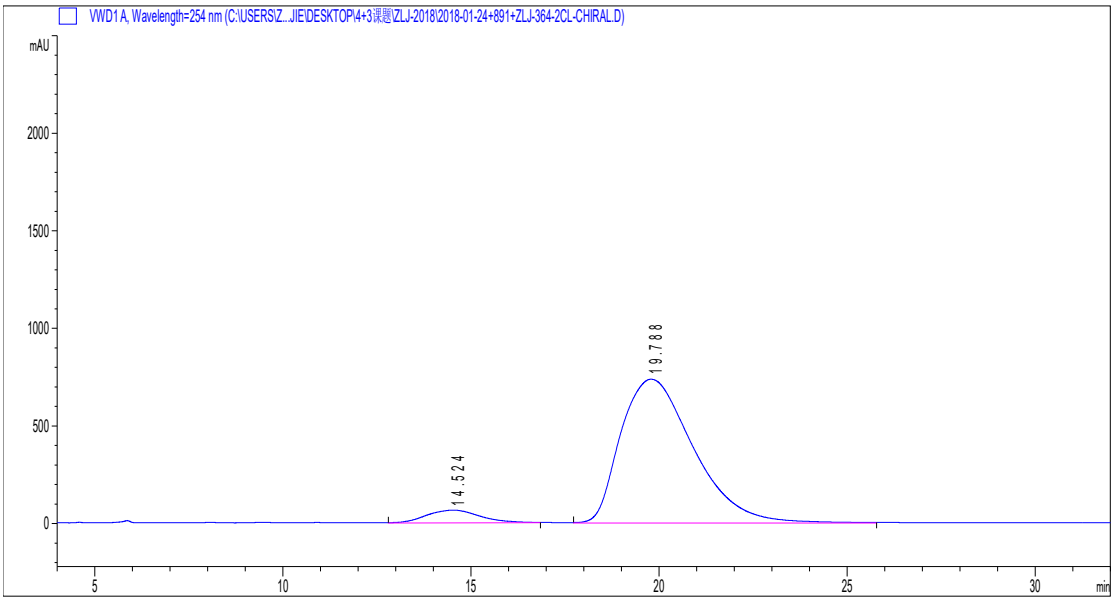
Peak #	RetTime [min]	Type	Width [min]	Area mAU *s	Height [mAU]	Area %
1	21.788	MM	1.4827	543.46332	6.10896	5.1437
2	36.847	BB	2.3535	1.00221e4	54.65178	94.8563

HPLC chromatogram of racemic 3ae



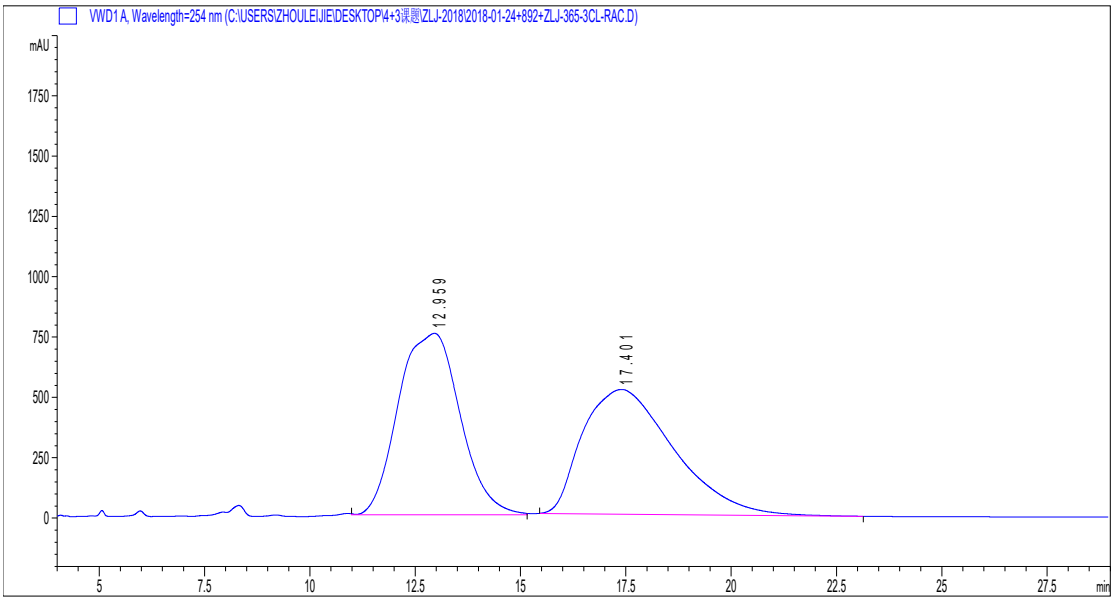
Peak #	RetTime [min]	Type	Width [min]	Area mAU *s	Height [mAU]	Area %
1	14.422	BB	1.5698	1.34650e4	128.67667	50.0716
2	20.586	BB	1.9649	1.34266e4	95.05569	49.9284

HPLC chromatogram of chiral 3ae



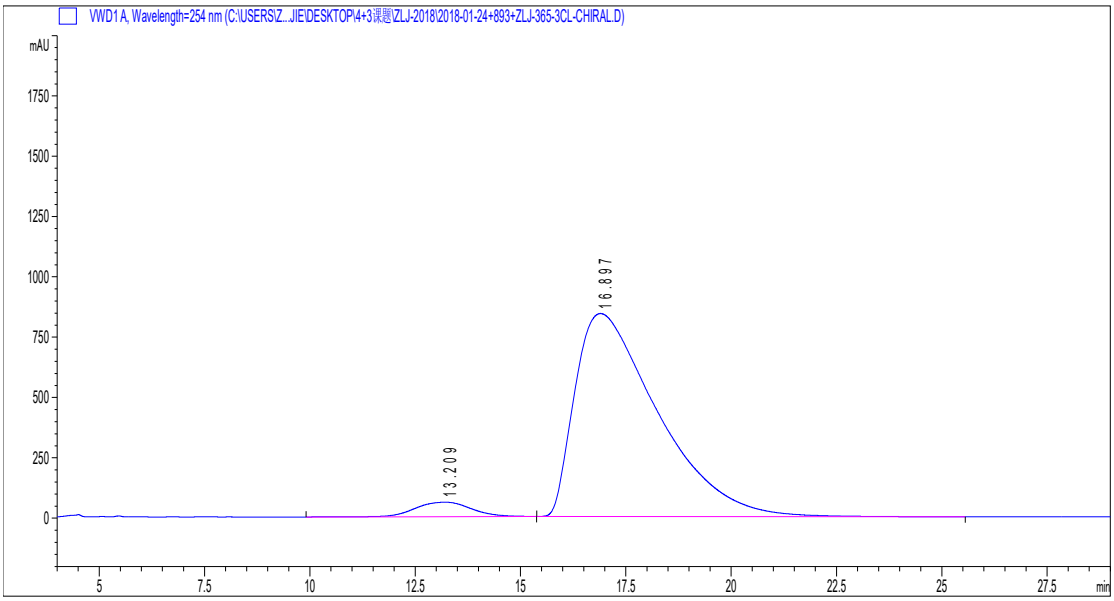
Peak #	RetTime [min]	Type	Width [min]	Area mAU *s	Height [mAU]	Area %
1	14.524	MM	1.6378	6297.70264	64.08868	5.9759
2	19.788	MM	2.2437	9.90877e4	736.03674	94.0241

HPLC chromatogram of racemic 3af



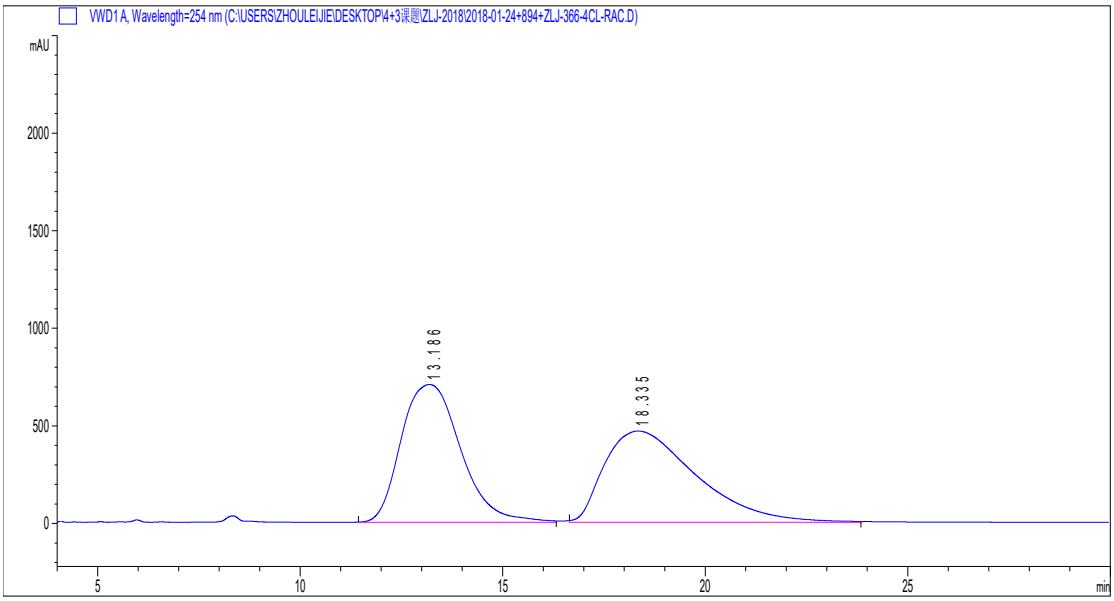
Peak #	RetTime [min]	Type	Width [min]	Area mAU *s	Height [mAU]	Area %
1	12.959	MM	1.6969	7.65656e4	752.01770	49.6961
2	17.401	BB	2.0378	7.75019e4	516.73785	50.3039

HPLC chromatogram of chiral 3af



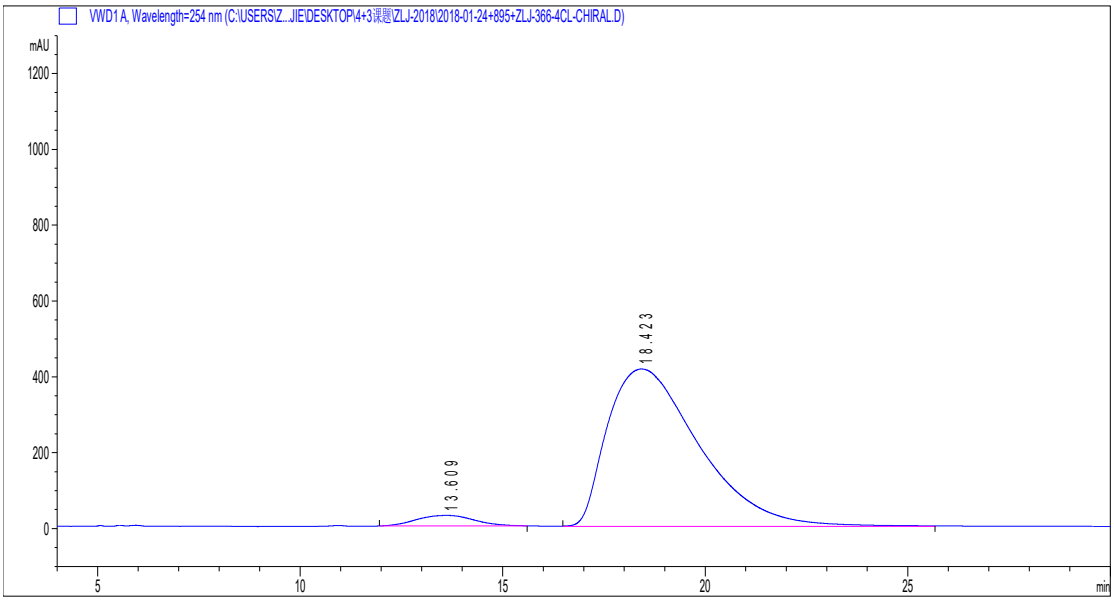
Peak #	RetTime [min]	Type	Width [min]	Area mAU *s	Height [mAU]	Area %
1	13.209	BB	1.4260	5528.79248	60.11185	4.5745
2	16.897	BB	2.0723	1.15333e5	841.36493	95.4255

HPLC chromatogram of racemic 3ag



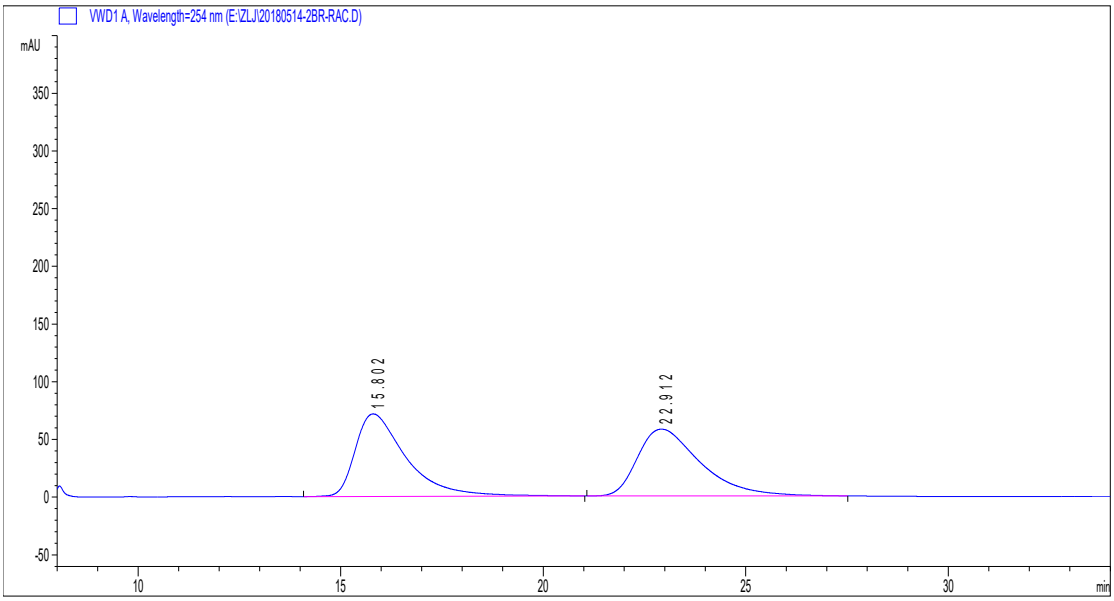
Peak #	RetTime [min]	Type	Width [min]	Area mAU *s	Height [mAU]	Area %
1	13.186	MM	1.7035	7.21974e4	706.36517	49.5292
2	18.335	MM	2.6227	7.35700e4	467.52097	50.4708

HPLC chromatogram of chiral 3ag



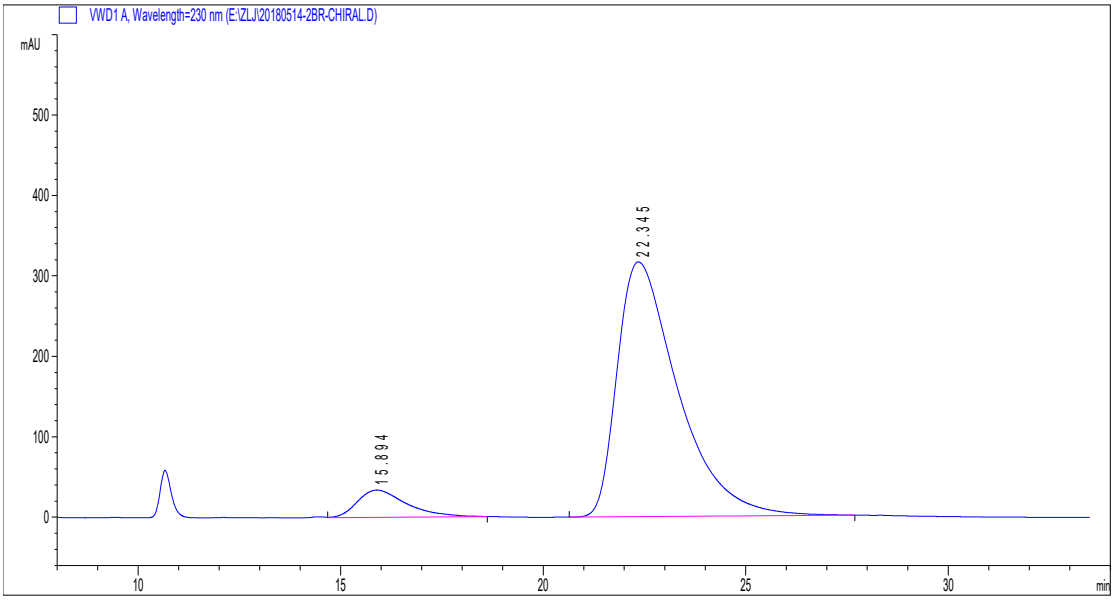
Peak #	RetTime [min]	Type	Width [min]	Area mAU *s	Height [mAU]	Area %
1	13.609	MM	1.6799	2814.68921	27.92580	4.1177
2	18.423	MM	2.6285	6.55407e4	415.57944	95.8823

HPLC chromatogram of racemic 3ah



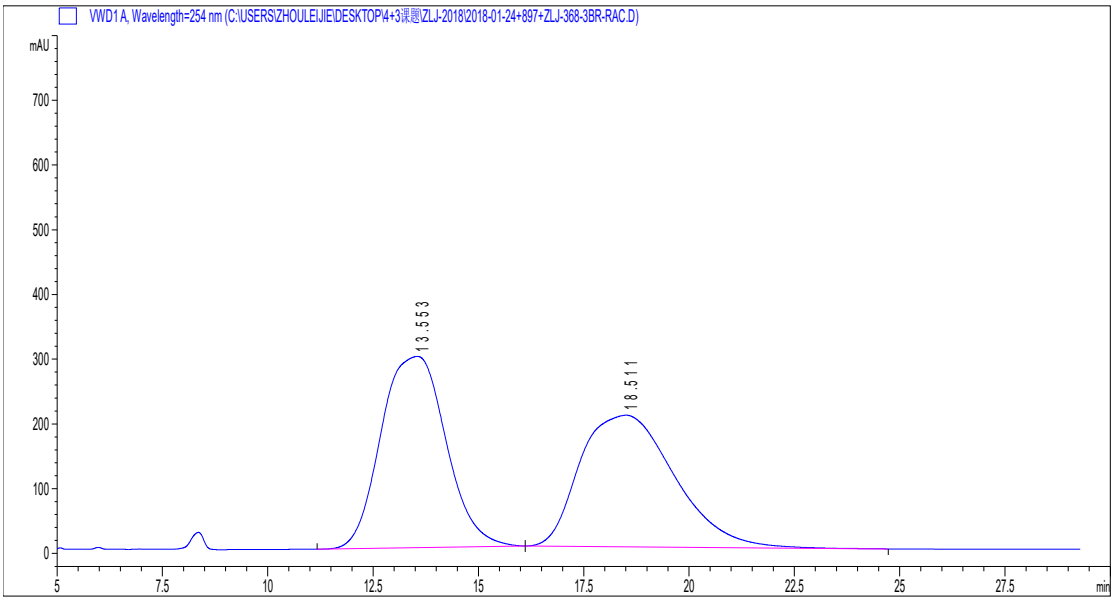
Peak #	RetTime [min]	Type	Width [min]	Area mAU *s	Height [mAU]	Area %
1	15.802	BB	1.2698	6233.68799	71.54839	49.9656
2	22.912	BB	1.5724	6242.26367	57.89722	50.0344

HPLC chromatogram of chiral 3ah



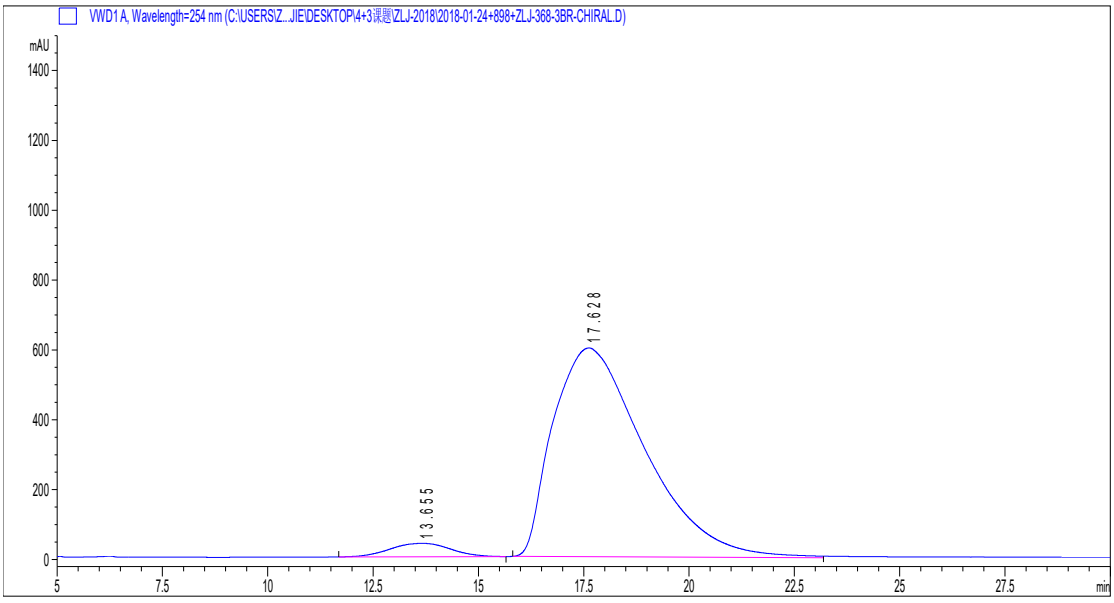
Peak #	RetTime [min]	Type	Width [min]	Area mAU *s	Height [mAU]	Area %
1	15.894	VB	1.2390	2844.57104	33.92020	7.9385
2	22.345	BB	1.5178	3.29882e4	316.76563	92.0615

HPLC chromatogram of racemic 3ai



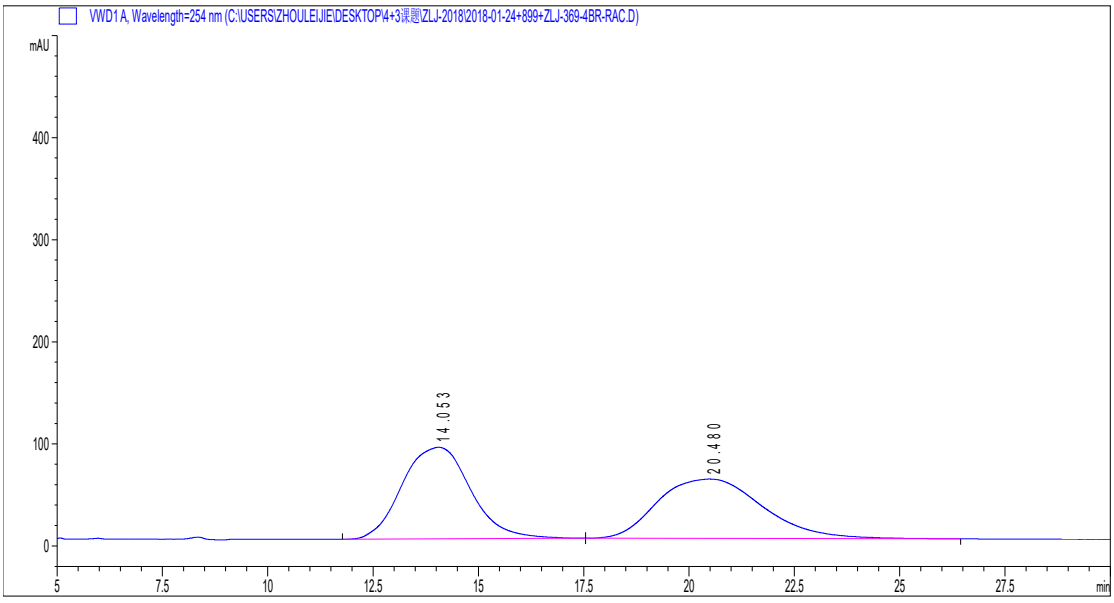
Peak #	RetTime [min]	Type	Width [min]	Area mAU *s	Height [mAU]	Area %
1	13.553	BB	1.6225	3.16643e4	295.41220	50.0351
2	18.511	BB	2.2603	3.16199e4	203.21127	49.9649

HPLC chromatogram of chiral 3ai



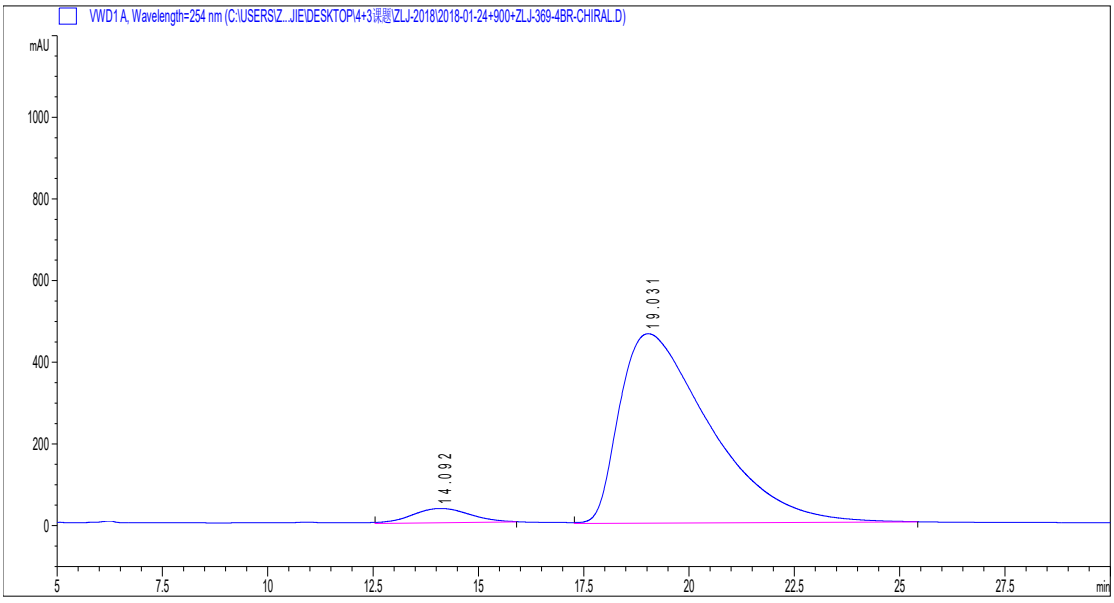
Peak #	RetTime [min]	Type	Width [min]	Area mAU *s	Height [mAU]	Area %
1	13.655	BB	1.4756	3806.37793	38.09774	4.0381
2	17.628	MM	2.5223	9.04546e4	597.68903	95.9619

HPLC chromatogram of racemic 3aj



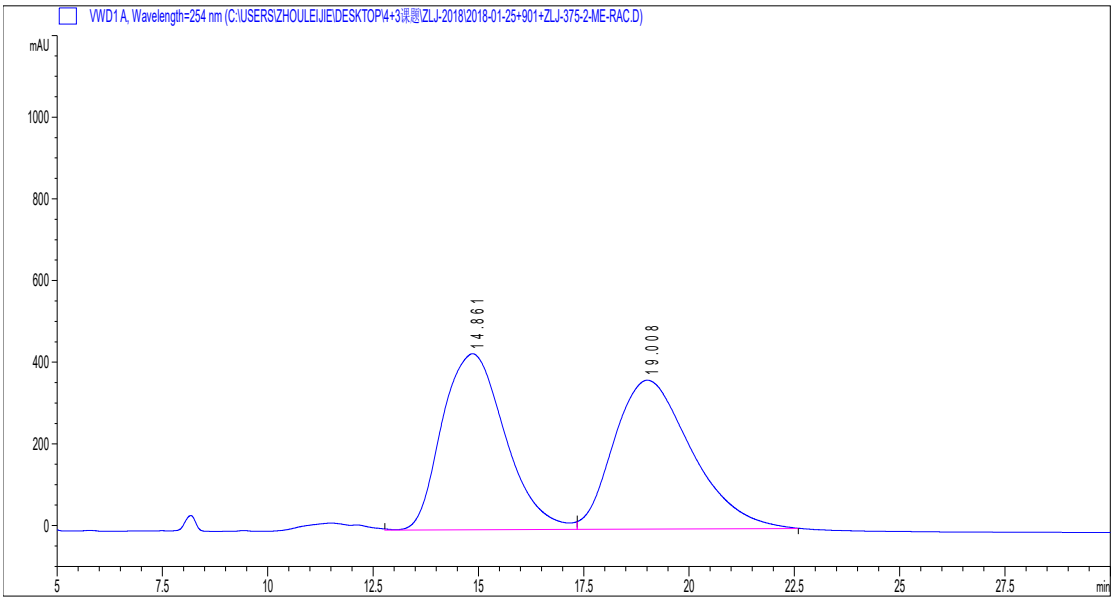
Peak #	RetTime [min]	Type	Width [min]	Area mAU *s	Height [mAU]	Area %
1	14.053	BB	1.6592	1.01329e4	89.74683	50.1354
2	20.480	BB	2.3520	1.00781e4	58.14829	49.8646

HPLC chromatogram of chiral 3aj



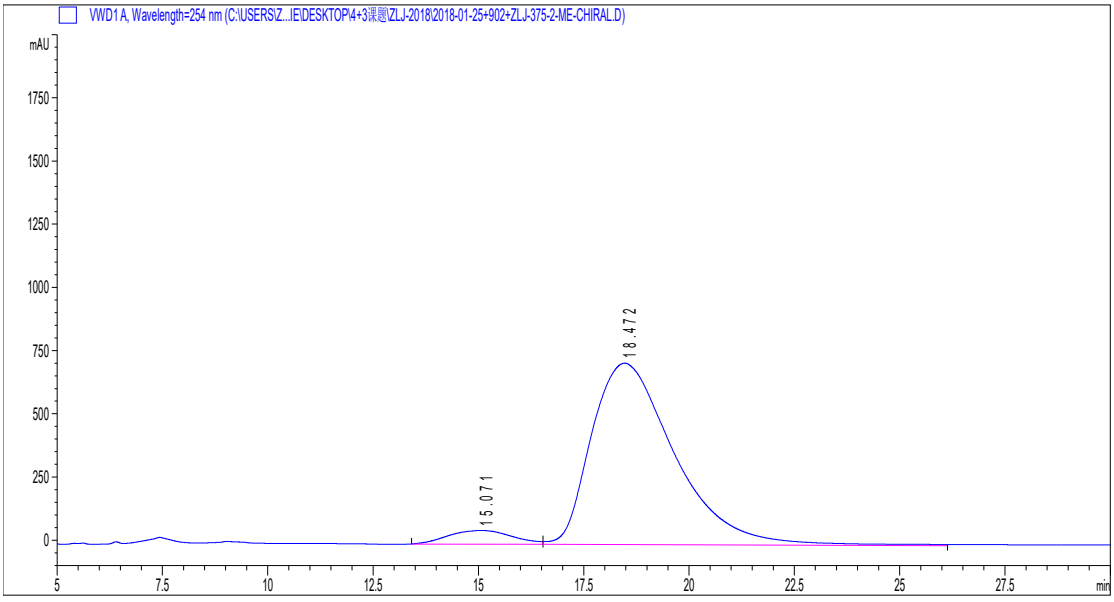
Peak #	RetTime [min]	Type	Width [min]	Area mAU *s	Height [mAU]	Area %
1	14.092	MM	1.6161	3406.59277	35.13179	4.6725
2	19.031	MM	2.4955	6.95009e4	464.17151	95.3275

HPLC chromatogram of racemic 3ak



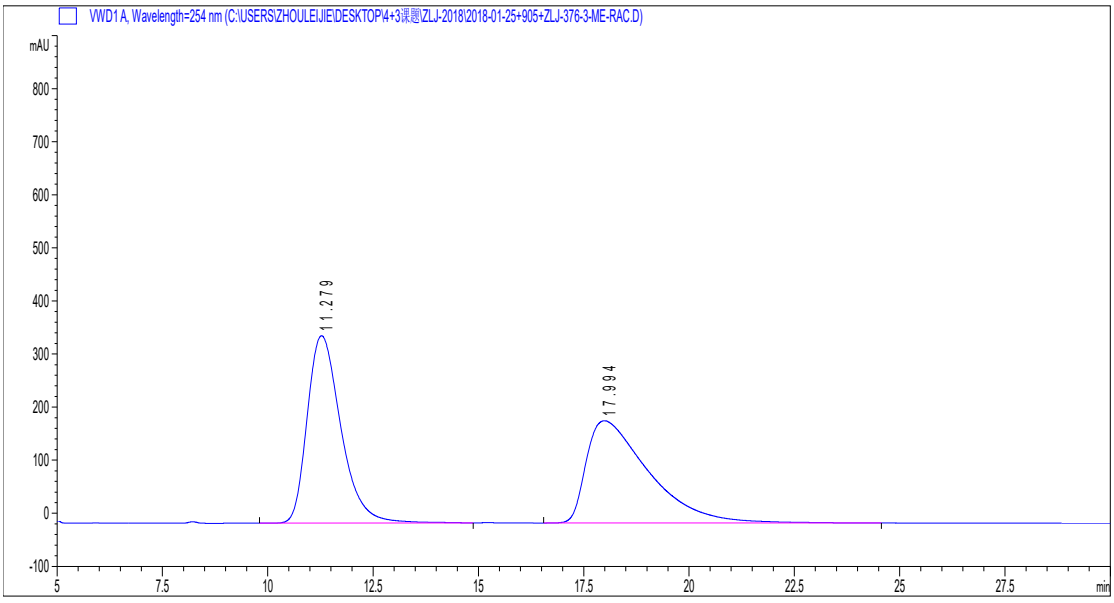
Peak #	RetTime [min]	Type	Width [min]	Area mAU *s	Height [mAU]	Area %
1	14.861	MF	1.7412	4.50648e4	431.36615	49.0270
2	19.008	FM	2.1398	4.68535e4	364.92972	50.9730

HPLC chromatogram of chiral 3ak



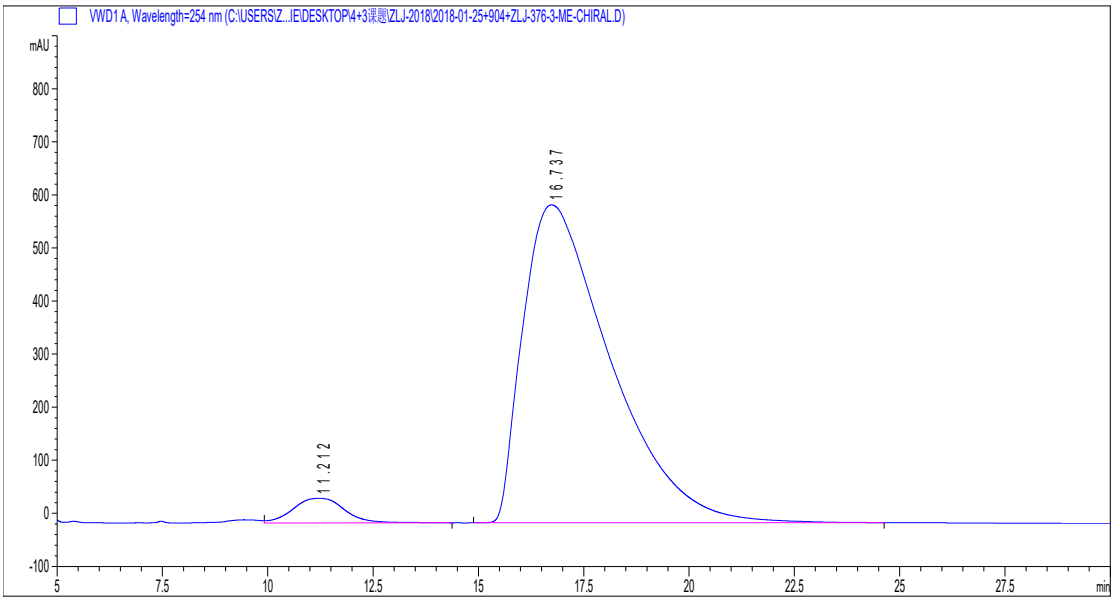
Peak #	RetTime [min]	Type	Width [min]	Area mAU *s	Height [mAU]	Area %
1	15.071	MF	1.7693	5754.56201	54.20819	5.5048
2	18.472	FM	2.2930	9.87829e4	718.00647	94.4952

HPLC chromatogram of racemic 3al



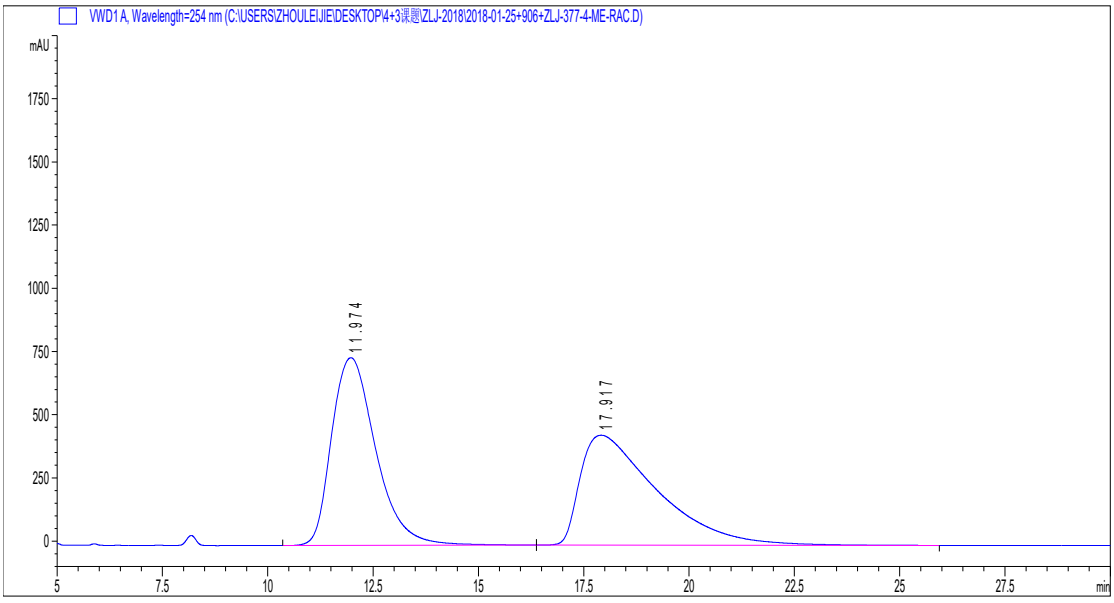
Peak #	RetTime [min]	Type	Width [min]	Area mAU *s	Height [mAU]	Area %
1	11.279	BB	0.8606	1.96235e4	352.97681	49.7204
2	17.994	BB	1.5372	1.98442e4	192.57141	50.2796

HPLC chromatogram of chiral 3al



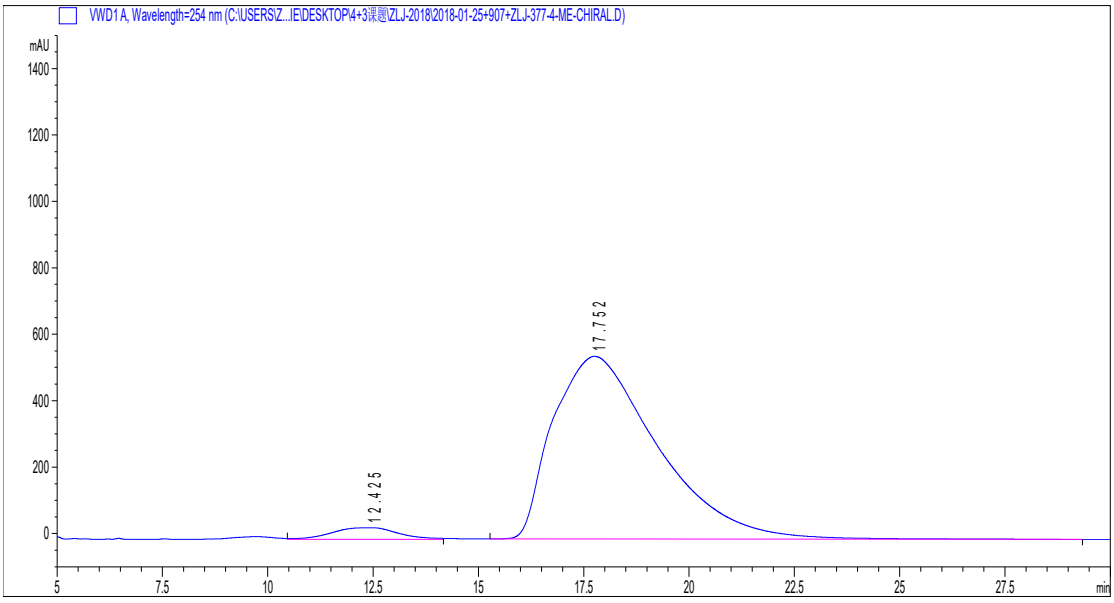
Peak #	RetTime [min]	Type	Width [min]	Area mAU *s	Height [mAU]	Area %
1	11.212	VB	1.3255	3920.01294	46.12577	4.3350
2	16.737	BB	2.1773	8.65065e4	598.86676	95.6650

HPLC chromatogram of racemic 3am



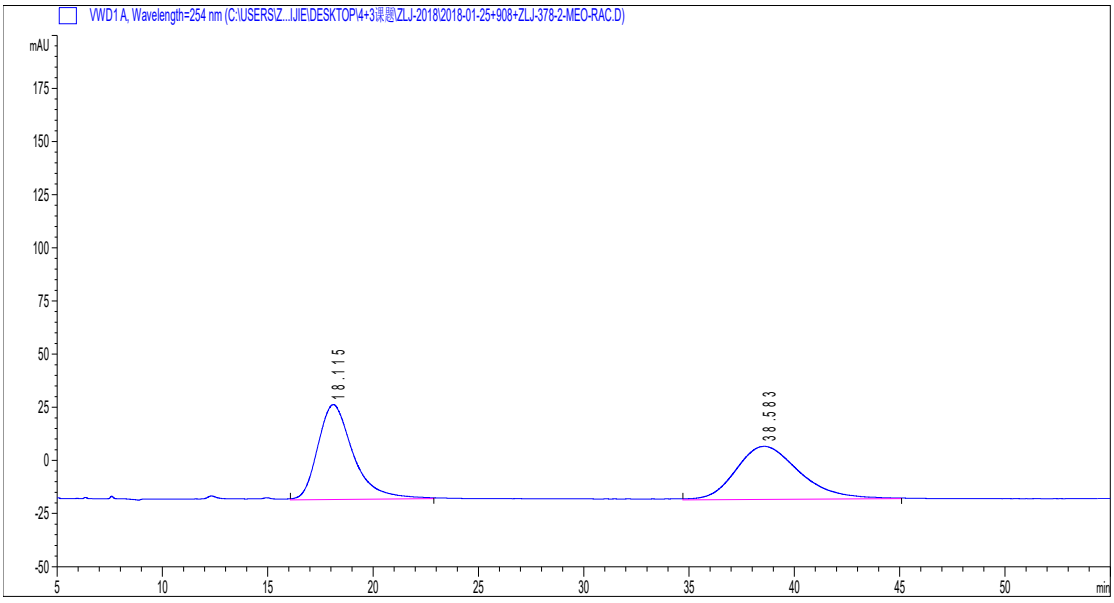
Peak #	RetTime [min]	Type	Width [min]	Area mAU *s	Height [mAU]	Area %
1	11.974	BB	1.1338	5.40383e4	742.70728	49.5783
2	17.917	BB	1.8224	5.49576e4	434.57230	50.4217

HPLC chromatogram of chiral 3am



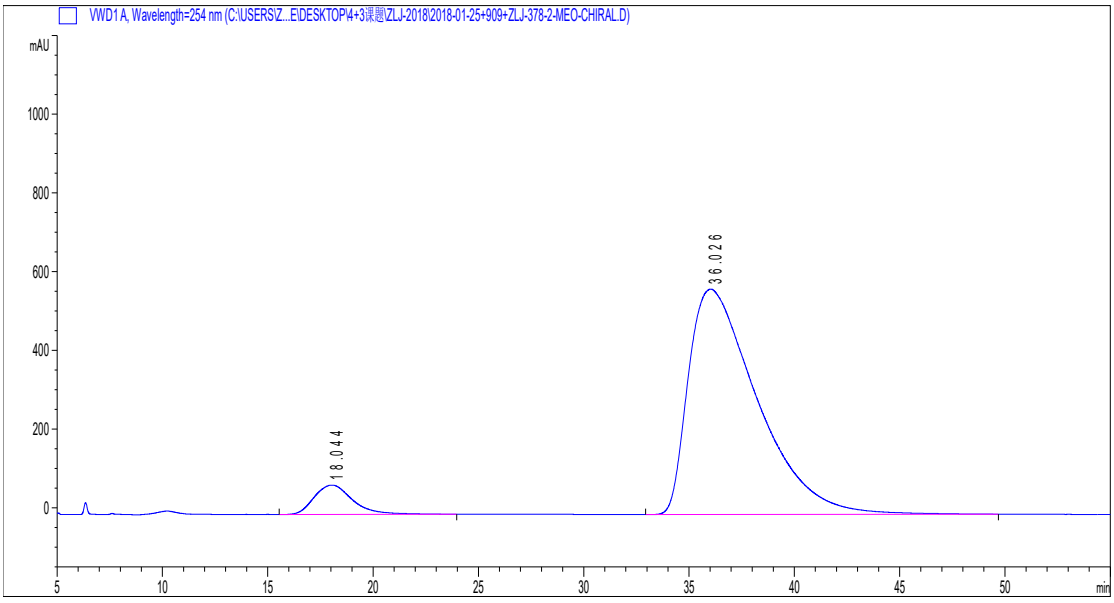
Peak #	RetTime [min]	Type	Width [min]	Area mAU *s	Height [mAU]	Area %
1	12.425	MM	1.8022	3799.59814	35.13946	3.8484
2	17.752	BB	2.4410	9.49317e4	549.92957	96.1516

HPLC chromatogram of racemic 3an



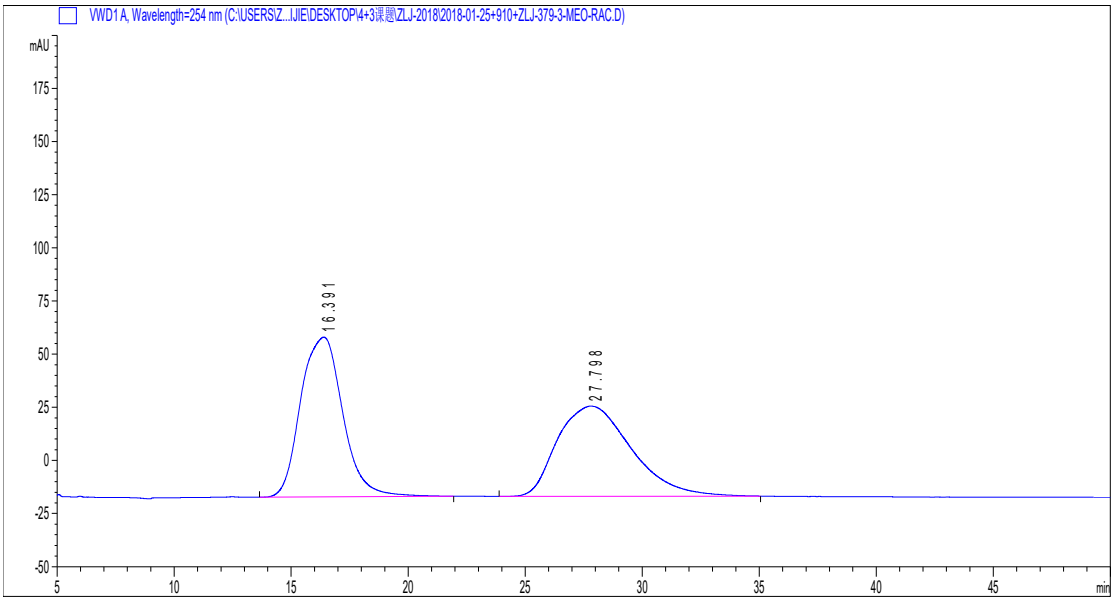
Peak #	RetTime [min]	Type	Width [min]	Area mAU *s	Height [mAU]	Area %
1	18.115	MM	1.9502	5226.22803	44.66338	49.8594
2	38.583	MM	3.5071	5255.70264	24.97655	50.1406

HPLC chromatogram of chiral 3an



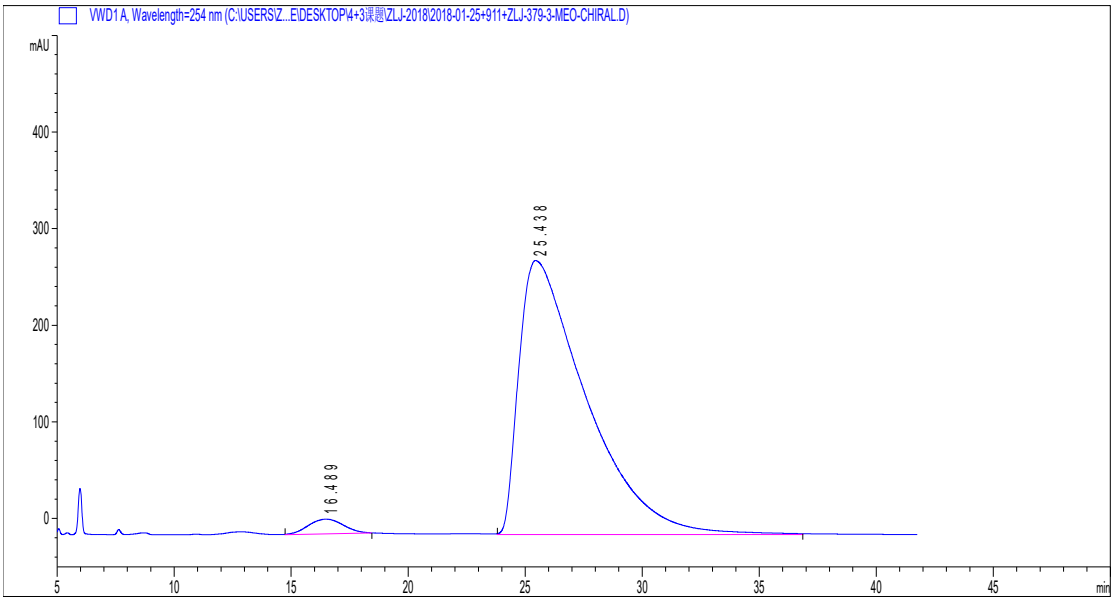
Peak #	RetTime [min]	Type	Width [min]	Area mAU *s	Height [mAU]	Area %
1	18.044	BB	1.8600	9594.81641	74.87750	6.8560
2	36.026	BB	3.2002	1.30353e5	572.97150	93.1440

HPLC chromatogram of racemic 3ao



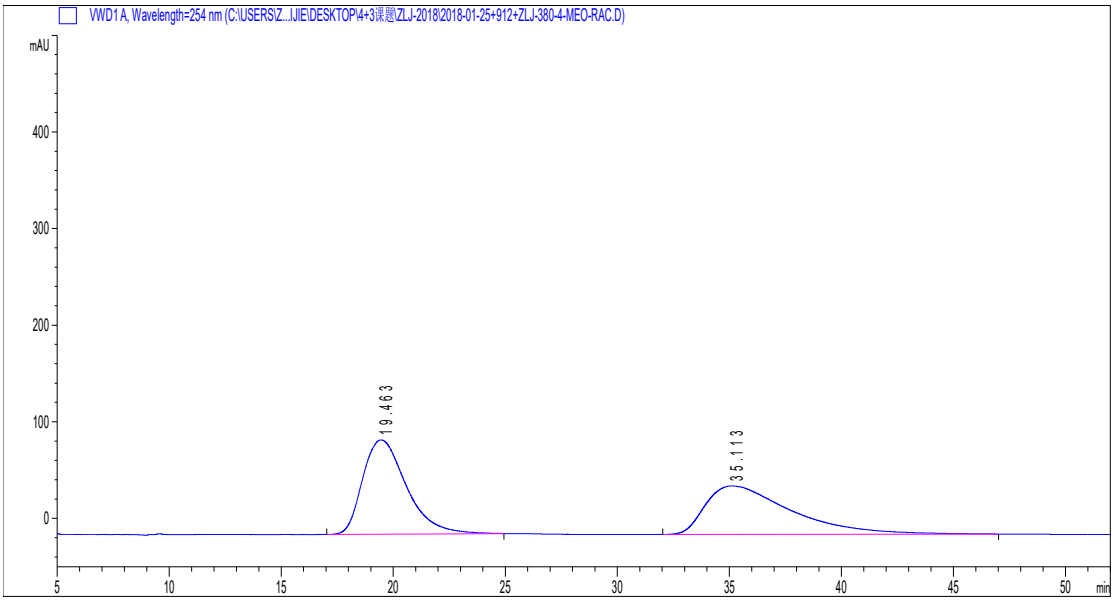
Peak #	RetTime [min]	Type	Width [min]	Area mAU *s	Height [mAU]	Area %
1	16.391	BB	1.8299	9400.32324	75.17247	50.2229
2	27.798	BB	2.6131	9316.87891	42.52491	49.7771

HPLC chromatogram of chiral 3ao



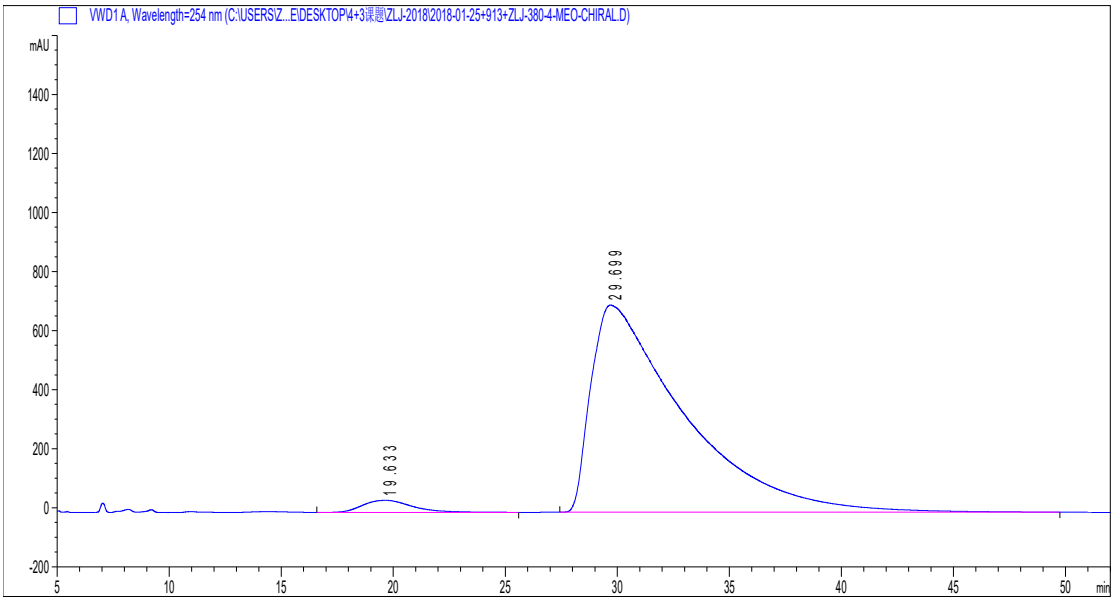
Peak #	RetTime [min]	Type	Width [min]	Area mAU *s	Height [mAU]	Area %
1	16.489	MM	1.7389	1585.78540	15.19889	2.7244
2	25.438	MM	3.3285	5.66209e4	283.51816	97.2756

HPLC chromatogram of racemic 3ap



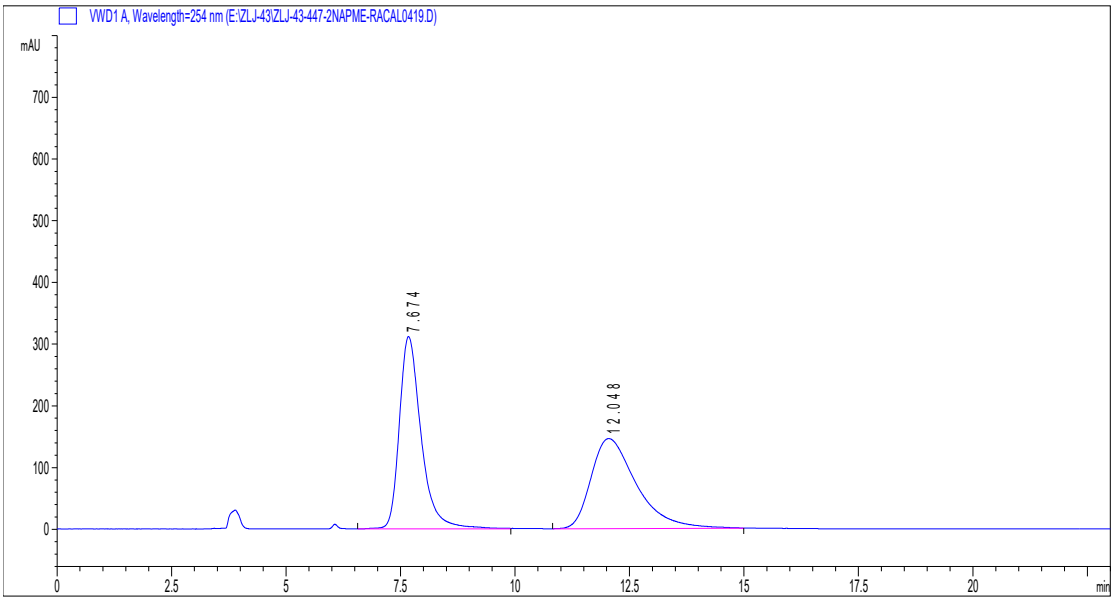
Peak #	RetTime [min]	Type	Width [min]	Area mAU *s	Height [mAU]	Area %
1	19.463	BB	1.9735	1.32223e4	97.48007	49.9724
2	35.113	BB	3.1261	1.32369e4	50.15385	50.0276

HPLC chromatogram of chiral 3ap



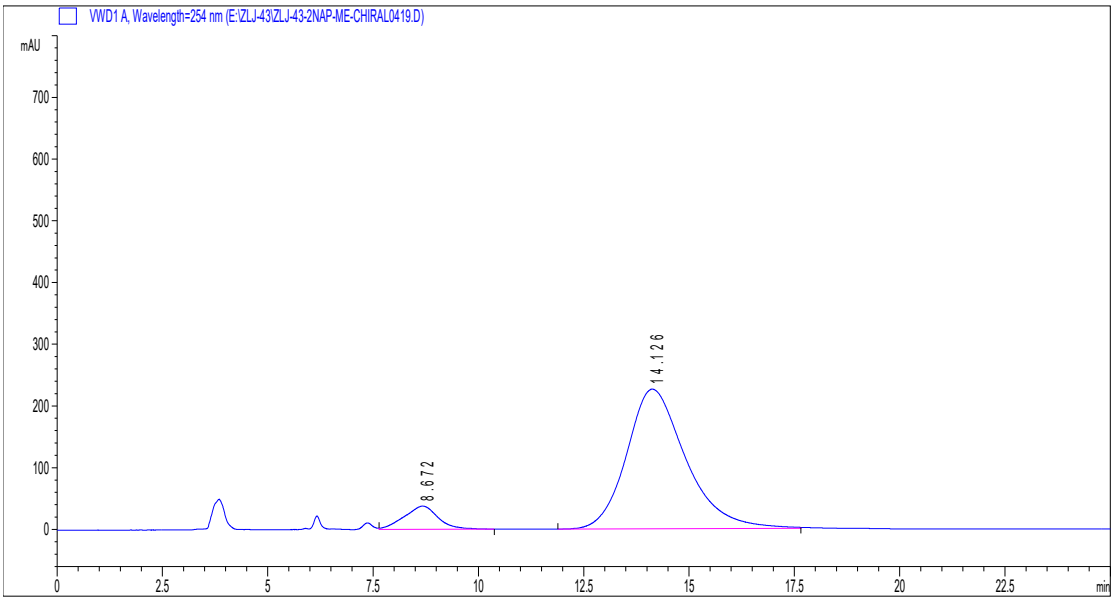
Peak #	RetTime [min]	Type	Width [min]	Area mAU *s	Height [mAU]	Area %
1	19.633	BB	2.2160	6328.25146	40.94850	3.0380
2	29.699	BB	3.5409	2.01976e5	701.33636	96.9620

HPLC chromatogram of racemic 3aq



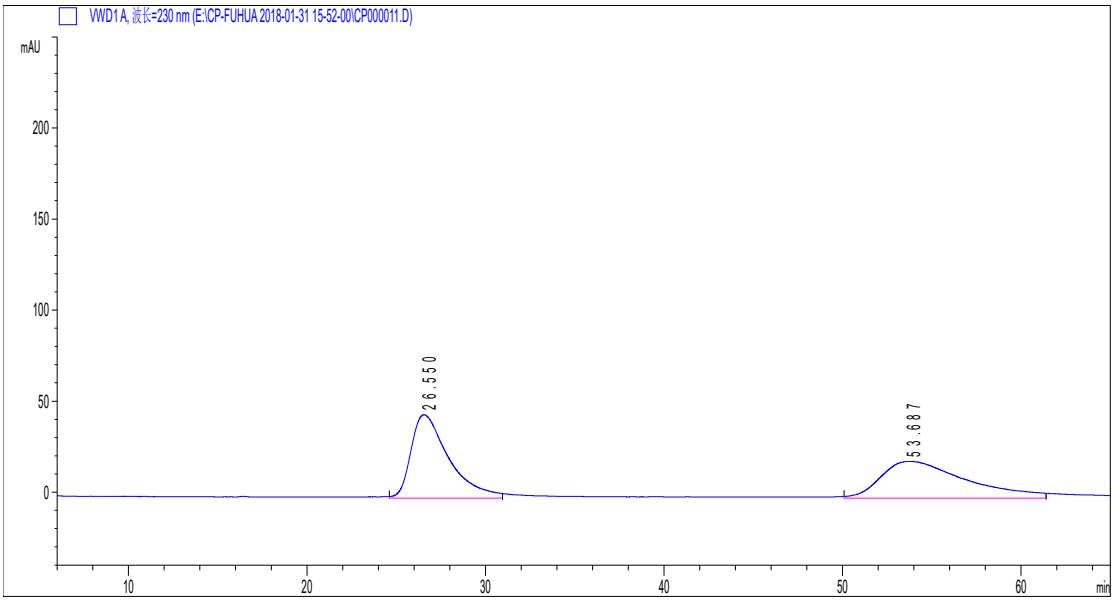
Peak #	RetTime [min]	Type	Width [min]	Area mAU *s	Height [mAU]	Area %
1	7.674	VV	0.5006	1.02921e4	311.44464	50.6257
2	12.048	VV	0.9659	1.00377e4	145.86292	49.3743

HPLC chromatogram of chiral 3aq



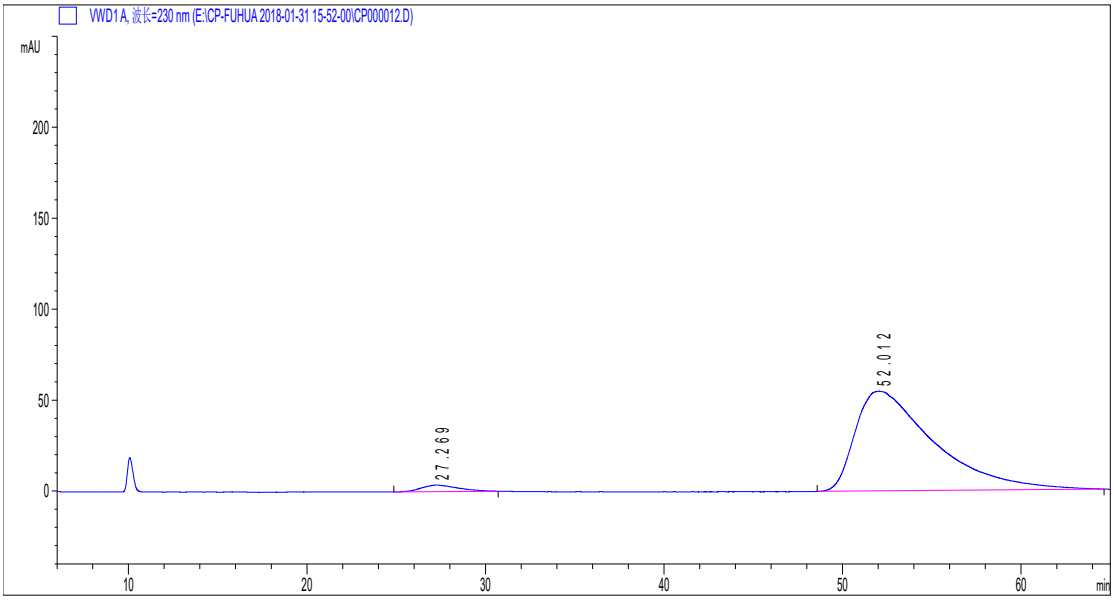
Peak #	RetTime [min]	Type	Width [min]	Area mAU *s	Height [mAU]	Area %
1	8.672	VB	0.7750	2121.59595	37.75135	8.7559
2	14.126	VV	1.3280	2.21090e4	226.22629	91.2441

HPLC chromatogram of racemic 3ar



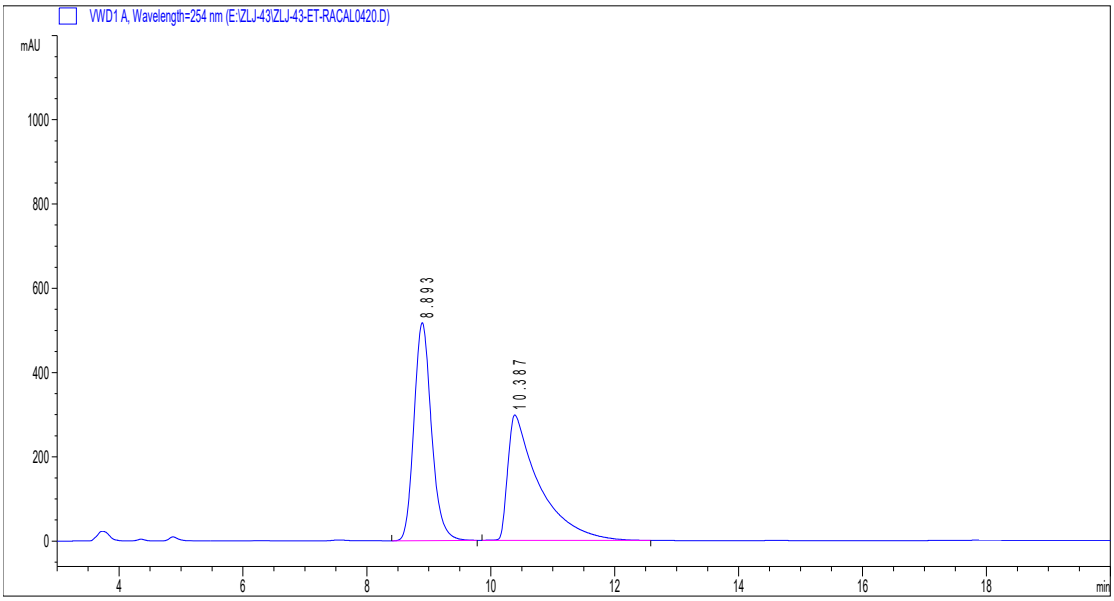
Peak #	RetTime [min]	Type	Width [min]	Area mAU *s	Height [mAU]	Area %
1	26.550	MM	2.4616	6775.16553	45.87218	50.1346
2	53.687	MM	5.5454	6738.78320	20.25343	49.8654

HPLC chromatogram of chiral 3ar



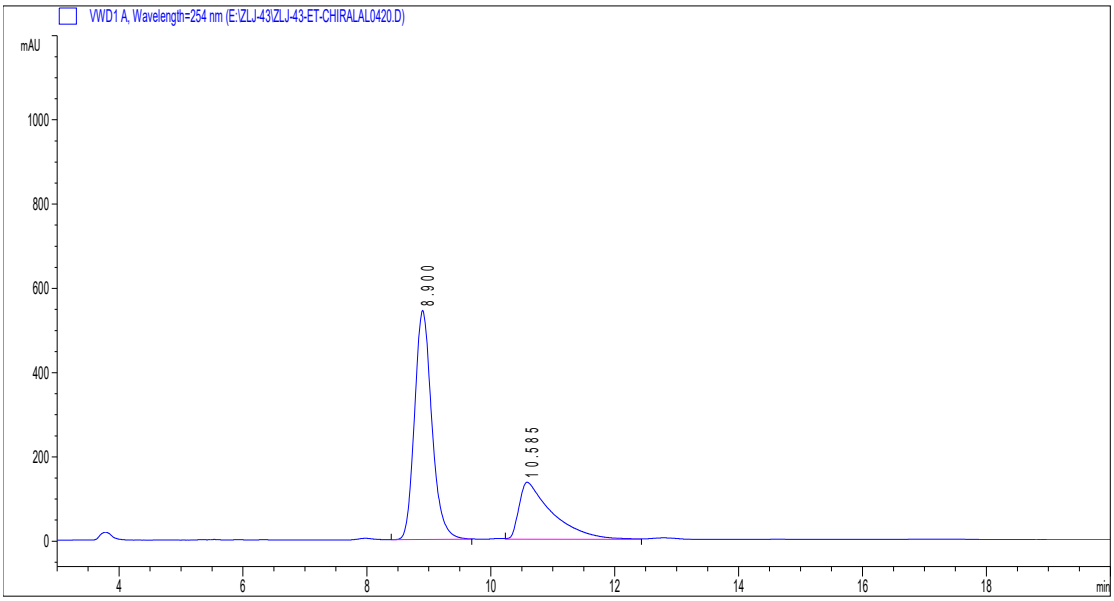
Peak #	RetTime [min]	Type	Width [min]	Area mAU *s	Height [mAU]	Area %
1	27.269	BB	1.6797	513.32013	3.59964	2.9663
2	52.012	BB	3.5875	1.67918e4	54.78497	97.0337

HPLC chromatogram of racemic 3as



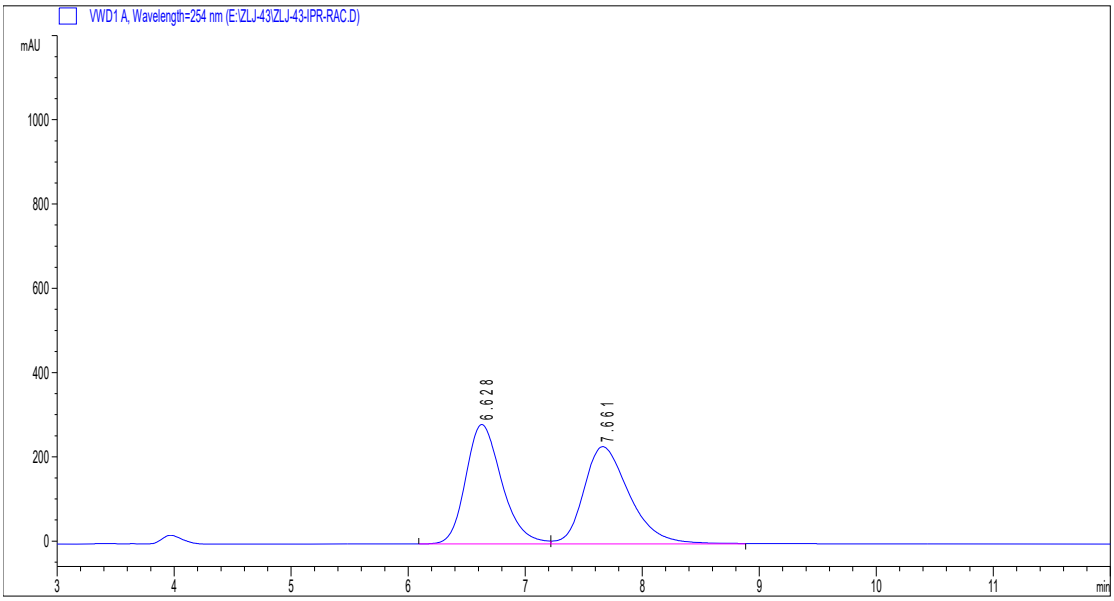
Peak #	RetTime [min]	Type	Width [min]	Area mAU *s	Height [mAU]	Area %
1	8.893	BV	0.3014	1.01417e4	517.47821	49.3273
2	10.387	BB	0.4869	1.04183e4	297.73486	50.6727

HPLC chromatogram of chiral 3as



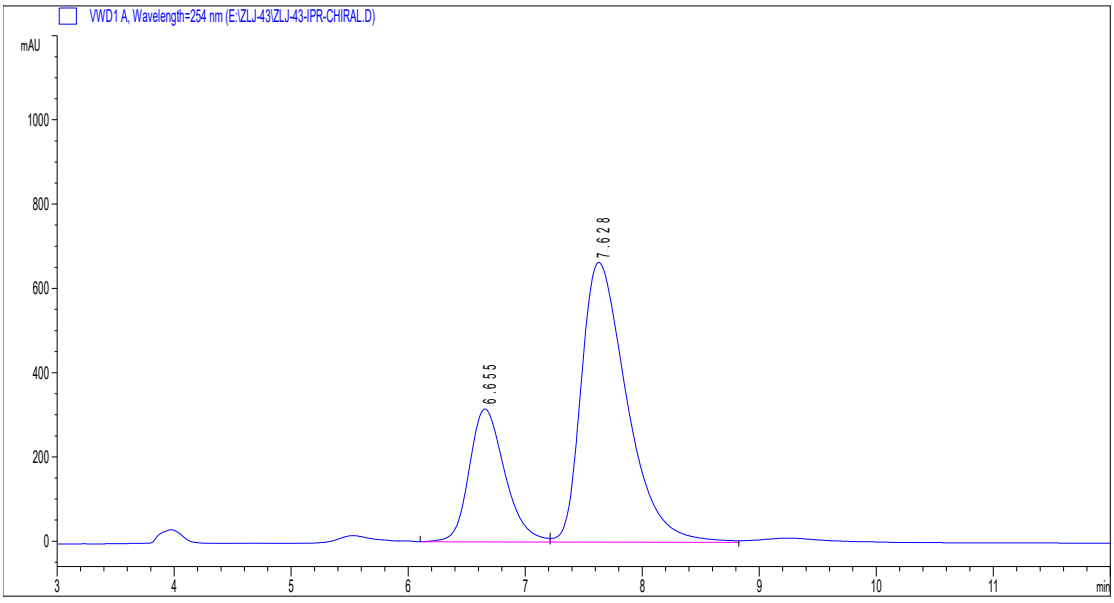
Peak #	RetTime [min]	Type	Width [min]	Area mAU *s	Height [mAU]	Area %
1	8.900	BV	0.2990	1.05364e4	543.47723	67.8183
2	10.585	VV	0.5103	4999.81836	135.12714	32.1817

HPLC chromatogram of racemic 3at



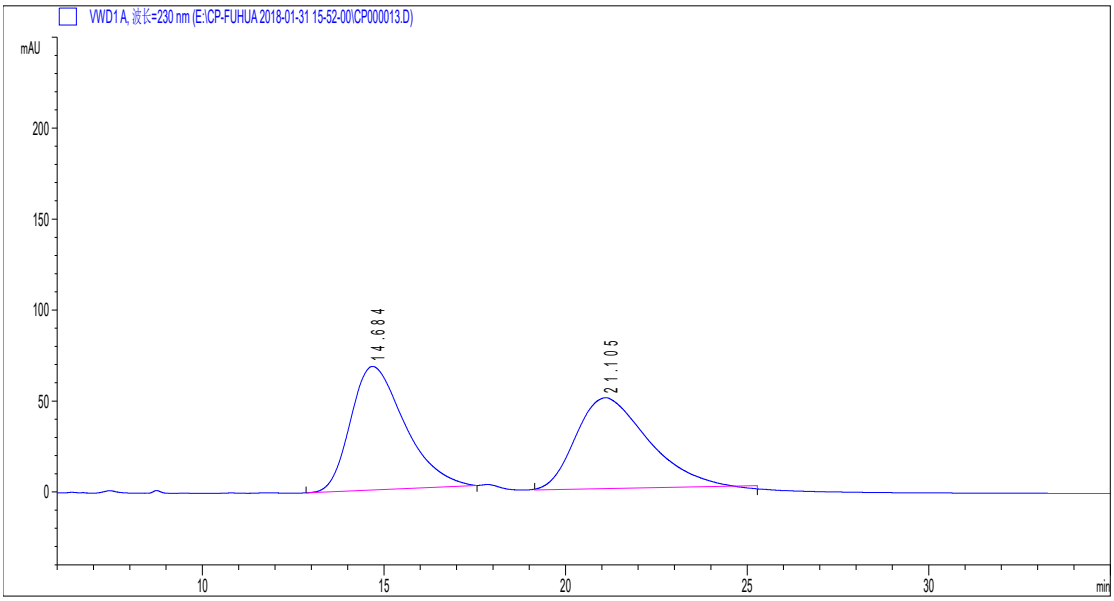
Peak #	RetTime [min]	Type	Width [min]	Area mAU *s	Height [mAU]	Area %
1	6.628	BV	0.3305	6086.93896	283.53439	49.3679
2	7.661	VV	0.4131	6242.80762	230.81627	50.6321

HPLC chromatogram of chiral 3at



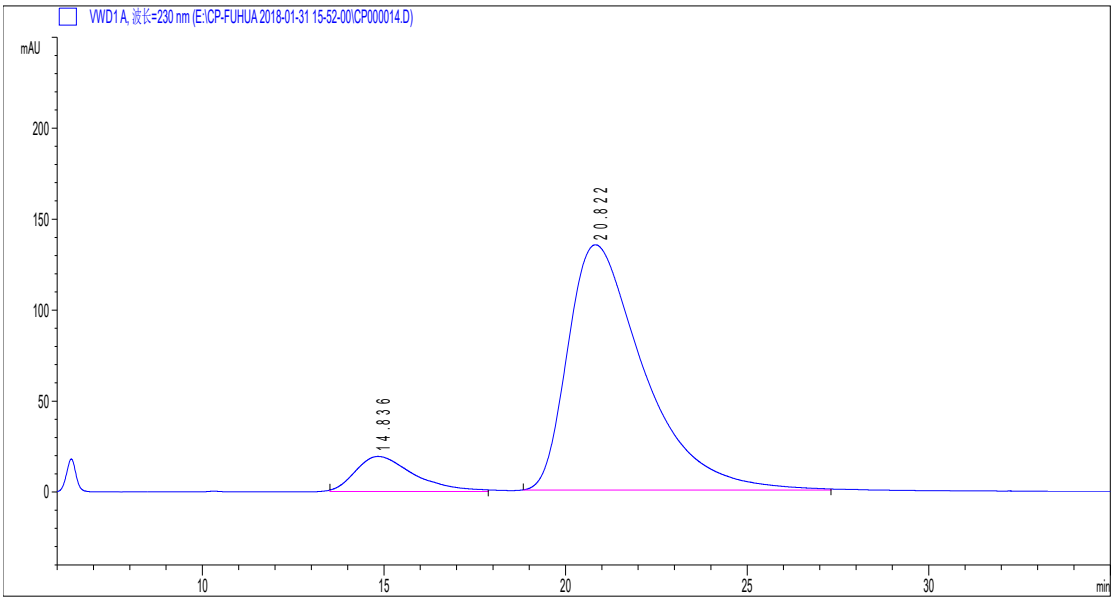
Peak #	RetTime [min]	Type	Width [min]	Area mAU *s	Height [mAU]	Area %
1	6.655	BV	0.3248	6652.19336	315.28662	27.0341
2	7.628	VV	0.4130	1.79545e4	663.95990	72.9659

HPLC chromatogram of racemic 3au



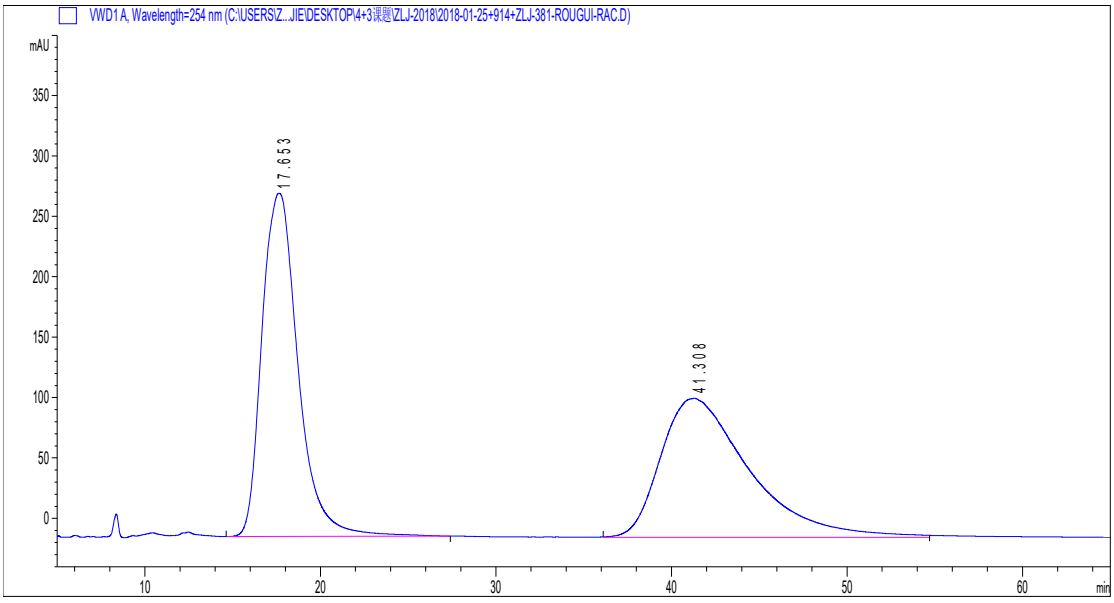
Peak #	RetTime [min]	Type	Width [min]	Area mAU *s	Height [mAU]	Area %
1	14.684	BB	1.5702	7037.23877	67.90141	50.4395
2	21.105	MM	2.3057	6914.59619	49.98221	49.5605

HPLC chromatogram of chiral 3au



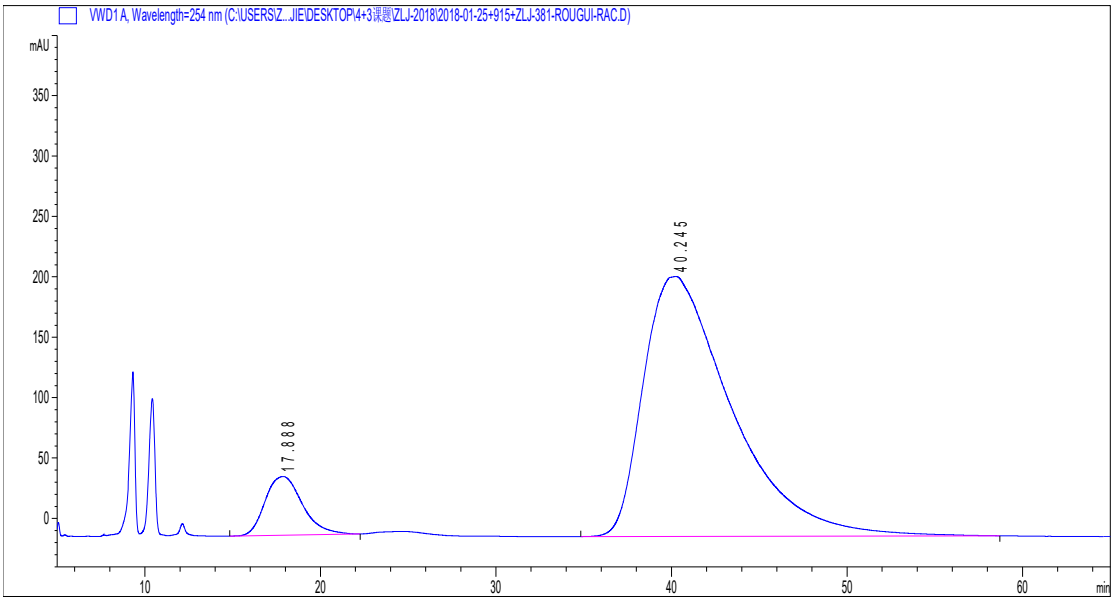
Peak #	RetTime [min]	Type	Width [min]	Area mAU *s	Height [mAU]	Area %
1	14.836	MM	1.8585	2149.77466	19.27889	9.8458
2	20.822	MM	2.4328	1.96848e4	134.85883	90.1542

HPLC chromatogram of racemic 3av



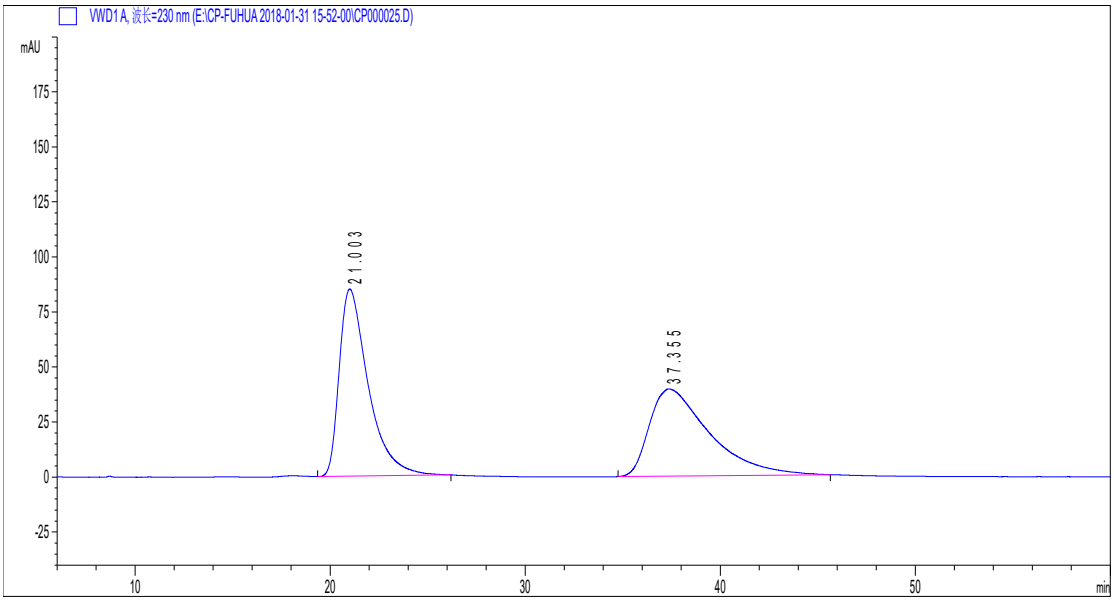
Peak #	RetTime [min]	Type	Width [min]	Area mAU *s	Height [mAU]	Area %
1	17.653	BB	2.2201	4.06590e4	284.19955	50.1346
2	41.308	MM	5.8479	4.04406e4	115.25602	49.8654

HPLC chromatogram of chiral 3av



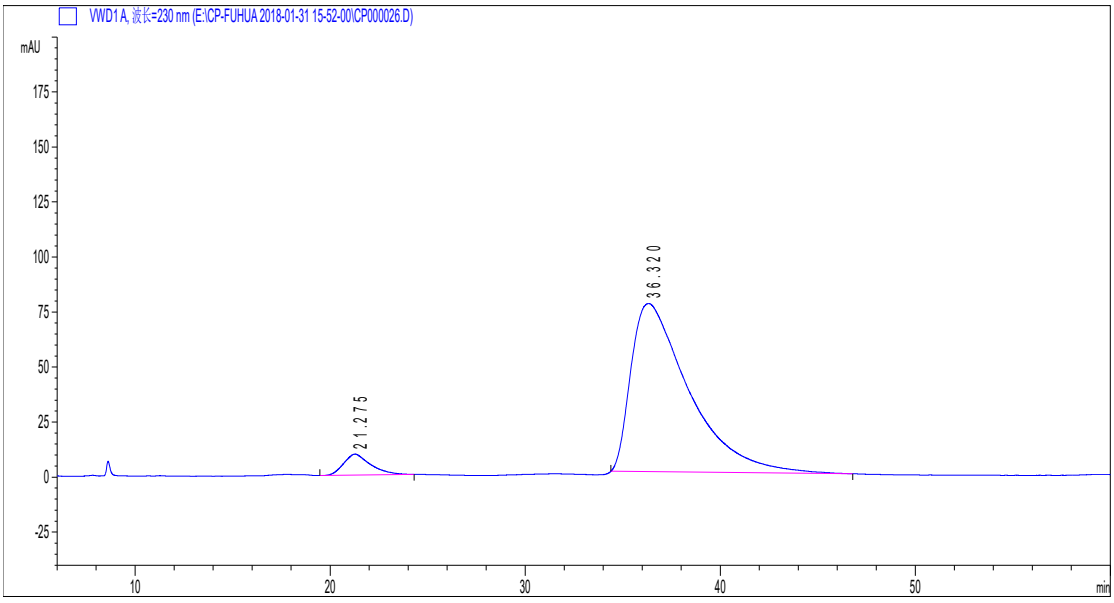
Peak #	RetTime [min]	Type	Width [min]	Area mAU *s	Height [mAU]	Area %
1	17.888	BB	2.0296	7193.11230	48.71615	8.7302
2	40.245	BB	4.1995	7.51999e4	215.27043	91.2698

HPLC chromatogram of racemic 3ba



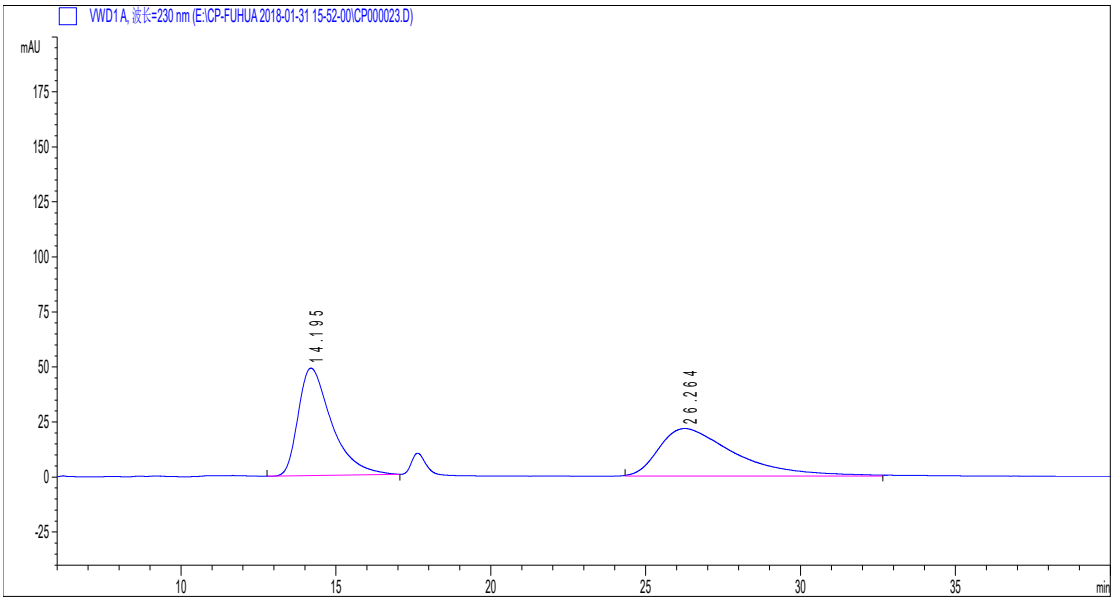
Peak #	RetTime [min]	Type	Width [min]	Area mAU *s	Height [mAU]	Area %
1	21.003	BB	1.5464	8779.60254	85.05949	50.9617
2	37.355	BB	2.5689	8448.22754	39.64881	49.0383

HPLC chromatogram of chiral 3ba



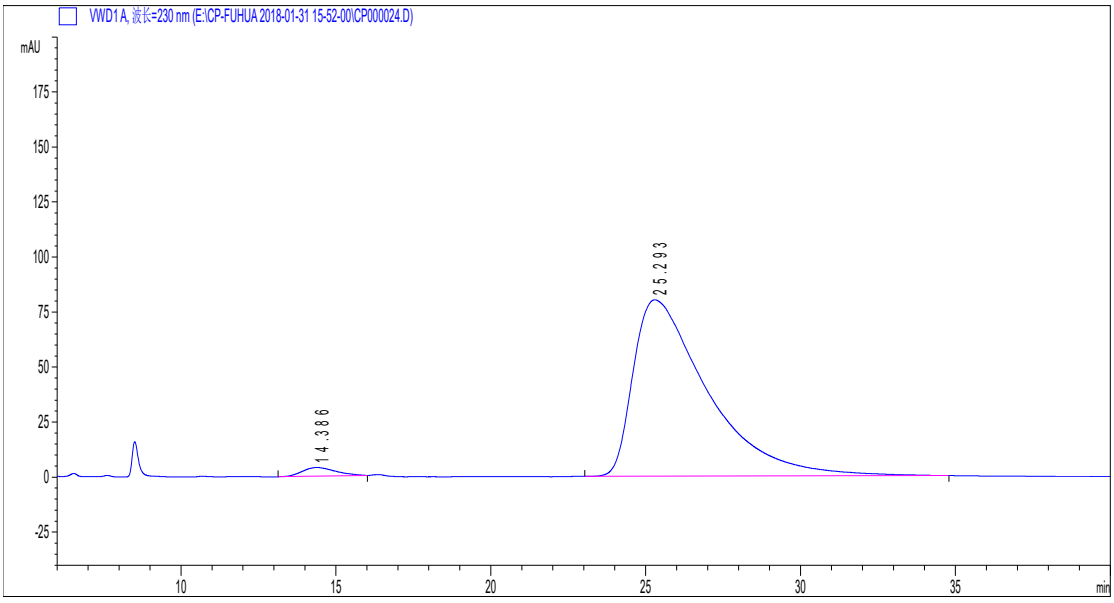
Peak #	RetTime [min]	Type	Width [min]	Area mAU *s	Height [mAU]	Area %
1	21.275	BB	1.2560	917.82092	9.60534	5.4823
2	36.320	BB	2.6407	1.58237e4	76.44106	94.5177

HPLC chromatogram of racemic 3cw



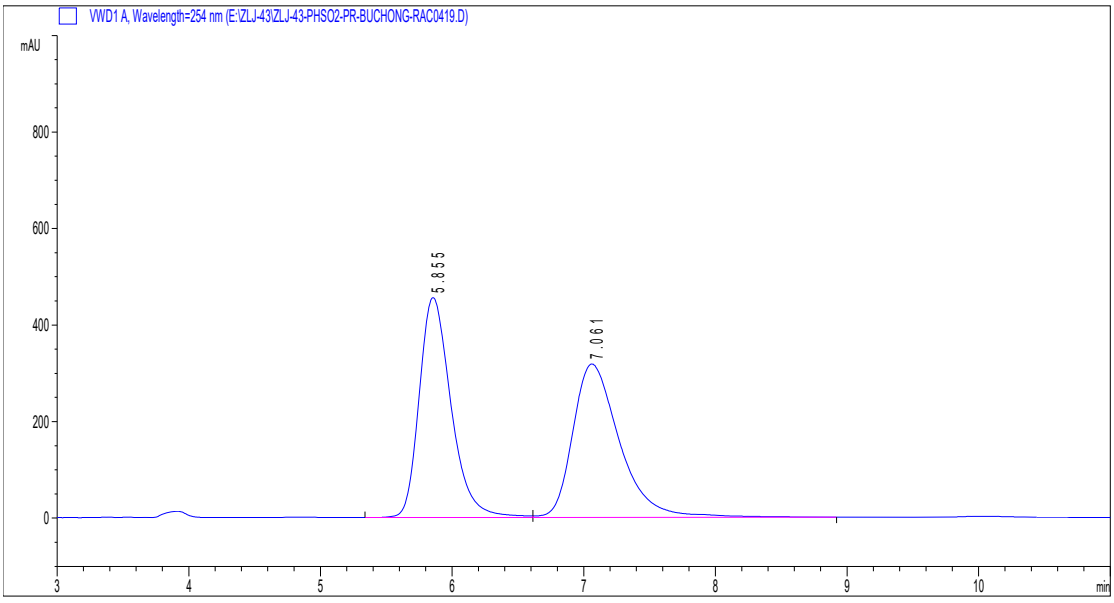
Peak #	RetTime [min]	Type	Width [min]	Area mAU *s	Height [mAU]	Area %
1	14.195	BB	1.1167	3670.27686	48.85522	49.8371
2	26.264	MM	2.8416	3694.27271	21.66780	50.1629

HPLC chromatogram of chiral 3cw



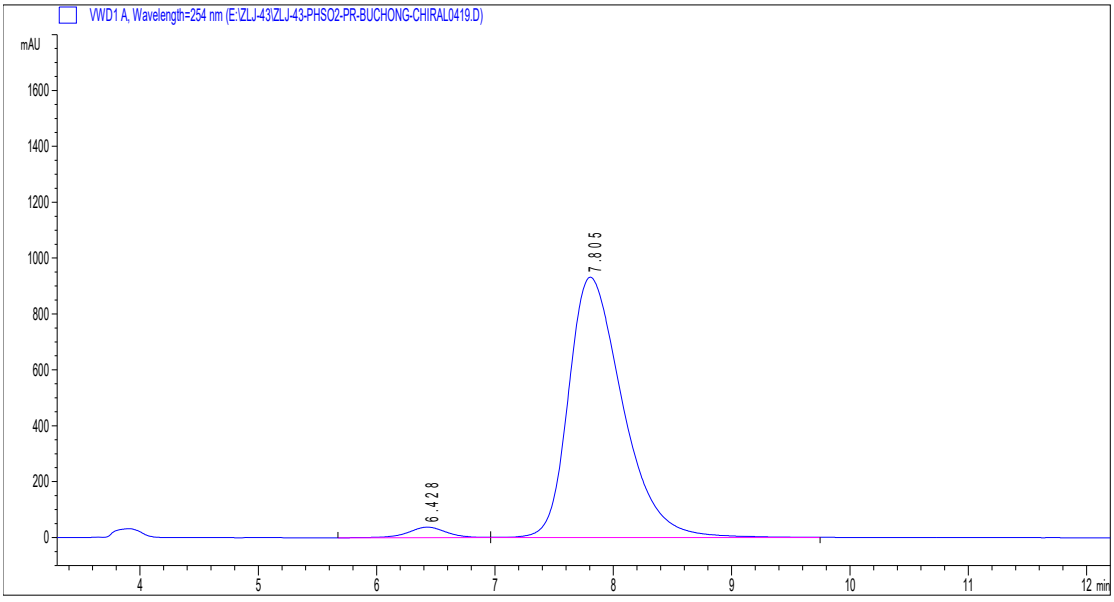
Peak #	RetTime [min]	Type	Width [min]	Area mAU *s	Height [mAU]	Area %
1	14.386	BB	0.9004	292.59311	3.92457	2.1384
2	25.293	BB	2.3256	1.33902e4	80.17490	97.8616

HPLC chromatogram of racemic 3dw



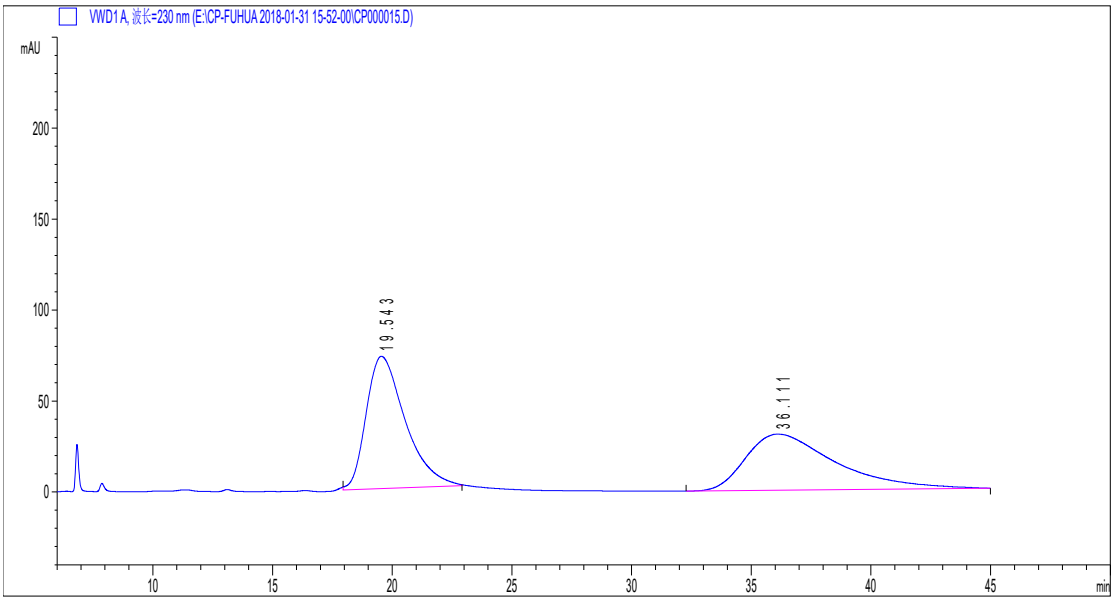
Peak #	RetTime [min]	Type	Width [min]	Area mAU *s	Height [mAU]	Area %
1	5.855	BV	0.2587	7657.32031	455.54147	49.4278
2	7.061	VB	0.3766	7834.61914	317.65585	50.5722

HPLC chromatogram of chiral 3dw



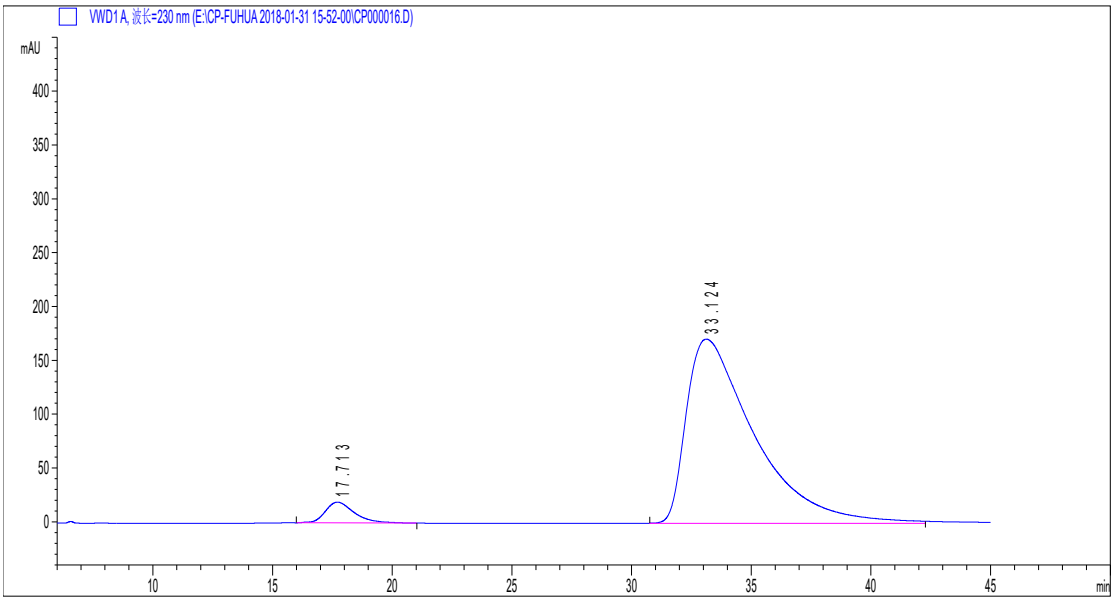
Peak #	RetTime [min]	Type	Width [min]	Area mAU *s	Height [mAU]	Area %
1	6.428	BV	0.3346	854.65118	37.87884	2.8047
2	7.805	VV	0.4857	2.96171e4	932.24622	97.1953

HPLC chromatogram of racemic 3ew



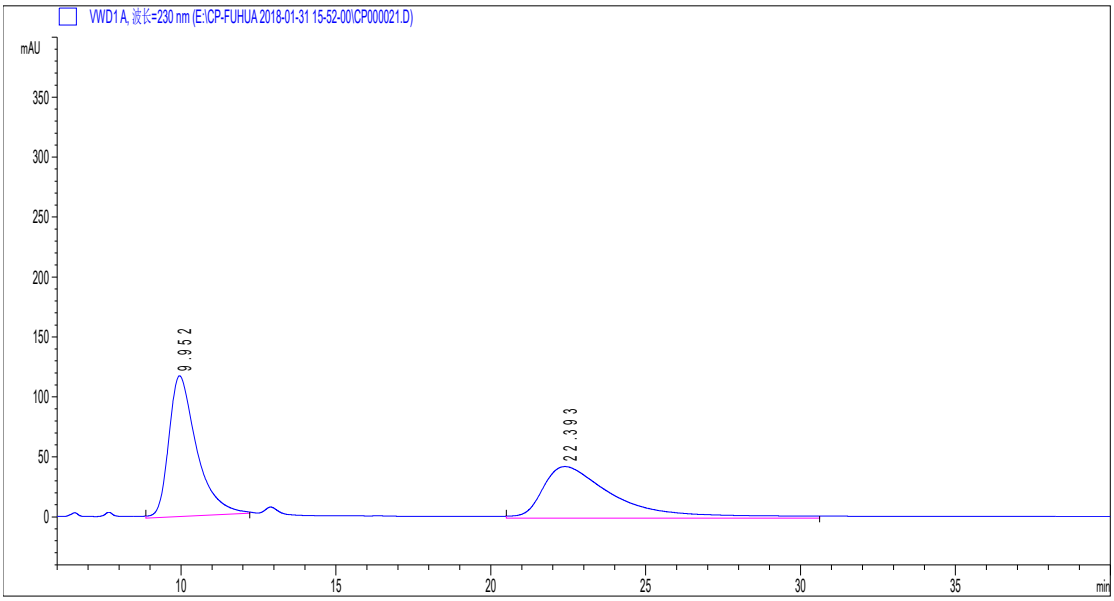
Peak #	RetTime [min]	Type	Width [min]	Area mAU *s	Height [mAU]	Area %
1	19.543	MM	1.8911	8252.50098	72.72974	50.6464
2	36.111	BBA	3.0688	8041.86230	30.85065	49.3536

HPLC chromatogram of chiral 3ew



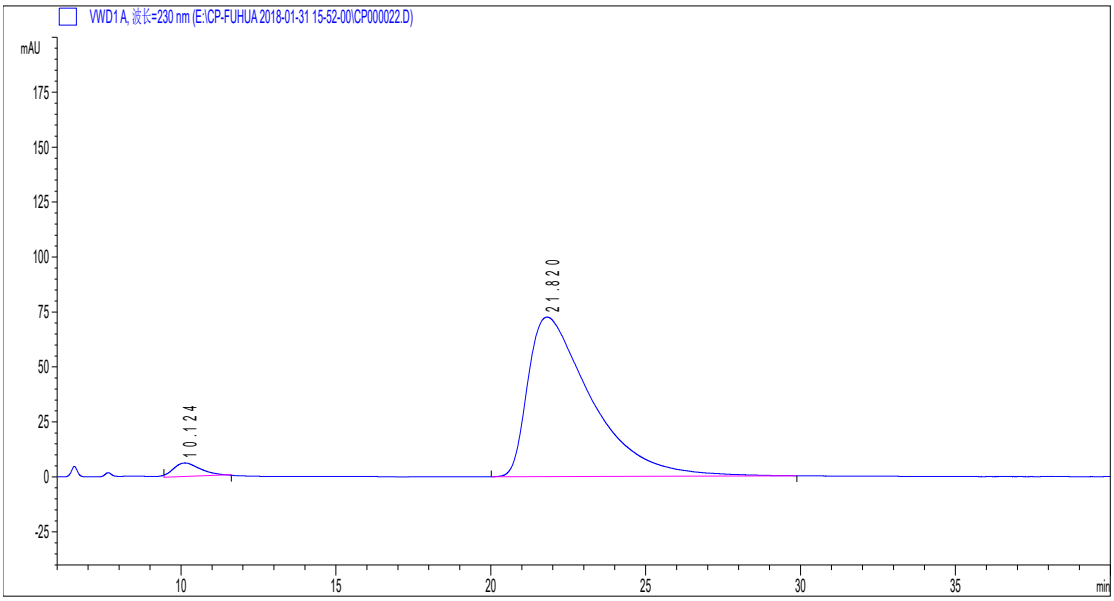
Peak #	RetTime [min]	Type	Width [min]	Area mAU *s	Height [mAU]	Area %
1	17.713	BB	1.2214	1632.57947	19.29815	4.6151
2	33.124	MM	3.2897	3.37425e4	170.95107	95.3849

HPLC chromatogram of racemic 3fw



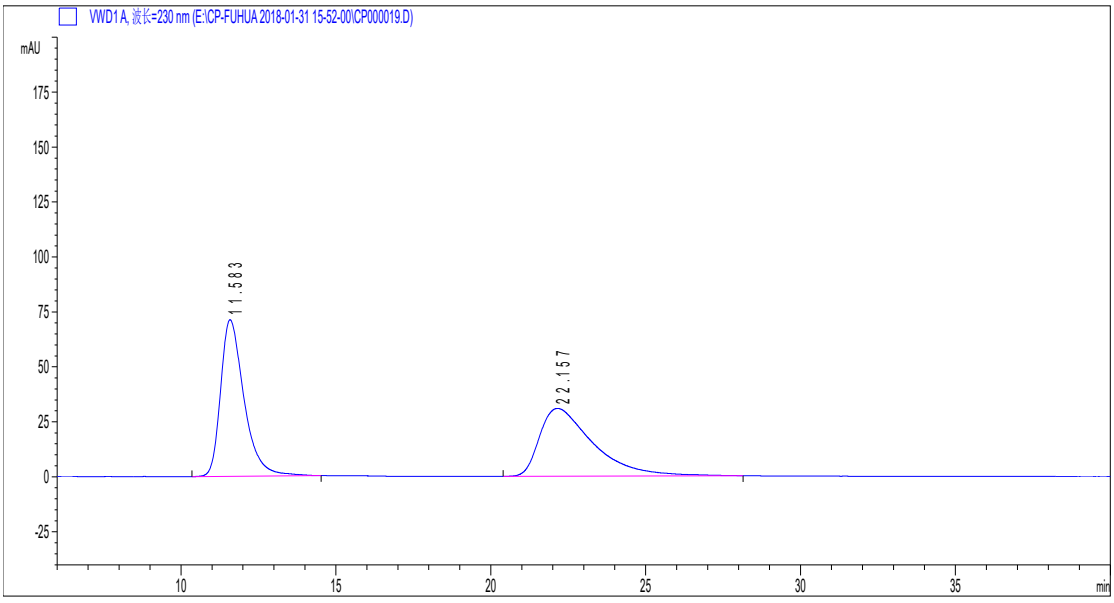
Peak #	RetTime [min]	Type	Width [min]	Area mAU *s	Height [mAU]	Area %
1	9.952	MM	1.0394	7311.81543	117.24369	51.2730
2	22.393	MM	2.6982	6948.75049	42.92192	48.7270

HPLC chromatogram of chiral 3fw



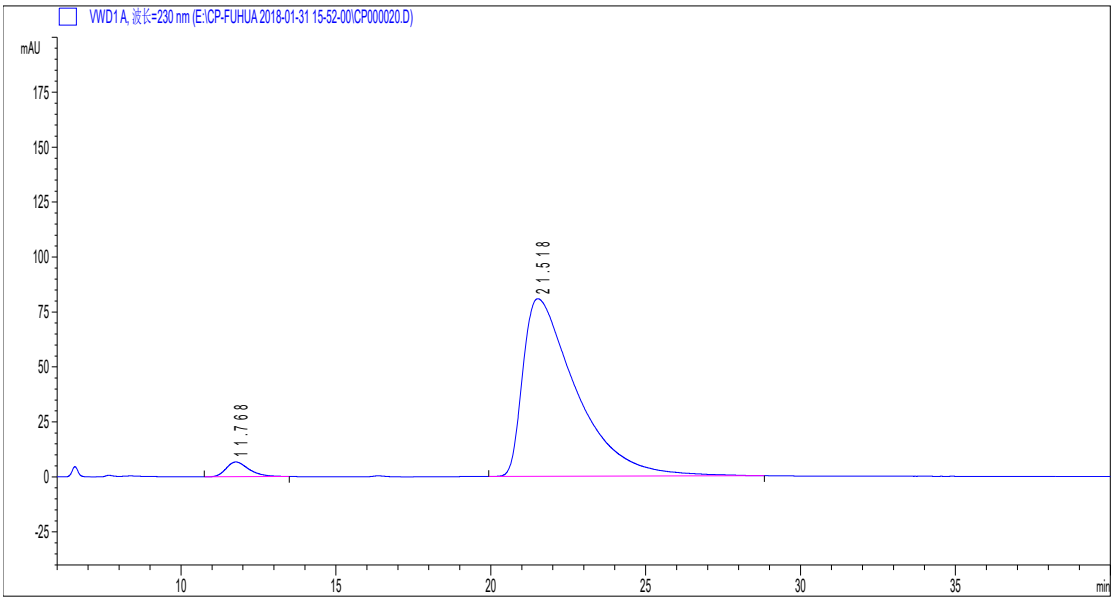
Peak #	RetTime [min]	Type	Width [min]	Area mAU *s	Height [mAU]	Area %
1	10.124	MM	0.9884	363.74335	6.13369	3.4024
2	21.820	BB	2.0501	1.03271e4	72.51881	96.5976

HPLC chromatogram of racemic 3gw



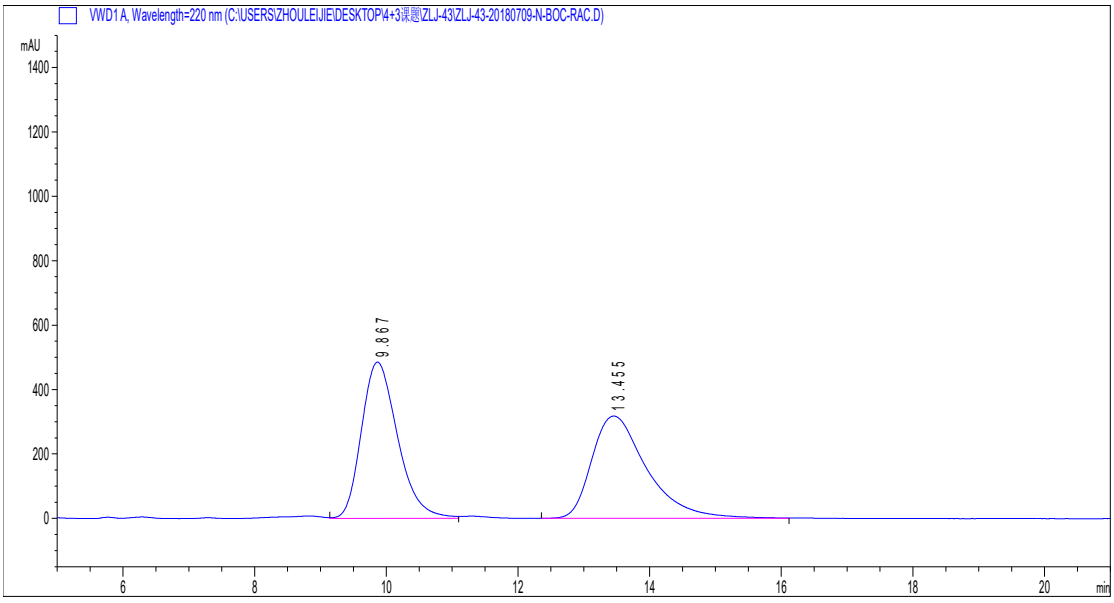
Peak #	RetTime [min]	Type	Width [min]	Area mAU *s	Height [mAU]	Area %
1	11.583	BB	0.7949	3743.49414	71.25246	50.2400
2	22.157	BB	1.6939	3707.73535	30.83807	49.7600

HPLC chromatogram of chiral 3gw



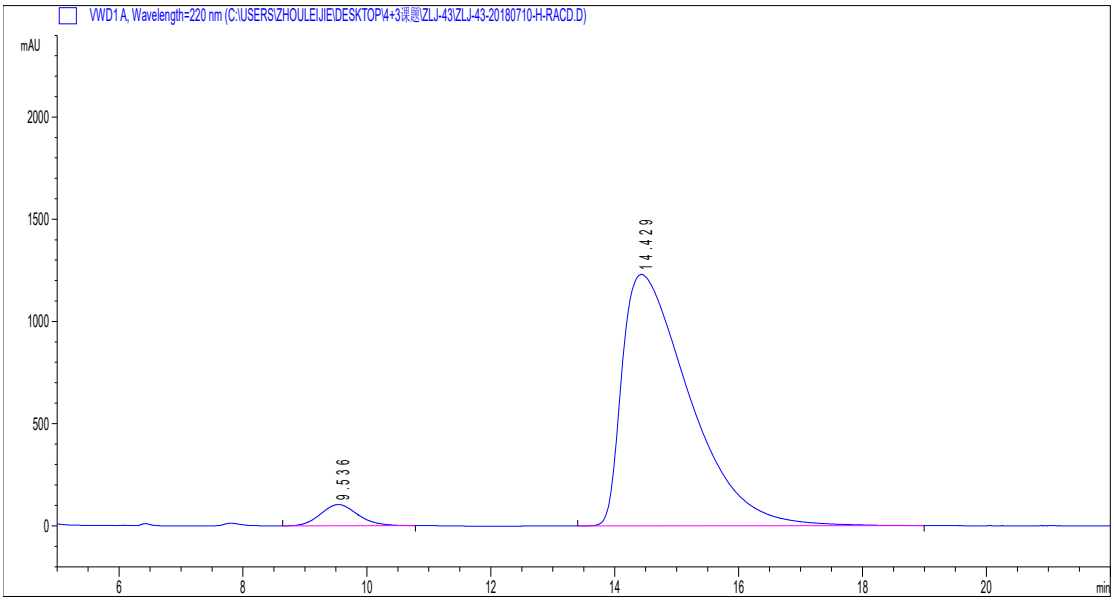
Peak #	RetTime [min]	Type	Width [min]	Area mAU *s	Height [mAU]	Area %
1	11.768	BB	0.7632	344.95825	6.69039	3.4398
2	21.518	BB	1.7095	9683.57227	80.81606	96.5602

HPLC chromatogram of racemic 5



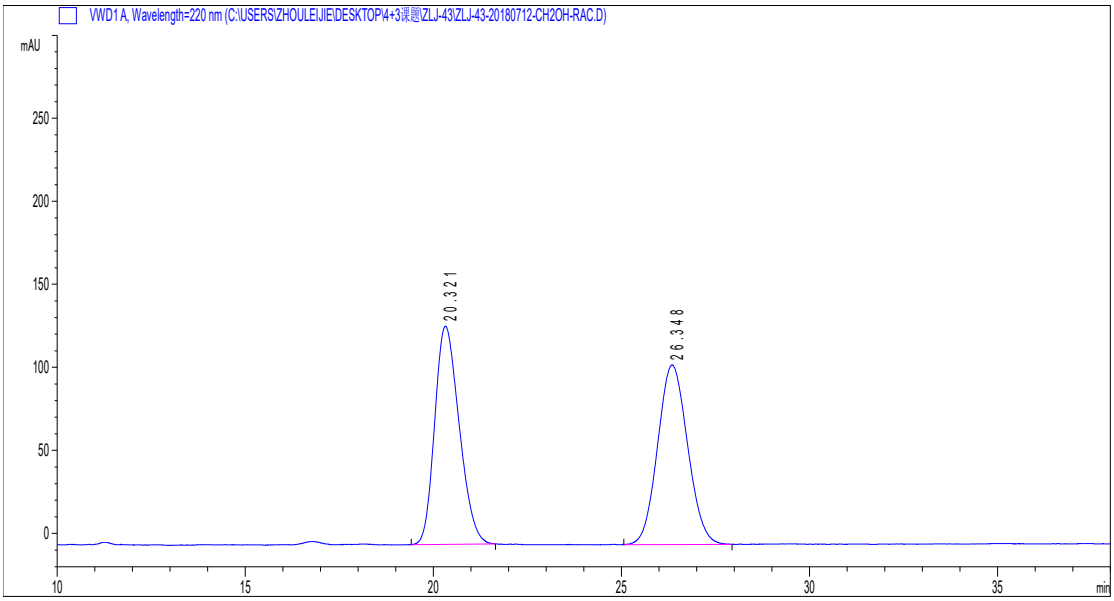
Peak #	RetTime [min]	Type	Width [min]	Area mAU *s	Height [mAU]	Area %
1	9.867	VV	0.5911	1.85279e4	485.19034	50.1325
2	13.455	BV	0.8661	1.84300e4	317.68961	49.8675

HPLC chromatogram of chiral 5



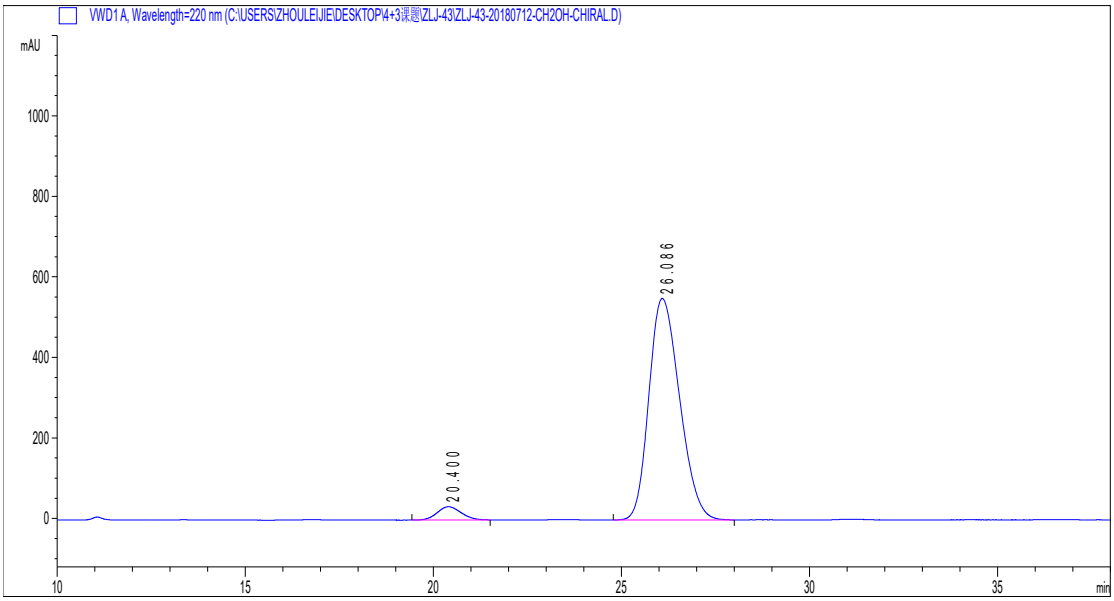
Peak #	RetTime [min]	Type	Width [min]	Area mAU *s	Height [mAU]	Area %
1	9.536	VV	0.6365	4348.20947	103.94975	4.4667
2	14.429	VV	1.0259	9.29997e4	1230.54968	95.5333

HPLC chromatogram of racemic 6



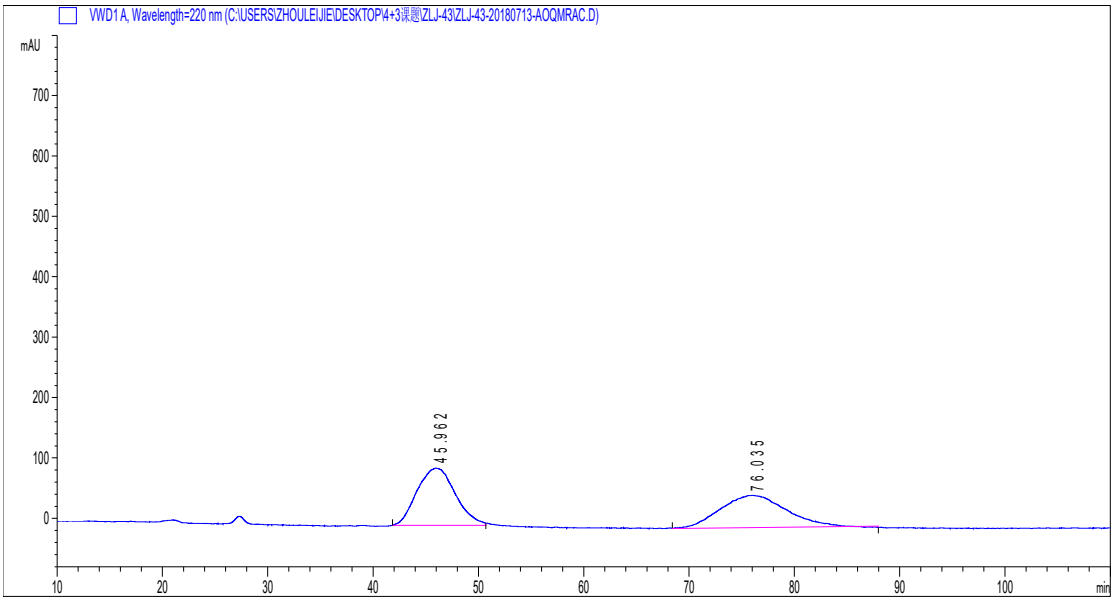
Peak #	RetTime [min]	Type	Width [min]	Area mAU *s	Height [mAU]	Area %
1	20.321	VB	0.6930	5955.31934	131.45966	49.8569
2	26.348	VB	0.8600	5989.51367	108.17847	50.1431

HPLC chromatogram of chiral 6



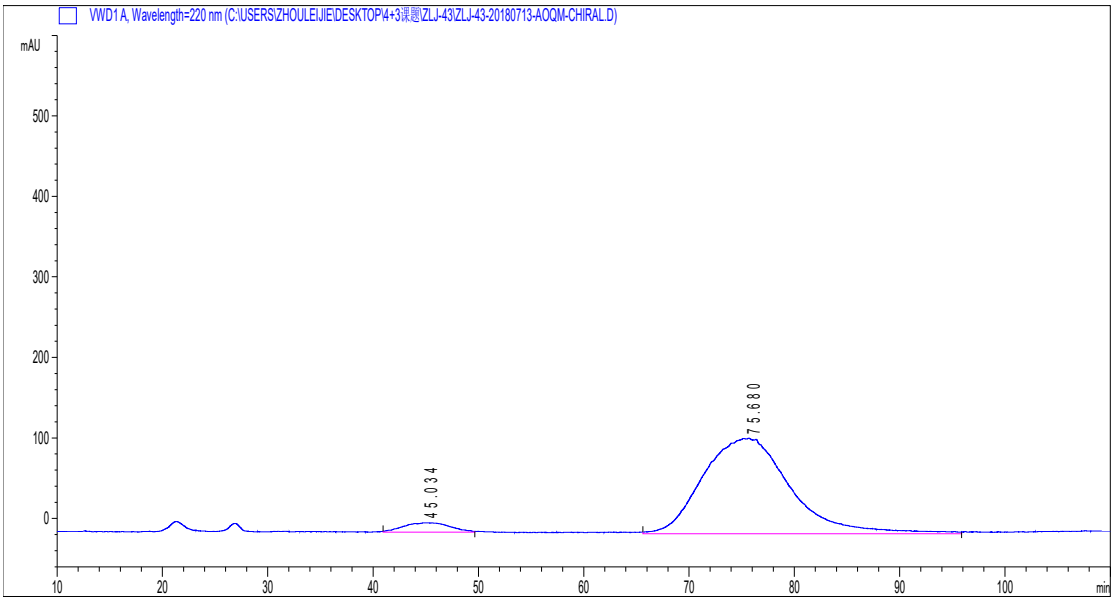
Peak #	RetTime [min]	Type	Width [min]	Area mAU *s	Height [mAU]	Area %
1	20.400	VV	0.6509	1466.57275	32.91055	4.4908
2	26.086	BV	0.8738	3.11905e4	550.31885	95.5092

HPLC chromatogram of racemic 8



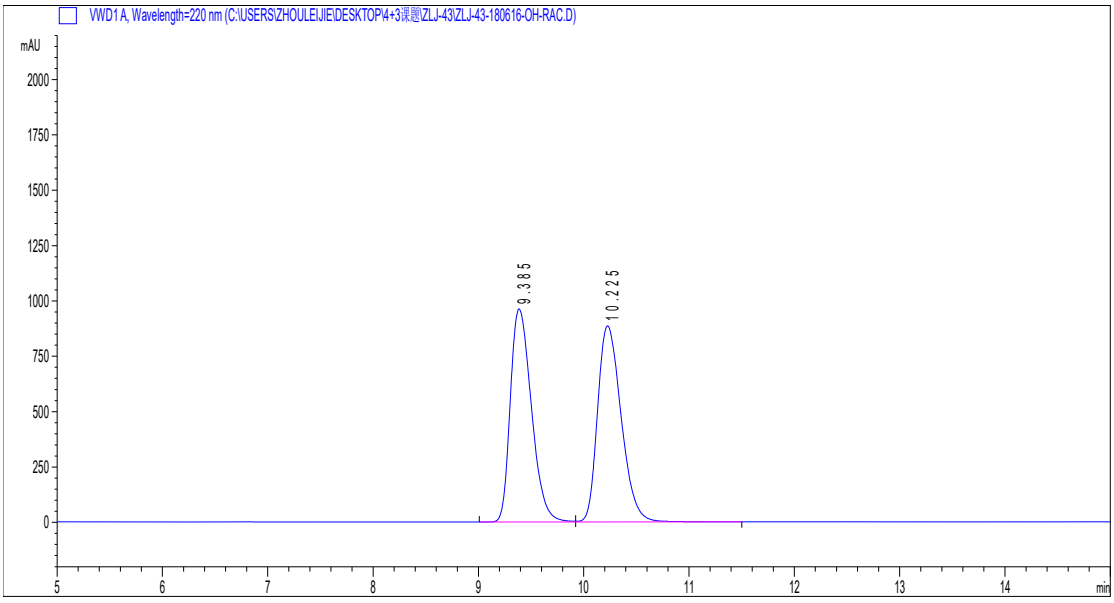
Peak #	RetTime [min]	Type	Width [min]	Area mAU *s	Height [mAU]	Area %
1	45.962	BV	2.9418	2.37742e4	94.51763	50.8097
2	76.035	MM	7.1942	2.30164e4	53.32178	49.1903

HPLC chromatogram of chiral 8



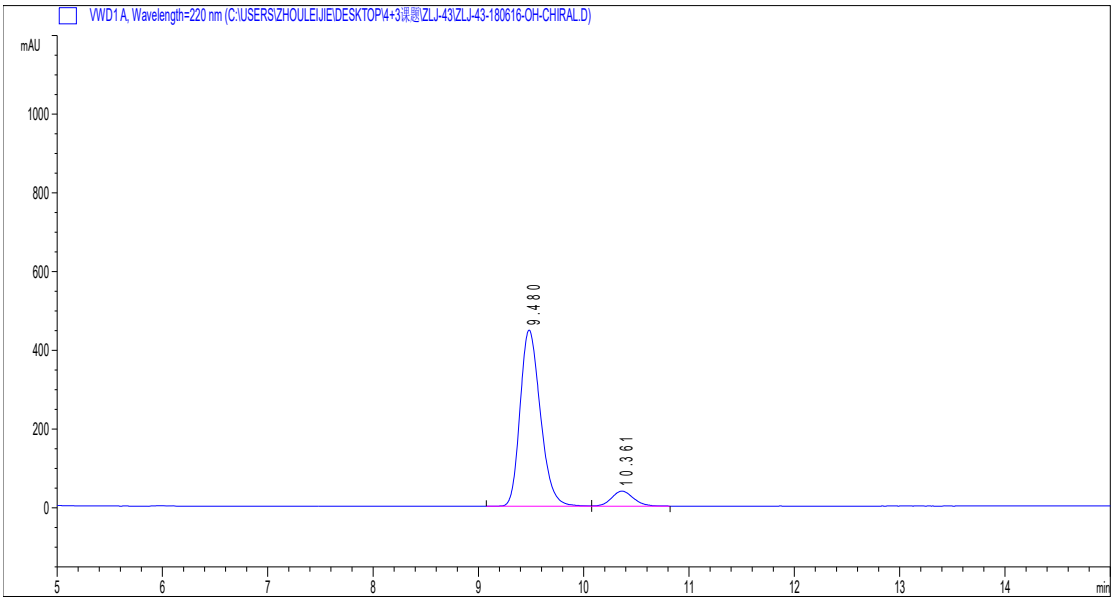
Peak #	RetTime [min]	Type	Width [min]	Area mAU *s	Height [mAU]	Area %
1	45.034	MM	5.1610	3591.82153	11.59933	4.9927
2	75.680	MM	9.6084	6.83500e4	118.55909	95.0073

HPLC chromatogram of racemic 2a



Peak #	RetTime [min]	Type	Width [min]	Area mAU *s	Height [mAU]	Area %
1	9.385	BV	0.2189	1.33666e4	962.18610	49.2395
2	10.225	VV	0.2441	1.37795e4	885.63794	50.7605

HPLC chromatogram of chiral 2a



Peak #	RetTime [min]	Type	Width [min]	Area mAU *s	Height [mAU]	Area %
1	9.480	BV	0.2084	5984.49756	447.58490	91.5305
2	10.361	VV	0.2217	553.75403	38.16028	8.4695

X-Ray Crystallography Data

Crystallographic data for **3aa** has been deposited with the Cambridge Crystallographic Data Centre as deposition number CCDC 1857263. These data can be obtained free of charge via www.ccdc.cam.ac.uk/data_request/cif, or by emailing data_request@ccdc.cam.ac.uk, or by contacting The Cambridge Crystallographic Data Centre, 12, Union Road, Cambridge CB2 1EZ, UK; fax: +44 1223 336033.

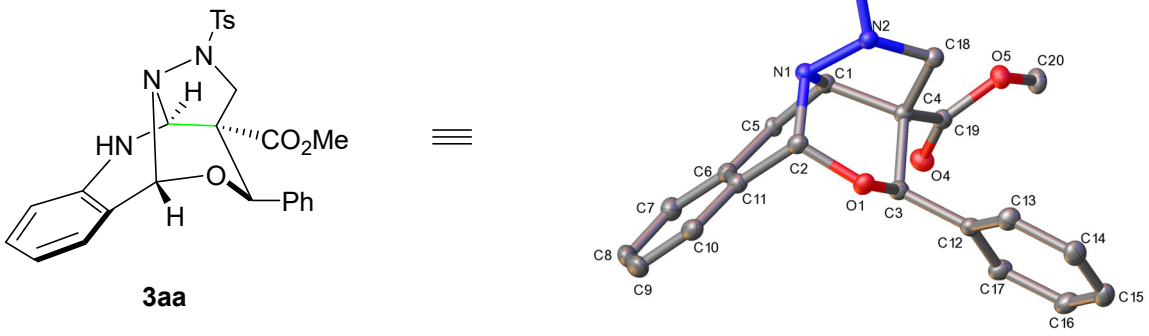


Table S1. Crystal data and structure refinement for **3aa**.

Identification code	**3aa**	
Empirical formula	C27 H25 N2 O5 S	
Formula weight	489.55	
Temperature	173.15 K	
Wavelength	0.71073 Å	
Crystal system	Monoclinic	
Space group	P 1 21 1	
Unit cell dimensions	a = 6.5581(12) Å	a= 90°.
	b = 10.9280(19) Å	b= 92.794(3)°.
	c = 16.216(3) Å	g = 90°.
Volume	1160.8(4) Å^3	

Z	2
Density (calculated)	1.401 Mg/m^3
Absorption coefficient	0.183 mm^{-1}
F(000)	514
Crystal size	0.366 x 0.319 x 0.203 mm^3
Theta range for data collection	2.515 to 27.495°.
Index ranges	-8<=h<=8, -14<=k<=14, -21<=l<=21
Reflections collected	13224
Independent reflections	5290 [R(int) = 0.0474]
Completeness to theta = 25.242°	99.4 %
Absorption correction	Semi-empirical from equivalents
Max. and min. transmission	1.00000 and 0.73515
Refinement method	Full-matrix least-squares on F^3
Data / restraints / parameters	5290 / 1 / 318
Goodness-of-fit on F^2	1.057
Final R indices [I>2sigma(I)]	R1 = 0.0409, wR2 = 0.1085
R indices (all data)	R1 = 0.0418, wR2 = 0.1093
Absolute structure parameter	0.01(3)
Extinction coefficient	n/a
Largest diff. peak and hole	0.390 and -0.270 $e.Å^{-3}$

Table S2. Atomic coordinates (x 10^4) and equivalent isotropic displacement parameters ($Å^2$ x 10^3) for **3aa**. U (eq) is defined as one third of the trace of the orthogonalized U^{ij} tensor.

	x	y	z	U(eq)
S1	-141(1)	4316(1)	4086(1)	27(1)

O1	1336(3)	4879(2)	1587(1)	28(1)
O2	-1283(3)	5431(2)	4121(1)	34(1)
O3	-1154(4)	3165(2)	4146(1)	36(1)
O4	7234(3)	3359(2)	2130(1)	32(1)
O5	5544(3)	1878(2)	2766(1)	30(1)
N1	2037(4)	5387(2)	3024(2)	25(1)
N2	870(3)	4299(2)	3172(1)	25(1)
C1	4156(4)	4926(2)	3002(2)	25(1)
C2	1377(5)	5830(3)	2195(2)	28(1)
C3	3182(4)	4179(3)	1564(2)	26(1)
C4	3799(4)	3755(3)	2459(2)	25(1)
C5	5509(4)	5849(2)	2731(2)	20(1)
C6	4800(5)	6844(3)	2273(2)	30(1)
C7	6071(5)	7816(3)	2084(2)	37(1)
C8	5338(6)	8775(3)	1603(2)	45(1)
C9	3298(7)	8808(3)	1324(2)	45(1)
C10	2012(6)	7862(3)	1519(2)	36(1)
C11	2751(5)	6876(3)	1988(2)	31(1)
C12	2808(4)	3145(3)	955(2)	27(1)
C13	864(5)	2630(3)	823(2)	32(1)
C14	567(5)	1679(3)	263(2)	36(1)
C15	2150(5)	1225(3)	-167(2)	36(1)

C16	4098(5)	1731(3)	-35(2)	36(1)
C17	4409(5)	2686(3)	516(2)	33(1)
C18	1987(4)	3193(3)	2892(2)	26(1)
C19	5720(4)	2987(2)	2437(2)	24(1)
C20	7390(5)	1140(3)	2764(2)	34(1)
C21	1892(4)	4375(3)	4827(2)	26(1)
C22	2884(5)	5486(3)	4985(2)	29(1)
C23	4683(5)	5488(3)	5476(2)	34(1)
C24	5486(4)	4415(3)	5817(2)	33(1)
C25	4412(5)	3318(3)	5677(2)	35(1)
C26	2640(5)	3298(3)	5182(2)	31(1)
C27	7440(5)	4434(4)	6341(2)	47(1)

Table S3. Bond lengths [Å] and angles [°] for **3aa**.

S1-O2	1.433(2)
S1-O3	1.428(2)
S1-N2	1.653(2)
S1-C21	1.753(3)
O1-C2	1.432(3)
O1-C3	1.434(3)

O4-C19	1.203(3)
O5-C19	1.332(3)
O5-C20	1.455(3)
N1-N2	1.440(3)
N1-C1	1.480(4)
N1-C2	1.474(4)
N2-C18	1.495(4)
C1-H1	1.0000
C1-C4	1.565(4)
C1-C5	1.427(3)
C2-H2	1.0000
C2-C11	1.503(4)
C3-H3	1.0000
C3-C4	1.557(4)
C3-C12	1.513(4)
C4-C18	1.538(4)
C4-C19	1.515(4)
C5-H5	0.9500
C5-C6	1.384(4)
C6-C7	1.394(4)
C6-C11	1.400(4)
C7-H7	0.9500

C7-C8	1.378(5)
C8-H8	0.9500
C8-C9	1.392(6)
C9-H9	0.9500
C9-C10	1.381(5)
C10-H10	0.9500
C10-C11	1.392(4)
C12-C13	1.400(4)
C12-C17	1.391(4)
C13-H13	0.9500
C13-C14	1.388(4)
C14-H14	0.9500
C14-C15	1.371(5)
C15-H15	0.9500
C15-C16	1.399(5)
C16-H16	0.9500
C16-C17	1.382(4)
C17-H17	0.9500
C18-H18A	0.9900
C18-H18B	0.9900
C20-H20A	0.9800
C20-H20B	0.9800

C20-H20C	0.9800
C21-C22	1.394(4)
C21-C26	1.389(4)
C22-H22	0.9500
C22-C23	1.391(4)
C23-H23	0.9500
C23-C24	1.390(5)
C24-C25	1.403(5)
C24-C27	1.503(4)
C25-H25	0.9500
C25-C26	1.380(5)
C26-H26	0.9500
C27-H27A	0.9800
C27-H27B	0.9800
C27-H27C	0.9800

O2-S1-N2	106.20(13)
O2-S1-C21	108.81(14)
O3-S1-O2	120.02(12)
O3-S1-N2	105.05(13)
O3-S1-C21	109.06(14)
N2-S1-C21	106.91(12)

C2-O1-C3	114.7(2)
C19-O5-C20	114.5(2)
N2-N1-C1	103.3(2)
N2-N1-C2	106.7(2)
C2-N1-C1	108.9(2)
N1-N2-S1	112.29(17)
N1-N2-C18	110.15(18)
C18-N2-S1	120.33(19)
N1-C1-H1	108.6
N1-C1-C4	100.2(2)
C4-C1-H1	108.6
C5-C1-N1	111.4(2)
C5-C1-H1	108.6
C5-C1-C4	118.9(2)
O1-C2-N1	112.6(2)
O1-C2-H2	107.9
O1-C2-C11	112.9(2)
N1-C2-H2	107.9
N1-C2-C11	107.5(2)
C11-C2-H2	107.9
O1-C3-H3	108.7
O1-C3-C4	108.4(2)

O1-C3-C12	107.8(2)
C4-C3-H3	108.7
C12-C3-H3	108.7
C12-C3-C4	114.4(2)
C3-C4-C1	107.8(2)
C18-C4-C1	99.6(2)
C18-C4-C3	111.9(2)
C19-C4-C1	111.4(2)
C19-C4-C3	108.8(2)
C19-C4-C18	116.8(2)
C1-C5-H5	119.2
C6-C5-C1	121.5(2)
C6-C5-H5	119.2
C5-C6-C7	121.9(3)
C5-C6-C11	119.3(3)
C7-C6-C11	118.9(3)
C6-C7-H7	119.7
C8-C7-C6	120.5(3)
C8-C7-H7	119.7
C7-C8-H8	119.8
C7-C8-C9	120.5(3)
C9-C8-H8	119.8

C8-C9-H9	120.2
C10-C9-C8	119.6(3)
C10-C9-H9	120.2
C9-C10-H10	119.8
C9-C10-C11	120.3(3)
C11-C10-H10	119.8
C6-C11-C2	118.9(2)
C10-C11-C2	120.9(3)
C10-C11-C6	120.2(3)
C13-C12-C3	121.1(3)
C17-C12-C3	120.1(3)
C17-C12-C13	118.8(3)
C12-C13-H13	120.0
C14-C13-C12	119.9(3)
C14-C13-H13	120.0
C13-C14-H14	119.4
C15-C14-C13	121.2(3)
C15-C14-H14	119.4
C14-C15-H15	120.4
C14-C15-C16	119.2(3)
C16-C15-H15	120.4
C15-C16-H16	119.9

C17-C16-C15	120.2(3)
C17-C16-H16	119.9
C12-C17-H17	119.6
C16-C17-C12	120.8(3)
C16-C17-H17	119.6
N2-C18-C4	102.5(2)
N2-C18-H18A	111.3
N2-C18-H18B	111.3
C4-C18-H18A	111.3
C4-C18-H18B	111.3
H18A-C18-H18B	109.2
O4-C19-O5	124.2(3)
O4-C19-C4	121.8(3)
O5-C19-C4	114.0(2)
O5-C20-H20A	109.5
O5-C20-H20B	109.5
O5-C20-H20C	109.5
H20A-C20-H20B	109.5
H20A-C20-H20C	109.5
H20B-C20-H20C	109.5
C22-C21-S1	119.4(2)
C26-C21-S1	119.6(2)

C26-C21-C22	120.6(2)
C21-C22-H22	120.6
C23-C22-C21	118.8(3)
C23-C22-H22	120.6
C22-C23-H23	119.3
C24-C23-C22	121.4(3)
C24-C23-H23	119.3
C23-C24-C25	118.6(3)
C23-C24-C27	120.6(3)
C25-C24-C27	120.7(3)
C24-C25-H25	119.7
C26-C25-C24	120.6(3)
C26-C25-H25	119.7
C21-C26-H26	120.1
C25-C26-C21	119.8(3)
C25-C26-H26	120.1
C24-C27-H27A	109.5
C24-C27-H27B	109.5
C24-C27-H27C	109.5
H27A-C27-H27B	109.5
H27A-C27-H27C	109.5
H27B-C27-H27C	109.5

Symmetry transformations used to generate equivalent atoms:

Table S4. Anisotropic displacement parameters ($Å^2$ x 10^3) for **3aa**. The anisotropic displacement factor exponent takes the form: $-2p^2$ [h^2 $a^{*2}U^{11}$ + ... + 2 h k a* b* U^{12}]

	U^{11}	U^{22}	U^{33}	U^{23}	U^{13}	U^{12}
S1	26(1)	30(1)	24(1)	-2(1)	2(1)	-1(1)
O1	30(1)	29(1)	25(1)	-2(1)	-6(1)	3(1)
O2	31(1)	39(1)	31(1)	-3(1)	1(1)	7(1)
O3	36(1)	40(1)	31(1)	-4(1)	5(1)	-12(1)
O4	26(1)	35(1)	34(1)	4(1)	2(1)	-2(1)
O5	28(1)	26(1)	36(1)	1(1)	2(1)	-1(1)
N1	26(1)	25(1)	23(1)	1(1)	0(1)	-2(1)
N2	28(1)	25(1)	23(1)	-1(1)	0(1)	-3(1)
C1	26(1)	25(1)	22(1)	1(1)	-3(1)	-1(1)
C2	33(1)	28(1)	23(1)	0(1)	-2(1)	4(1)
C3	26(1)	27(1)	24(1)	1(1)	1(1)	-2(1)
C4	24(1)	28(1)	23(1)	-1(1)	-2(1)	-3(1)
C5	19(1)	19(1)	22(1)	0(1)	-3(1)	-4(1)
C6	42(2)	24(1)	24(1)	-2(1)	3(1)	-3(1)
C7	46(2)	31(2)	34(2)	-4(1)	2(1)	-9(1)
C8	73(2)	27(1)	34(2)	2(1)	4(2)	-15(2)

C9	78(3)	28(1)	30(2)	6(1)	-2(2)	1(2)
C10	53(2)	31(2)	26(1)	0(1)	-2(1)	5(1)
C11	42(2)	26(1)	24(1)	-1(1)	1(1)	0(1)
C12	32(1)	28(1)	21(1)	2(1)	-3(1)	-2(1)
C13	30(1)	34(1)	30(1)	-2(1)	-5(1)	1(1)
C14	36(2)	34(2)	35(2)	-1(1)	-10(1)	-7(1)
C15	49(2)	29(1)	29(2)	-2(1)	-10(1)	1(1)
C16	43(2)	40(2)	26(1)	-4(1)	2(1)	3(1)
C17	34(2)	39(2)	25(1)	-2(1)	-1(1)	-3(1)
C18	26(1)	26(1)	26(1)	-1(1)	0(1)	-2(1)
C19	24(1)	26(1)	23(1)	-1(1)	-3(1)	-2(1)
C20	34(2)	25(1)	43(2)	-2(1)	4(1)	2(1)
C21	31(1)	25(1)	23(1)	-2(1)	3(1)	1(1)
C22	39(2)	23(1)	24(1)	0(1)	-3(1)	-1(1)
C23	42(2)	33(2)	27(1)	-4(1)	0(1)	-8(1)
C24	32(1)	45(2)	23(1)	0(1)	0(1)	-2(2)
C25	43(2)	33(2)	30(2)	4(1)	1(1)	9(1)
C26	38(2)	24(1)	30(1)	2(1)	2(1)	-1(1)
C27	38(2)	65(2)	37(2)	4(2)	-9(1)	2(2)

Table S5. Hydrogen coordinates (x 10^4) and isotropic displacement parameters ($Å^2$ x 10^2) for **3aa**.

	x	y	z	U(eq)
H1	4622	4666	3572	29
H2	-41	6158	2224	34
H3	4286	4716	1362	31
H5	6929	5780	2869	24
H7	7454	7818	2288	44
H8	6231	9418	1462	54
H9	2793	9477	1000	55
H10	616	7884	1333	44
H13	-250	2932	1116	38
H14	-757	1337	175	43
H15	1926	575	-550	43
H16	5210	1417	-324	44
H17	5732	3033	595	39
H18A	1120	2694	2505	31
H18B	2459	2678	3366	31
H20A	7958	1176	2216	50
H20B	7062	290	2896	50

H20C	8394	1458	3177	50
H22	2341	6227	4761	35
H23	5377	6240	5581	41
H25	4909	2582	5925	42
H26	1933	2549	5084	37
H27A	8436	4961	6082	71
H27B	7986	3601	6393	71
H27C	7172	4753	6891	71

Table S6. Torsion angles [°] for **3aa**.

S1-N2-C18-C4	-140.32(19)
S1-C21-C22-C23	-170.1(2)
S1-C21-C26-C25	170.9(2)
O1-C2-C11-C6	-90.4(3)
O1-C2-C11-C10	89.4(3)
O1-C3-C4-C1	-60.5(3)
O1-C3-C4-C18	48.0(3)
O1-C3-C4-C19	178.6(2)
O1-C3-C12-C13	-30.4(3)
O1-C3-C12-C17	149.8(3)

O2-S1-N2-N1	54.3(2)
O2-S1-N2-C18	-173.5(2)
O2-S1-C21-C22	-36.2(3)
O2-S1-C21-C26	150.9(2)
O3-S1-N2-N1	-177.52(18)
O3-S1-N2-C18	-45.4(2)
O3-S1-C21-C22	-168.8(2)
O3-S1-C21-C26	18.3(3)
N1-N2-C18-C4	-7.3(3)
N1-C1-C4-C3	69.1(2)
N1-C1-C4-C18	-47.8(2)
N1-C1-C4-C19	-171.7(2)
N1-C1-C5-C6	-21.9(4)
N1-C2-C11-C6	34.4(3)
N1-C2-C11-C10	-145.8(3)
N2-S1-C21-C22	78.1(3)
N2-S1-C21-C26	-94.8(2)
N2-N1-C1-C4	44.0(2)
N2-N1-C1-C5	170.8(2)
N2-N1-C2-O1	-48.3(3)
N2-N1-C2-C11	-173.3(2)
C1-N1-N2-S1	113.31(19)

C1-N1-N2-C18	-23.7(2)
C1-N1-C2-O1	62.6(3)
C1-N1-C2-C11	-62.4(3)
C1-C4-C18-N2	33.1(2)
C1-C4-C19-O4	-64.7(3)
C1-C4-C19-O5	116.9(3)
C1-C5-C6-C7	172.8(3)
C1-C5-C6-C11	-7.4(4)
C2-O1-C3-C4	50.1(3)
C2-O1-C3-C12	174.4(2)
C2-N1-N2-S1	-131.93(19)
C2-N1-N2-C18	91.0(2)
C2-N1-C1-C4	-69.2(3)
C2-N1-C1-C5	57.6(3)
C3-O1-C2-N1	-51.4(3)
C3-O1-C2-C11	70.6(3)
C3-C4-C18-N2	-80.6(3)
C3-C4-C19-O4	54.0(3)
C3-C4-C19-O5	-124.5(2)
C3-C12-C13-C14	-179.7(3)
C3-C12-C17-C16	179.1(3)
C4-C1-C5-C6	93.8(3)

C4-C3-C12-C13	90.2(3)
C4-C3-C12-C17	-89.6(3)
C5-C1-C4-C3	-52.5(3)
C5-C1-C4-C18	-169.3(2)
C5-C1-C4-C19	66.8(3)
C5-C6-C7-C8	177.8(3)
C5-C6-C11-C2	0.5(4)
C5-C6-C11-C10	-179.3(3)
C6-C7-C8-C9	2.2(5)
C7-C6-C11-C2	-179.8(3)
C7-C6-C11-C10	0.4(4)
C7-C8-C9-C10	-1.0(5)
C8-C9-C10-C11	-0.5(5)
C9-C10-C11-C2	-179.1(3)
C9-C10-C11-C6	0.8(5)
C11-C6-C7-C8	-1.9(4)
C12-C3-C4-C1	179.2(2)
C12-C3-C4-C18	-72.2(3)
C12-C3-C4-C19	58.3(3)
C12-C13-C14-C15	0.1(5)
C13-C12-C17-C16	-0.7(5)
C13-C14-C15-C16	0.2(5)
C14-C15-C16-C17	-0.8(5)
C15-C16-C17-C12	1.0(5)

C17-C12-C13-C14	0.1(4)
C18-C4-C19-O4	-178.2(3)
C18-C4-C19-O5	3.4(3)
C19-C4-C18-N2	153.1(2)
C20-O5-C19-O4	2.8(4)
C20-O5-C19-C4	-178.8(2)
C21-S1-N2-N1	-61.7(2)
C21-S1-N2-C18	70.4(2)
C21-C22-C23-C24	-0.8(5)
C22-C21-C26-C25	-1.8(4)
C22-C23-C24-C25	-1.9(5)
C22-C23-C24-C27	179.5(3)
C23-C24-C25-C26	2.7(5)
C24-C25-C26-C21	-0.9(5)
C26-C21-C22-C23	2.6(4)
C27-C24-C25-C26	-178.7(3)

Symmetry transformations used to generate equivalent atoms:

Table S7. Hydrogen bonds for **3aa** [Å and °].

D-H...A	d(D-H)	d(H...A)	d(D...A)	<(DHA)