

Electronic Supplementary Information

Tandem Nucleophilic Addition-Cycloaddition of Arynes with α -Iminoesters: Two Concurrent Pathways to Imidazolidines

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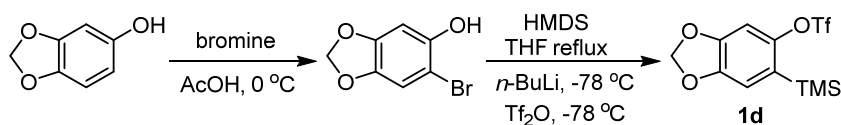
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General Information

All reactions were performed under Ar 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). ^1H and ^{13}C NMR spectra were recorded in CDCl_3 using a 300MHz NMR instrument (referenced internally to Me_4Si). Chemical shifts (δ , ppm) are relative to tetramethylsilane (TMS) with the resonance of the non-deuterated solvent or TMS as the internal standard. ^1H NMR data are reported as follows: chemical shift, multiplicity (s = singlet; d = doublet; q = quartet; m = multiplet), 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 V Plus polarimeter. Accurate mass measurements were performed using an Agilent instrument with the ESI-MS technique. HPLC analysis was performed on Agilent 1100 series and Agilent 1260 series, UV detection monitored at 254 nm, using a RC-OD, Chiralpak IA column, Lux Cellulose-1 column (OOG-4459-EO), Lux Amylose-2 column (OOG-4472-EO), and Lux Cellulose-2 column (OOG-4457-EO) with hexane and *i*-PrOH as solvents. X-ray crystallographic data were collected using a MM007HF Saturn724+.

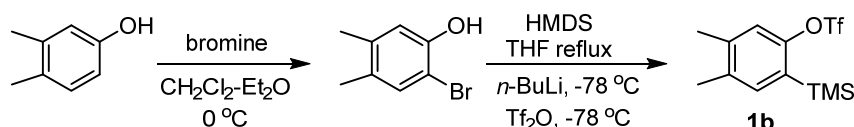
General Procedure for Preparation of Aryne **1**^[1]



To a solution of sesamol (3.0 g, 21.7 mmol) in AcOH (7 mL) was added a solution of bromine (1.0 mL, 19.4 mmol) in AcOH (4 mL) dropwise at 0 °C and the reaction mixture was stirred for 30 min at this temperature. Ice was put into this mixture and filtered off. The residual solid was washed with water and dried to afford 5-bromos sesamol as a faint green solid (2.6 g, 55%).

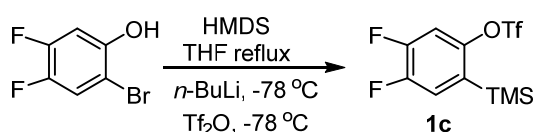
To a solution of 3-bromo-2-sesamol (1.21 g, 5.58 mmol) in THF (20 mL) was added HMDS (1.2 mL, 5.65 mmol) under argon atmosphere. The reaction mixture was refluxed for 2 h. After cooling to room temperature, the solvent was removed in vacuo. The residue was dissolved in THF (30 mL) under argon atmosphere and cooled to -78 °C. To

the solution was added *n*-butyllithium (5.36 mmol, 1.6 M solution in hexane) dropwise. After stirring at $-78\text{ }^{\circ}\text{C}$ for 1.5 h, Tf_2O (0.98 mL 58.4 mmol) was added to reaction mixture dropwise at $-78\text{ }^{\circ}\text{C}$. After stirring at $-78\text{ }^{\circ}\text{C}$ for 2 h, the reaction mixture was quenched with sat. NaHCO_3 aq. at $-78\text{ }^{\circ}\text{C}$ and this mixture was warmed to room temperature. The layers were separated without filtration, and then the aqueous layer was extracted with Et_2O three times. The combined organic layers were dried over Na_2SO_4 . The solvent was removed in vacuo, and the residue was purified by silica gel column chromatography with hexane to afford 6(trimethylsilyl)benzo[d][1,3]dioxol-5-yl trifluoromethanesulfonate **1d** as a light green liquid (284 mg, 15% yield).



To a solution of 3,4-xyleneol (9.8 g, 80 mmol) in CH_2Cl_2 (500 mL) and Et_2O (40 mL) was added dropwise a solution of bromine (4.1 mL, 80 mmol) in CH_2Cl_2 (160 mL) dropwise at $0\text{ }^{\circ}\text{C}$. After the addition was completed, the reaction was quenched with sat. Na_2SO_3 aq. at $0\text{ }^{\circ}\text{C}$ and this mixture was warmed to room temperature. The layers were separated, and then the aqueous layer was extracted with CH_2Cl_2 . The combined organic layers were washed with water and brine then dried over MgSO_4 . The solvent was removed in vacuo, and the residue was recrystallized from pentane to afford 2-bromo-4,5-xyleneol as a white solid (11.7 g, 72% yield).

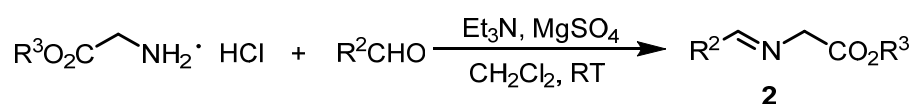
To a solution of 2-bromo-4,5-xyleneol (2.0 g, 10 mmol) in THF (15 mL) was added HMDS (2.2 mL, 10.5 mmol) under argon atmosphere. The reaction mixture was refluxed for 3 h. After cooling to room temperature, the solvent was removed in vacuo. The residue was dissolved in THF (30 mL) under argon atmosphere and cooled to $-78\text{ }^{\circ}\text{C}$. To the solution was added *n*-butyllithium (11 mmol, 2.65 M solution in hexane) dropwise. After stirring at $-78\text{ }^{\circ}\text{C}$ for 1 h, Tf_2O (2.0 mL, 11.9 mmol) was added to reaction mixture dropwise at $-78\text{ }^{\circ}\text{C}$. After stirring at $-78\text{ }^{\circ}\text{C}$ for 2 h, the reaction mixture was quenched with sat. NaHCO_3 aq. at $-78\text{ }^{\circ}\text{C}$ and this mixture was warmed to room temperature. The layers were separated, and then the aqueous layer was extracted with Et_2O twice. The combined organic layers were washed with brine and then dried over Na_2SO_4 . The solvent was removed in vacuo, and the residue was purified by silica gel column chromatography with hexane to afford 4,5-dimethyl-2-(trimethylsilyl)phenyl trifluoromethanesulfonate **1b** as a colorless liquid (1.28 g, 47% yield).



To a solution of 2-bromophenol (1.16g, 5.58 mmol) in THF (20 mL) was added HMDS (1.2 mL, 5.65 mmol) under

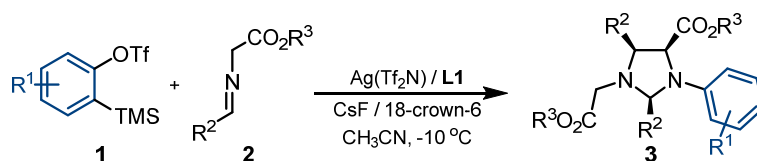
argon atmosphere. The reaction mixture was refluxed for 2 h. After cooling to room temperature, the solvent was removed in vacuo. The residue was dissolved in THF (30 mL) under argon atmosphere and cooled to $-78\text{ }^{\circ}\text{C}$. To the solution was added *n*-butyllithium (2.17 mmol, 2.4 M solution in hexane) dropwise. After stirring at $-78\text{ }^{\circ}\text{C}$ for 1.5 h, TiF_4 (0.98 mL 58.4 mmol) was added to reaction mixture dropwise at $-78\text{ }^{\circ}\text{C}$. After stirring at $-78\text{ }^{\circ}\text{C}$ for 2 h, the reaction mixture was quenched with sat. NaHCO_3 aq. At $-78\text{ }^{\circ}\text{C}$ and this mixture was warmed to room temperature. The layers were separated, and then the aqueous layer was extracted with Et_2O three times. The combined organic layers were dried over Na_2SO_4 . The solvent was removed in vacuo, and the residue was purified by silica gel column chromatography with hexane to afford 2-(trimethylsilyl)phenyl trifluoromethanesulfonate **1c** as a colorless liquid (524 mg, 28% yield).

General Procedure for Preparation of α -Iminoesters **2**^[2]



All α -iminoesters were prepared using the reported procedure. A suspension of ethyl/methyl/*t*-butyl/*n*-propyl glycinate hydrochloride (14.8 mmol), MgSO_4 (14.8 mmol) and Et_3N (14.8 mmol) in dry CH_2Cl_2 (36 mL) was stirred at room temperature for 1 h, and aldehyde (9.9 mmol) was added. After 12 h at room temperature, the mixture was filtered off and water (5 mL) was added. The organic layer was separated and the aqueous phase was extracted with CH_2Cl_2 (10 mL). The combined organic layers were washed with brine, dried over Na_2SO_4 , and evaporated under reduced pressure to afford azomethine ylide **2** which was used in the next step without further purification.

General Procedure for the Tandem Nucleophilic Addition-Cycloaddition.

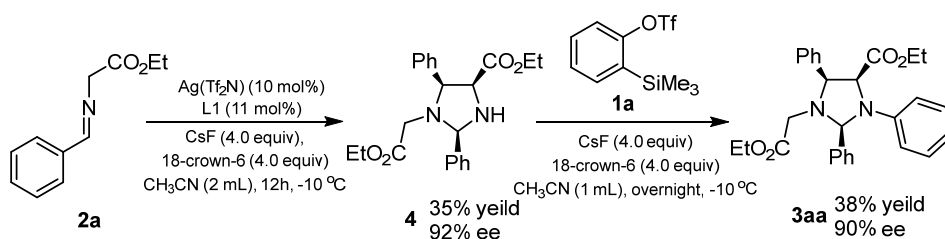


Under argon atmosphere (*Rc,Sp*)-PPFA (**L1**) (4.8 mg, 0.011 mmol) and $\text{Ag}(\text{Tf}_2\text{N})$ (3.8 mg, 0.01 mmol) were dissolved in 1 mL of acetonitrile, and stirred at $-10\text{ }^{\circ}\text{C}$ for about 30 min. Then azomethine ylides **2** (0.20 mmol) were added, the resulting mixture was stirred at $-10\text{ }^{\circ}\text{C}$ for about 30 min. Then, CsF (60.7 mg, 0.4 mmol), 18-crown-6 (105.7 mg, 0.4 mmol), aryne **1** (0.15 mmol), and 0.5 mL of acetonitrile were added sequentially. The resulting mixture was stirred at $-10\text{ }^{\circ}\text{C}$ for overnight. Once the starting material was completely consumed (monitored by TLC, petroleum ether/ EtOAc =10/1), the mixture was concentrated to dryness. The residue was purified through flash column chromatography (Petroleum ether/ EtOAc =30/1) to afford the corresponding cycloaddition product.

Tandem Nucleophilic Addition-Cycloaddition on the Gram Scale

Under argon atmosphere (*Rc,Sp*)-PPFA (**L1**) (48.0 mg, 0.11 mmol) and Ag(Tf₂N) (38.0 mg, 0.10 mmol) were dissolved in 7 mL of acetonitrile, and stirred at -10 °C for about 30 min. Then azomethine ylides **2a** (382.2 mg, 2.0 mmol) were added, the resulting mixture was stirred at -10 °C for about 1 h. Then, CsF (607.0 mg, 4.0 mmol), 18-crown-6 (1057.0 mg, 4.0 mmol), benzyne **1a** (447.0 mg, 0.15 mmol), and 3 mL of acetonitrile were added sequentially. The resulting mixture was stirred at -10 °C for 24 h and then was purified through flash column chromatography above to give the product **3aa** in 66 % yield (0.32 g). HPLC analysis: 90% ee (OOG-4459-EO, isopropanol/hexane = 7/93, 1.0 mL/min, UV: 254 nm), t_R = 6.7 min (major), 9.3 min (minor).

Procedure for the Control Experiment



Under argon atmosphere (*Rc,Sp*)-PPFA (**L1**) (4.8 mg, 0.011 mmol) and Ag(Tf₂N) (3.8 mg, 0.01 mmol) were dissolved in 1.5 mL of acetonitrile, and stirred at -10 °C for about 30 min. Then, CsF (60.7 mg, 0.4 mmol), 18-crown-6 (105.7 mg, 0.4 mmol), azomethine ylides **2a** (38.2 mg, 0.20 mmol) and 0.5 mL of acetonitrile were added sequentially. The resulting mixture was stirred at -10 °C for about 7 h. Once the starting material was completely consumed (monitored by TLC, Petroleum ether/EtOAc=3/1), the mixture was concentrated to dryness. The residue was purified through flash column chromatography (Petroleum ether/EtOAc=9/1) to afford the corresponding cycloaddition product **4**.

Under argon atmosphere imidazolidine **4** (28.7 mg, 0.075 mmol) were dissolved in 1 mL of acetonitrile, CsF (45.6 mg, 0.3 mmol), 18-crown-6 (79.3 mg, 0.3 mmol) and benzyne **1a** (14.9 mg, 0.05 mmol) were added sequentially. The resulting mixture was stirred at -10 °C for about 48 h. The mixture was concentrated to dryness. The residue was purified through flash column chromatography (Petroleum ether/EtOAc=9/1) to afford the corresponding cycloaddition product **3aa**.

References:

- (a) Ueta, Y; Mikami, K; Ito, S. *Angew. Chem. Int. Ed.* **2016**, 55(26):7525. (b) Zhang, T-Y; Lin, J-B; Li, Q-Z; Kang, J-C; Pan, J-L; Hou, S-H; Chen, C; Zhang, S-Y. *Org. Lett.* **2017**, 19, 1764.
- (a) Cabrera, S.; Gómez Arrayás R.; Carretero, J. C. *J. Am. Chem. Soc.* **2005**, 127, 16394. (b) Nájera, C.; de Garcia Retamosa, M.; Sansano, J. M. *Org. Lett.* **2007**, 9, 4025. (c) Ana López-Pérez, Javier, A.; Juan, C. C. *J. Am. Chem. Soc.* **2008**, 130, 10084.

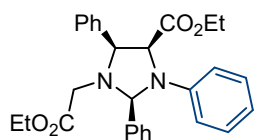
Optimization of Reaction Conditions

Table S1: Optimization of the Reaction Conditions

| Entry | 1a/2a (mmol) | Metal (0.01 mmol) | Ligand (0.011mmol) | Base/Additive (mmol) | Solvent (mL) | Yield (%) | ee (%) |
|-------|--------------|--|---------------------|-------------------------------|------------------------|-----------|--------|
| 1 | 1.0/2.2 | AgOTf | L1 | CsF/-, 0.3/- | CH ₃ CN 1.5 | 34 | 93 |
| 2 | 1.0/2.2 | Ag(Tf ₂ N) | L1 | CsF/-, 0.3/- | CH ₃ CN 1.5 | 20 | 91 |
| 3 | 1.0/2.2 | AgOTs | L1 | CsF/-, 0.3/- | CH ₃ CN 1.5 | 22 | 92 |
| 4 | 1.0/2.2 | AgNO ₃ | L1 | CsF/-, 0.3/- | CH ₃ CN 1.5 | 10 | 90 |
| 5 | 1.0/2.2 | AgOTf | L6 | CsF/-, 0.3/- | CH ₃ CN 1.5 | 13 | 72 |
| 6 | 1.0/2.2 | AgOTf | L5 | CsF/-, 0.3/- | CH ₃ CN 1.5 | 5 | 77 |
| 7 | 1.0/2.2 | AgOTf | L4 | CsF/-, 0.3/- | CH ₃ CN 1.5 | 9 | 89 |
| 8 | 1.0/2.2 | AgOTf | L2 | CsF/-, 0.3/- | CH ₃ CN 1.5 | 10 | 93 |
| 9 | 1.0/2.2 | AgOTf | L3 | CsF/-, 0.3/- | CH ₃ CN 1.5 | 24 | 83 |
| 10 | 1.0/2.2 | AgOTf | L8 | CsF/-, 0.3/- | CH ₃ CN 1.5 | NR | - |
| 11 | 1.0/2.2 | AgOTf | L7 | CsF/-, 0.3/- | CH ₃ CN 1.5 | 10 | 81 |
| 12 | 1.0/2.2 | AgOTf | L1 | NaF/-, 0.3/- | CH ₃ CN 1.5 | NR | - |
| 13 | 1.0/2.2 | AgOTf | L1 | TBAF/-, 0.3/- | CH ₃ CN 1.5 | 30 | 87 |
| 14 | 1.0/2.2 | AgOTf | L1 | KF/18-c-6, 0.3/0.03 | CH ₃ CN 1.5 | 12 | 88 |
| 15 | 1.0/2.2 | AgOTs | L1 | CsF/18-c-6, 0.3/0.3 | CH ₃ CN 1.5 | 53 | 93 |
| 16 | 1.0/2.2 | AgOTs | L2 | CsF/18-c-6, 0.3/0.3 | CH ₃ CN 2.0 | 52 | 94 |
| 17 | 1.0/2.2 | AgOTs | L3 | CsF/18-c-6, 0.3/0.3 | CH ₃ CN 2.0 | 49 | 89 |
| 18 | 1.0/2.2 | Ag(Tf ₂ N) | L1 | CsF/18-c-6, 0.3/0.3 | CH ₃ CN 1.5 | 53 | 95 |
| 19 | 1.0/2.2 | Ag(Tf ₂ N) | L2 | CsF/18-c-6, 0.3/0.3 | CH ₃ CN 2.0 | 51 | 95 |
| 20 | 1.0/2.2 | Ag(Tf ₂ N) | L3 | CsF/18-c-6, 0.3/0.3 | CH ₃ CN 2.0 | 52 | 90 |
| 21 | 1.0/2.2 | AgOTf | L1 | CsF/18-c-6, 0.3/0.3 | CH ₃ CN 1.5 | 51 | 93 |
| 22 | 1.0/2.2 | AgOTf | L2 | CsF/18-c-6, 0.3/0.3 | CH ₃ CN 1.5 | 48 | 94 |
| 23 | 1.0/2.2 | AgOTf | L3 | CsF/18-c-6, 0.3/0.3 | CH ₃ CN 1.5 | 49 | 88 |
| 24 | 1.0/2.2 | Ag(Tf ₂ N) | L1 | CsF/18-c-6, 0.3/0.3 | Tol 2.0 | trace | - |
| 25 | 1.0/2.2 | Ag(Tf ₂ N) | L1 | CsF/18-c-6, 0.3/0.3 | DCE 2.0 | 46 | 89 |
| 26 | 1.0/2.5 | Ag(Tf ₂ N) | L1 | CsF/18-c-6, 0.3/0.3 | CH ₃ CN 2.0 | 53 | 94 |
| 27 | 1.0/3.0 | Ag(Tf ₂ N) | L1 | CsF/18-c-6, 0.3/0.3 | CH ₃ CN 2.0 | 56 | 94 |
| 28 | 1.2/2.0 | Ag(Tf ₂ N) | L1 | CsF/18-c-6, 0.3/0.3 | CH ₃ CN 2.0 | 58 | 92 |
| 29 | 1.0/2.2 | Ag(Tf ₂ N) | L1 | CsF/18-c-6/4Å MS, 0.3/0.3/100 | CH ₃ CN 2.0 | 56 | 92 |
| 30 | 1.5/2.0 | Ag(Tf ₂ N) | L1 | CsF/18-c-6, 0.4/0.4 | CH ₃ CN 2.0 | 75 | 92 |
| 31 | 1.0/2.2 | Ag(Tf ₂ N) | L1 | CsF/18-c-6, 0.4/0.4 | CH ₃ CN 2.0 | 47 | 93 |
| 32 | 1.2/2.0 | Ag(Tf ₂ N) | L1 | CsF/18-c-6, 0.4/0.4 | CH ₃ CN 2.0 | 40 | 92 |
| 33 | 1.7/2.0 | Ag(Tf ₂ N) | L1 | CsF/18-c-6, 0.5/0.5 | CH ₃ CN 2.0 | 57 | 94 |
| 34 | 2.0/2.0 | Ag(Tf ₂ N) | L1 | CsF/18-c-6, 0.6/0.6 | CH ₃ CN 2.0 | 54 | 92 |
| 35 | 1.5/2.0 | Ag(Tf ₂ N) (three quarters) | L1 (three quarters) | CsF/18-c-6, 0.4/0.4 | CH ₃ CN 2.0 | 42 | 92 |

Characterization Data for the Tandem Nucleophilic Addition-Cycloaddition Products 3, and 4.

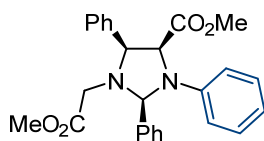
Ethyl (2S,4S,5S)-1-(2-ethoxy-2-oxoethyl)-2,3,5-triphenylimidazolidine-4-carboxylate (3aa)



3aa

Prepared according to the general procedure as described above in 75% yield (34.4 mg). (monitored by TLC, petroleum ether:EtOAc=10:1, $R_f = 0.6$) It was purified by flash chromatography (PE/EtOAc=25/1) to afford white solid. mp =100-101 °C; $[\alpha]_D^{25} = -28.9$ (c 0.80, CH₂Cl₂); ¹H NMR (300 MHz, Chloroform-*d*) δ 8.04 – 7.96 (m, 2H), 7.49 – 7.31 (m, 8H), 7.15 – 7.04 (m, 2H), 6.69 (t, $J = 7.3$ Hz, 1H), 6.44 (d, $J = 7.9$ Hz, 2H), 5.53 (s, 1H), 5.15 (d, $J = 8.6$ Hz, 1H), 4.52 (d, $J = 8.6$ Hz, 1H), 4.14 – 4.03 (m, 2H), 3.89 (dq, $J = 10.8$, 7.2 Hz, 1H), 3.64 (dq, $J = 10.7$, 7.2 Hz, 1H), 3.25 (s, 2H), 1.22 (t, $J = 7.1$ Hz, 3H), 0.90 (t, $J = 7.2$ Hz, 3H). ¹³C NMR (75 MHz, CDCl₃) δ 171.2, 169.9, 144.9, 140.0, 135.2, 128.7, 128.6, 128.3, 128.3, 128.2, 128.2, 117.4, 112.6, 79.7, 67.7, 65.8, 60.5, 59.9, 45.4, 13.9, 13.3; HRMS (ESI) calcd for C₂₈H₃₀N₂O₄H⁺ (M + H)⁺ 459.2278, found 459.2268; HPLC analysis: 93% ee (OOG-4459-EO, isopropanol/hexane = 7/93, 1.0 mL/min, UV: 254 nm), $t_R = 6.6$ min (major), 9.0 min (minor).

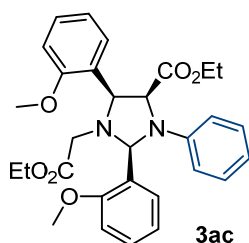
Methyl (2S,4S,5S)-1-(2-methoxy-2-oxoethyl)-2,3,5-triphenylimidazolidine-4-carboxylate (3ab)



3ab

Prepared according to the general procedure as described above in 73% yield (31.4 mg). It was purified by flash chromatography to afford white solid. mp =118-120 °C; $[\alpha]_D^{25} = -26.8$ (c 0.80, CH₂Cl₂); ¹H NMR (300 MHz, Chloroform-*d*) δ 8.02 – 7.93 (m, 2H), 7.48 – 7.31 (m, 8H), 7.10 (dd, $J = 8.7$, 7.3 Hz, 2H), 6.74 – 6.66 (m, 1H), 6.47 – 6.40 (m, 2H), 5.52 (s, 1H), 5.13 (d, $J = 8.6$ Hz, 1H), 4.55 (d, $J = 8.6$ Hz, 1H), 3.61 (s, 3H), 3.30 (s, 3H), 3.26 (s, 2H). ¹³C NMR (75 MHz, Chloroform-*d*) δ 171.6, 170.4, 144.8, 139.9, 135.1, 128.6, 128.4, 128.3, 128.2, 128.1, 117.5, 112.6, 79.7, 67.7, 65.7, 51.3, 50.9, 45.3; HRMS (ESI) calcd for C₂₆H₂₆N₂O₄H⁺ (M + H)⁺ 431.1965, found 431.1964; HPLC analysis: 95% ee (OOG-4459-EO, isopropanol/hexane = 7/93, 1.0 mL/min, UV: 254 nm), $t_R = 8.9$ min (major), 15.8 min (minor).

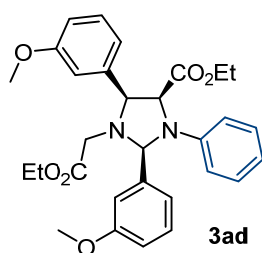
Ethyl (2S,4S,5S)-1-(2-ethoxy-2-oxoethyl)-2,5-bis(2-methoxyphenyl)-3-phenylimidazolidine-4-carboxylate (3ac)



3ac

Prepared according to the general procedure as described above in 61% yield (31.6 mg). It was purified by flash chromatography to afford pink solid. mp =183-184 °C; $[\alpha]_D^{25} = -24.4$ (c 0.67, CH₂Cl₂); ¹H NMR (300 MHz, Chloroform-*d*) δ 8.45 – 8.42 (m, 1H), 7.44 (dd, $J = 7.4$, 1.7 Hz, 1H), 7.33 – 7.22 (m, 2H), 7.10 (m, 2H), 7.06 – 6.97 (m, 1H), 6.95 – 6.86 (m, 3H), 6.67 (t, $J = 7.3$ Hz, 1H), 6.46 – 6.39 (m, 2H), 6.12 (s, 1H), 5.61 (d, $J = 8.5$ Hz, 1H), 4.63 (d, $J = 8.5$ Hz, 1H), 4.04 (qd, $J = 7.2$, 2.1 Hz, 2H), 3.91 (s, 3H), 3.87 (s, 3H), 3.82 – 3.74 (m, 1H), 3.63 – 3.52 (m, 1H), 3.32 (d, $J = 3.4$ Hz, 2H), 1.21 (t, $J = 7.1$ Hz, 3H), 0.89 (t, $J = 7.1$ Hz, 3H). ¹³C NMR (75 MHz, CDCl₃) δ 171.6, 170.4, 158.3, 157.5, 145.4, 130.3, 128.9, 128.5, 128.4, 127.8, 127.7, 123.9, 121.4, 120.1, 117.0, 112.5, 110.0, 109.3, 71.7, 66.1, 60.1, 59.6, 58.9, 55.3, 54.9, 46.2, 13.9, 13.4; HRMS (ESI) calcd for C₃₀H₃₄N₂O₆H⁺ (M + H)⁺ 519.2490, found 519.2488; HPLC analysis: 83% ee (OOG-4459-EO, isopropanol/hexane = 7/93, 1.0 mL/min, UV: 254 nm), $t_R = 9.6$ min (major), 6.7 min (minor).

Ethyl (2S,4S,5S)-1-(2-ethoxy-2-oxoethyl)-2,5-bis(3-methoxyphenyl)-3-phenylimidazolidine-4-carboxylate (3ad)



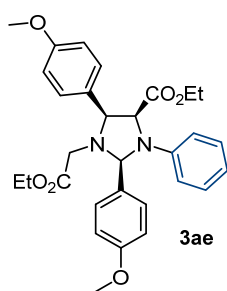
Prepared according to the general procedure as described above in 65% yield (33.7 mg).

It was purified by flash chromatography to afford brown wax; $[\alpha]_D^{25} = -38.3$ (*c* 0.61, CH₂Cl₂);

¹H NMR (300 MHz, Chloroform-*d*) δ 7.74 (dd, *J* = 2.7, 1.5 Hz, 1H), 7.48 – 7.45 (m, 1H), 7.35 – 7.23 (m, 2H), 7.13 – 7.10 (m, 2H), 7.03 – 6.98 (m, 2H), 6.91 – 6.84 (m, 2H), 6.73 – 6.66 (m, 1H), 6.46 – 6.42 (m, 2H), 5.48 (s, 1H), 5.09 (d, *J* = 8.6 Hz, 1H), 4.50 (d, *J* = 8.6 Hz, 1H), 4.12 – 4.04 (m, 2H), 3.92 (dt, *J* = 10.7, 7.1 Hz, 1H), 3.84 (s, 3H), 3.80 (s, 3H),

3.68 (dq, *J* = 10.7, 7.1 Hz, 1H), 3.27 (s, 2H), 1.22 (t, *J* = 7.1 Hz, 3H), 0.92 (t, *J* = 7.1 Hz, 3H). ¹³C NMR (75 MHz, CDCl₃) δ 171.0, 169.9, 159.5, 144.9, 141.9, 136.9, 129.1, 128.9, 128.6, 120.9, 117.3, 114.3, 113.8, 113.7, 112.5, 79.5, 67.5, 65.7, 60.4, 59.9, 54.9, 54.9, 45.5, 13.9, 13.4; HRMS (ESI) calcd for C₃₀H₃₄N₂O₆H⁺ (*M* + *H*)⁺ 519.2490, found 519.2489; HPLC analysis: 90% ee (OOG-4459-EO, isopropanol/hexane = 7/93, 1.0 mL/min, UV: 254 nm), *t*_R = 7.2 min (major), 8.0 min (minor).

Ethyl (2S,4S,5S)-1-(2-ethoxy-2-oxoethyl)-2,5-bis(4-methoxyphenyl)-3-phenylimidazolidine-4-carboxylate (3ae)



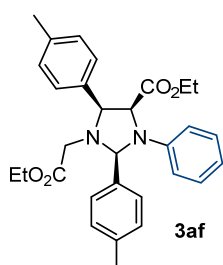
Prepared according to the general procedure as described above in 67% yield (34.8 mg). It

was purified by flash chromatography to afford white solid. mp = 132–133 °C; $[\alpha]_D^{25} = -23.6$ (*c*

0.61, CH₂Cl₂); ¹H NMR (300 MHz, Chloroform-*d*) δ 7.89 (d, *J* = 8.7 Hz, 2H), 7.34 (d, *J* = 8.7 Hz, 2H), 7.15 – 7.03 (m, 2H), 6.98 – 6.84 (m, 4H), 6.68 (tt, *J* = 7.3, 1.0 Hz, 1H), 6.44 (dt, *J* = 7.8, 1.0 Hz, 2H), 5.46 (s, 1H), 5.05 (d, *J* = 8.5 Hz, 1H), 4.45 (d, *J* = 8.5 Hz, 1H), 4.07 (qd, *J* = 7.2, 0.7 Hz, 2H), 3.93 (dq, *J* = 10.7, 7.1 Hz, 1H), 3.82 (s, 3H), 3.81 (s, 3H), 3.71 (dq, *J* = 10.7, 7.2 Hz, 1H), 3.22 (s, 2H), 1.21 (t, *J* = 7.1 Hz, 3H), 0.96 (t, *J* = 7.2 Hz, 3H). ¹³C NMR (75 MHz,

CDCl₃) δ 171.4, 170.0, 159.5, 159.5, 145.0, 132.0, 129.8, 129.4, 128.6, 127.1, 117.2, 113.6, 113.5, 112.6, 79.1, 67.6, 65.0, 60.5, 59.9, 55.0, 54.9, 45.4, 13.9, 13.4; HRMS (ESI) calcd for C₃₀H₃₄N₂O₆H⁺ (*M* + *H*)⁺ 519.2490, found 519.2488; HPLC analysis: 93% ee (OOG-4459-EO, isopropanol/hexane = 7/93, 1.0 mL/min, UV: 254 nm), *t*_R = 10.0 min (major), 15.0 min (minor).

Ethyl (2S,4S,5S)-1-(2-ethoxy-2-oxoethyl)-3-phenyl-2,5-di-*p*-tolylimidazolidine-4-carboxylate (3af)



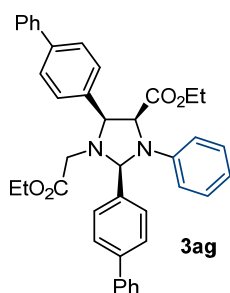
Prepared according to the general procedure as described above in 80% yield (38.9 mg). It

was purified by flash chromatography to afford white solid. mp = 124–125 °C; $[\alpha]_D^{25} = -32.0$ (*c*

0.82, CH₂Cl₂); ¹H NMR (300 MHz, Chloroform-*d*) δ 7.89 – 7.83 (m, 2H), 7.33 – 7.28 (m, 2H), 7.25 – 7.20 (m, 2H), 7.18 – 7.06 (m, 4H), 6.68 (tt, *J* = 7.3, 1.0 Hz, 1H), 6.44 (dt, *J* = 8.0, 1.0 Hz, 2H), 5.49 (s, 1H), 5.10 (d, *J* = 8.5 Hz, 1H), 4.48 (d, *J* = 8.7 Hz, 1H), 4.08 (qd, *J* = 7.1, 1.4 Hz, 2H), 3.90 (dq, *J* = 10.7, 7.1 Hz, 1H), 3.70 (dq, *J* = 10.7, 7.1 Hz, 1H), 3.24 (d, *J* = 1.0 Hz, 2H), 2.37 (s, 3H), 2.35 (s, 3H), 1.22 (t, *J* = 7.1 Hz, 3H), 0.93 (t, *J* = 7.1 Hz, 3H). ¹³C NMR (75

MHz, CDCl₃) δ 171.3, 170.0, 145.1, 138.0, 137.9, 137.0, 132.1, 128.9, 128.8, 128.6, 128.5, 128.2, 117.2, 112.6, 79.4, 67.7, 65.4, 60.4, 59.9, 45.4, 21.0, 20.8, 13.9, 13.3; HRMS (ESI) calcd for C₃₀H₃₄N₂O₄H⁺ (*M* + *H*)⁺ 487.2591, found 487.2587; HPLC analysis: 90% ee (IA, isopropanol/hexane = 7/93, 1.0 mL/min, UV: 254 nm), *t*_R = 16.4 min (major), 18.6 min (minor).

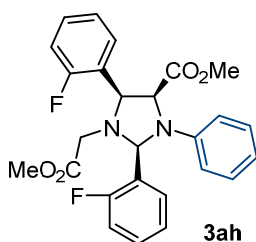
Ethyl (2S,4S,5S)-2,5-di([1,1'-biphenyl]-4-yl)-1-(2-ethoxy-2-oxoethyl)-3-phenylimidazolidine-4-carboxylate (3ag)



Prepared according to the general procedure as described above in 82% yield (50.2 mg). It was purified by flash chromatography to afford yellow solid. mp =82-83 °C; $[\alpha]_D^{25} = -19.7$ (c 0.97, CH₂Cl₂); ¹H NMR (300 MHz, Chloroform-*d*) δ 8.13 – 8.08 (m, 2H), 7.72 – 7.58 (m, 8H), 7.56 – 7.44 (m, 6H), 7.43 – 7.34 (m, 2H), 7.15 (dd, *J* = 8.5, 7.1 Hz, 2H), 6.74 (t, *J* = 7.3 Hz, 1H), 6.52 (d, *J* = 8.1 Hz, 2H), 5.63 (s, 1H), 5.25 (d, *J* = 8.5 Hz, 1H), 4.60 (d, *J* = 8.6 Hz, 1H), 4.13 (qd, *J* = 7.1, 1.3 Hz, 2H), 3.93 (dq, *J* = 10.7, 7.1 Hz, 1H), 3.73 (dq, *J* = 10.7, 7.1 Hz, 1H), 3.36 (s, 2H), 1.33 – 1.25 (t, *J* = 7.1 Hz, 3H), 0.92 (t, *J* = 7.1 Hz, 3H). ¹³C NMR (75 MHz, CDCl₃) δ 171.2, 170.05, 144.9, 141.3, 141.2, 140.7, 140.4, 139.1, 134.3, 129.1, 128.7, 128.7,

128.5, 128.4, 127.1, 127.1, 126.9, 126.9, 126.8, 126.7, 117.5, 112.7, 79.4, 67.7, 65.6, 60.6, 60.0, 45.6, 14.0, 13.3; HRMS (ESI) calcd for C₄₀H₃₈N₂O₄H⁺ (M + H)⁺ 611.2904, found 611.2902; HPLC analysis: 90% ee (OOG-4459-EO, isopropanol/hexane = 7/93, 1.0 mL/min, UV: 254 nm), t_R = 13.0 min (major), 10.7 min (minor).

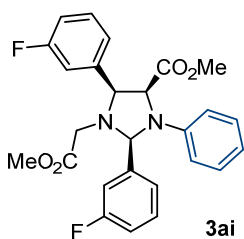
Methyl (2S,4S,5S)-2,5-bis(2-fluorophenyl)-1-(2-methoxy-2-oxoethyl)-3-phenylimidazolidine-4-carboxylate (3ah)



Prepared according to the general procedure as described above in 93% yield (43.3 mg). It was purified by flash chromatography to afford yellow wax; $[\alpha]_D^{25} = -16.7$ (c 0.91, CH₂Cl₂); ¹H NMR (300 MHz, Chloroform-*d*) δ 8.48 (td, *J* = 7.7, 1.9 Hz, 1H), 7.51 – 7.44 (m, 1H), 7.38 – 7.28 (m, 2H), 7.25 – 7.18 (m, 1H), 7.17 – 7.07 (m, 5H), 6.77 – 6.70 (m, 1H), 6.46 – 6.40 (m, 2H), 6.09 (s, 1H), 5.58 (d, *J* = 8.6 Hz, 1H), 4.67 (d, *J* = 8.6 Hz, 1H), 3.63 (s, 3H), 3.35 (s, 2H), 3.26 (s, 3H). ¹³C NMR (75 MHz, CDCl₃) δ 171.5, 170.0, 163.1 (d, *J*_{C-F} = 13.4 Hz), 159.9 (d, *J*_{C-F} = 10.7 Hz), 144.5, 130.9 (d, *J*_{C-F} = 3.3 Hz), 129.9 (d, *J*_{C-F} = 8.3 Hz), 129.5

(d, *J*_{C-F} = 8.3 Hz), 128.8, 128.2 (d, *J*_{C-F} = 3.5 Hz), 126.4 (d, *J*_{C-F} = 9.7 Hz), 125.1 (d, *J*_{C-F} = 3.4 Hz), 123.9 (d, *J*_{C-F} = 3.6 Hz), 122.4 (d, *J*_{C-F} = 12.3 Hz), 117.9, 115.0 (d, *J*_{C-F} = 21.5 Hz), 114.3 (d, *J*_{C-F} = 21.8 Hz), 112.4, 71.3, 71.3, 66.3, 58.0, 57.9, 51.2, 51.0, 45.5; HRMS (ESI) calcd for C₂₆H₂₄N₂F₂O₄H⁺ (M + H)⁺ 467.1777, found 467.1776; HPLC analysis: 93% ee (OOG-4459-EO, isopropanol/hexane = 7/93, 1.0 mL/min, UV: 254 nm), t_R = 8.3 min (major), 9.5 min (minor).

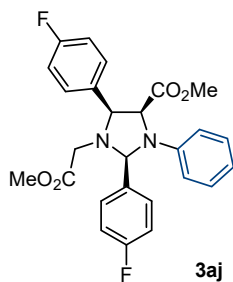
Methyl (2S,4S,5S)-2,5-bis(3-fluorophenyl)-1-(2-methoxy-2-oxoethyl)-3-phenylimidazolidine-4-carboxylate (3ai)



Prepared according to the general procedure as described above in 99% yield (46.1 mg). It was purified by flash chromatography to afford light yellow solid. mp =138-139 °C; $[\alpha]_D^{25} = -17.5$ (c 0.72, CH₂Cl₂); ¹H NMR (300 MHz, Chloroform-*d*) δ 7.84 (dt, *J* = 9.7, 2.2 Hz, 1H), 7.66 (dt, *J* = 7.5, 1.2 Hz, 1H), 7.44 – 7.30 (m, 2H), 7.22 – 7.00 (m, 6H), 6.73 (t, *J* = 7.4 Hz, 1H), 6.44 – 6.36 (m, 2H), 5.53 (s, 1H), 5.13 (d, *J* = 8.5 Hz, 1H), 4.55 (d, *J* = 8.6 Hz, 1H), 3.65 (s, 3H), 3.37 (s, 3H), 3.27 (s, 2H). ¹³C NMR (75 MHz, CDCl₃) δ 171.3, 170.0, 164.5 (d, *J*_{C-F} = 21.4 Hz), 161.2 (d, *J*_{C-F} = 21.5 Hz), 144.4, 142.7 (d, *J*_{C-F} = 6.4 Hz), 137.7 (d, *J*_{C-F} = 6.9 Hz), 129.8 (d, *J*_{C-F} = 8.0 Hz), 129.6 (d, *J*_{C-F} = 8.1 Hz), 128.7, 124.2 (d, *J*_{C-F} = 2.7 Hz), 123.8 (d, *J*_{C-F} = 2.9 Hz), 117.9, 115.7 (d, *J*_{C-F} = 15.5 Hz), 115.5, 115.3 (d, *J*_{C-F} = 5.4 Hz), 114.9 (d, *J*_{C-F} = 22.3 Hz), 112.6, 79.0, 67.4, 65.2,

51.5, 51.1, 45.2; HRMS (ESI) calcd for C₂₆H₂₄N₂F₂O₄H⁺ (M + H)⁺ 467.1777, found 467.1776; HPLC analysis: 84% ee (OOG-4457-EO, isopropanol/hexane = 7/93, 1.0 mL/min, UV: 254 nm), t_R = 6.5 min (major), 5.7 min (minor).

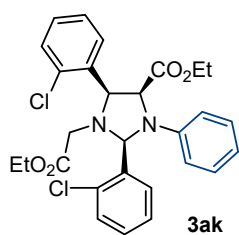
Methyl (2S,4S,5S)-2,5-bis(4-fluorophenyl)-1-(2-methoxy-2-oxoethyl)-3-phenylimidazolidine-4-carboxylate (3aj)



Prepared according to the general procedure as described above in 91% yield (42.4 mg). It was purified by flash chromatography to afford yellow wax; $[\alpha]_D^{25} = -26.7$ (*c* 0.69, CH₂Cl₂); ¹H NMR (300 MHz, Chloroform-*d*) δ 7.88 – 7.81 (m, 1H), 7.66 (dt, *J* = 7.5, 1.2 Hz, 1H), 7.43 – 7.31 (m, 2H), 7.22 – 7.18 (m, 1H), 7.16 – 7.01 (m, 5H), 6.73 (t, *J* = 7.4 Hz, 1H), 6.44 – 6.39 (m, 2H), 5.53 (s, 1H), 5.13 (d, *J* = 8.5 Hz, 1H), 4.55 (d, *J* = 8.6 Hz, 1H), 3.65 (s, 3H), 3.37 (s, 3H), 3.27 (s, 2H). ¹³C NMR (75 MHz, CDCl₃) δ 171.6, 170.1, 164.3 (d, *J*_{C-F} = 12.2 Hz), 161.1 (d, *J*_{C-F} = 12.6 Hz), 144.5, 135.5 (d, *J*_{C-F} = 2.8 Hz), 130.6 (d, *J*_{C-F} = 3.2 Hz), 130.4 (d, *J*_{C-F} = 8.3 Hz), 129.7 (d, *J*_{C-F} = 8.0 Hz), 128.7, 117.8, 115.2 (d, *J*_{C-F} = 21.4 Hz), 112.6, 79.0, 67.5, 64.9, 51.4, 51.0, 45.2;

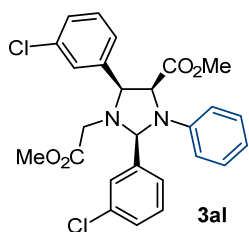
HRMS (ESI) calcd for C₂₆H₂₄N₂F₂O₄H⁺ (*M* + *H*)⁺ 467.1777, found 467.1776; HPLC analysis: 92% ee (OOG-4459-EO, isopropanol/hexane = 7/93, 1.0 mL/min, UV: 254 nm), *t*_R = 8.4 min (major), 7.4 min (minor).

Ethyl (2S,4S,5S)-2,5-bis(2-chlorophenyl)-1-(2-ethoxy-2-oxoethyl)-3-phenylimidazolidine-4-carboxylate (3ak)



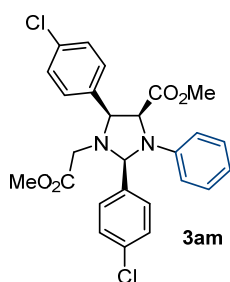
Prepared according to the general procedure as described above in 74% yield (38.9 mg). It was purified by flash chromatography to afford yellow wax; $[\alpha]_D^{25} = -33.9$ (*c* 0.88, CH₂Cl₂); ¹H NMR (300 MHz, Chloroform-*d*) δ 8.71 (dd, *J* = 7.7, 1.9 Hz, 1H), 7.56 – 7.50 (m, 1H), 7.44 – 7.31 (m, 3H), 7.30 – 7.21 (m, 3H), 7.19 – 7.10 (m, 2H), 6.73 (t, *J* = 7.3 Hz, 1H), 6.44 – 6.39 (m, 2H), 6.24 (s, 1H), 5.78 (d, *J* = 8.7 Hz, 1H), 4.76 (d, *J* = 8.7 Hz, 1H), 4.21 – 4.00 (m, 2H), 3.84 (dq, *J* = 10.7, 7.1 Hz, 1H), 3.55 (dq, *J* = 10.7, 7.1 Hz, 1H), 3.30 (s, 2H), 1.22 (t, *J* = 7.1 Hz, 3H), 0.88 (t, *J* = 7.1 Hz, 3H). ¹³C NMR (75 MHz, CDCl₃) δ 171.1, 169.7, 144.6, 137.2, 135.1, 133.9, 133.0, 131.6, 129.5, 129.2, 128.9, 128.8, 128.7, 128.3, 127.8, 126.6, 117.8, 112.5, 74.6, 65.5, 61.7, 60.5, 60.1, 45.3, 13.9, 13.3; HRMS (ESI) calcd for C₂₈H₂₈N₂Cl₂O₄H⁺ (*M* + *H*)⁺ 527.1499, found 527.1498; HPLC analysis: 82% ee (OOG-4459-EO, isopropanol/hexane = 7/93, 1.0 mL/min, UV: 254 nm), *t*_R = 6.8 min (major), 5.3 min (minor).

Methyl (2S,4S,5S)-2,5-bis(3-chlorophenyl)-1-(2-methoxy-2-oxoethyl)-3-phenylimidazolidine-4-carboxylate (3al)



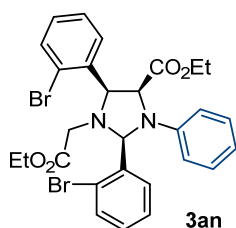
Prepared according to the general procedure as described above in 73% yield (36.4 mg). It was purified by flash chromatography to afford yellow solid. mp = 136–138 °C; $[\alpha]_D^{25} = -25.9$ (*c* 0.94, CH₂Cl₂); ¹H NMR (300 MHz, Chloroform-*d*) δ 8.01 (d, *J* = 2.0 Hz, 1H), 7.84 (dt, *J* = 6.5, 2.4 Hz, 1H), 7.41 – 7.23 (m, 6H), 7.20 – 7.03 (m, 2H), 6.74 (t, *J* = 7.3 Hz, 1H), 6.50 – 6.27 (m, 2H), 5.50 (s, 1H), 5.09 (d, *J* = 8.5 Hz, 1H), 4.54 (d, *J* = 8.6 Hz, 1H), 3.65 (s, 3H), 3.39 (s, 3H), 3.25 (s, 2H). ¹³C NMR (75 MHz, CDCl₃) δ 171.2, 169.9, 144.4, 142.0, 137.1, 134.3, 129.6, 128.8, 128.7, 128.6, 128.1, 126.8, 126.3, 118.0, 112.6, 79.0, 67.5, 65.2, 51.5, 51.1, 45.1; HRMS (ESI) calcd for C₂₆H₂₄N₂Cl₂O₄H⁺ (*M* + *H*)⁺ 499.1186, found 499.1177; HPLC analysis: 91% ee (OOG-4472-EO, isopropanol/hexane = 7/93, 1.0 mL/min, UV: 254 nm), *t*_R = 10.0 min (major), 11.6 min (minor).

Methyl (2S,4S,5S)-2,5-bis(4-chlorophenyl)-1-(2-methoxy-2-oxoethyl)-3-phenylimidazolidine-4-carboxylate (3am)



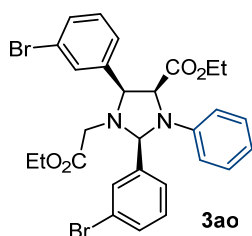
Prepared according to the general procedure as described above in 81% yield (40.3 mg). It was purified by flash chromatography to afford yellow solid. mp = 182-183 °C; $[\alpha]_D^{25} = -18.0$ (*c* 0.67, CH₂Cl₂); ¹H NMR (300 MHz, Chloroform-*d*) δ 7.92 (d, *J* = 8.4 Hz, 2H), 7.39 (d, *J* = 8.4 Hz, 2H), 7.34 (s, 4H), 7.21 – 6.95 (m, 2H), 6.79 – 6.68 (m, 1H), 6.55 – 6.30 (m, 2H), 5.48 (s, 1H), 5.09 (d, *J* = 8.6 Hz, 1H), 4.53 (d, *J* = 8.6 Hz, 1H), 3.62 (s, 3H), 3.34 (s, 3H), 3.21 (s, 2H). ¹³C NMR (75 MHz, CDCl₃) δ 171.4, 170.0, 144.4, 138.3, 134.2, 134.2, 133.4, 130.0, 129.4, 128.7, 128.6, 128.5, 117.9, 112.6, 78.9, 67.4, 65.0, 51.5, 51.1, 45.1; HRMS (ESI) calcd for C₂₆H₂₄N₂Cl₂O₄H⁺ (*M* + *H*)⁺ 499.1186, found 499.1181; HPLC analysis: 90% ee (OOG-4459-EO, isopropanol/hexane = 7/93, 1.0 mL/min, UV: 254 nm), *t*_R = 8.7 min (major), 6.9 min (minor).

Ethyl (2S,4S,5S)-2,5-bis(2-bromophenyl)-1-(2-ethoxy-2-oxoethyl)-3-phenylimidazolidine-4-carboxylate (3an)



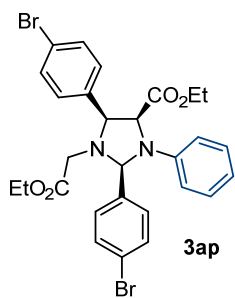
Prepared according to the general procedure as described above in 73% yield (45.0 mg). It was purified by flash chromatography to afford yellow wax; $[\alpha]_D^{25} = -36.1$ (*c* 0.67, CH₂Cl₂); ¹H NMR (300 MHz, Chloroform-*d*) δ 8.74 (dd, *J* = 7.9, 1.8 Hz, 1H), 7.63 – 7.47 (m, 3H), 7.44 – 7.36 (m, 1H), 7.30 (td, *J* = 7.6, 1.4 Hz, 1H), 7.23 – 7.10 (m, 4H), 6.75 (d, *J* = 7.3 Hz, 1H), 6.49 – 6.34 (m, 2H), 6.17 (s, 1H), 5.76 (d, *J* = 8.7 Hz, 1H), 4.77 (d, *J* = 8.8 Hz, 1H), 4.20 – 4.03 (m, 2H), 3.84 (dq, *J* = 10.7, 7.1 Hz, 1H), 3.54 (dq, *J* = 10.7, 7.1 Hz, 1H), 3.29 (s, 2H), 1.23 (t, *J* = 7.1 Hz, 3H), 0.88 (t, *J* = 7.1 Hz, 3H). ¹³C NMR (75 MHz, CDCl₃) δ 171.1, 169.8, 144.6, 138.6, 134.6, 132.5, 132.1, 131.7, 129.8, 129.3, 129.1, 128.8, 128.4, 127.2, 125.5, 124.3, 117.8, 112.7, 77.3, 65.3, 64.3, 60.5, 60.2, 45.2, 13.9, 13.3; HRMS (ESI) calcd for C₂₈H₂₈N₂Br₂O₄H⁺ (*M* + *H*)⁺ 615.0489, found 615.0488; HPLC analysis: 83% ee (OOG-4459-EO, isopropanol/hexane = 7/93, 1.0 mL/min, UV: 254 nm), *t*_R = 7.1 min (major), 5.4 min (minor).

Ethyl (2S,4S,5S)-2,5-bis(3-bromophenyl)-1-(2-ethoxy-2-oxoethyl)-3-phenylimidazolidine-4-carboxylate (3ao)



Prepared according to the general procedure as described above in 57% yield (35.1 mg). It was purified by flash chromatography to afford yellow wax; $[\alpha]_D^{25} = -18.5$ (*c* 0.53, CH₂Cl₂); ¹H NMR (300 MHz, Chloroform-*d*) δ 8.14 (t, *J* = 1.8 Hz, 1H), 7.90 (dt, *J* = 7.6, 1.3 Hz, 1H), 7.59 – 7.45 (m, 3H), 7.37 – 7.27 (m, 2H), 7.25 – 7.07 (m, 3H), 6.77 – 6.69 (m, 1H), 6.44 – 6.37 (m, 2H), 5.47 (s, 1H), 5.07 (d, *J* = 8.6 Hz, 1H), 4.51 (d, *J* = 8.7 Hz, 1H), 4.10 (q, *J* = 7.1 Hz, 2H), 3.87 (dq, *J* = 39.2, 7.2 Hz, 2H), 3.23 (s, 2H), 1.24 (t, *J* = 7.1 Hz, 3H), 1.05 (t, *J* = 7.2 Hz, 3H). ¹³C NMR (75 MHz, CDCl₃) δ 170.8, 169.5, 144.5, 142.4, 137.4, 131.7, 131.5, 131.5, 131.1, 129.9, 129.8, 128.8, 127.3, 127.0, 122.4, 117.9, 112.6, 79.1, 67.6, 65.3, 60.9, 60.2, 45.5, 13.9, 13.5; HRMS (ESI) calcd for C₂₈H₂₈N₂Br₂O₄H⁺ (*M* + *H*)⁺ 615.0489, found 615.0491; HPLC analysis: 86% ee (OOG-4459-EO, isopropanol/hexane = 7/93, 1.0 mL/min, UV: 254 nm), *t*_R = 8.2 min (major), 7.4 min (minor).

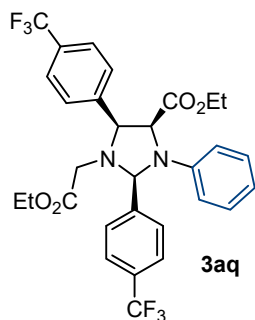
Ethyl (2S,4S,5S)-2,5-bis(4-bromophenyl)-1-(2-ethoxy-2-oxoethyl)-3-phenylimidazolidine-4-carboxylate (3ap)



Prepared according to the general procedure as described above in 82% yield (50.5 mg). It was purified by flash chromatography to afford yellow wax; $[\alpha]_D^{25} = -17.3$ (*c* 0.73, CH₂Cl₂); ¹H NMR (300 MHz, Chloroform-*d*) δ 8.01 – 7.74 (m, 2H), 7.60 – 7.44 (m, 4H), 7.32 – 7.20 (m, 2H), 7.11 (dd, *J* = 8.8, 7.4 Hz, 2H), 6.72 (td, *J* = 7.3, 1.0 Hz, 1H), 6.39 (dd, *J* = 8.8, 1.1 Hz, 2H), 5.49 (s, 1H), 5.10 (d, *J* = 8.5 Hz, 1H), 4.50 (d, *J* = 8.6 Hz, 1H), 4.09 (qd, *J* = 7.1, 0.7 Hz, 2H), 3.91 (dq, *J* = 10.7, 7.1 Hz, 1H), 3.70 (dq, *J* = 10.8, 7.2 Hz, 1H), 3.19 (s, 2H), 1.22 (t, *J* = 7.1 Hz, 3H), 0.94 (t, *J* = 7.2 Hz, 3H). ¹³C NMR (75 MHz, CDCl₃) δ 170.9, 169.5,

144.4, 139.0, 134.1, 131.5, 131.384, 130.4, 129.9, 128.7, 122.5, 122.3, 117.8, 112.6, 79.0, 67.3, 65.1, 60.7, 60.2, 45.3, 13.9, 13.3; HRMS (ESI) calcd for C₂₈H₂₈N₂Br₂O₄H⁺ (*M* + *H*)⁺ 615.0489, found 615.0485; HPLC analysis: 91% ee (OOG-4459-EO, isopropanol/hexane = 7/93, 1.0 mL/min, UV: 254 nm), *t_R* = 6.6 min (major), 9.0 min (minor).

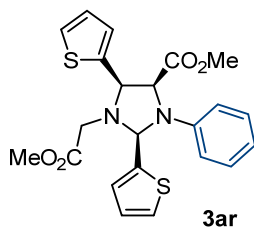
Ethyl (2S,4S,5S)-1-(2-ethoxy-2-oxoethyl)-3-phenyl-2,5-bis(4-(trifluoromethyl)phenyl)imidazolidine-4-carboxylate (3aq)



Prepared according to the general procedure as described above in 84% yield (49.9 mg). It was purified by flash chromatography to afford yellow wax; $[\alpha]_D^{25} = -11.5$ (*c* 0.61, CH₂Cl₂); ¹H NMR (300 MHz, Chloroform-*d*) δ 8.15 (d, *J* = 8.0 Hz, 2H), 7.85 – 7.45 (m, 6H), 7.18 – 7.05 (m, 2H), 6.74 (t, *J* = 7.3 Hz, 1H), 6.39 (d, *J* = 8.1 Hz, 2H), 5.62 (s, 1H), 5.25 (d, *J* = 8.6 Hz, 1H), 4.58 (d, *J* = 8.6 Hz, 1H), 4.11 (q, *J* = 7.1 Hz, 2H), 3.88 (dq, *J* = 10.8, 7.1 Hz, 1H), 3.64 (dq, *J* = 10.8, 7.2 Hz, 1H), 3.21 (s, 2H), 1.23 (t, *J* = 7.2 Hz, 3H), 0.86 (t, *J* = 7.2 Hz, 3H). ¹³C NMR (75 MHz, CDCl₃) δ 170.7, 169.4, 144.2, 144.0, 139.3, 130.9 (d, *J_{C-F}* = 4.0 Hz), 130.5 (d, *J_{C-F}* = 3.4 Hz), 129.0, 128.8, 128.7, 125.3 (q, *J_{C-F}* = 3.6 Hz), 125.2 (q, *J_{C-F}* = 3.7 Hz), 118.1, 112.5,

79.0, 67.4, 65.4, 60.8, 60.3, 45.4, 13.8, 13.1; HRMS (ESI) calcd for C₃₀H₂₈N₂F₂O₄H⁺ (*M* + *H*)⁺ 594.1953, found 594.1952; HPLC analysis: 91% ee (OOG-4457-EO, isopropanol/hexane = 7/93, 1.0 mL/min, UV: 254 nm), *t_R* = 5.3 min (major), 4.5 min (minor).

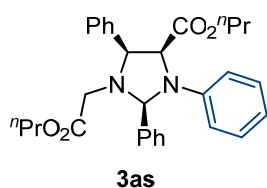
Methyl (2S,4S,5R)-1-(2-methoxy-2-oxoethyl)-3-phenyl-2,5-di(thiophen-2-yl)imidazolidine-4-carboxylate (3ar)



Prepared according to the general procedure as described above in 76% yield (33.6 mg). It was purified by flash chromatography to afford red wax; $[\alpha]_D^{25} = -12.1$ (*c* 0.68, CH₂Cl₂); ¹H NMR (300 MHz, Chloroform-*d*) δ 7.41 – 7.29 (m, 1H), 7.19 – 7.11 (m, 1H), 7.04 – 6.97 (m, 1H), 6.75 (td, *J* = 7.4, 1.1 Hz, 0H), 6.60 – 6.52 (m, 1H), 5.92 (s, 0H), 5.45 (d, *J* = 8.3 Hz, 0H), 4.52 (d, *J* = 8.3 Hz, 0H), 3.66 (s, 1H), 3.56 (s, 1H), 3.49 (d, *J* = 3.4 Hz, 1H). ¹³C

NMR (75 MHz, CDCl₃) δ 171.3, 170.3, 144.8, 144.5, 138.4, 128.7, 127.7, 127.2, 127.1, 126.5, 125.8, 125.4, 117.9, 112.6, 74.7, 67.5, 60.8, 51.7, 51.1, 45.0; HRMS (ESI) calcd for C₂₂H₂₂N₂O₄S₂H⁺ (*M* + *H*)⁺ 443.1094, found 443.1093; HPLC analysis: 69% ee (OOG-4459-EO, isopropanol/hexane = 7/93, 1.0 mL/min, UV: 254 nm), *t_R* = 14.2 min (major), 17.5 min (minor).

Propyl (2S,4S,5S)-1-(2-oxo-2-propoxyethyl)-2,3,5-triphenylimidazolidine-4-carboxylate (3as)



3as

Prepared according to the general procedure as described above in 61% yield (29.6 mg).

It was purified by flash chromatography to afford light yellow solid. mp =80-81 °C;

$[\alpha]_D^{25} = -25.0$ (*c* 0.69, CH₂Cl₂); ¹H NMR (300 MHz, Chloroform-*d*) δ 8.05 – 7.89 (m, 2H),

7.54 – 7.30 (m, 8H), 7.09 (dd, *J* = 8.7, 7.3 Hz, 2H), 6.69 (t, *J* = 7.4 Hz, 2H), 6.43 (dt, *J* =

7.0, 1.1 Hz, 2H), 5.52 (s, 1H), 5.13 (d, *J* = 8.6 Hz, 1H), 4.53 (d, *J* = 8.6 Hz, 1H), 3.99 (td,

J = 6.7, 2.5 Hz, 2H), 3.84 (dt, *J* = 10.6, 6.7 Hz, 2H), 3.48 (dt, *J* = 10.7, 6.7 Hz, 1H), 3.24 (s, 2H), 1.61 (h, *J* = 7.2 Hz,

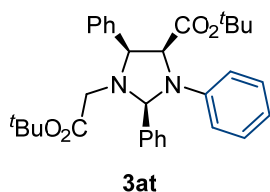
2H), 1.34 – 1.22 (m, 2H), 0.90 (t, *J* = 7.4 Hz, 3H), 0.73 (t, *J* = 7.4 Hz, 3H). ¹³C NMR (75 MHz, CDCl₃) δ 171.3,

170.0, 144.9, 140.0, 135.2, 128.6, 128.6, 128.3, 128.3, 128.2, 128.2, 117.4, 112.6, 79.7, 67.7, 66.2, 65.8, 65.5, 45.4,

21.6, 21.2, 10.04, 9.95; HRMS (ESI) calcd for C₃₀H₃₄N₂O₄H⁺ (*M* + *H*)⁺ 487.2591, found 487.2589; HPLC analysis:

94% ee (OOG-4457-EO, isopropanol/hexane = 7/93, 1.0 mL/min, UV: 254 nm), *t*_R = 6.9 min (major), 5.4 min (minor).

tert-Butyl (2S,4S,5S)-1-(2-(*tert*-butoxy)-2-oxoethyl)-2,3,5-triphenylimidazolidine-4-carboxylate (3at)



3at

Prepared according to the general procedure as described above in 73% yield (37.5 mg).

It was purified by flash chromatography to afford light yellow solid. mp =150-152 °C;

$[\alpha]_D^{25} = -32.3$ (*c* 0.63, CH₂Cl₂); ¹H NMR (300 MHz, Chloroform-*d*) δ 8.09 – 7.74 (m, 2H),

7.50 – 7.28 (m, 8H), 7.09 (dd, *J* = 8.7, 7.2 Hz, 2H), 6.68 (t, *J* = 7.3 Hz, 1H), 6.52 – 6.33

(m, 2H), 5.51 (s, 1H), 5.14 (d, *J* = 8.8 Hz, 1H), 4.41 (d, *J* = 8.9 Hz, 1H), 3.34 – 3.00 (m,

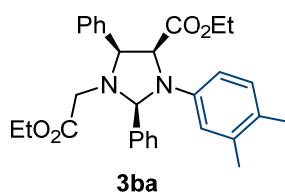
2H), 1.42 (s, 9H), 1.17 (s, 9H). ¹³C NMR (75 MHz, CDCl₃) δ 170.1, 169.4, 145.2, 140.4, 135.5, 128.8, 128.6, 128.5,

128.2, 128.1, 127.9, 117.1, 112.6, 80.9, 80.6, 79.6, 68.0, 65.6, 46.3, 27.9, 27.3; HRMS (ESI) calcd for C₃₂H₃₈N₂O₄H⁺

(*M* + *H*)⁺ 515.2904, found 515.2902; HPLC analysis: 95% ee (OOG-4472-EO, isopropanol/hexane = 7/93, 1.0

mL/min, UV: 254 nm), *t*_R = 6.2 min (major), 5.1 min (minor).

Ethyl (2S,4S,5S)-3-(3,4-dimethylphenyl)-1-(2-ethoxy-2-oxoethyl)-2,5-diphenylimidazolidine-4-carboxylate (3ba)



3ba

Prepared according to the general procedure as described above in 70% yield (34.0 mg).

It was purified by flash chromatography to afford light yellow wax; $[\alpha]_D^{25} = -19.3$ (*c* 0.57,

CH₂Cl₂); ¹H NMR (300 MHz, Chloroform-*d*) δ 8.22 – 7.74 (m, 2H), 7.56 – 7.14 (m, 8H),

6.85 (d, *J* = 8.2 Hz, 1H), 6.35 – 6.02 (m, 2H), 5.49 (s, 1H), 5.12 (d, *J* = 8.6 Hz, 1H), 4.50

(d, *J* = 8.7 Hz, 1H), 4.08 (q, *J* = 7.1 Hz, 2H), 3.91 (dq, *J* = 10.7, 7.1 Hz, 1H), 3.65 (dq, *J*

= 10.7, 7.2 Hz, 1H), 3.24 (s, 2H), 2.11 (s, 3H), 2.09 (s, 3H), 1.22 (t, *J* = 7.1 Hz, 3H), 0.93 (t, *J* = 7.2 Hz, 3H). ¹³C

NMR (75 MHz, CDCl₃) δ 171.4, 169.9, 143.2, 140.3, 136.6, 135.3, 129.7, 128.7, 128.3, 128.2, 128.2, 128.1, 128.1,

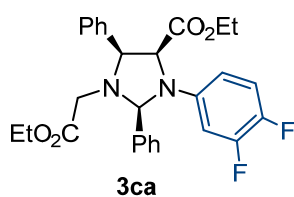
125.3, 114.2, 110.1, 79.8, 67.9, 65.8, 60.4, 59.9, 45.6, 19.9, 18.2, 13.9, 13.3; HRMS (ESI) calcd for C₃₀H₃₄N₂O₄H⁺

(*M* + *H*)⁺ 487.2591, found 487.2588; HPLC analysis: 94% ee (OOG-4459-EO, isopropanol/hexane = 7/93, 1.0

mL/min, UV: 254 nm), *t*_R = 6.1 min (major), 8.9 min (minor).

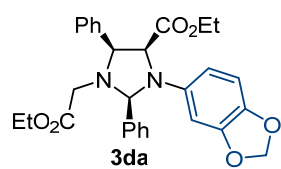
Ethyl (2S,4S,5S)-3-(3,4-difluorophenyl)-1-(2-ethoxy-2-oxoethyl)-2,5-diphenylimidazolidine-4-carboxylate

(3ca)



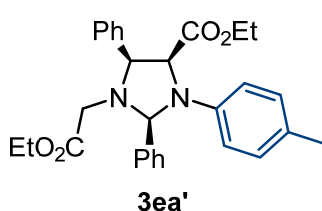
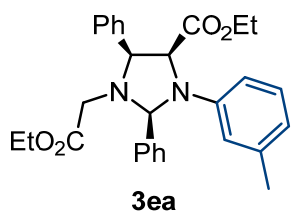
Prepared according to the general procedure as described above in 62% yield (30.6 mg). It was purified by flash chromatography to afford light red wax; $[\alpha]_D^{25} = -22.9$ (*c* 0.21, CH₂Cl₂); ¹H NMR (300 MHz, Chloroform-*d*) δ 8.03 – 7.84 (m, 2H), 7.47 – 7.31 (m, 8H), 6.86 (dt, *J* = 10.1, 9.0 Hz, 1H), 6.20 (ddd, *J* = 13.3, 6.6, 3.0 Hz, 1H), 6.09 – 6.00 (m, 1H), 5.47 (s, 1H), 5.16 (d, *J* = 8.6 Hz, 1H), 4.43 (d, *J* = 8.6 Hz, 1H), 4.09 (qd, *J* = 7.1, 1.6 Hz, 2H), 3.87 (dq, *J* = 10.7, 7.1 Hz, 1H), 3.61 (dq, *J* = 10.7, 7.2 Hz, 1H), 3.31 – 3.12 (m, 2H), 1.21 (t, *J* = 7.1 Hz, 3H), 0.87 (t, *J* = 7.2 Hz, 3H). ¹³C NMR (75 MHz, CDCl₃) δ 170.7, 169.9, 141.9 (d, *J*_{C-F} = 8.8 Hz), 139.3, 134.8, 128.5 (d, *J*_{C-F} = 26.3 Hz), 128.5 (d, *J*_{C-F} = 11.0 Hz), 128.2, 117.0, 116.9 (dd, *J*_{C-F} = 18.0, 1.7 Hz), 116.7, 107.6, 107.5 (dd, *J*_{C-F} = 5.4, 3.2 Hz), 107.4, 101.5 (d, *J*_{C-F} = 22.0 Hz), 79.7, 67.7, 65.6, 60.7, 60.0, 45.1, 13.9, 13.2; HRMS (ESI) calcd for C₂₈H₂₈N₂F₂O₄H⁺ (M + H)⁺ 495.2090, found 495.2087; HPLC analysis: 97% ee (OOG-4459-EO, isopropanol/hexane = 7/93, 1.0 mL/min, UV: 254 nm), *t*_R = 6.5 min (major), 10.1 min (minor).

Ethyl (2S,4S,5S)-3-(benzo[d][1,3]dioxol-5-yl)-1-(2-ethoxy-2-oxoethyl)-2,5-diphenylimidazolidine-4-carboxylate (3da)



Prepared according to the general procedure as described above in 70% yield (35.1 mg). It was purified by flash chromatography to afford brown wax; $[\alpha]_D^{25} = -7.5$ (*c* 0.63, CH₂Cl₂); ¹H NMR (300 MHz, Chloroform-*d*) δ 8.01 – 7.87 (m, 2H), 7.46 – 7.29 (m, 8H), 6.57 (d, *J* = 8.5 Hz, 1H), 6.08 (d, *J* = 2.5 Hz, 1H), 5.83 (dd, *J* = 8.5, 2.5 Hz, 1H), 5.78 (s, 2H), 5.46 (s, 1H), 5.14 (d, *J* = 8.6 Hz, 1H), 4.44 (d, *J* = 8.6 Hz, 1H), 4.14 – 4.02 (m, 2H), 3.86 (dq, *J* = 10.7, 7.1 Hz, 1H), 3.61 (dq, *J* = 10.6, 7.2 Hz, 1H), 3.22 (d, *J* = 2.3 Hz, 2H), 1.21 (t, *J* = 7.1 Hz, 3H), 0.88 (t, *J* = 7.1 Hz, 3H). ¹³C NMR (75 MHz, CDCl₃) δ 171.2, 169.9, 147.7, 140.9, 140.0, 139.3, 135.2, 128.6, 128.4, 128.3, 128.2, 128.1, 108.1, 104.5, 100.2, 95.5, 80.0, 68.3, 65.7, 60.5, 59.9, 45.4, 13.9, 13.3; HRMS (ESI) calcd for C₂₉H₃₀N₂O₆H⁺ (M + H)⁺ 503.2177, found 503.2176; HPLC analysis: 96% ee (OOG-4459-EO, isopropanol/hexane = 7/93, 1.0 mL/min, UV: 254 nm), *t*_R = 9.8 min (major), 15.7 min (minor).

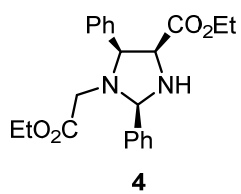
Ethyl (2S,4S,5S)-1-(2-ethoxy-2-oxoethyl)-2,5-diphenyl-3-(*m*-tolyl)imidazolidine-4-carboxylate (3ea) and Ethyl (2S,4S,5S)-1-(2-ethoxy-2-oxoethyl)-2,5-diphenyl-3-(*p*-tolyl)imidazolidine-4-carboxylate (3ea')



The mixture of **3ea** and **3ea'**, prepared according to the general procedure as described above in 69% yield (32.6 mg, yellow liquid). The two regioisomers could not be separated by flash chromatography. The ratio (**3ea** : **3ea'**) is around 60:40 according to ¹H NMR. ¹H NMR (300 MHz, Chloroform-*d*) δ 8.11 – 7.89 (2H),

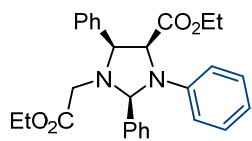
7.47 – 7.31 (8H), 7.05 – 6.47 (2H), 6.38 – 6.21 (2H), 5.51 (1H), 5.13 (1H), 4.50 (1H), 4.08 (2H), 3.99 – 3.80 (1H), 3.64 (1H), 3.24 (2H), 2.19 and 2.17 (3H, 4-CH₃C₆H₄ and 3-CH₃C₆H₄), 1.22 (3H), 0.91 (3H). ¹³C NMR (75 MHz, CDCl₃) δ 171.30, 171.24, 145.00, 142.74, 140.16, 138.28, 135.30, 135.24, 129.13, 128.65, 128.27, 128.18, 128.13, 126.45, 118.36, 113.39, 112.52, 109.84, 79.74, 79.68, 67.82, 67.73, 65.80, 65.74, 60.42, 59.91, 45.53, 45.47, 21.43, 19.85, 13.90, 13.31.

Ethyl (2R,4S,5S)-1-(2-ethoxy-2-oxoethyl)-2,5-diphenylimidazolidine-4-carboxylate (4)

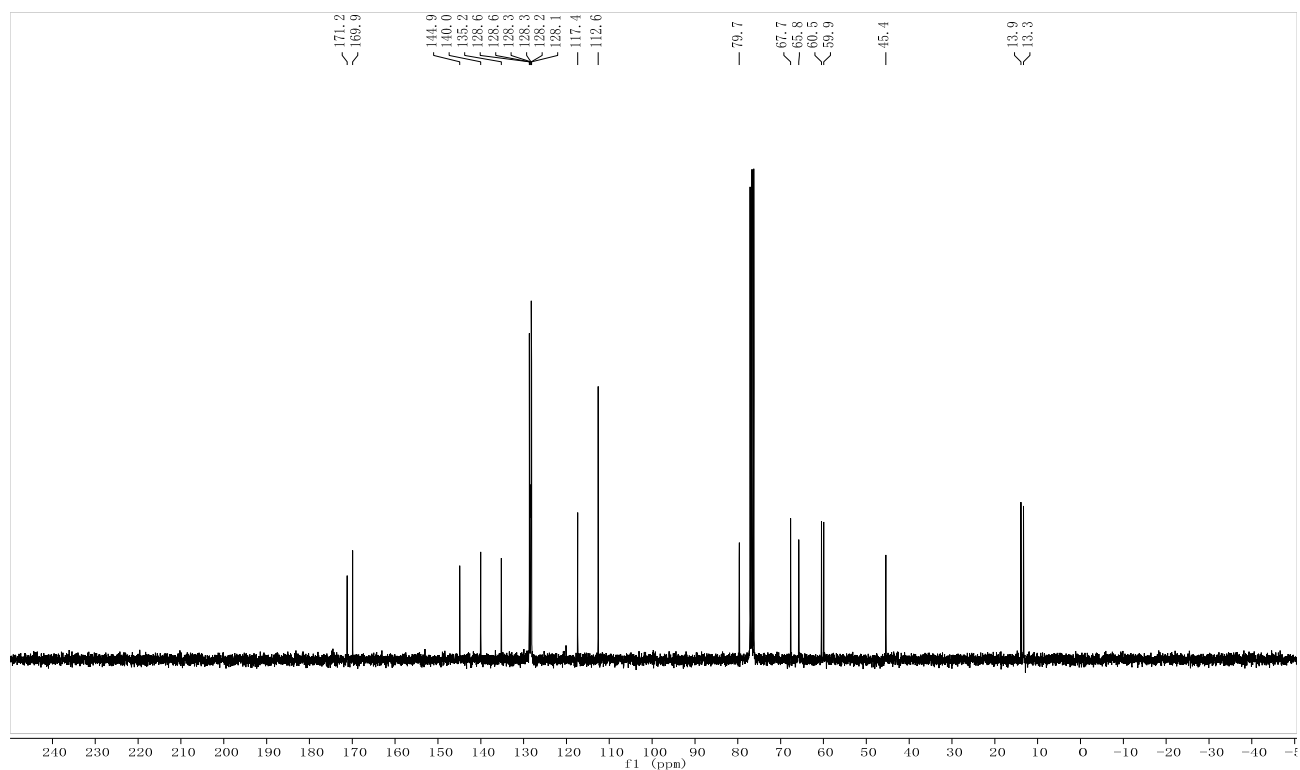
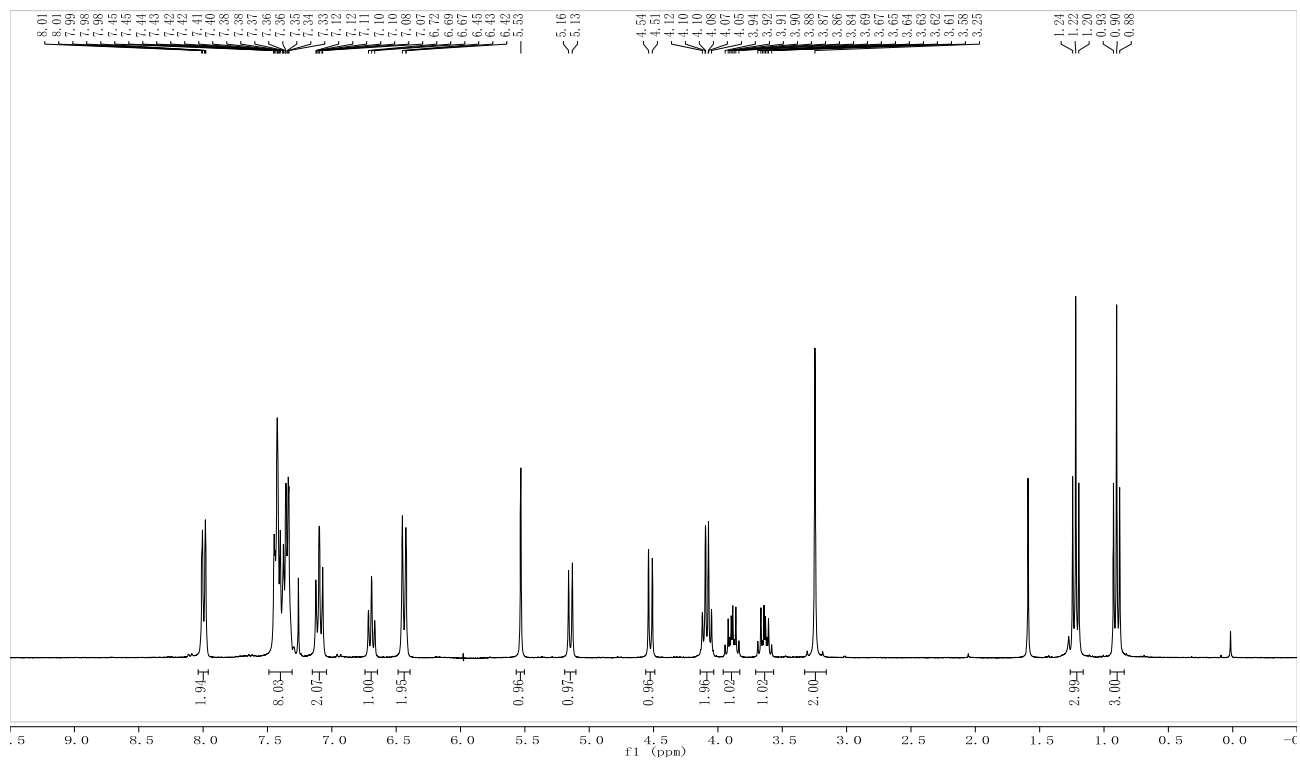


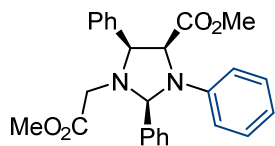
Prepared according to the above procedure as described above in 35% yield (13.4 mg). It was purified by flash chromatography (11% EtOAc/PE) to afford colorless liquid; $[\alpha]_D^{25} = +68.4$ (*c* 0.67, CH₂Cl₂); ¹H NMR (300 MHz, DMSO-*d*₆) δ 7.79 – 7.64 (m, 2H), 7.51 – 7.40 (m, 4H), 7.37 (d, *J* = 2.0 Hz, 3H), 7.33 – 7.27 (m, 1H), 5.12 (s, 1H), 4.71 (d, *J* = 9.4 Hz, 1H), 4.35 (d, *J* = 9.4 Hz, 1H), 4.02 (q, *J* = 7.1 Hz, 1H), 3.75 (dq, *J* = 10.7, 7.1 Hz, 2H), 3.47 (dq, *J* = 10.7, 7.2 Hz, 0H), 3.38 – 3.16 (m, 2H), 2.92 (s, 1H), 1.18 (t, *J* = 7.1 Hz, 1H), 0.82 (t, *J* = 7.2 Hz, 1H); ¹³C NMR (75 MHz, CDCl₃) δ 170.9, 170.1, 138.7, 138.3, 128.7, 128.5, 128.0, 127.8, 127.7, 127.6, 79.5, 67.1, 64.4, 60.6, 59.9, 47.5, 13.8, 13.2; HRMS (ESI) calcd for C₂₂H₂₇N₂O₄ (M + H)⁺ 383.1965, found 383.1961; HPLC analysis: 92% ee (RC-OD, isopropanol/hexane = 7/93, 1.0 mL/min, UV: 254 nm), *t*_R = 8.2 min (major), 10.6 min (minor).

¹H and ¹³C NMR Spectra of All Products 3, and 4.

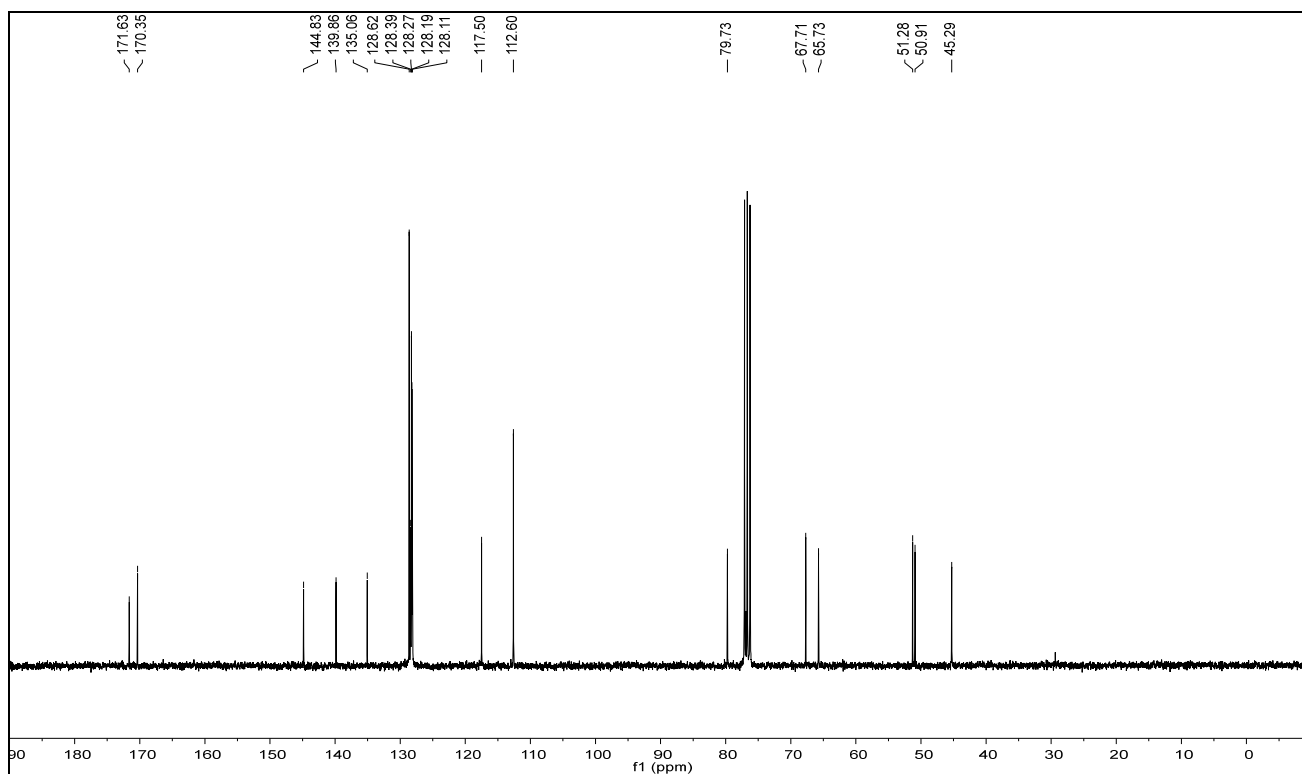
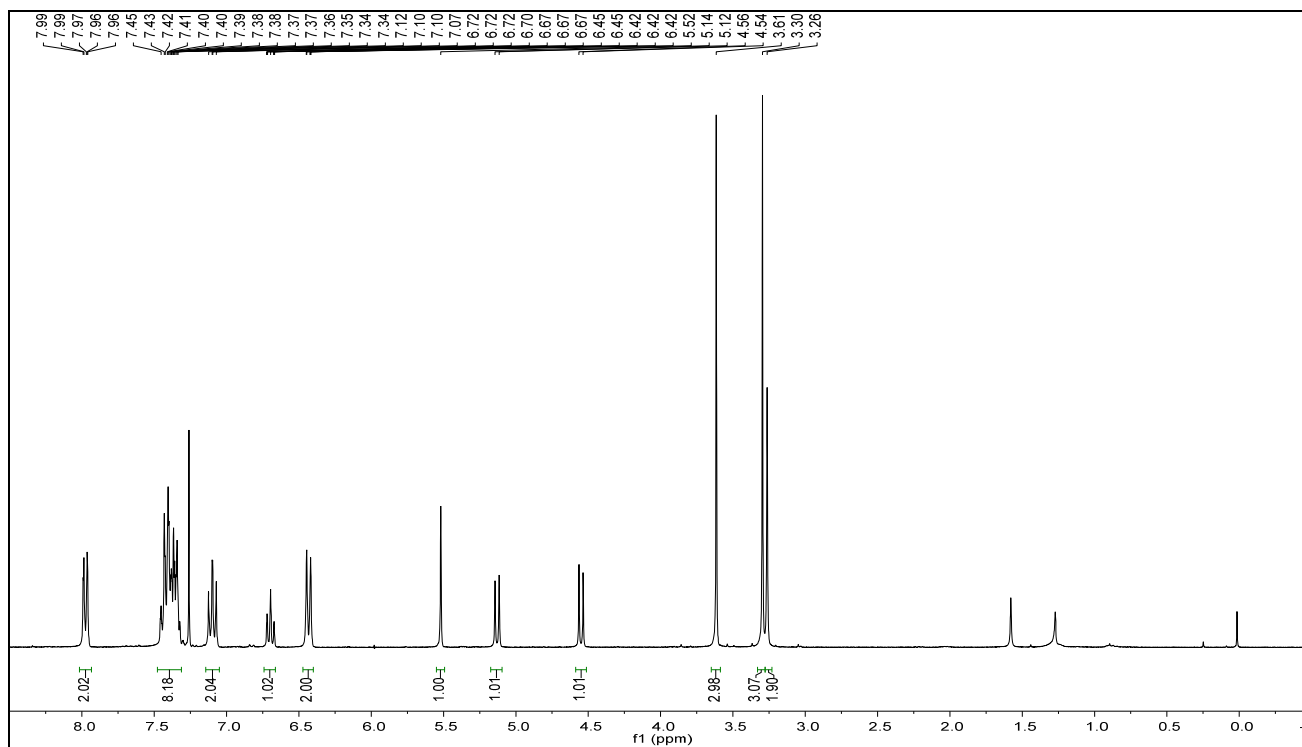


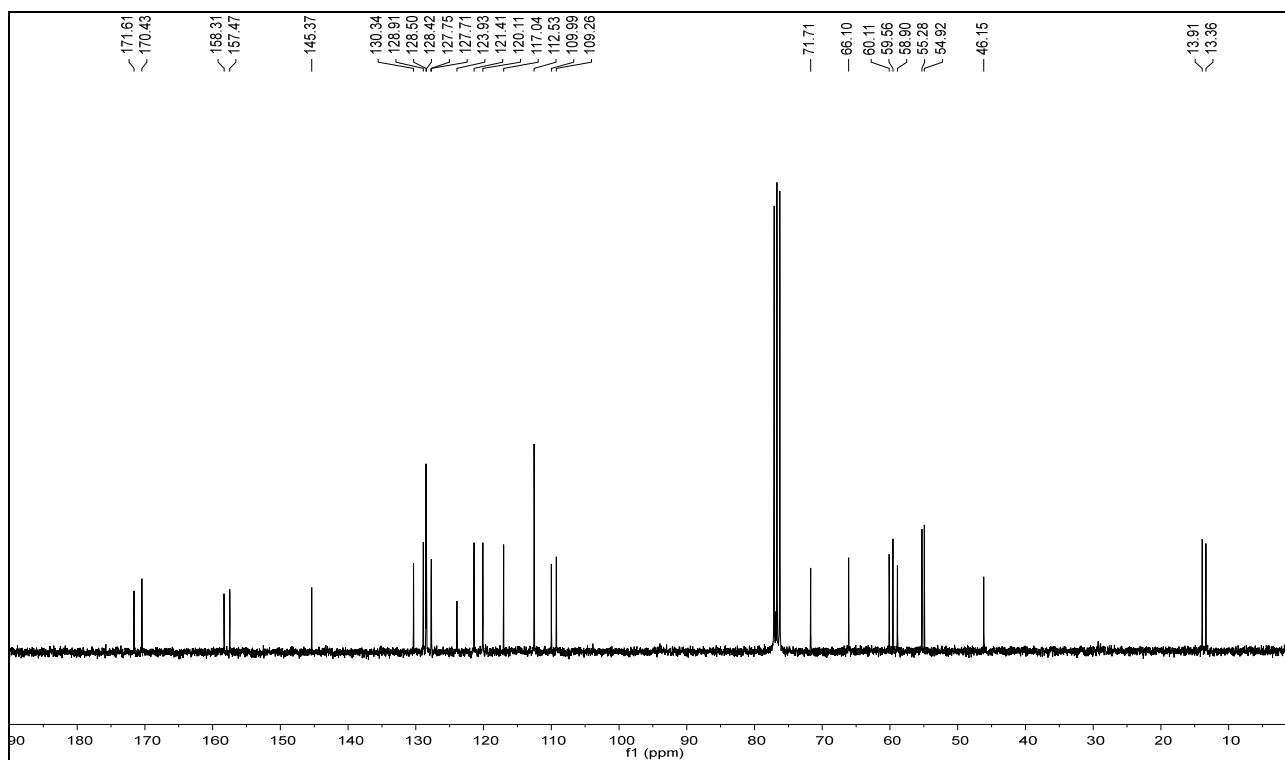
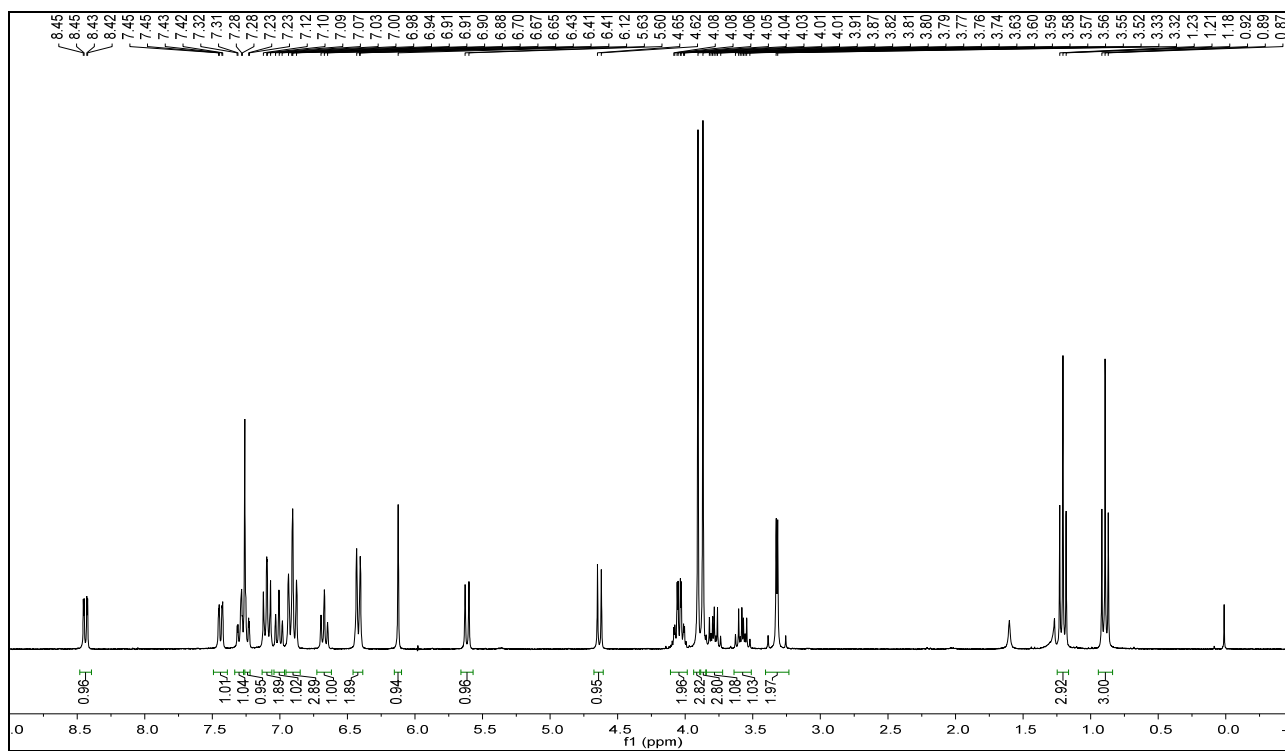
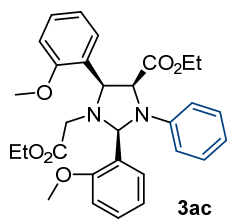
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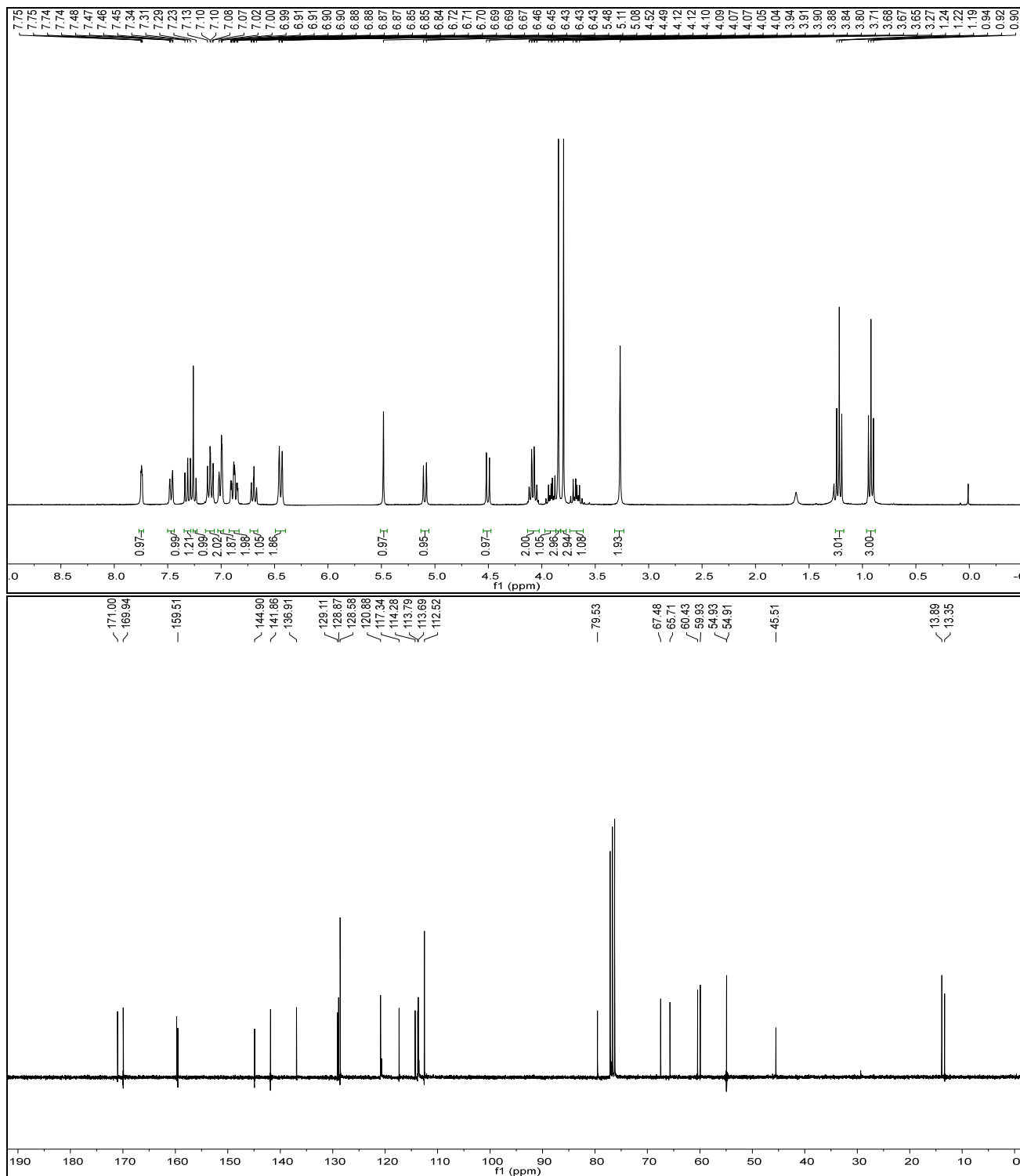
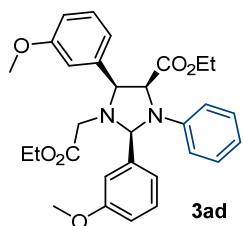


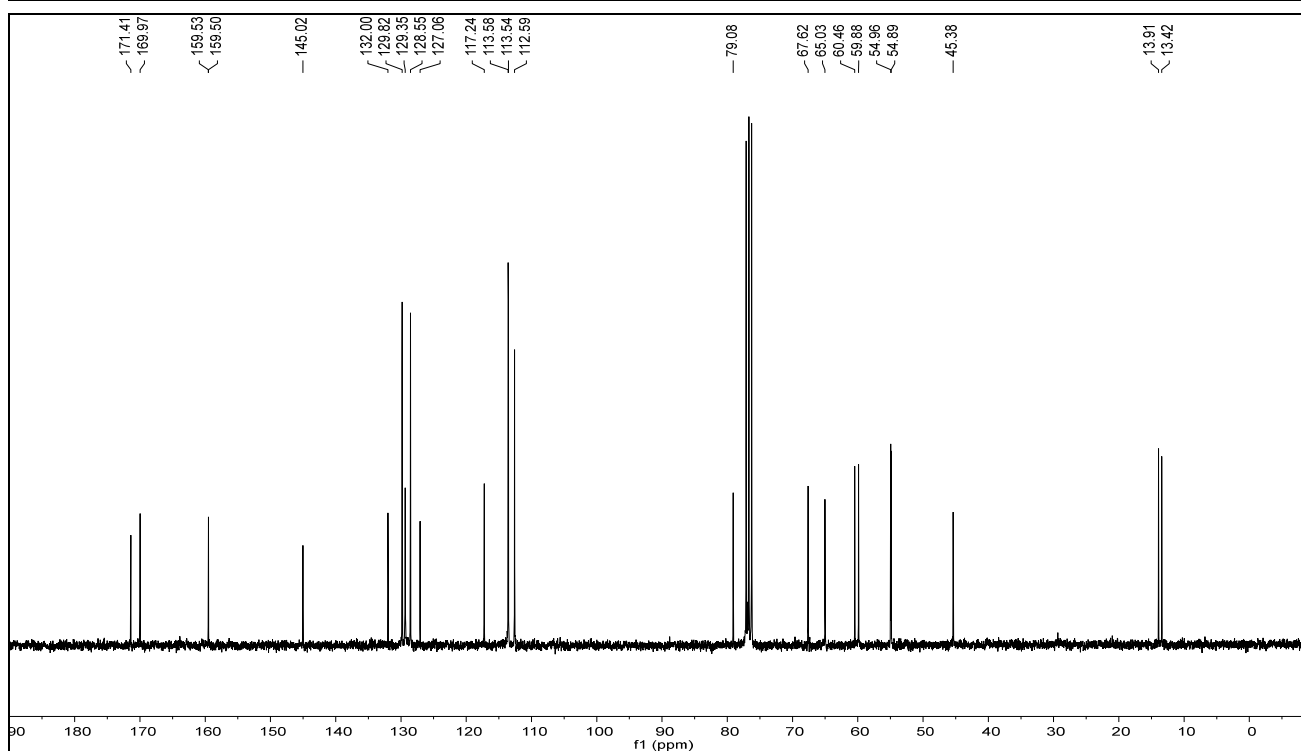
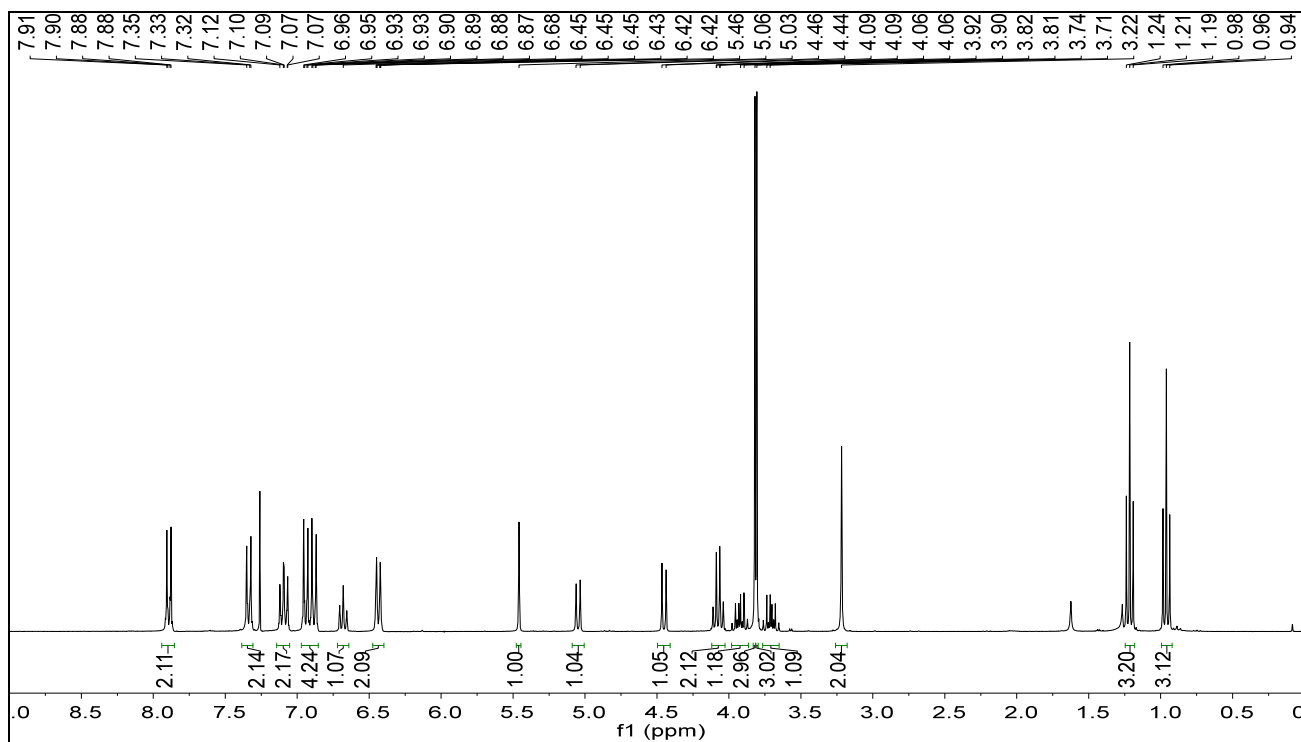
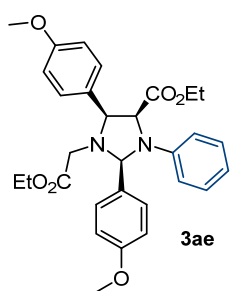


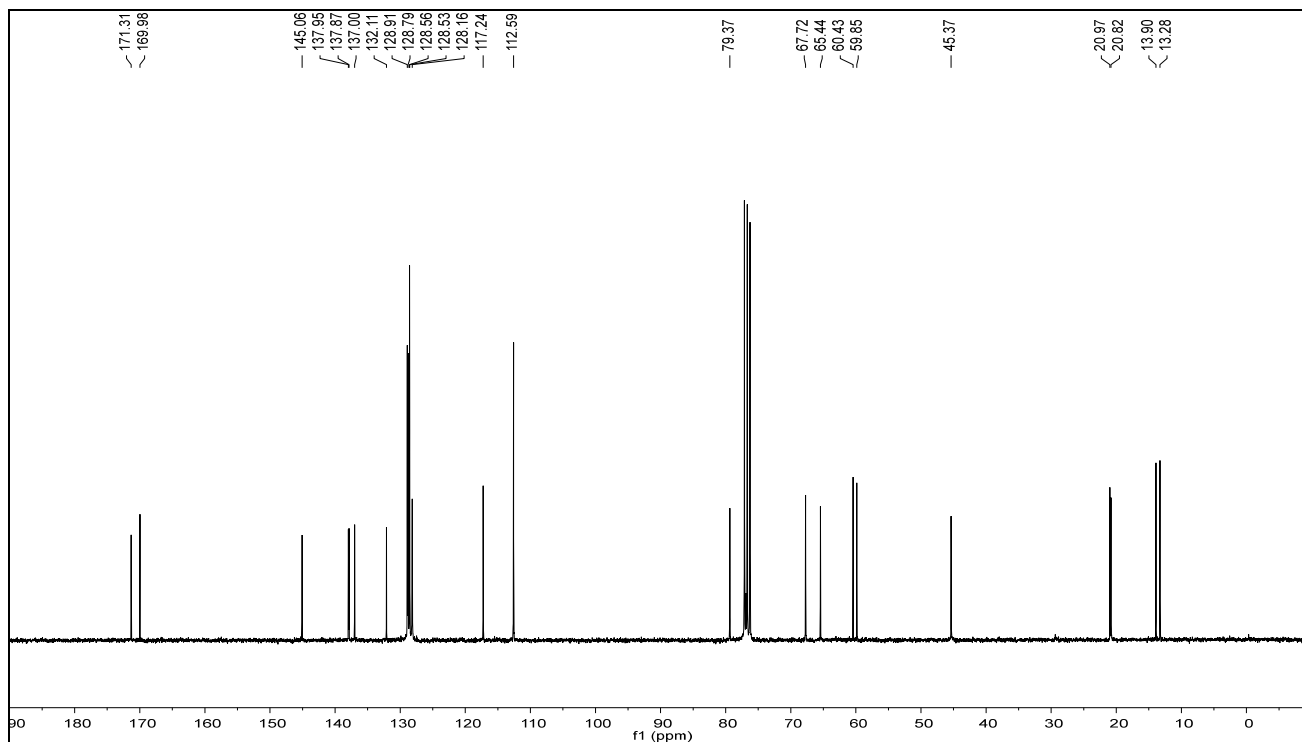
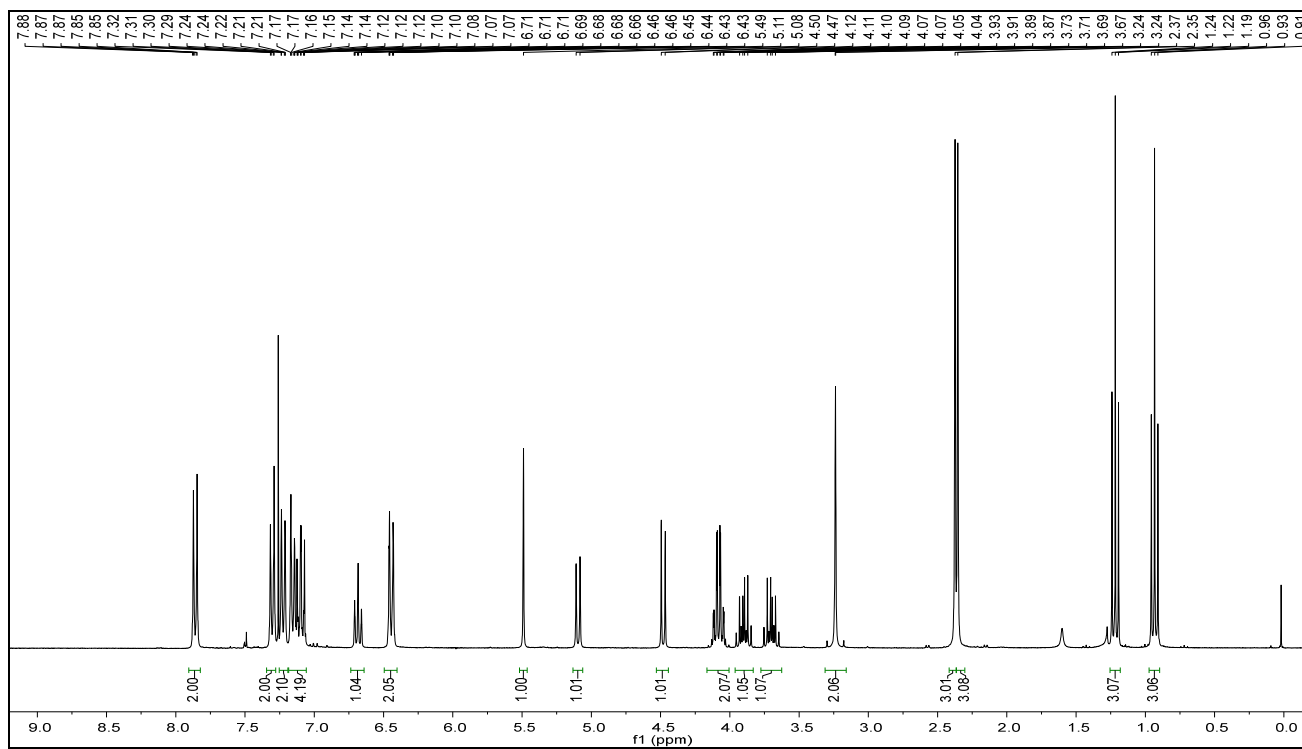
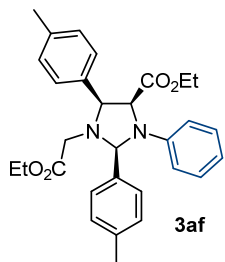
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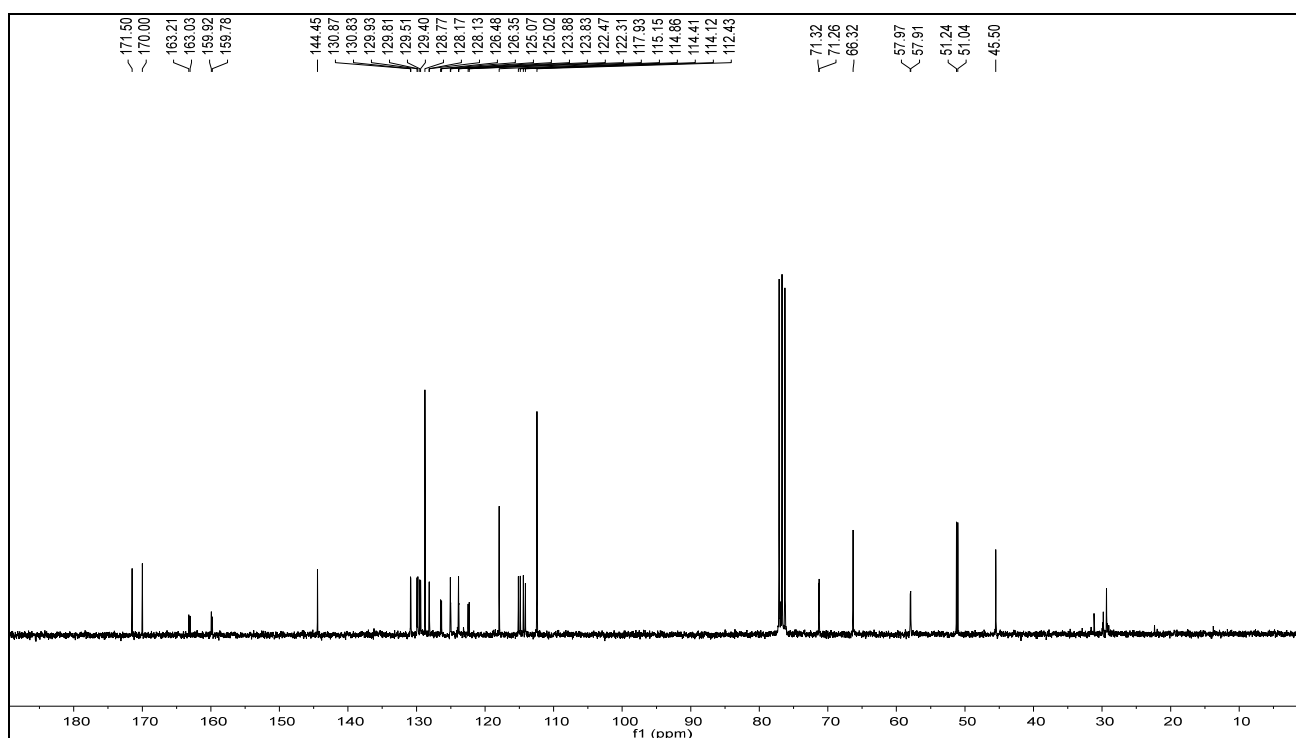
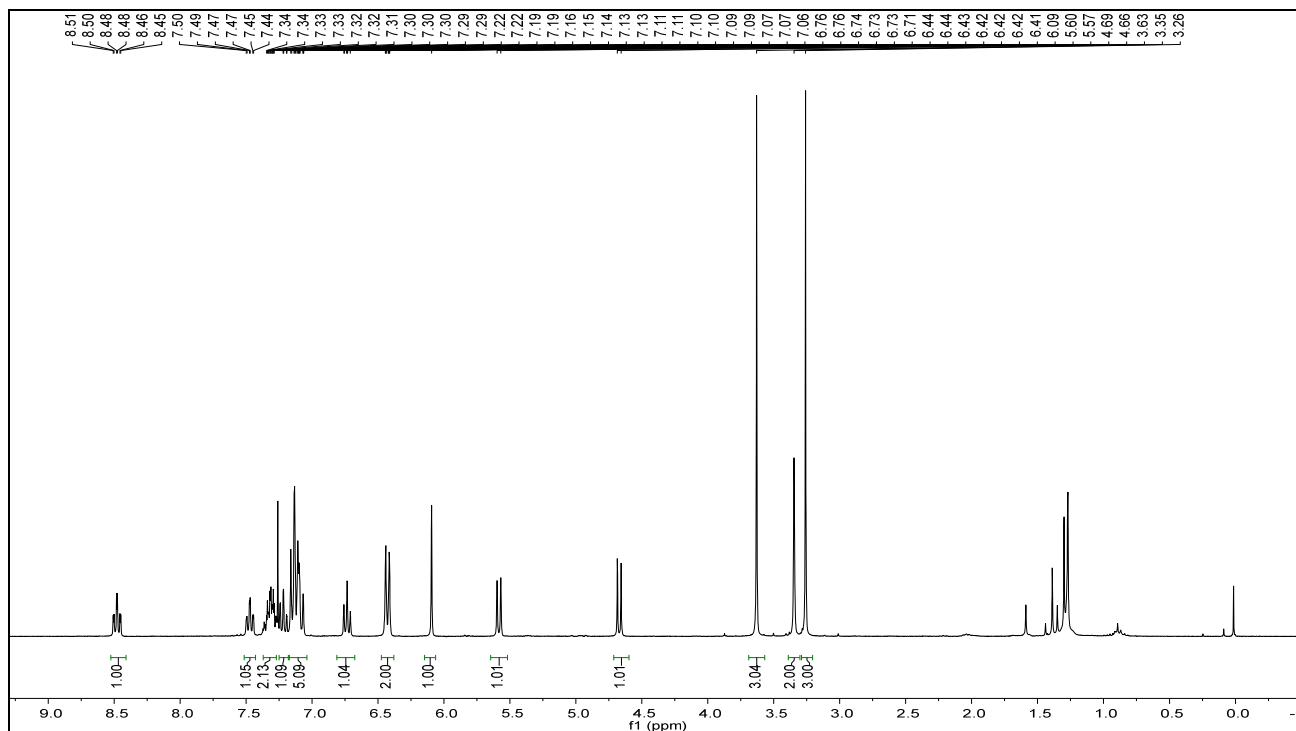
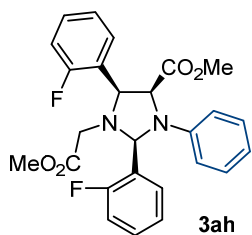


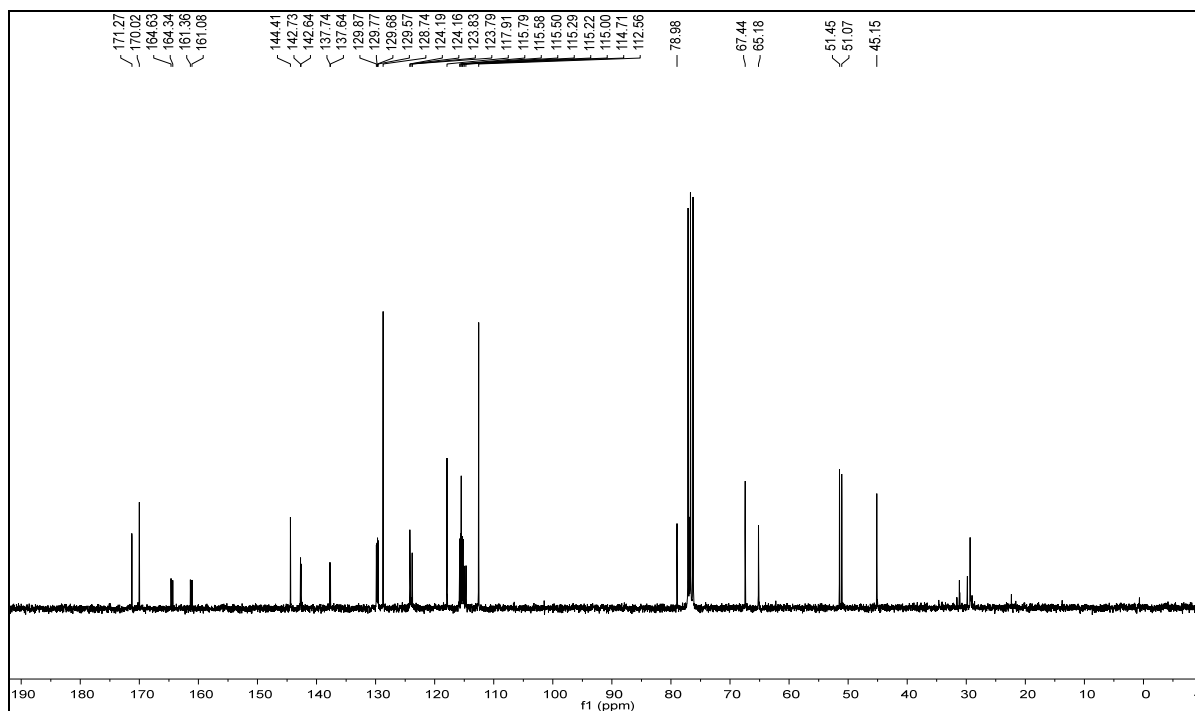
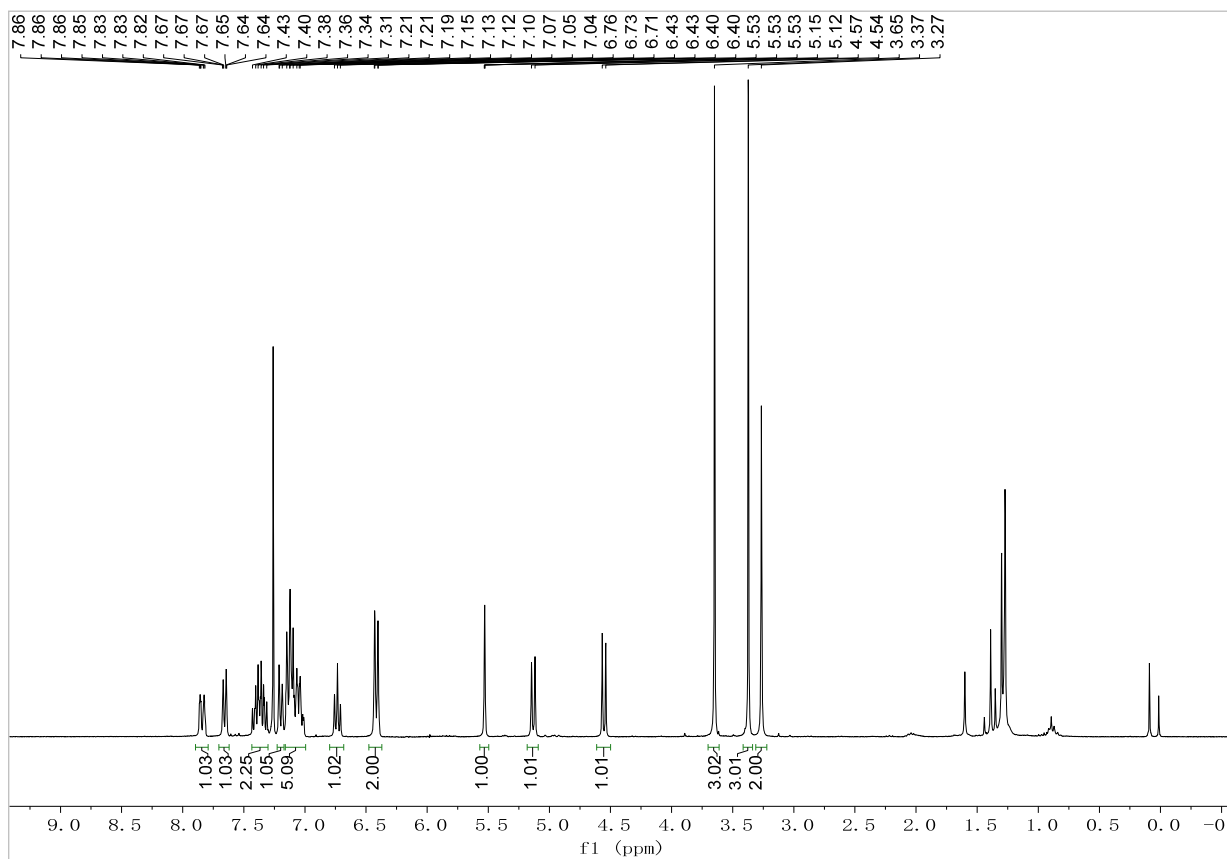
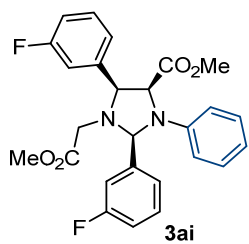


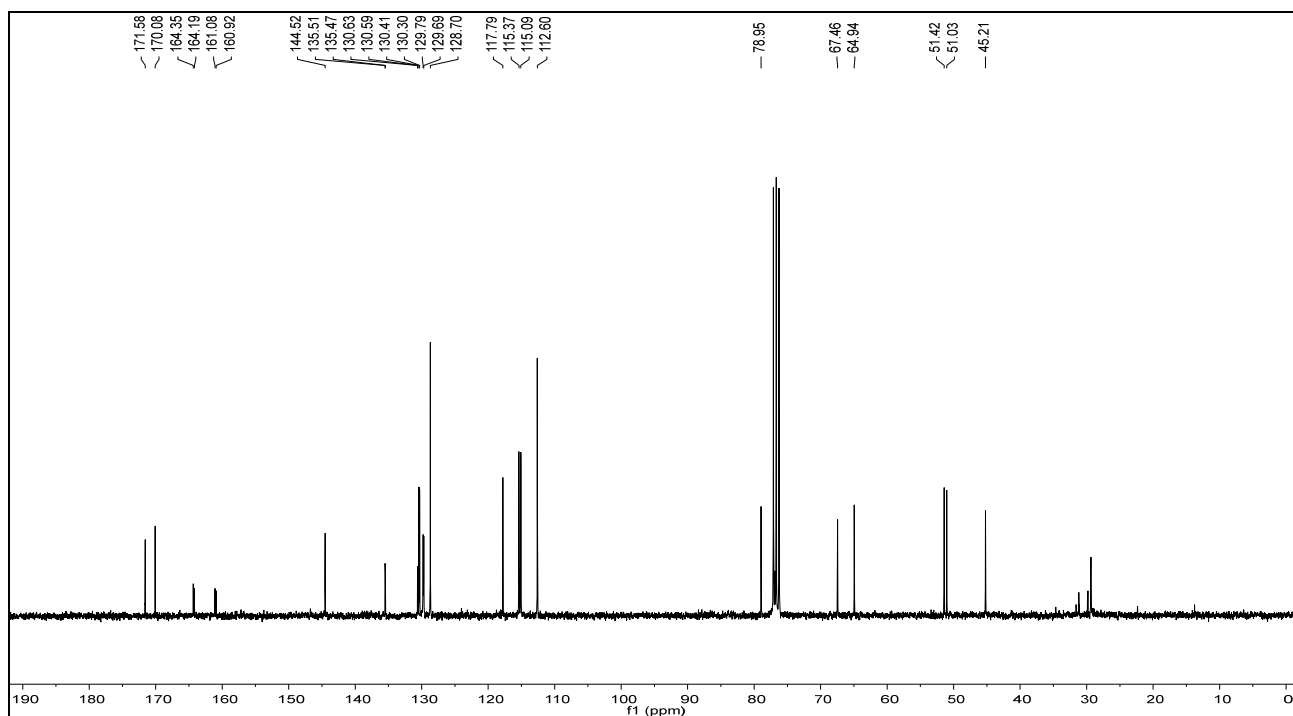
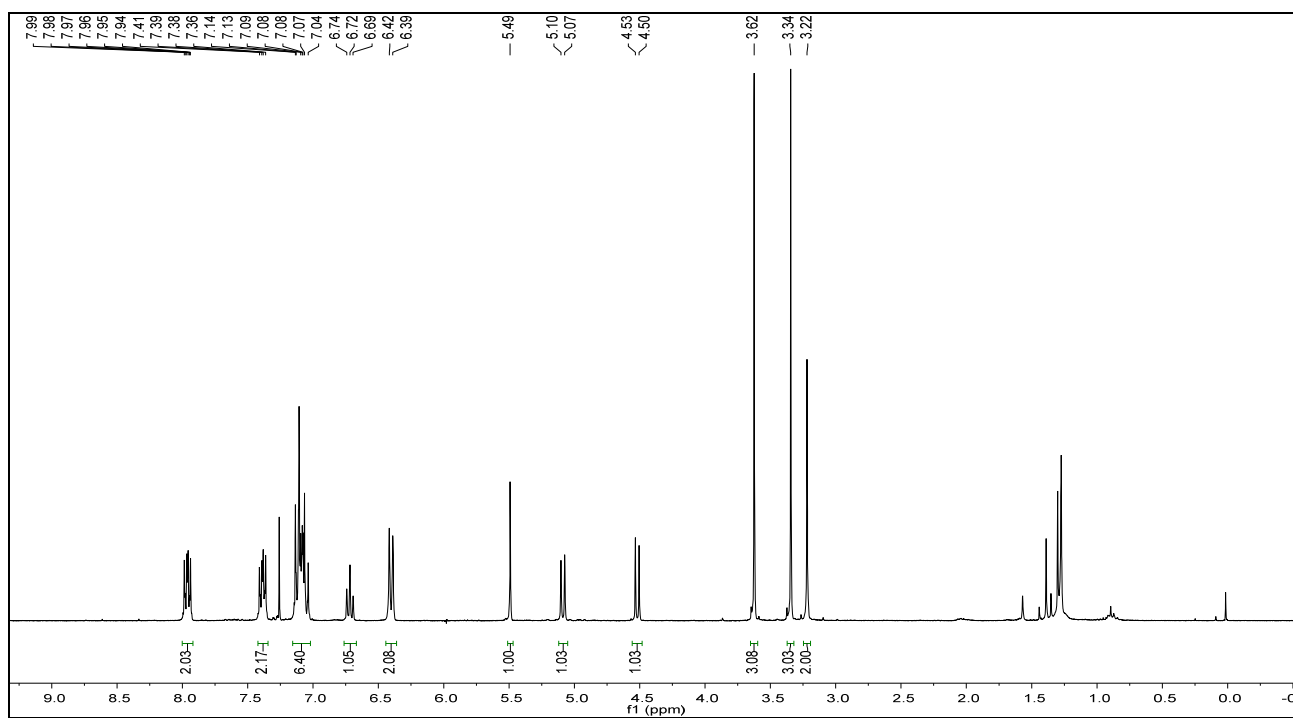
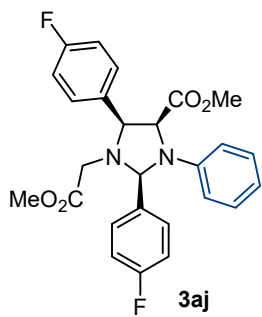


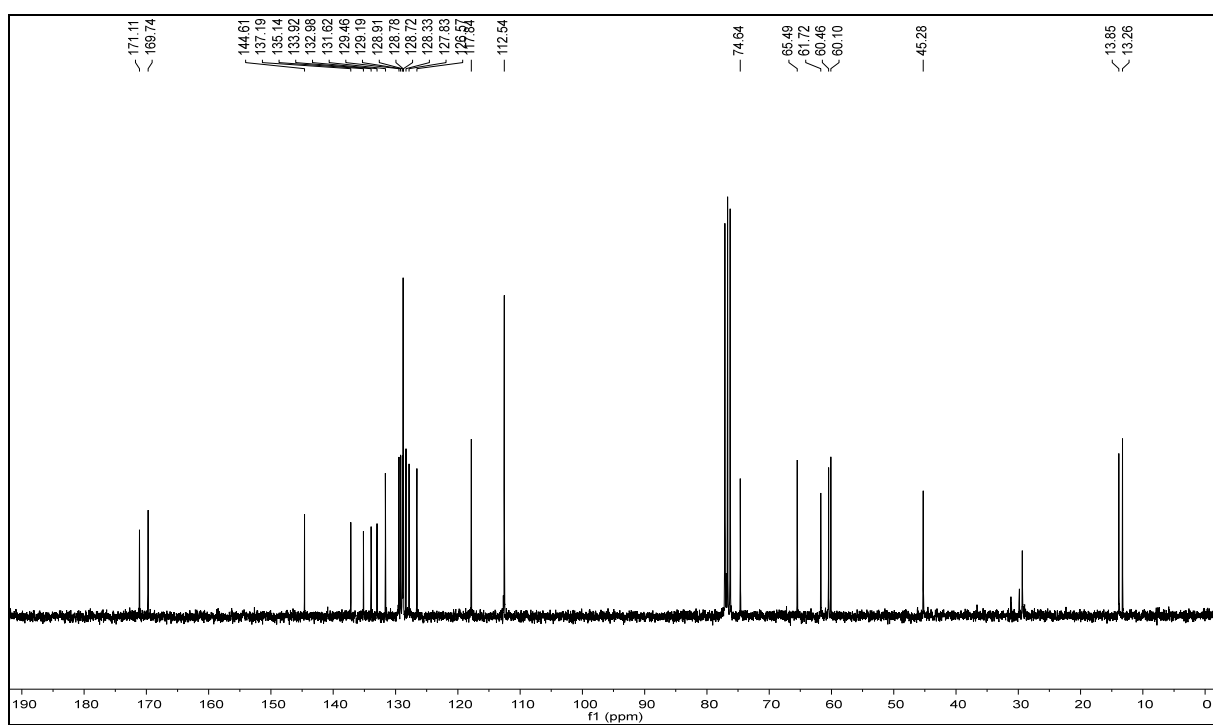
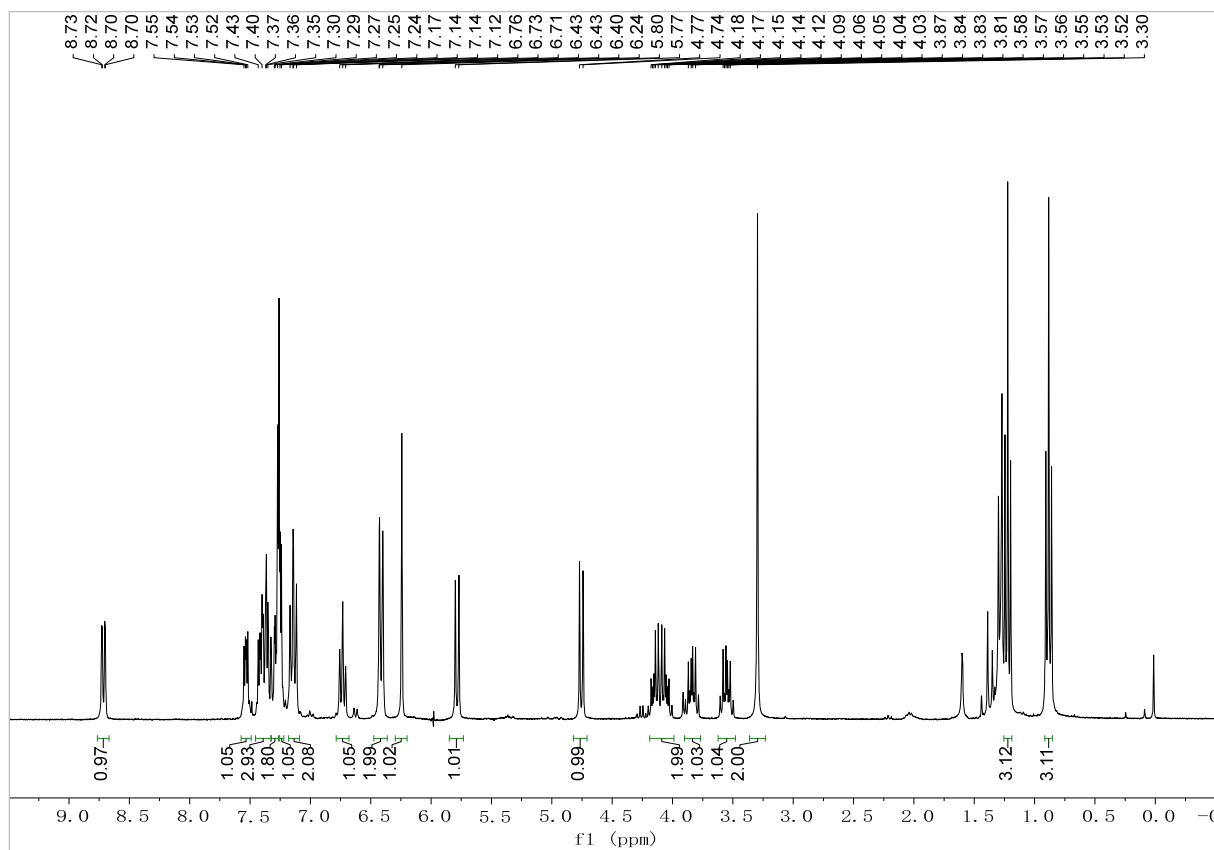
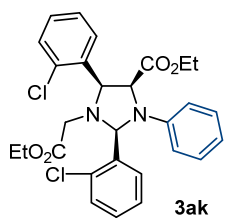


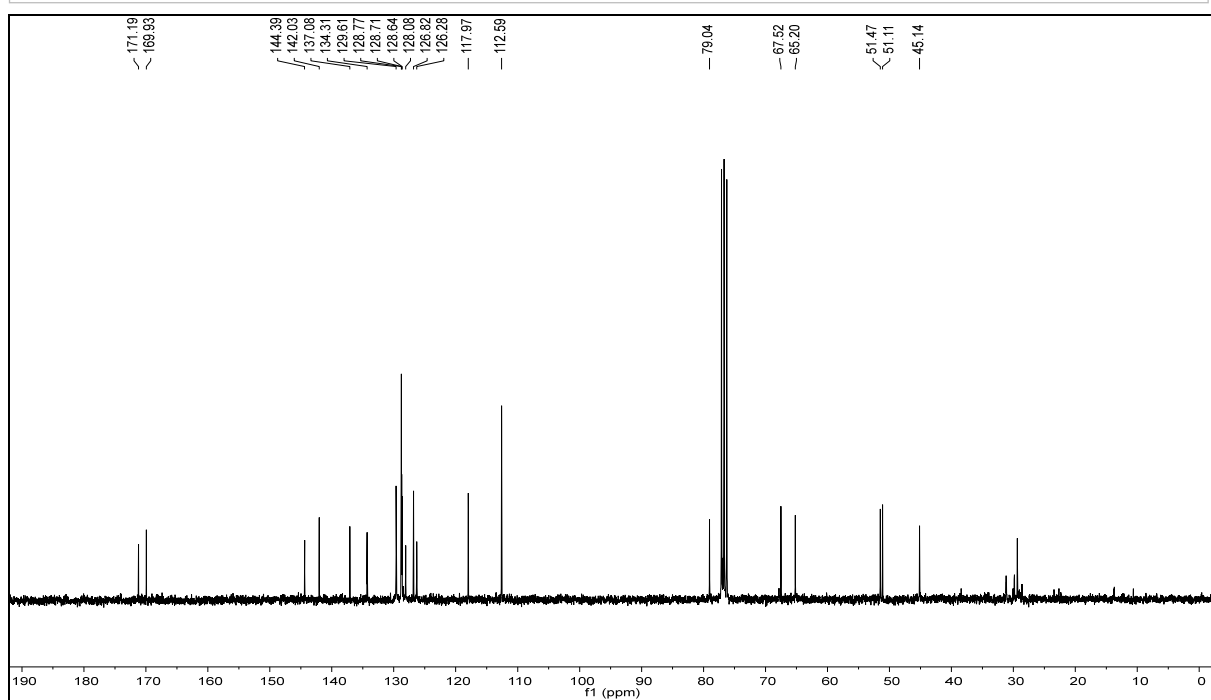
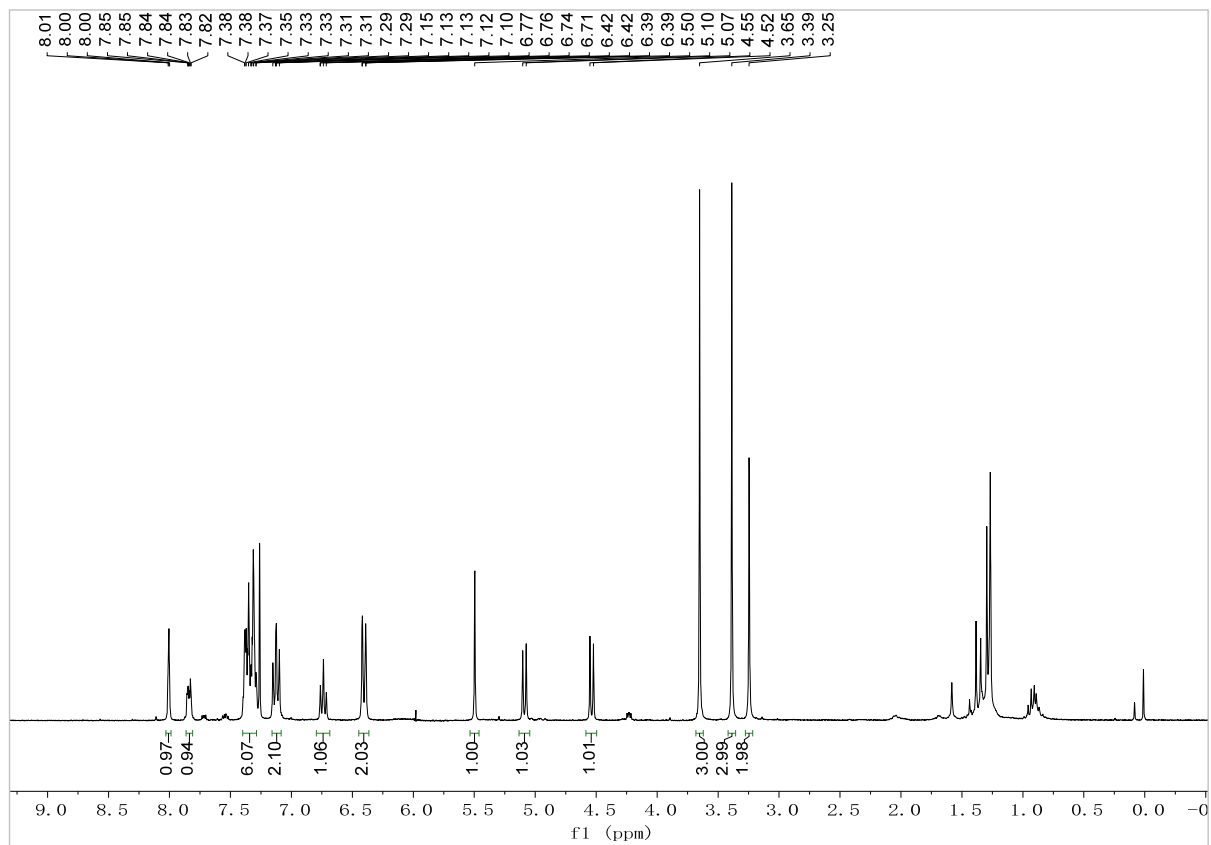
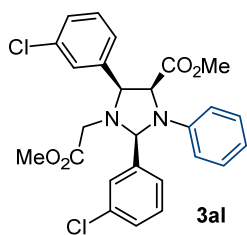


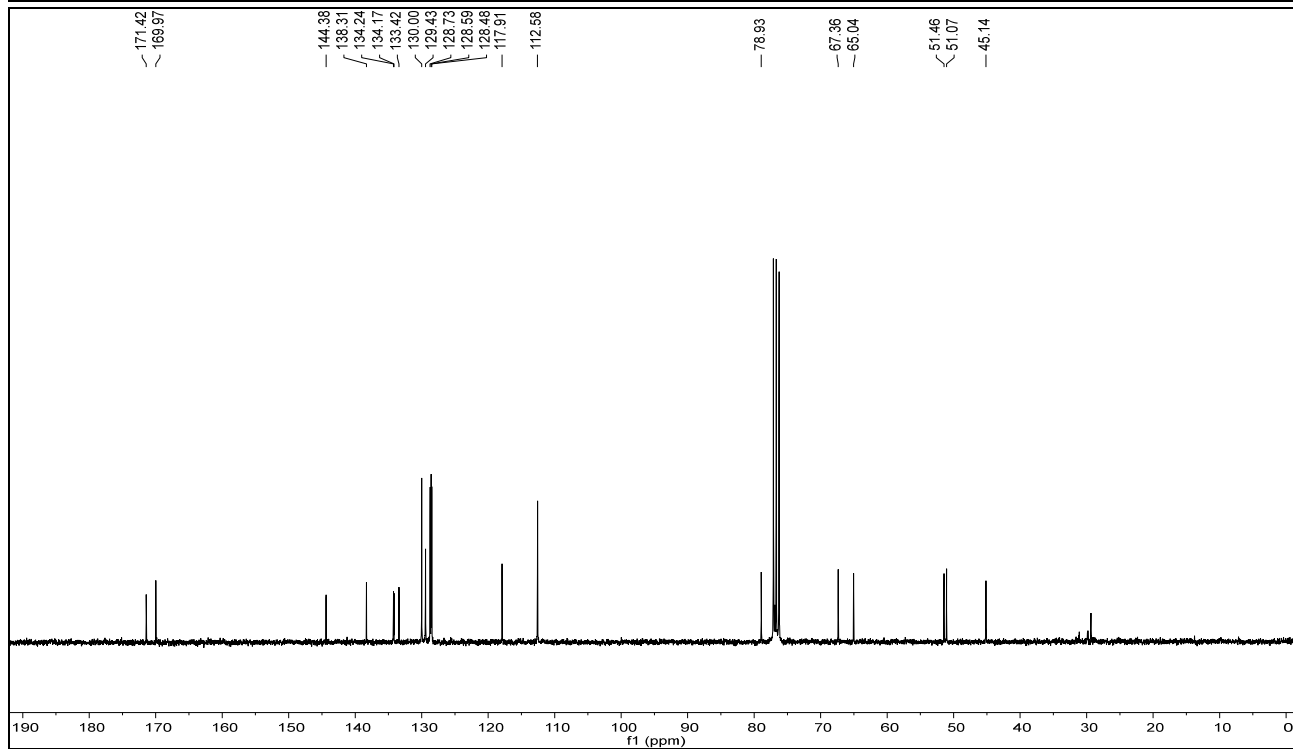
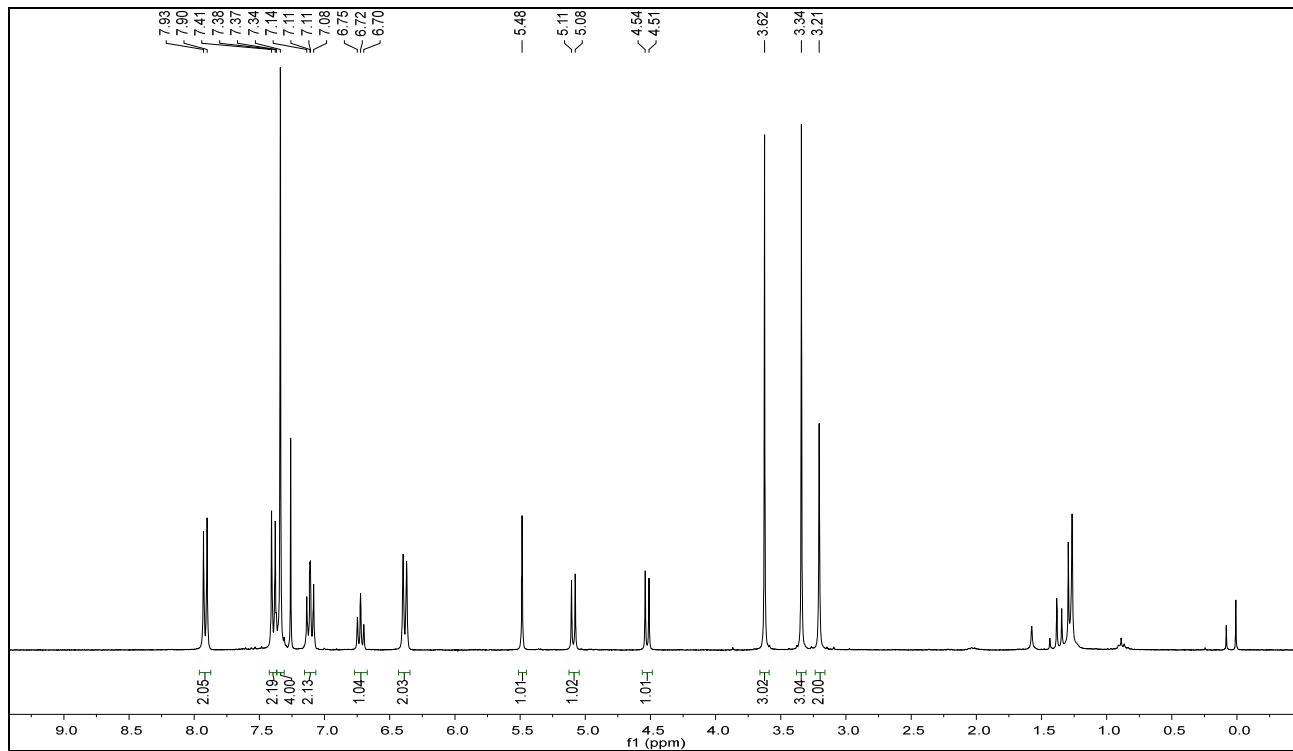
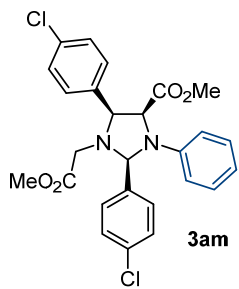


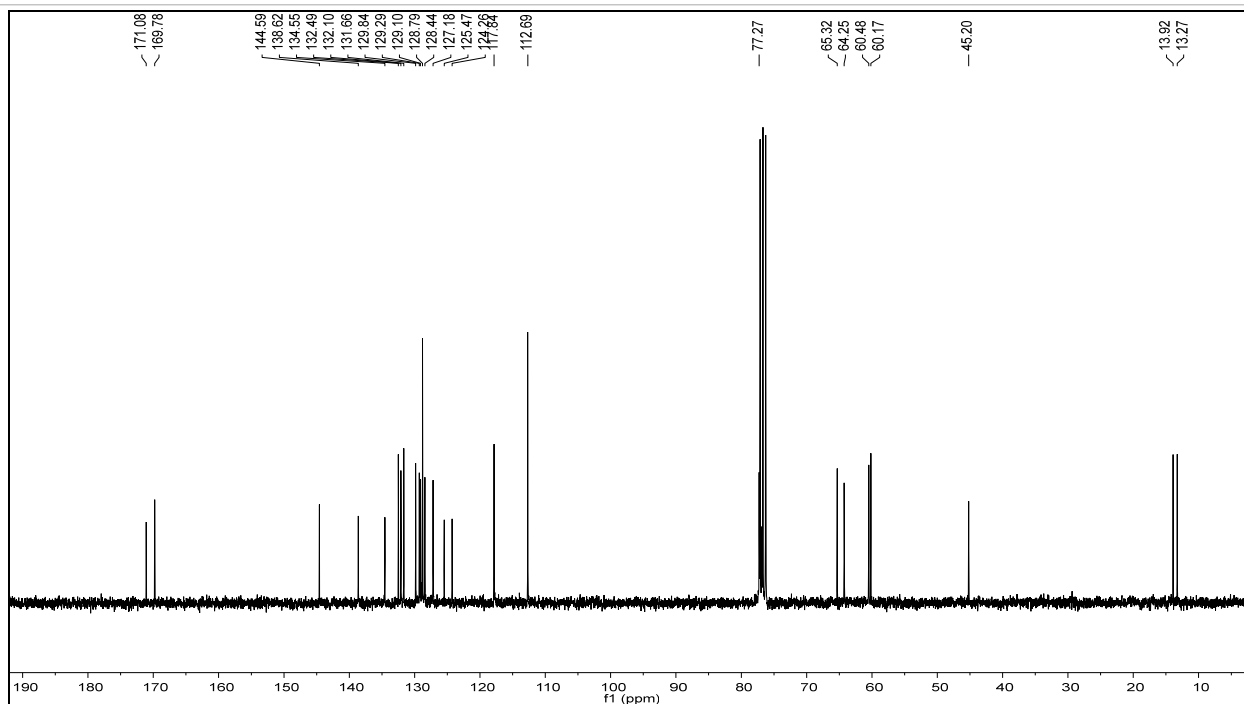
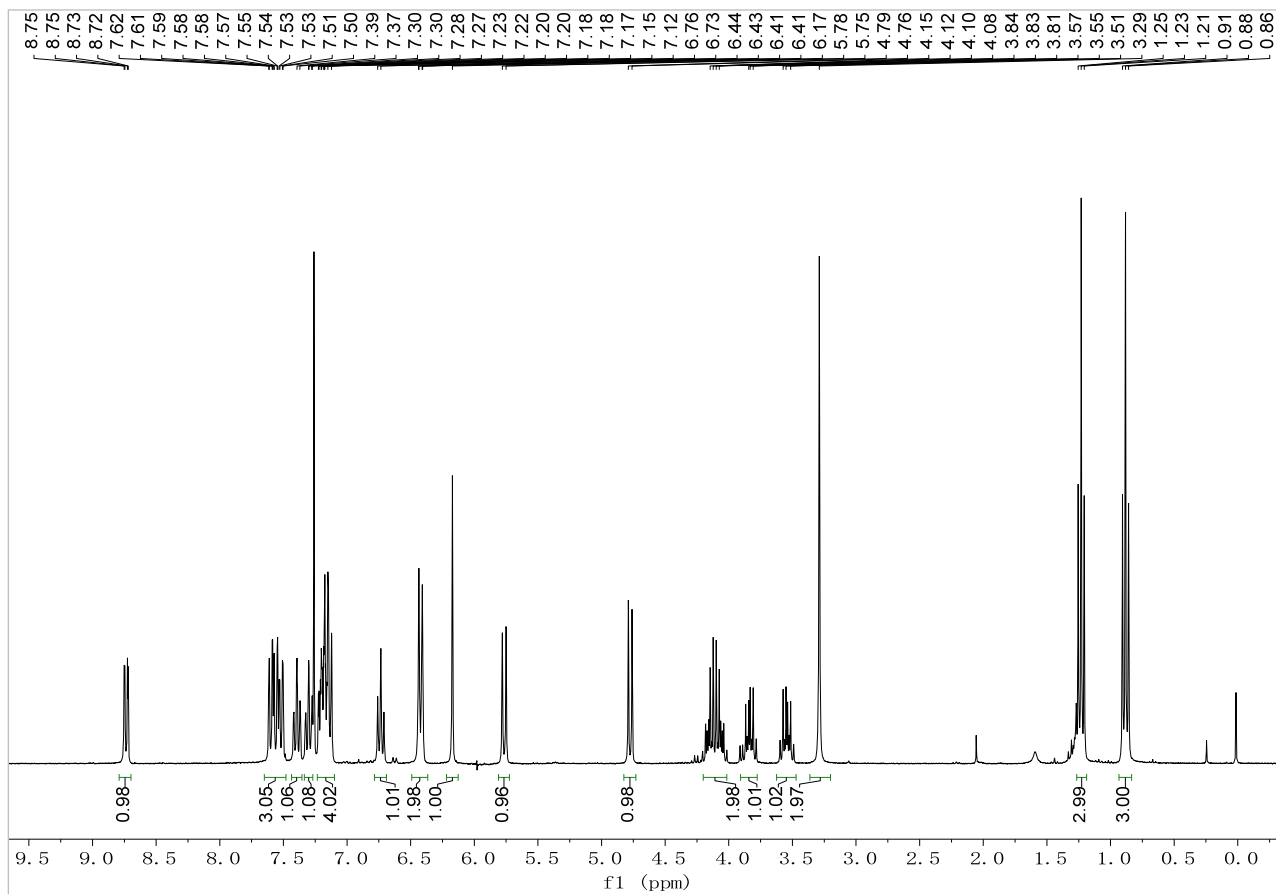
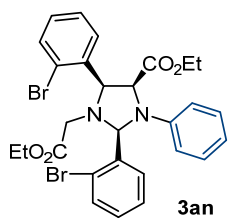


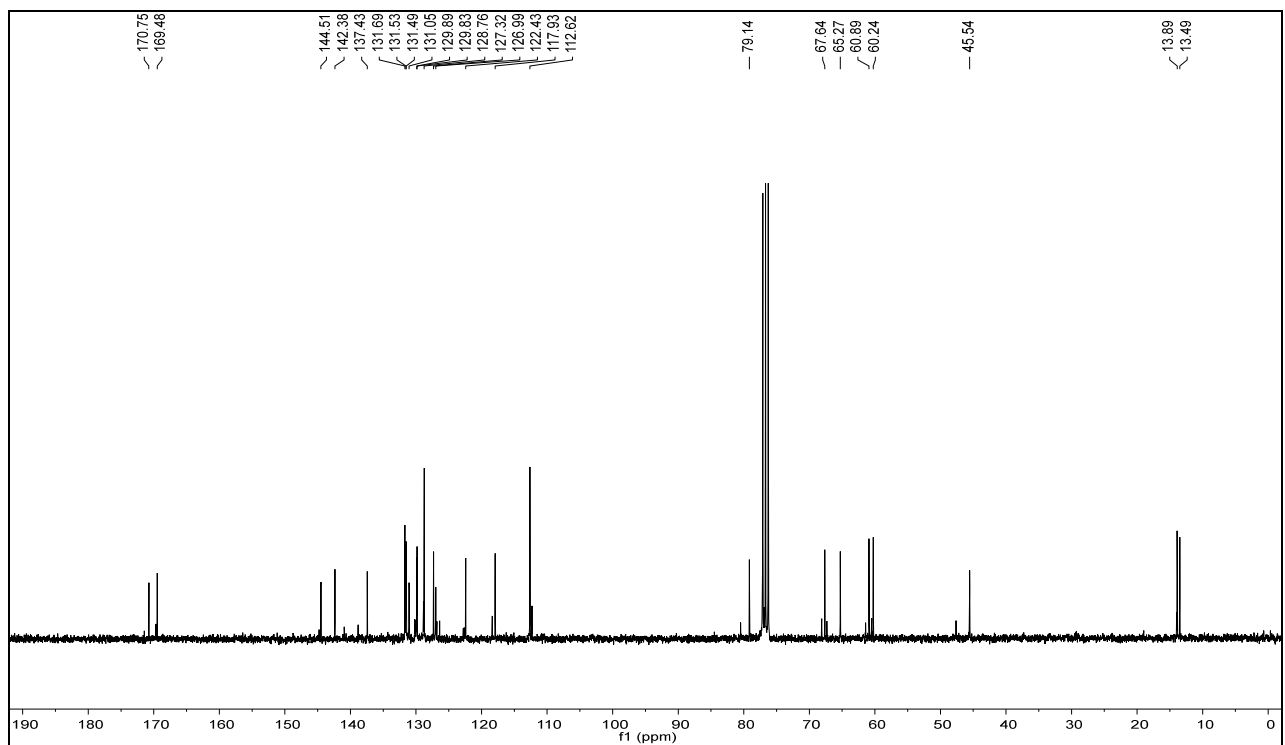
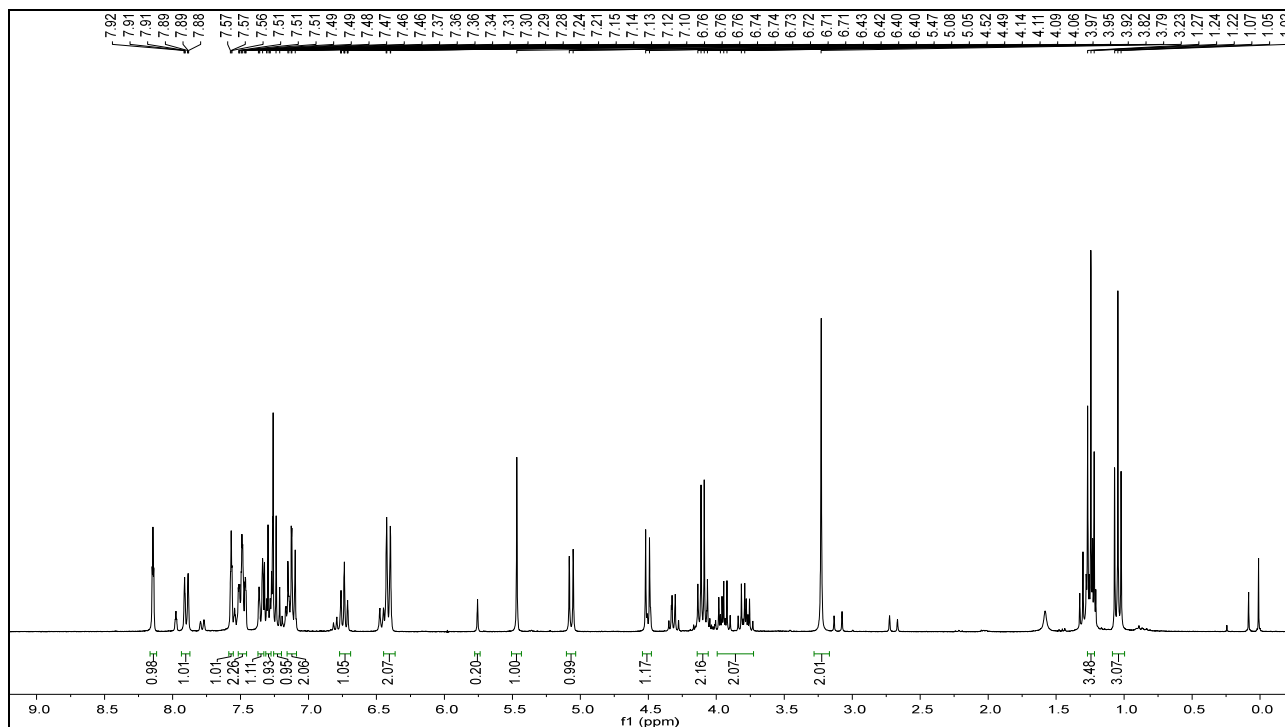
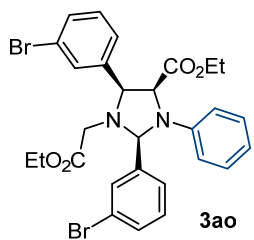


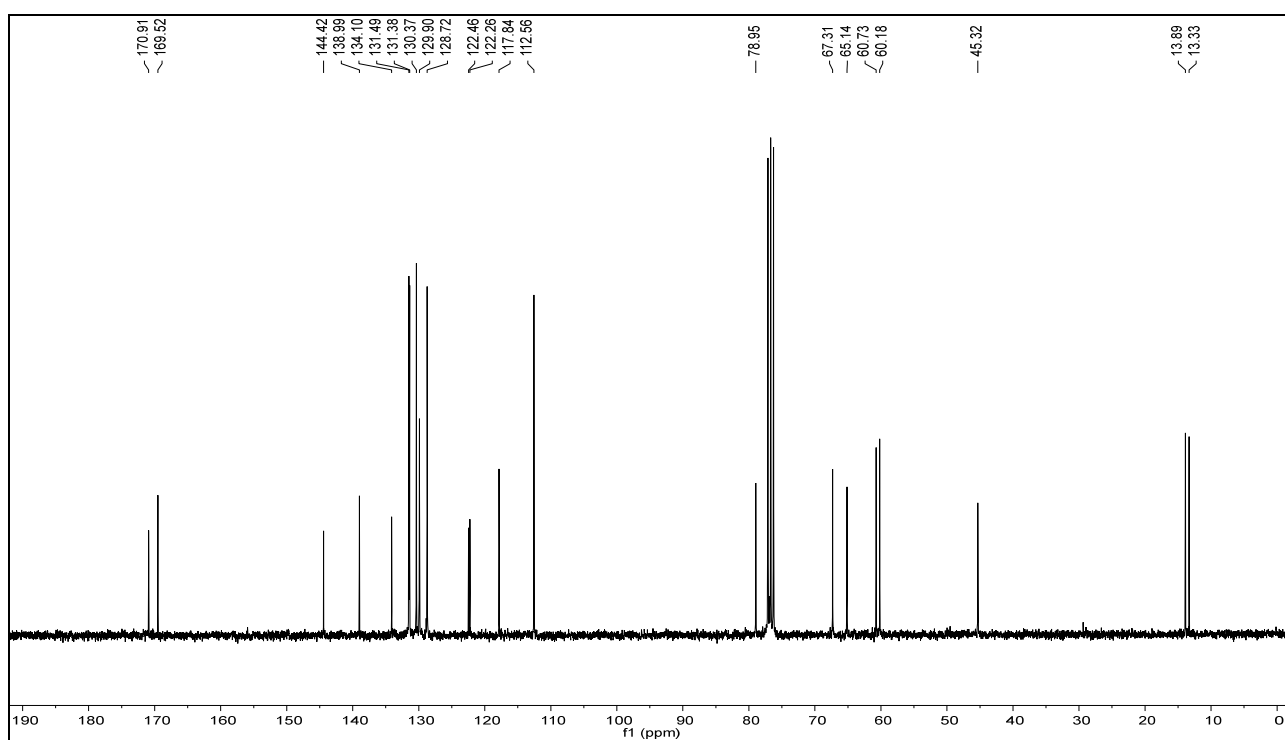
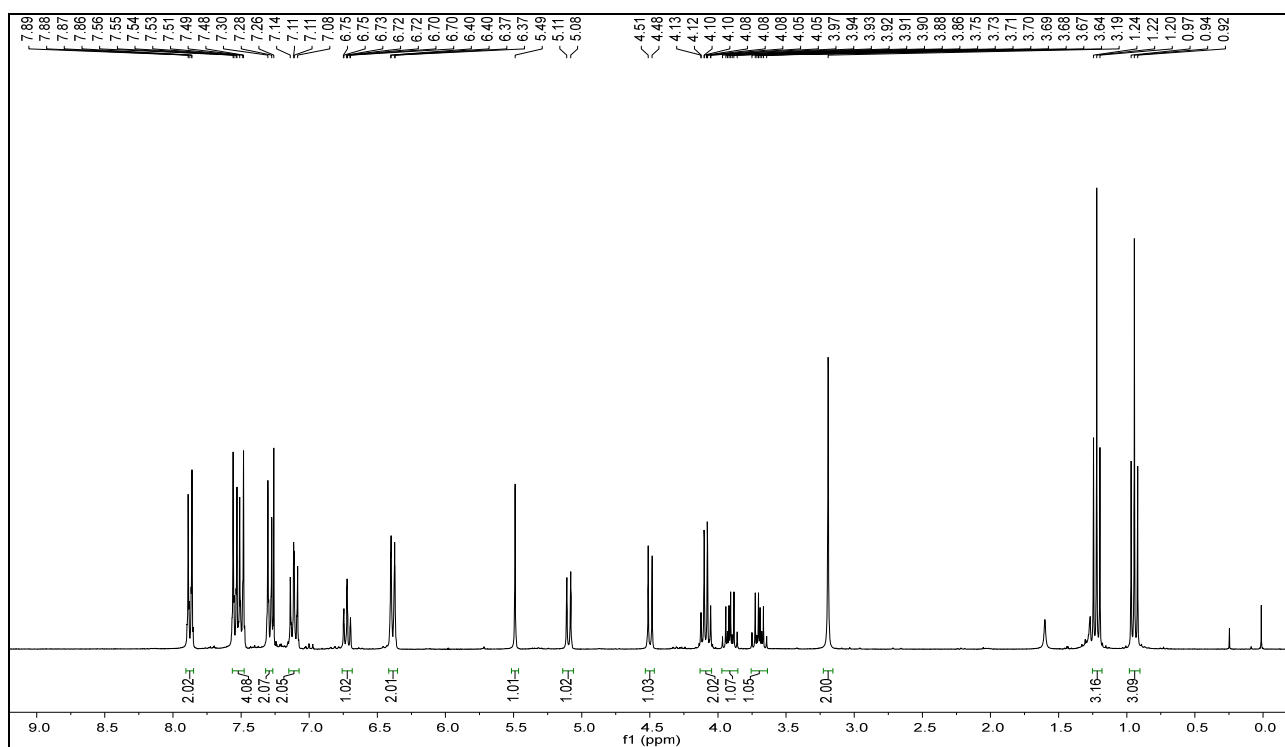
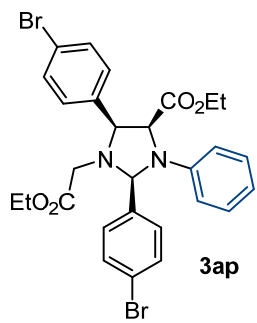


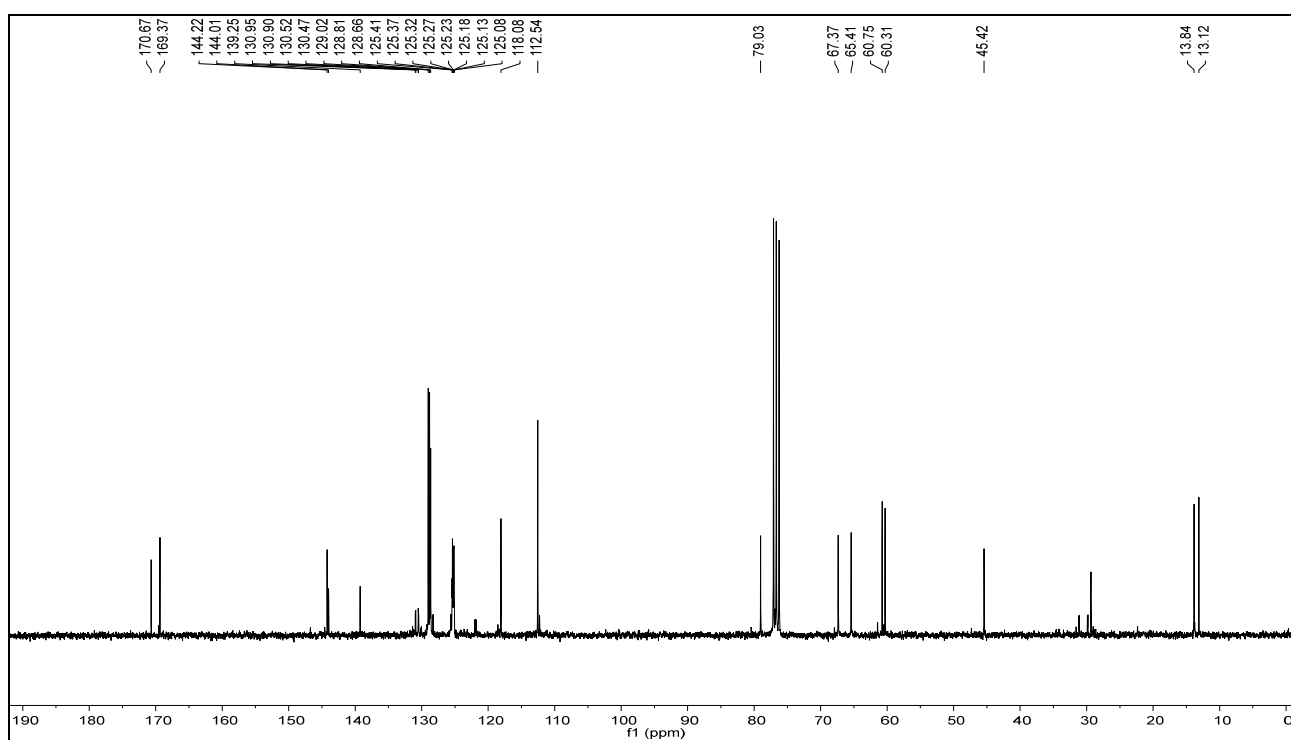
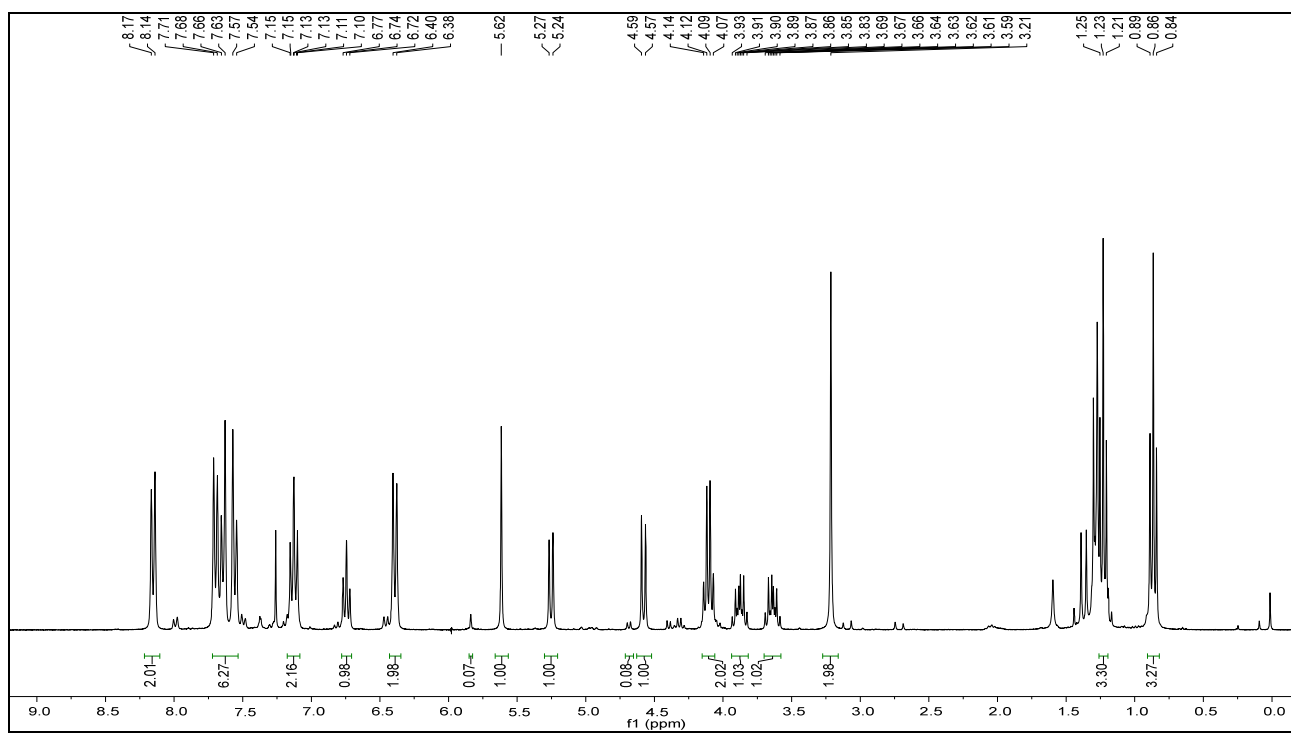
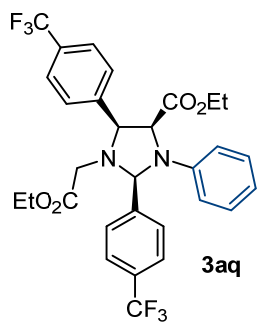


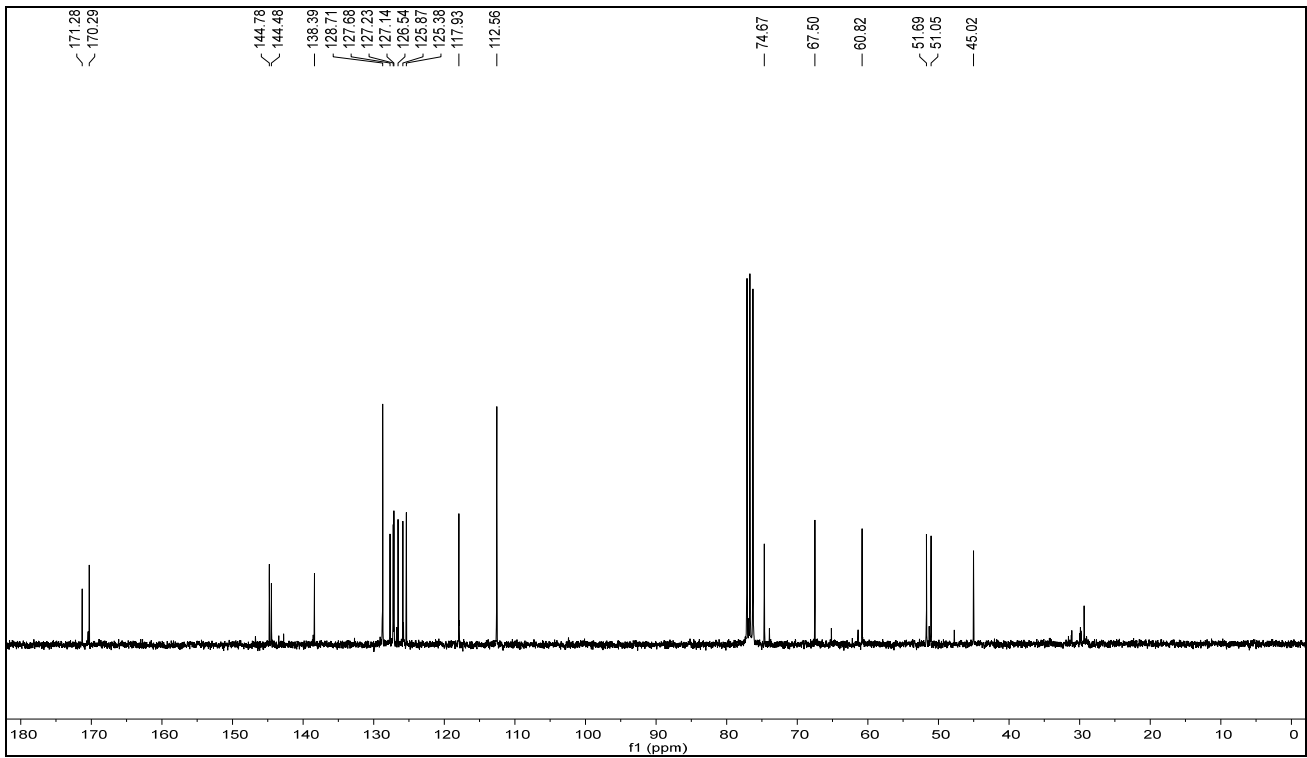
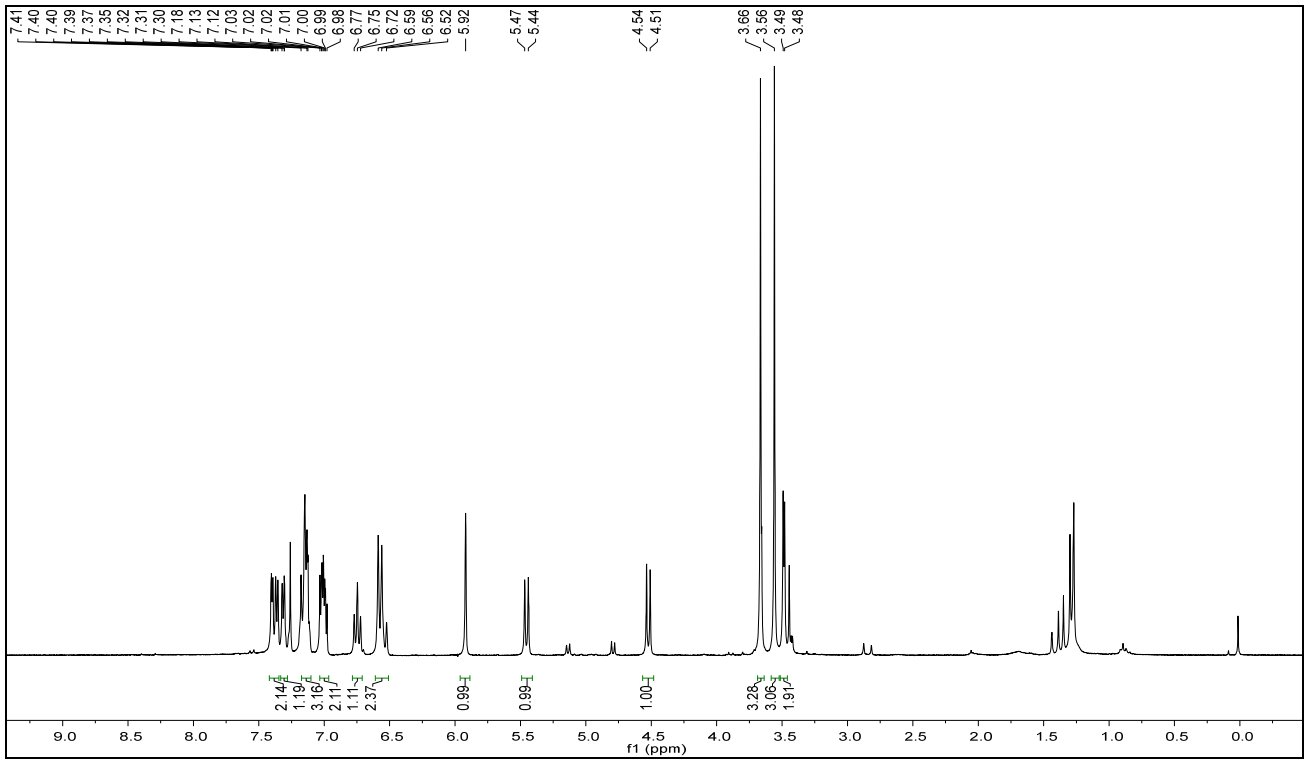
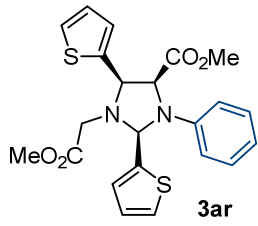


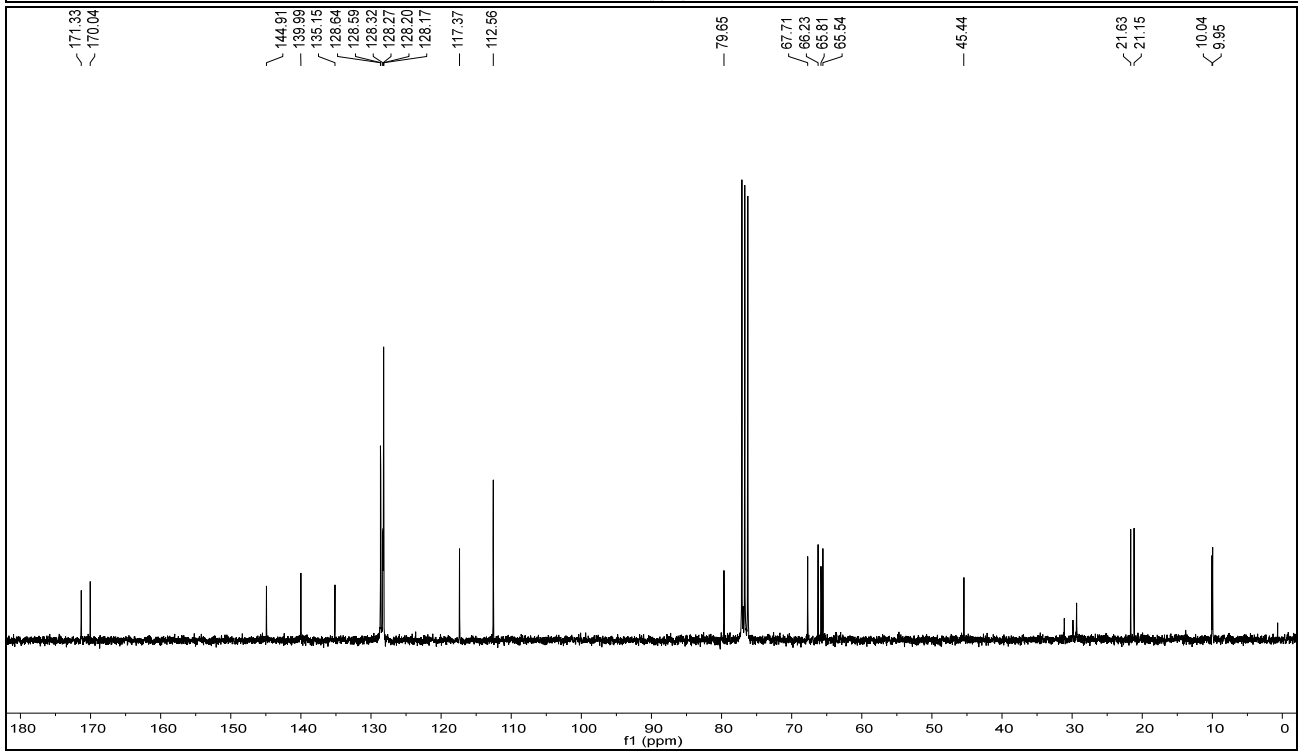
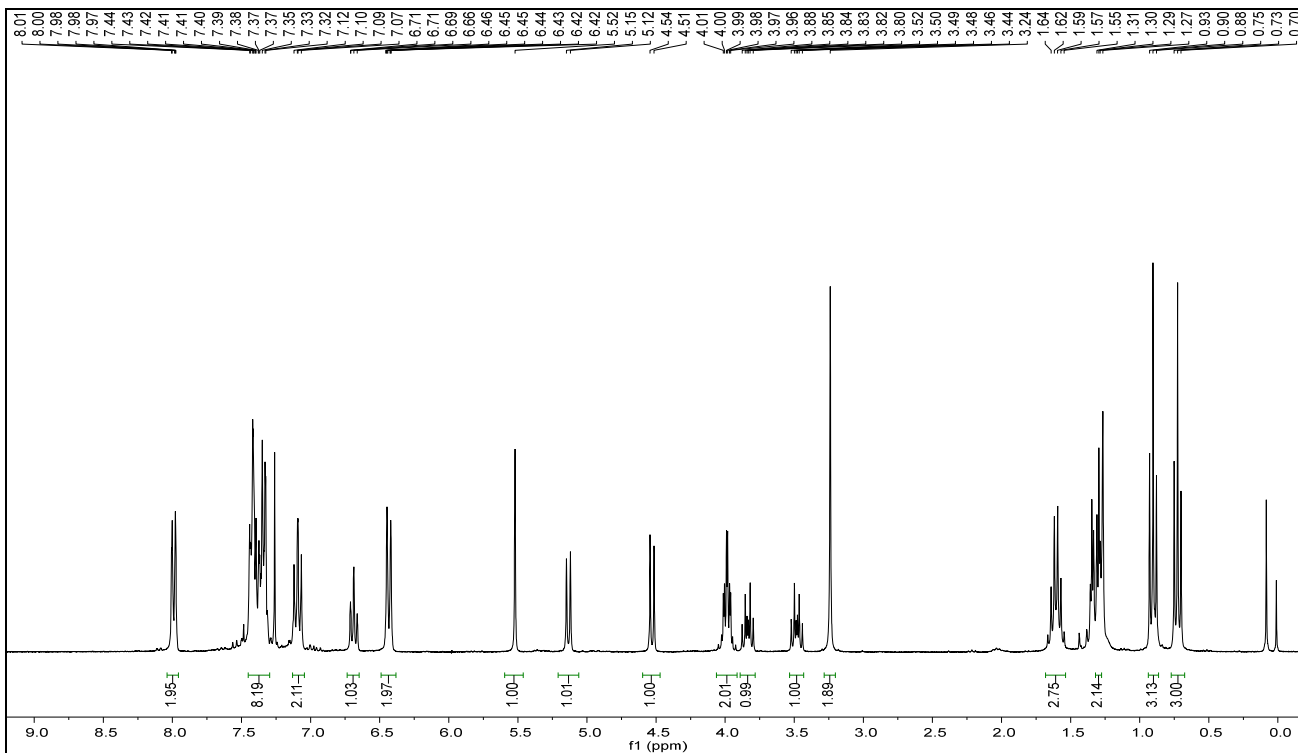
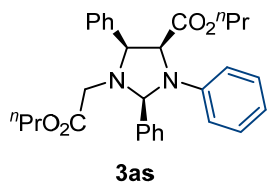


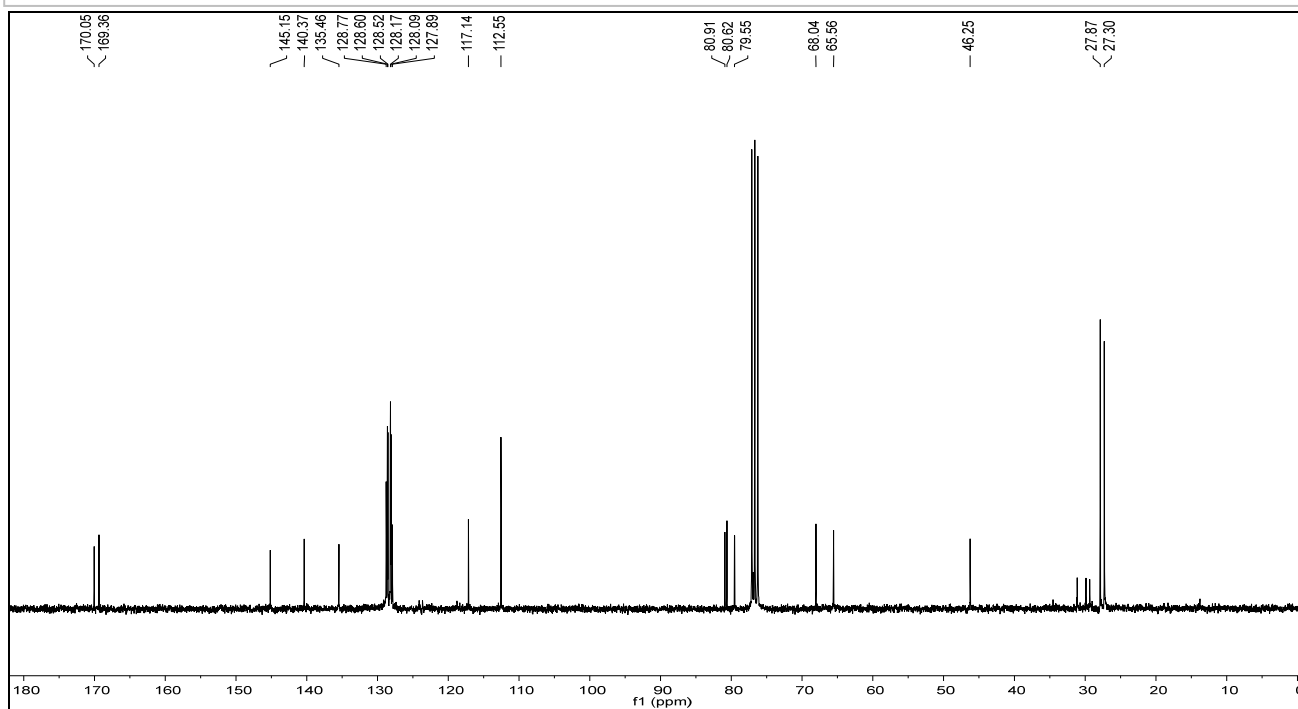
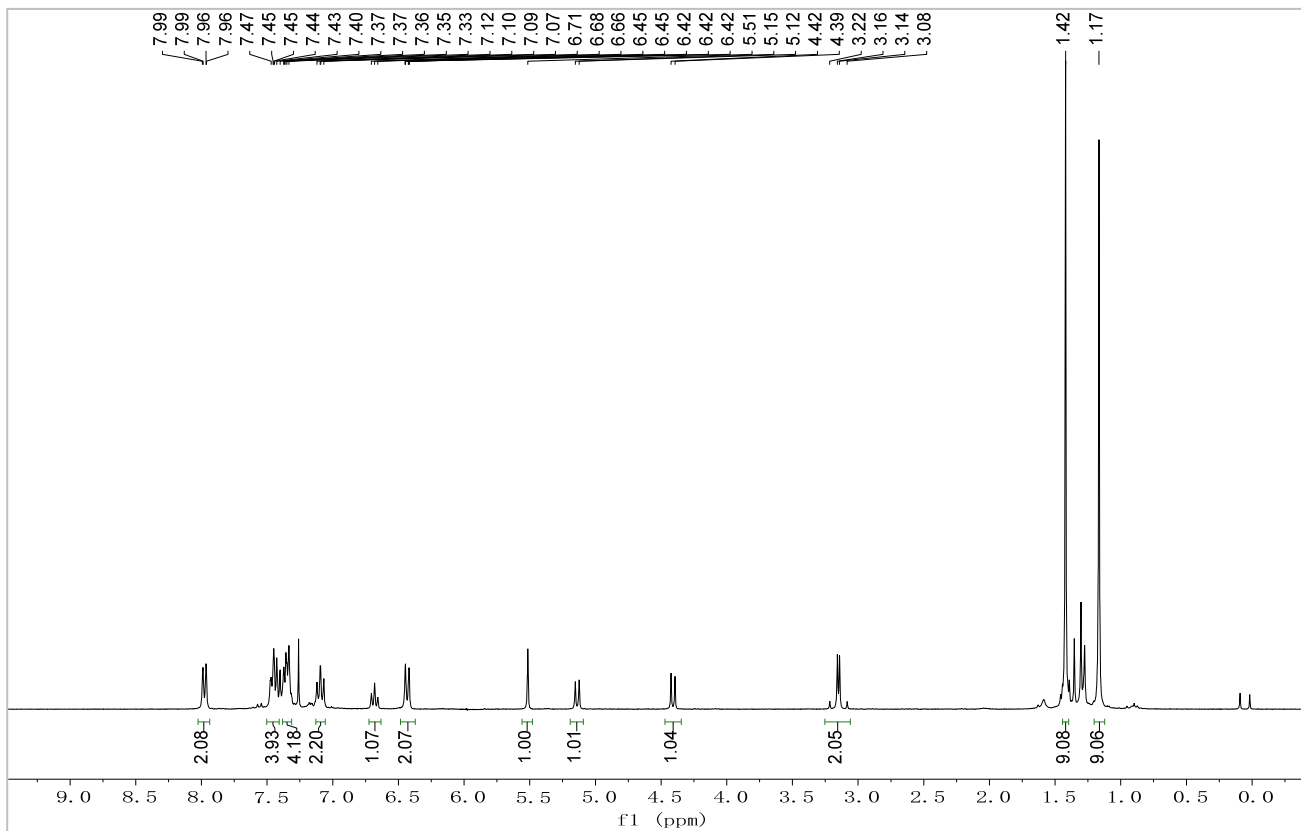
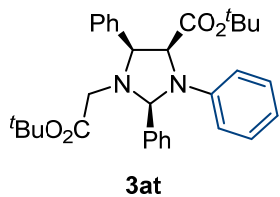


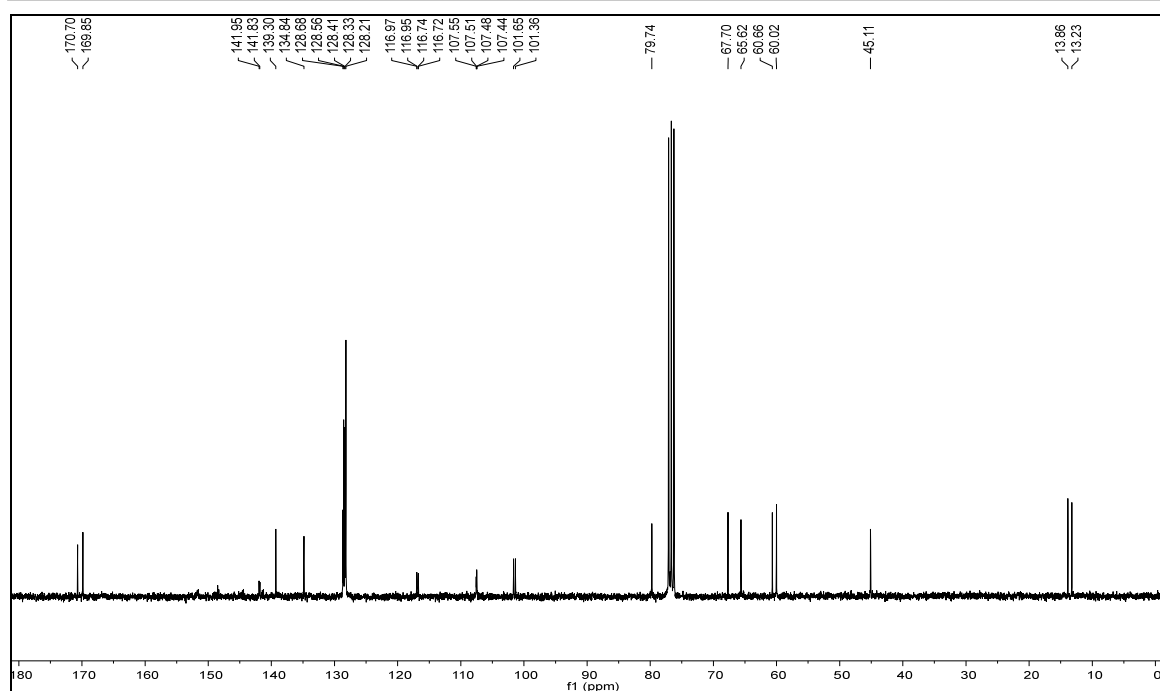
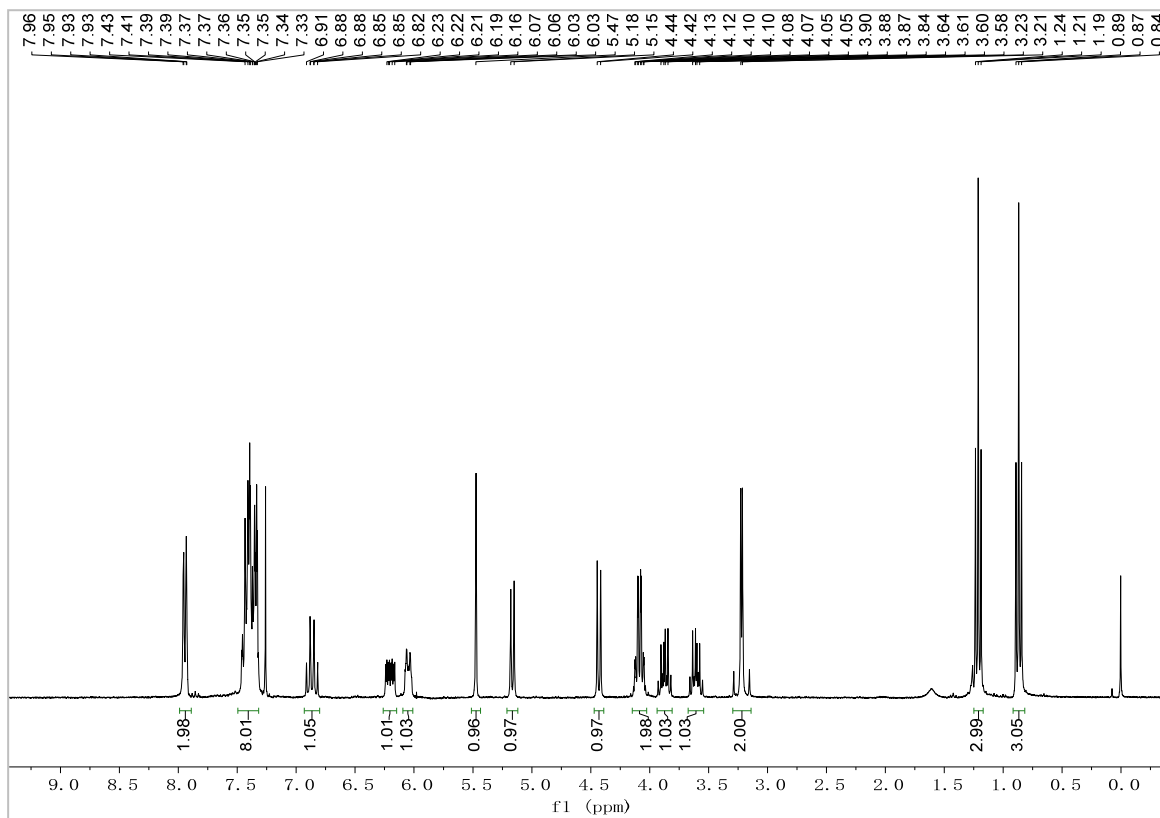
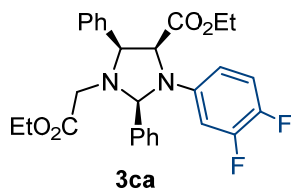


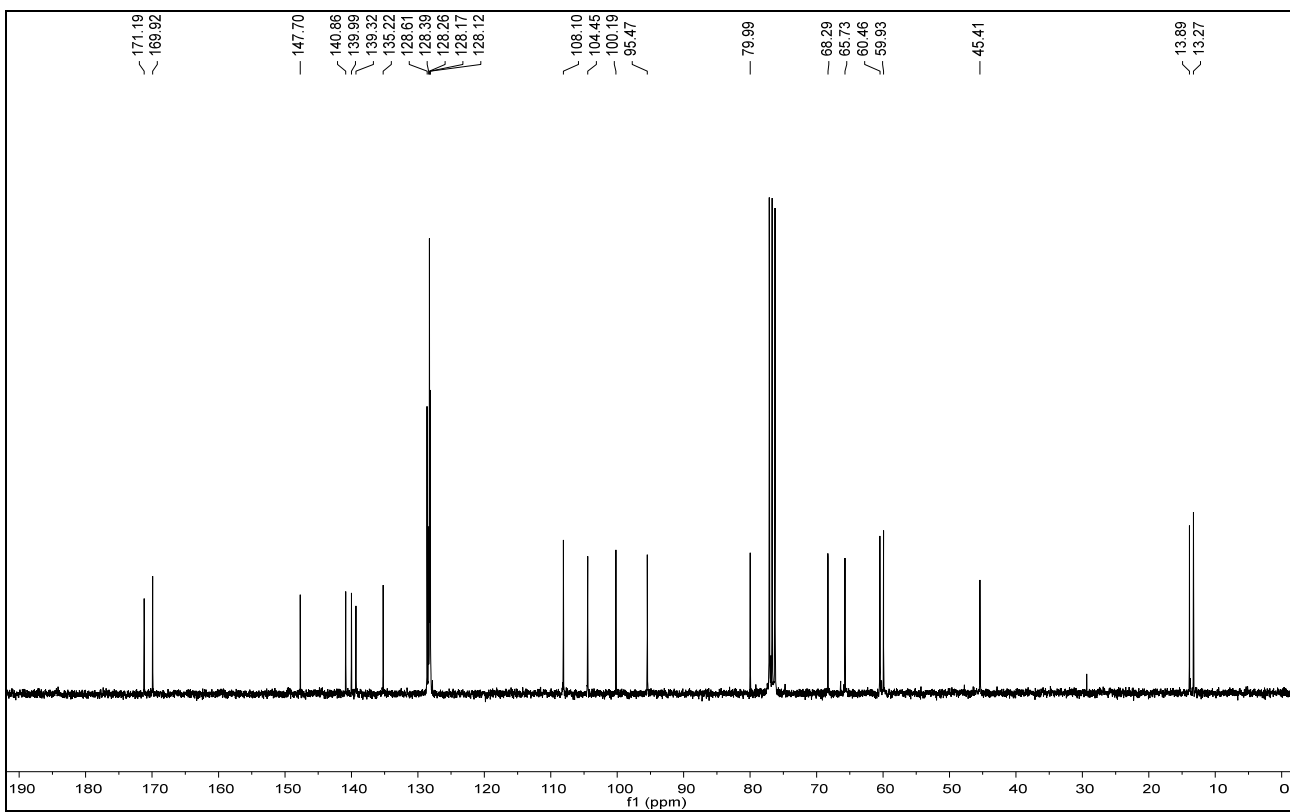
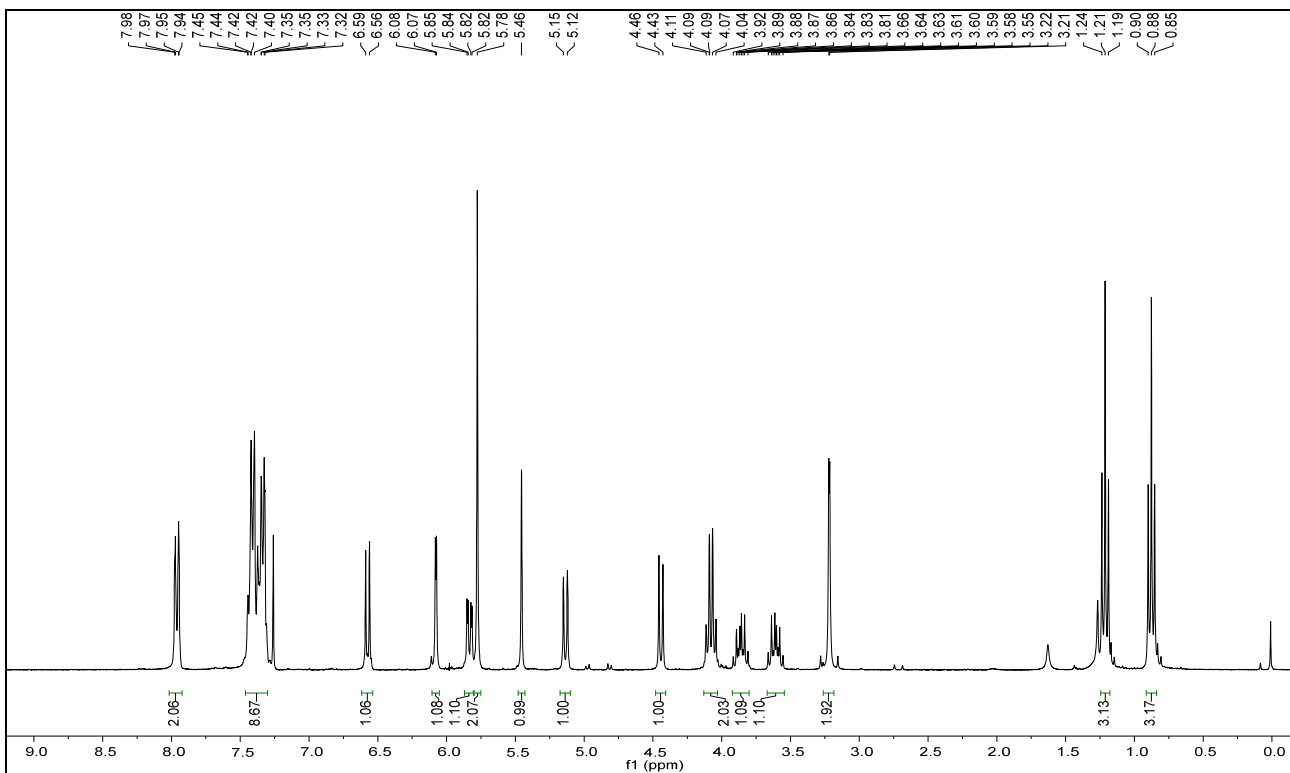
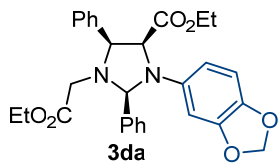


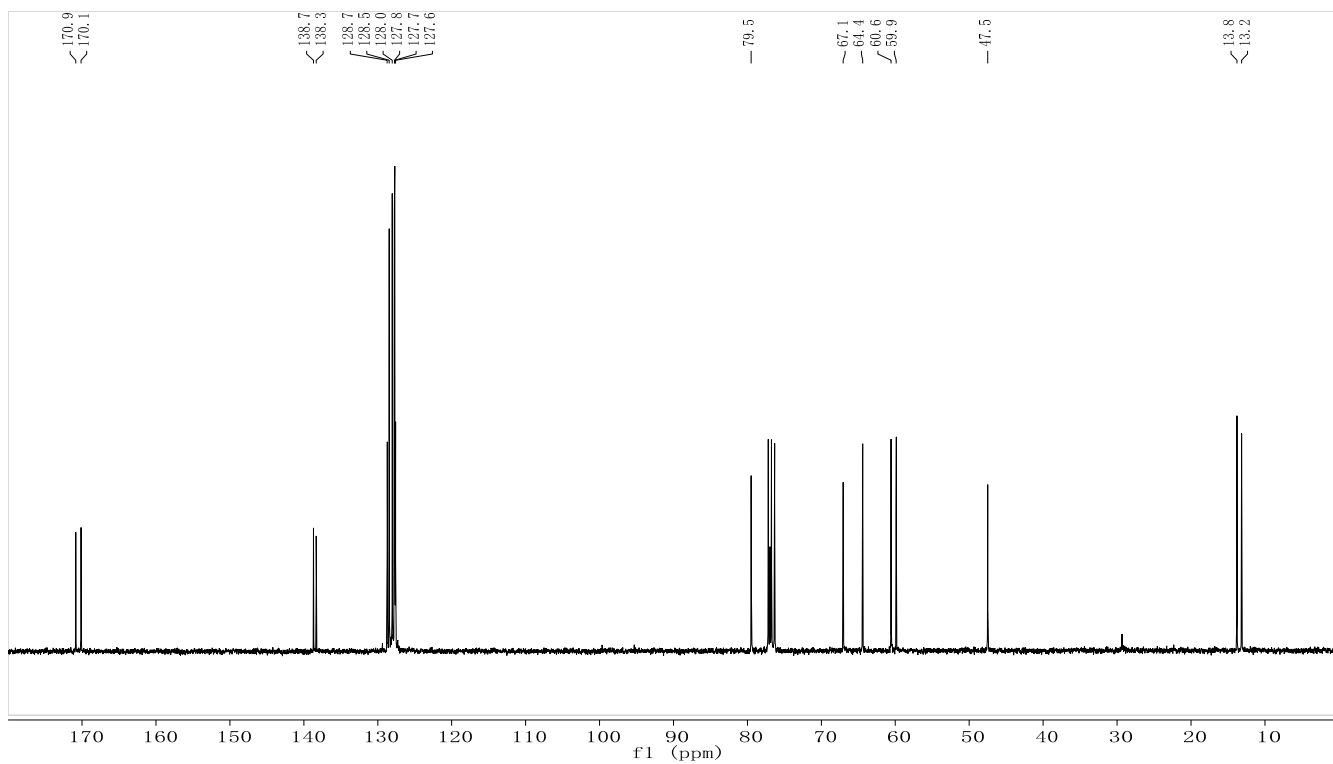
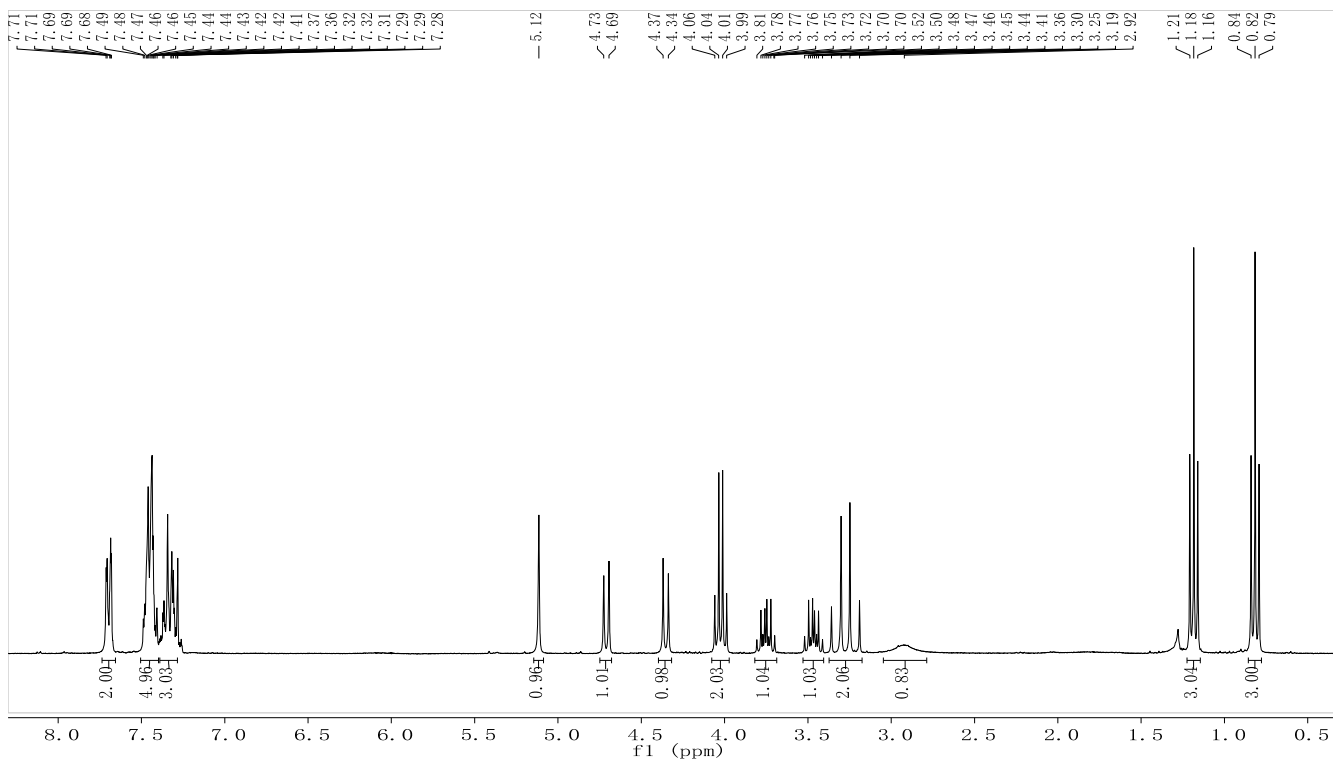
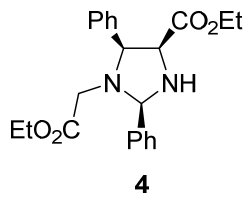






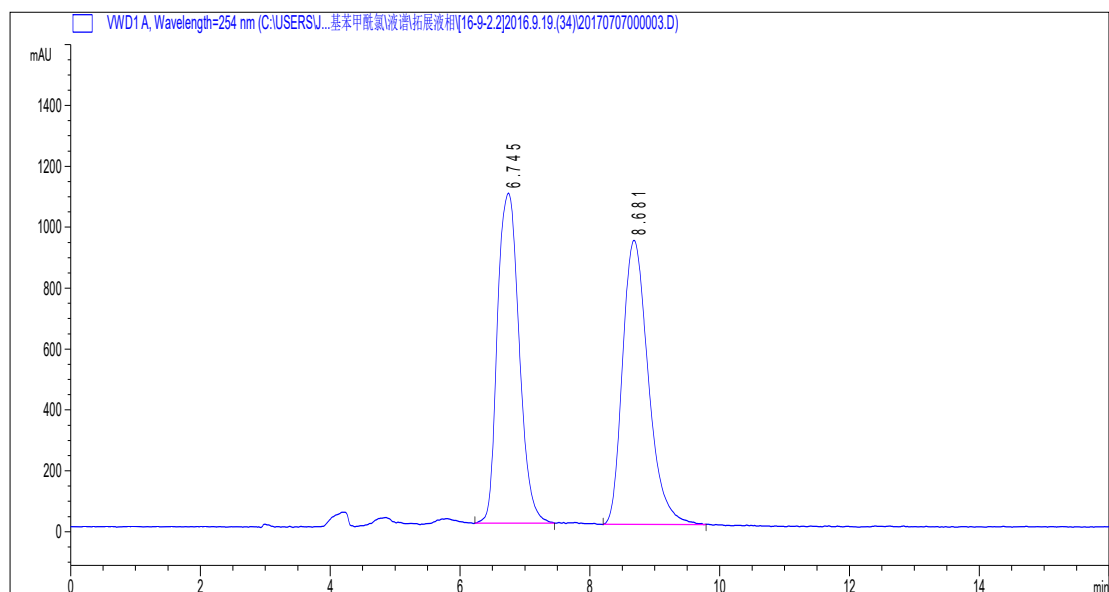






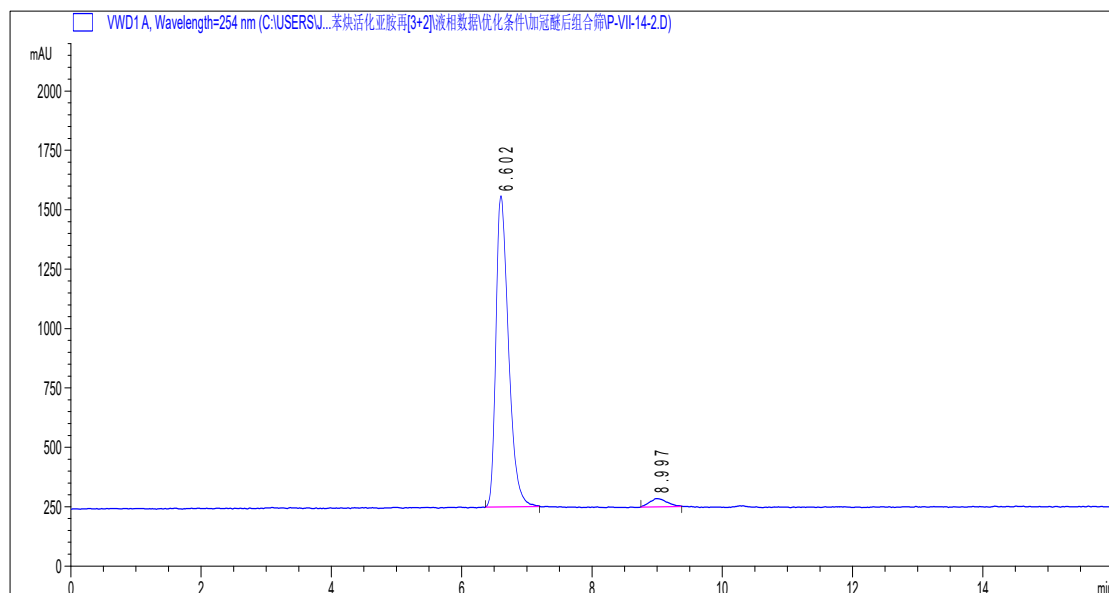
HPLC Chromatograms of All Products 3, and 4.

HPLC chromatogram of racemic 3aa



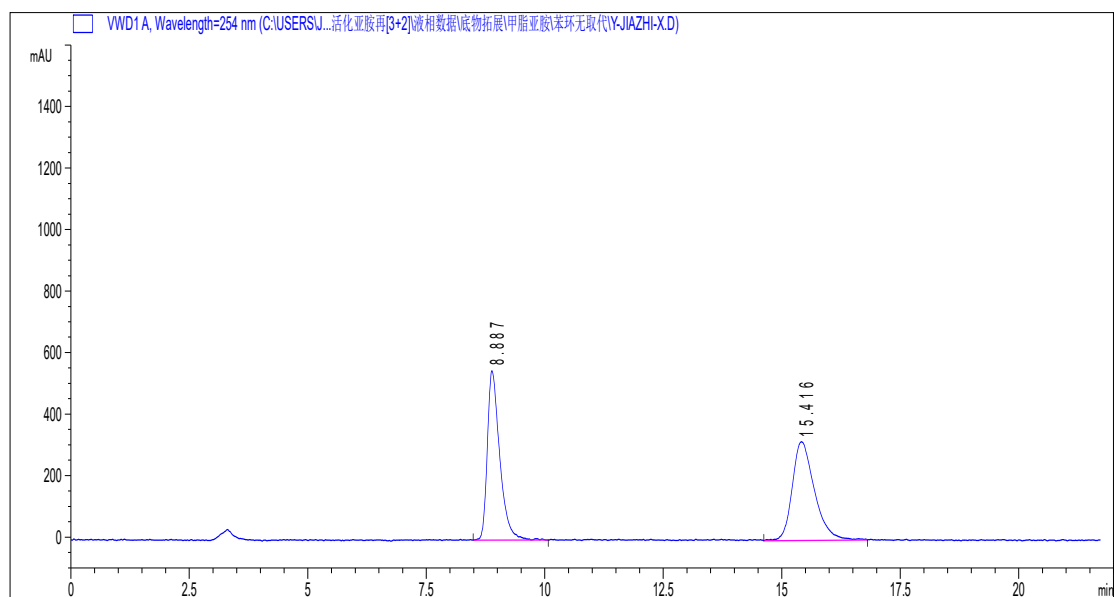
| Peak | RetTime/min | Type | Width/min | Area/mAU*s | Height/mAU | Area/% |
|------|-------------|------|-----------|------------|------------|---------|
| 1 | 6.746 | MM | 0.3878 | 2.52241e4 | 1084.01196 | 49.5500 |
| 2 | 8.681 | MM | 0.4589 | 2.56823e4 | 932.72485 | 50.4500 |

HPLC chromatogram of chiral 3aa



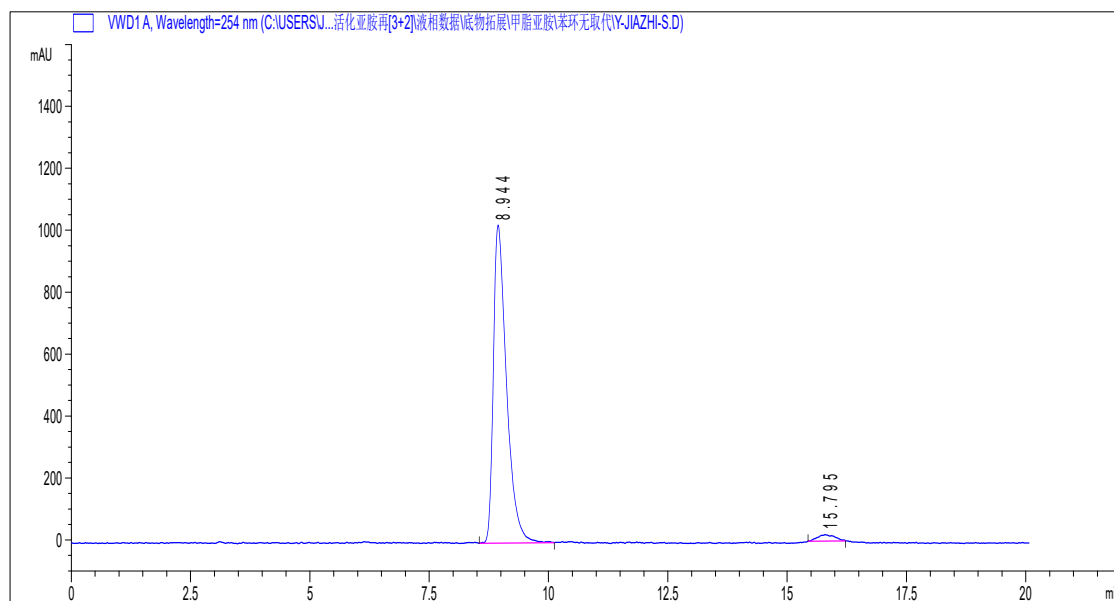
| Peak | RetTime/min | Type | Width/min | Area/mAU*s | Height/mAU | Area/% |
|------|-------------|------|-----------|------------|------------|---------|
| 1 | 6.602 | MM | 0.2241 | 1.76243e4 | 1310.81702 | 96.3727 |
| 2 | 8.997 | MM | 0.3103 | 663.34265 | 35.63121 | 3.6273 |

HPLC chromatogram of racemic 3ab



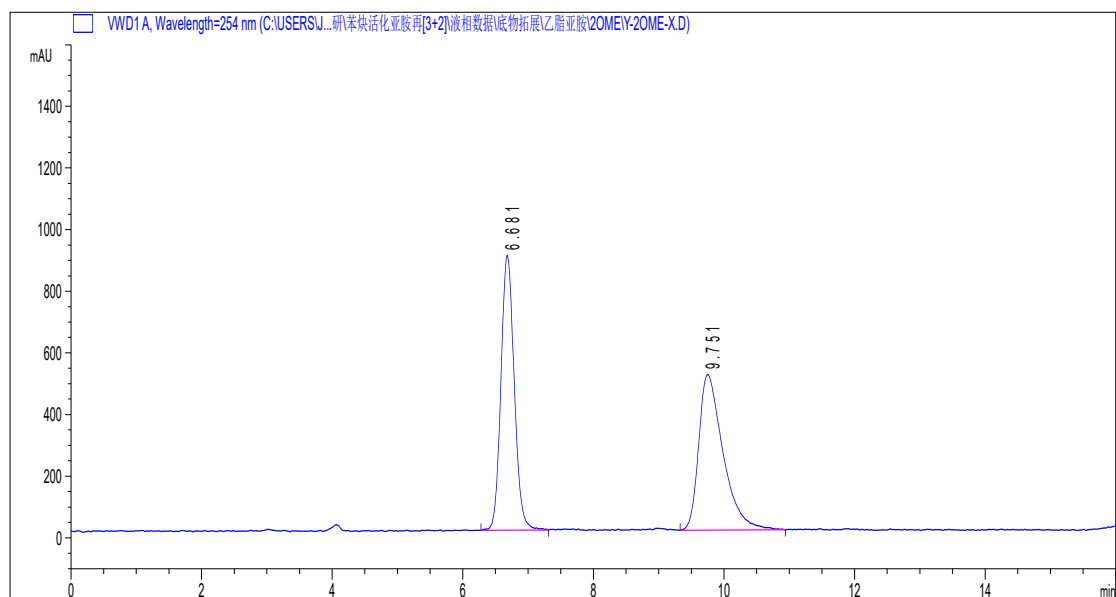
| Peak | RetTime/min | Type | Width/min | Area/mAU*s | Height/mAU | Area/% |
|------|-------------|------|-----------|------------|------------|---------|
| 1 | 8.887 | BB | 0.2733 | 1.00098e4 | 550.59241 | 48.9424 |
| 2 | 15.416 | BB | 0.4881 | 1.04424e4 | 320.27115 | 51.0576 |

HPLC chromatogram of chiral 3ab



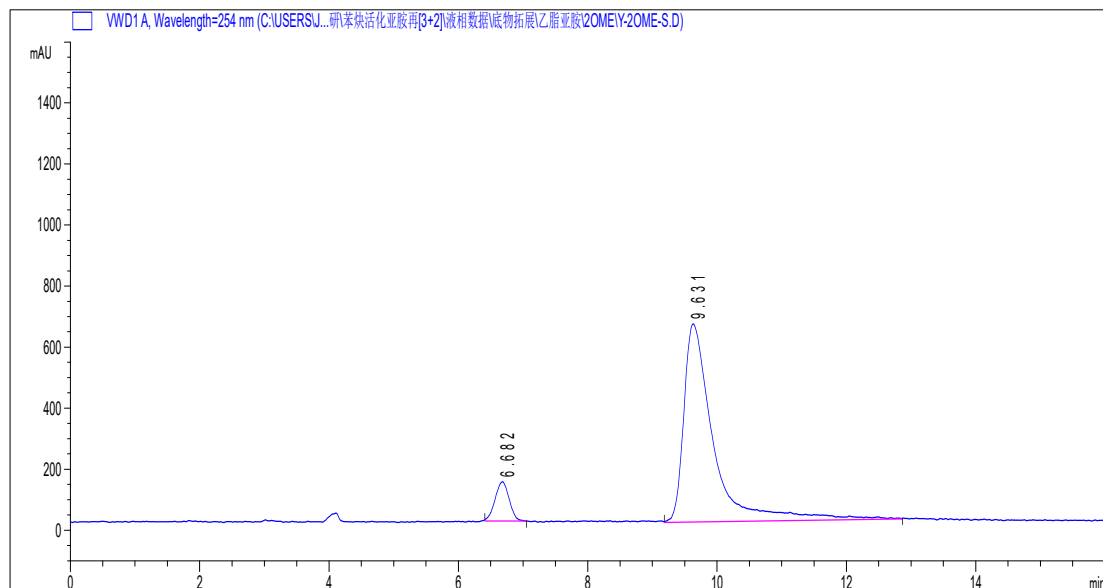
| Peak | RetTime/min | Type | Width/min | Area/mAU*s | Height/mAU | Area/% |
|------|-------------|------|-----------|------------|------------|---------|
| 1 | 8.944 | BB | 0.2874 | 1.96537e4 | 1026.64563 | 97.4178 |
| 2 | 15.795 | MM | 0.4137 | 520.94598 | 20.98643 | 2.5822 |

HPLC chromatogram of racemic 3ac



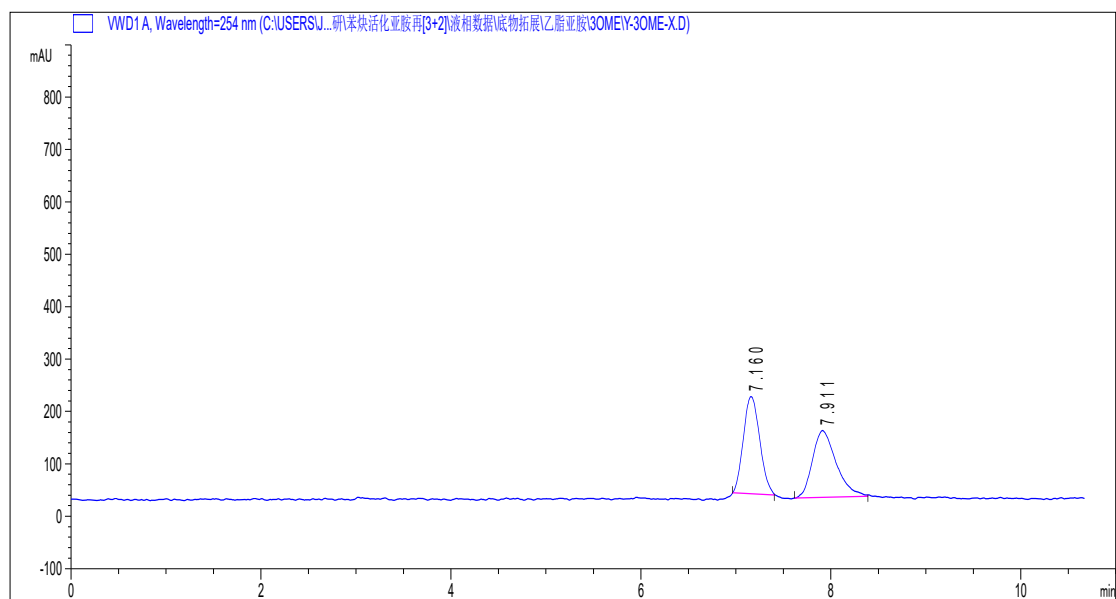
| Peak | RetTime/min | Type | Width/min | Area/mAU*s | Height/mAU | Area/% |
|------|-------------|------|-----------|------------|------------|---------|
| 1 | 6.681 | BB | 0.2204 | 1.26116e4 | 891.19440 | 49.1308 |
| 2 | 9.751 | BB | 0.3923 | 1.30579e4 | 504.33975 | 50.8692 |

HPLC chromatogram of chiral 3ac



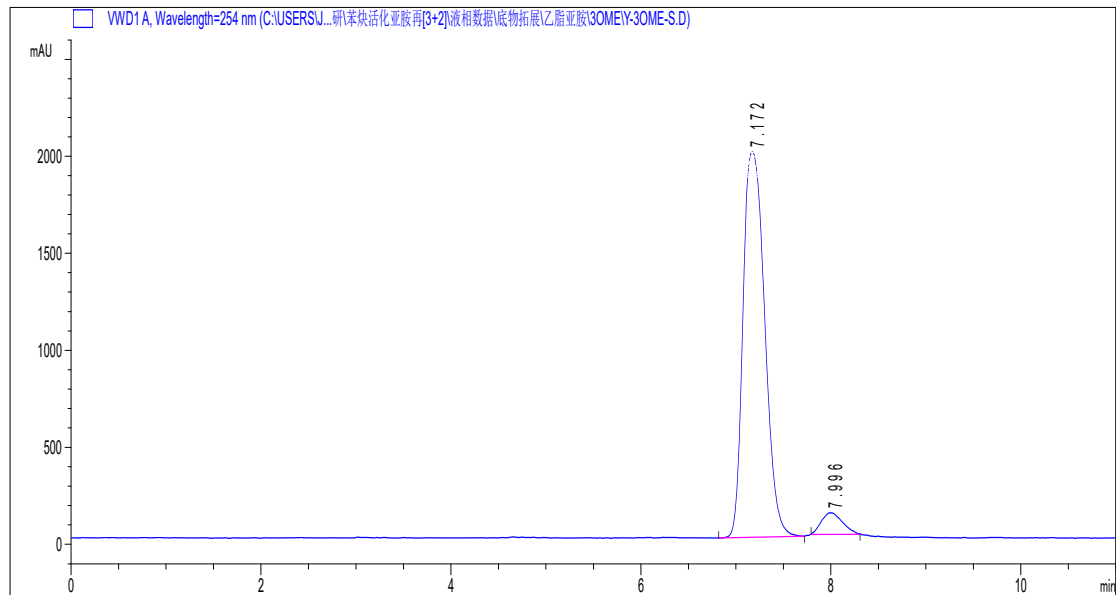
| Peak | RetTime/min | Type | Width/min | Area/mAU*s | Height/mAU | Area/% |
|------|-------------|------|-----------|------------|------------|---------|
| 1 | 6.682 | MM | 0.2524 | 1947.54211 | 128.61499 | 8.5613 |
| 2 | 9.631 | MM | 0.5340 | 2.08005e4 | 649.15533 | 91.4387 |

HPLC chromatogram of racemic 3ad



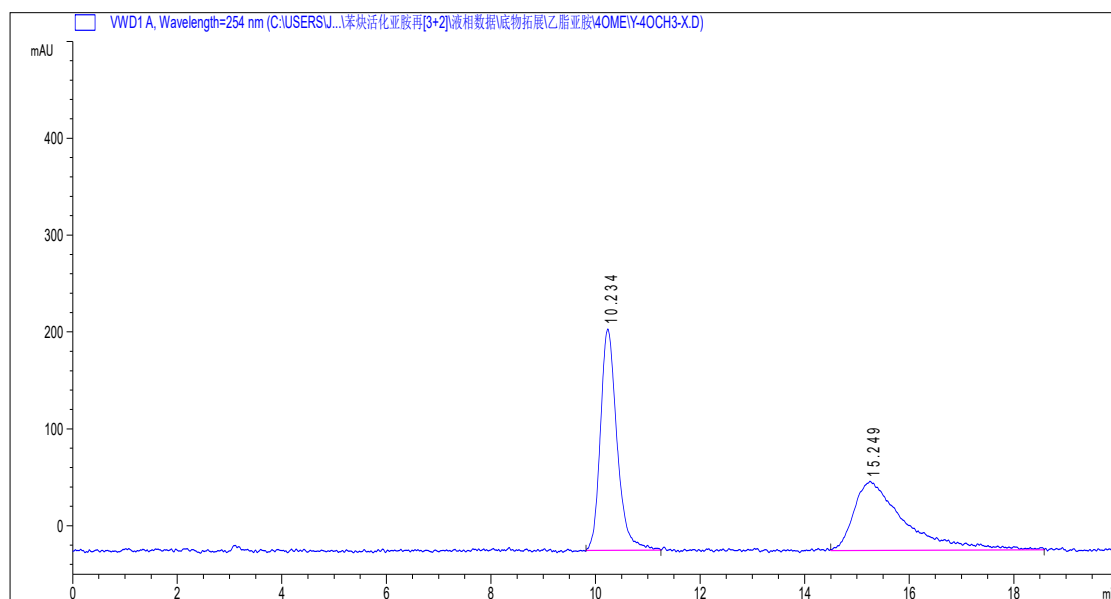
| Peak | RetTime/min | Type | Width/min | Area/mAU*s | Height/mAU | Area/% |
|------|-------------|------|-----------|------------|------------|---------|
| 1 | 7.160 | MM | 0.1997 | 2224.70679 | 185.67969 | 50.1241 |
| 2 | 7.911 | MM | 0.2890 | 2213.69214 | 127.64575 | 49.8759 |

HPLC chromatogram of chiral 3ad



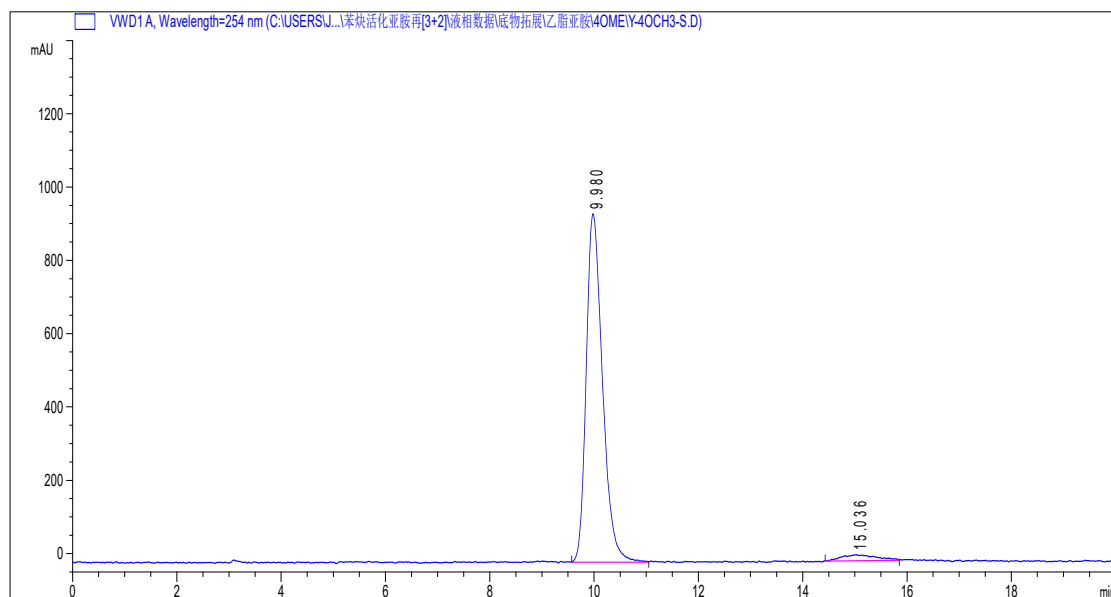
| Peak | RetTime/min | Type | Width/min | Area/mAU*s | Height/mAU | Area/% |
|------|-------------|------|-----------|------------|------------|---------|
| 1 | 7.712 | MM | 0.2640 | 3.14709e4 | 1986.81689 | 94.7854 |
| 2 | 7.996 | MM | 0.2577 | 1731.34827 | 111.96774 | 5.2146 |

HPLC chromatogram of racemic 3ae



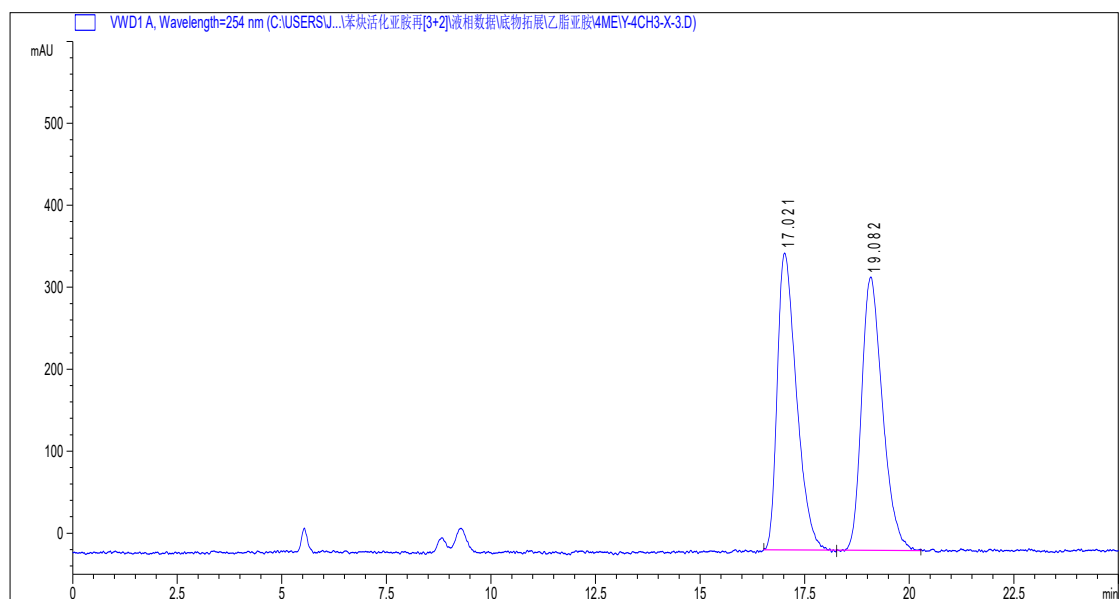
| Peak | RetTime/min | Type | Width/min | Area/mAU*s | Height/mAU | Area/% |
|------|-------------|------|-----------|------------|------------|----------|
| 1 | 10.234 | MM | 0.3672 | 5035.21094 | 228.51926 | 51.18171 |
| 2 | 15.249 | MM | 1.1210 | 4802.70020 | 71.40487 | 48.81829 |

HPLC chromatogram of chiral 3ae



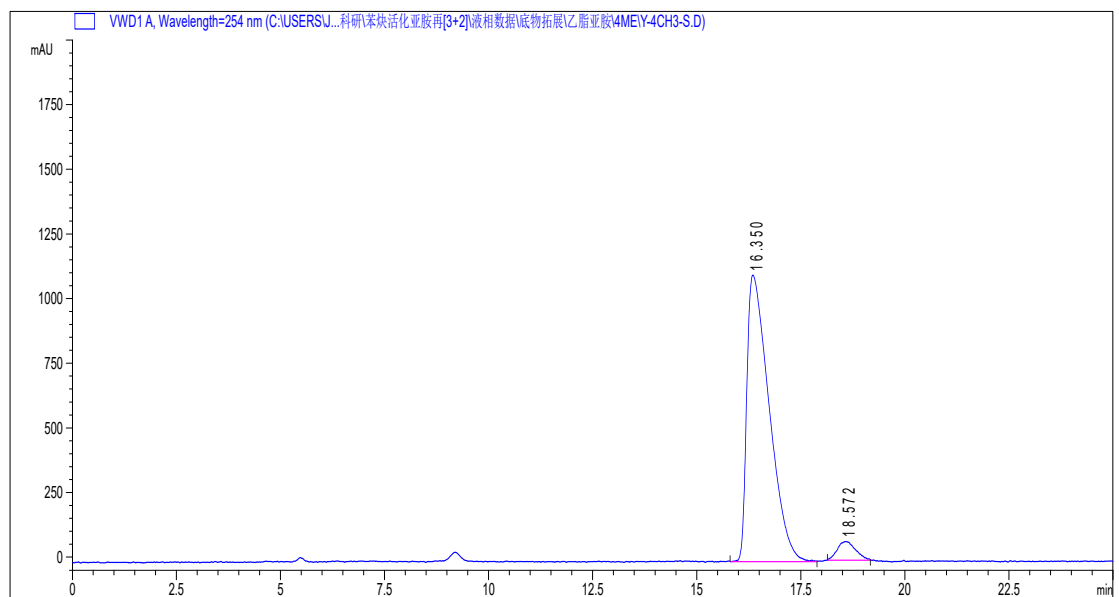
| Peak | RetTime/min | Type | Width/min | Area/mAU*s | Height/mAU | Area/% |
|------|-------------|------|-----------|------------|------------|----------|
| 1 | 9.980 | MM | 0.3604 | 2.05563e4 | 950.55249 | 96.28603 |
| 2 | 15.036 | MM | 0.8059 | 792.90137 | 16.39833 | 3.71397 |

HPLC chromatogram of racemic 3af



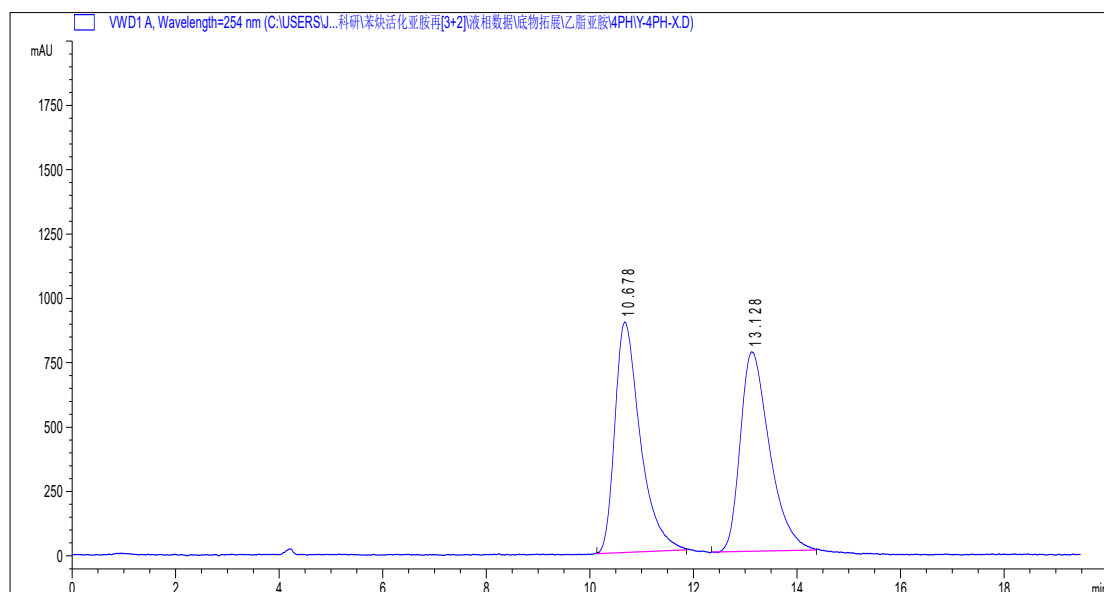
| Peak | RetTime/min | Type | Width/min | Area/mAU*s | Height/mAU | Area/% |
|------|-------------|------|-----------|------------|------------|----------|
| 1 | 17.021 | MM | 0.5317 | 1.15543e4 | 362.16711 | 49.92744 |
| 2 | 19.082 | FM | 0.5795 | 1.15879e4 | 333.27933 | 50.07256 |

HPLC chromatogram of chiral 3af



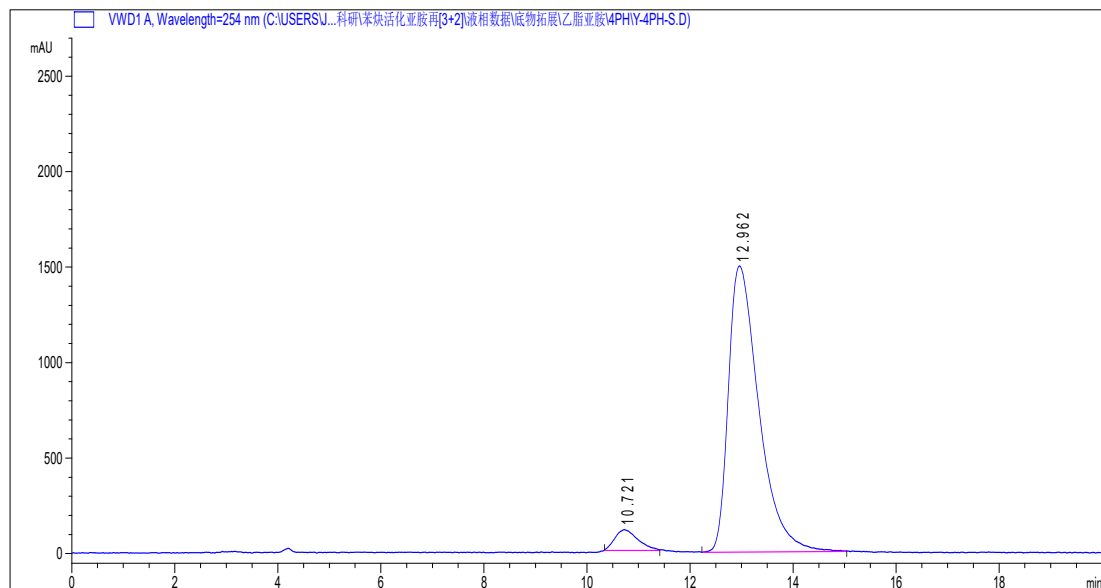
| Peak | RetTime/min | Type | Width/min | Area/mAU*s | Height/mAU | Area/% |
|------|-------------|------|-----------|------------|------------|----------|
| 1 | 16.350 | MM | 0.6213 | 4.12947e4 | 1107.70410 | 94.89470 |
| 2 | 18.572 | MM | 0.5132 | 2221.64136 | 72.15144 | 5.10530 |

HPLC chromatogram of racemic 3ag



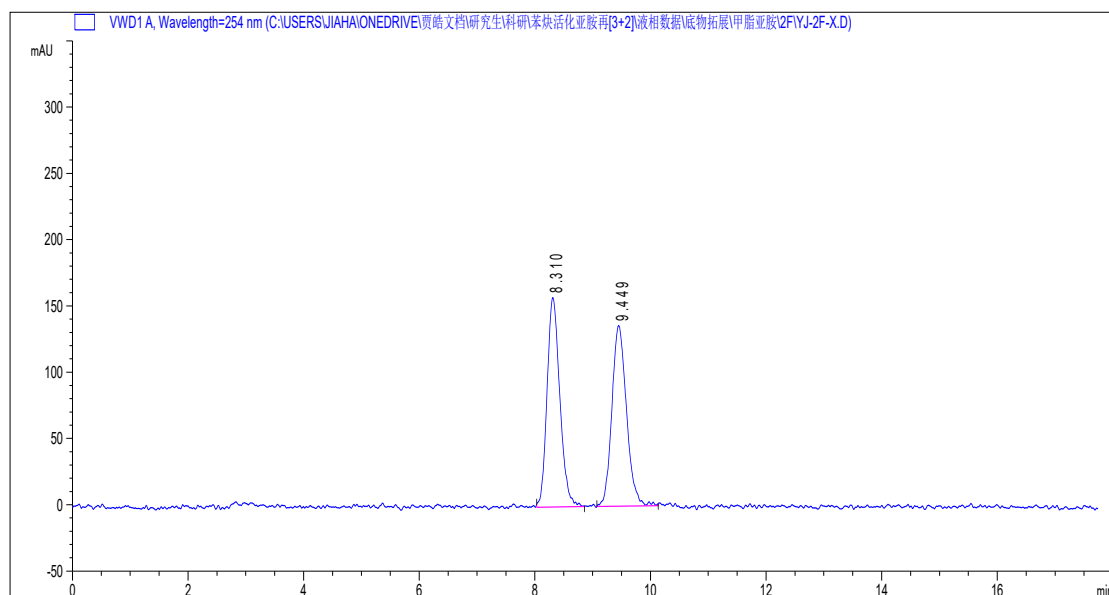
| Peak | RetTime/min | Type | Width/min | Area/mAU*s | Height/mAU | Area/% |
|------|-------------|------|-----------|------------|------------|----------|
| 1 | 10.678 | BB | 0.5049 | 3.04668e4 | 894.98175 | 50.01150 |
| 2 | 13.128 | BB | 0.5722 | 3.04528e4 | 774.62701 | 49.98850 |

HPLC chromatogram of chiral 3ag



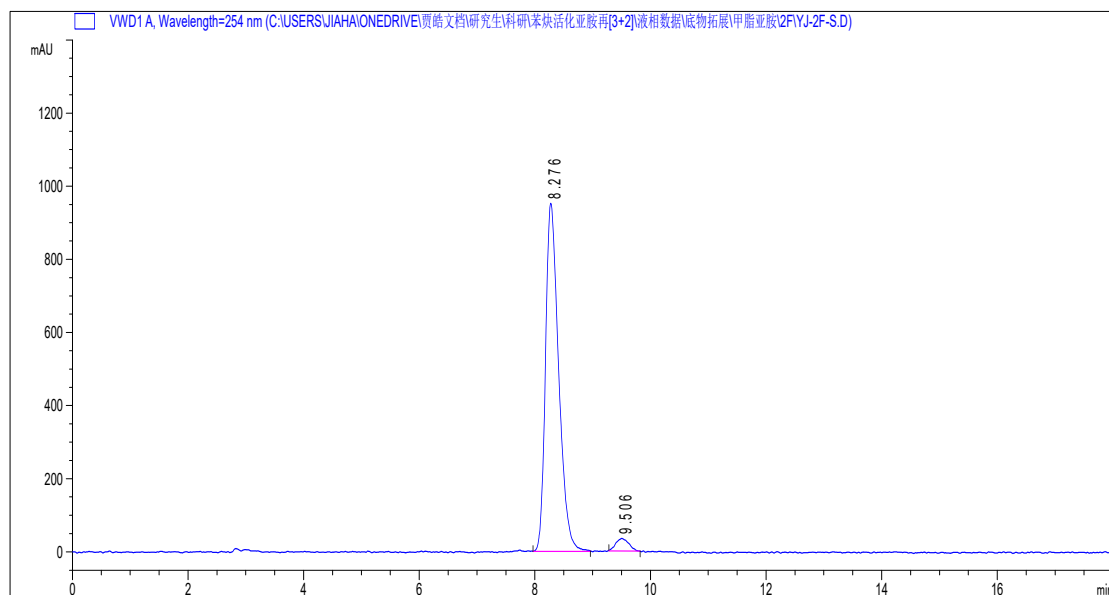
| Peak | RetTime/min | Type | Width/min | Area/mAU*s | Height/mAU | Area/% |
|------|-------------|------|-----------|------------|------------|----------|
| 1 | 10.721 | MM | 0.5138 | 3331.47900 | 108.07144 | 5.11952 |
| 2 | 12.962 | MM | 0.6863 | 6.17425e4 | 1499.43787 | 94.88048 |

HPLC chromatogram of racemic 3ah



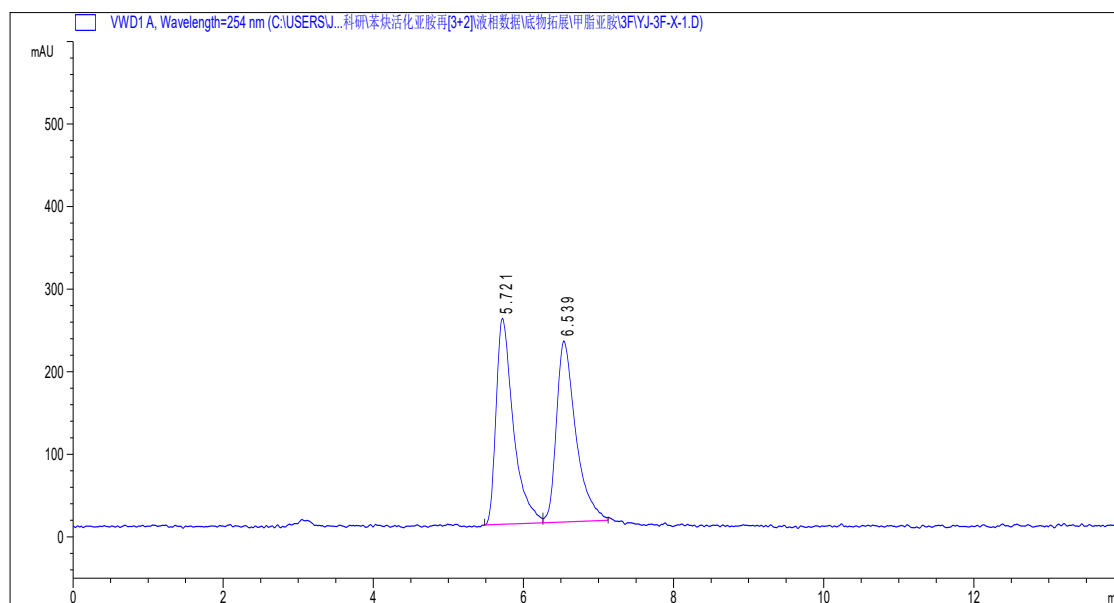
| Peak | RetTime/min | Type | Width/min | Area/mAU*s | Height/mAU | Area/% |
|------|-------------|------|-----------|------------|------------|----------|
| 1 | 8.310 | MM | 0.2560 | 2428.64478 | 158.14348 | 50.32796 |
| 2 | 9.449 | MM | 0.2929 | 2396.99292 | 136.41246 | 49.67204 |

HPLC chromatogram of chiral 3ah



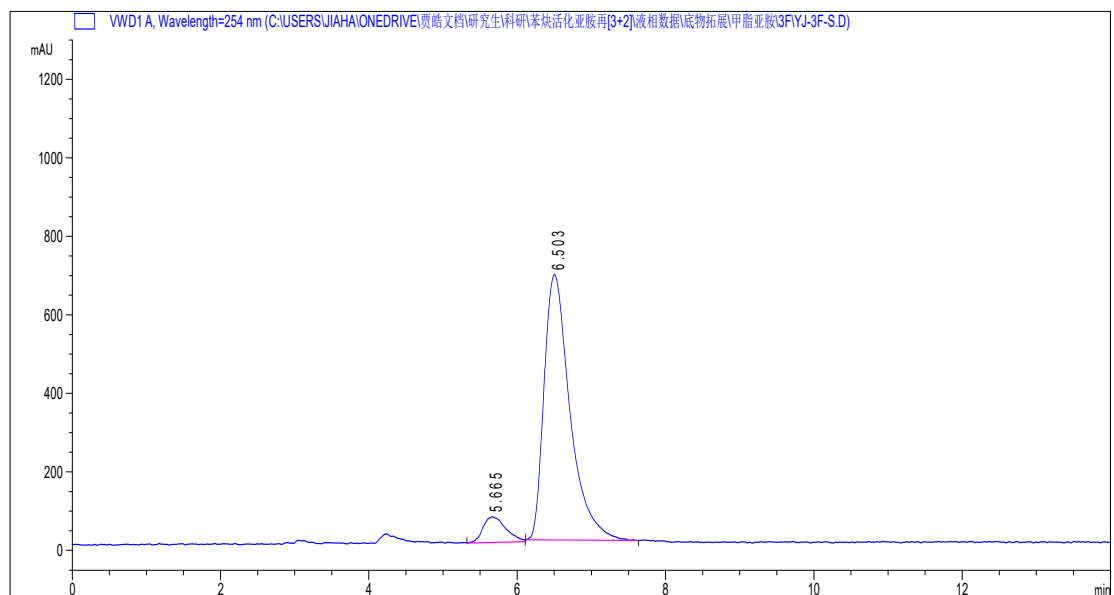
| Peak | RetTime/min | Type | Width/min | Area/mAU*s | Height/mAU | Area/% |
|------|-------------|------|-----------|------------|------------|----------|
| 1 | 8.276 | MM | 0.2632 | 1.50393e4 | 952.49768 | 96.59111 |
| 2 | 9.506 | MM | 0.2602 | 530.76447 | 34.00311 | 3.40889 |

HPLC chromatogram of racemic 3ai



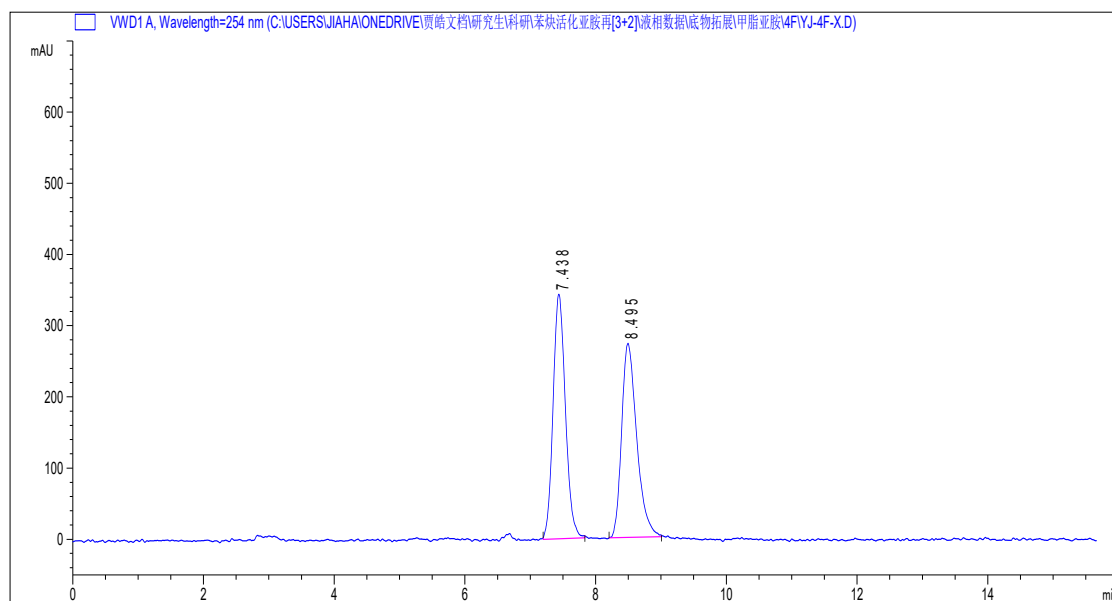
| Peak | RetTime/min | Type | Width/min | Area/mAU*s | Height/mAU | Area/% |
|------|-------------|------|-----------|------------|------------|----------|
| 1 | 5.721 | MM | 0.2385 | 3979.35132 | 249.45381 | 50.18739 |
| 2 | 6.539 | MM | 0.2772 | 3949.63550 | 219.16638 | 49.81261 |

HPLC chromatogram of chiral 3ai



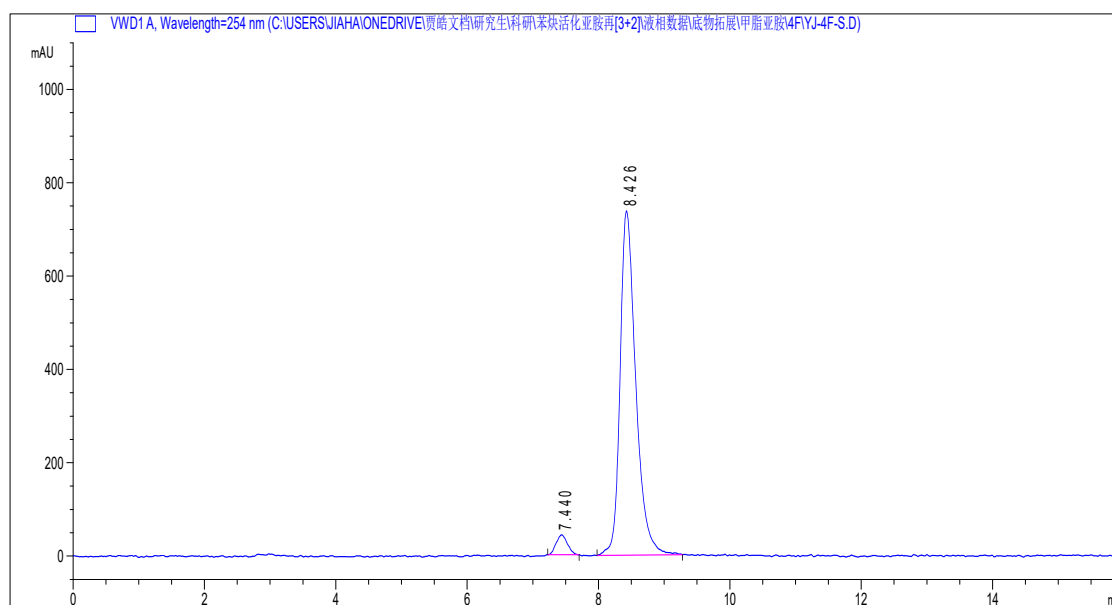
| Peak | RetTime/min | Type | Width/min | Area/mAU*s | Height/mAU | Area/% |
|------|-------------|------|-----------|------------|------------|----------|
| 1 | 5.665 | BV | 0.2884 | 1396.40735 | 65.02044 | 7.83710 |
| 2 | 6.503 | MM | 0.4048 | 1.64215e4 | 676.11810 | 92.16290 |

HPLC chromatogram of racemic 3aj



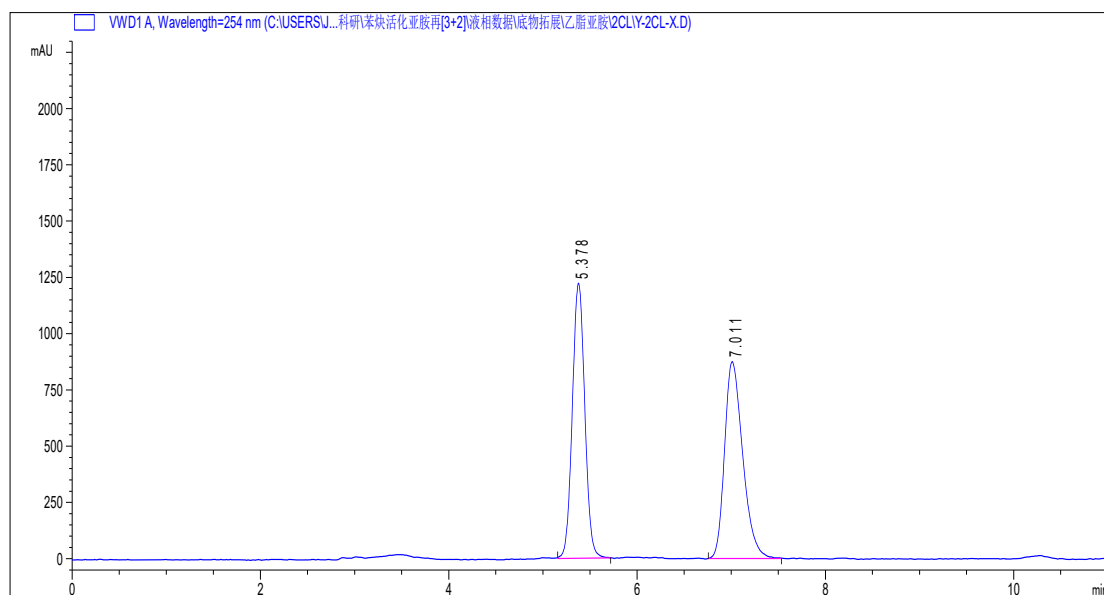
| Peak | RetTime/min | Type | Width/min | Area/mAU*s | Height/mAU | Area/% |
|------|-------------|------|-----------|------------|------------|----------|
| 1 | 7.438 | BB | 0.2027 | 4507.59863 | 343.31915 | 50.69024 |
| 2 | 8.495 | BB | 0.2430 | 4384.84082 | 272.63675 | 49.30976 |

HPLC chromatogram of chiral 3aj



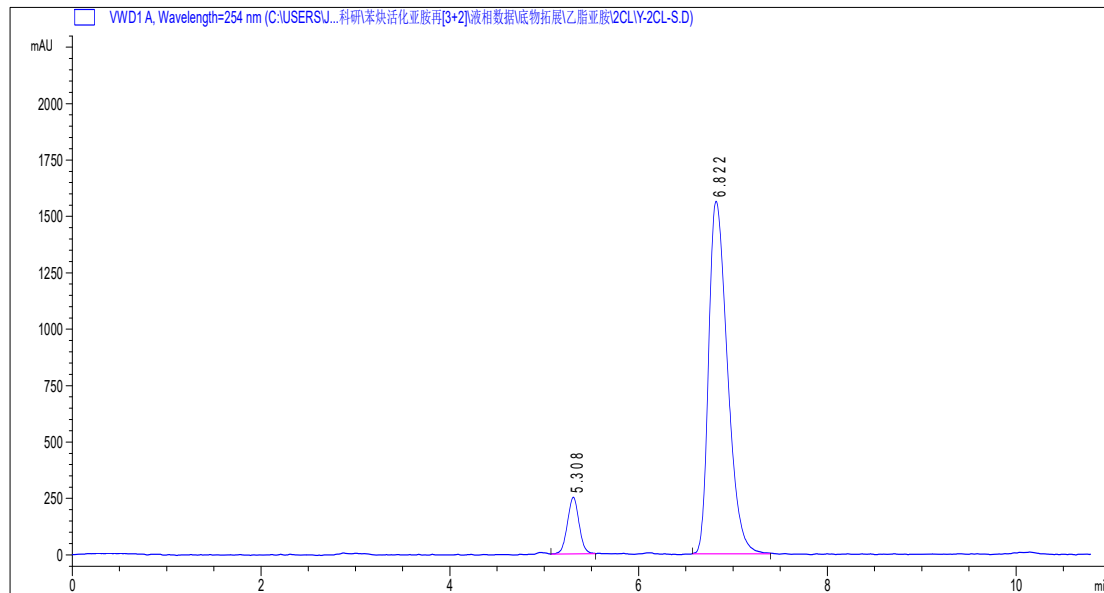
| Peak | RetTime/min | Type | Width/min | Area/mAU*s | Height/mAU | Area/% |
|------|-------------|------|-----------|------------|------------|----------|
| 1 | 7.440 | MM | 0.1980 | 504.96854 | 42.51554 | 3.96416 |
| 2 | 8.426 | MM | 0.2762 | 1.22334e4 | 738.15509 | 96.03584 |

HPLC chromatogram of racemic 3ak



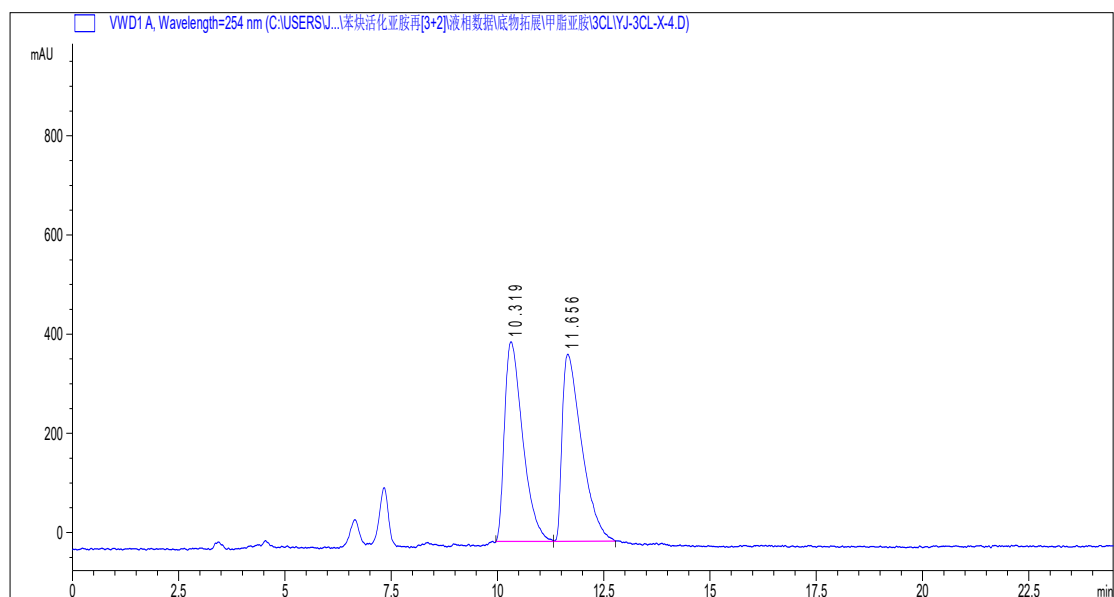
| Peak | RetTime/min | Type | Width/min | Area/mAU*s | Height/mAU | Area/% |
|------|-------------|------|-----------|------------|------------|----------|
| 1 | 5.378 | BB | 0.1453 | 1.12591e4 | 1222.59058 | 49.05972 |
| 2 | 7.011 | BB | 0.2056 | 1.16907e4 | 873.76263 | 50.94028 |

HPLC chromatogram of chiral 3ak



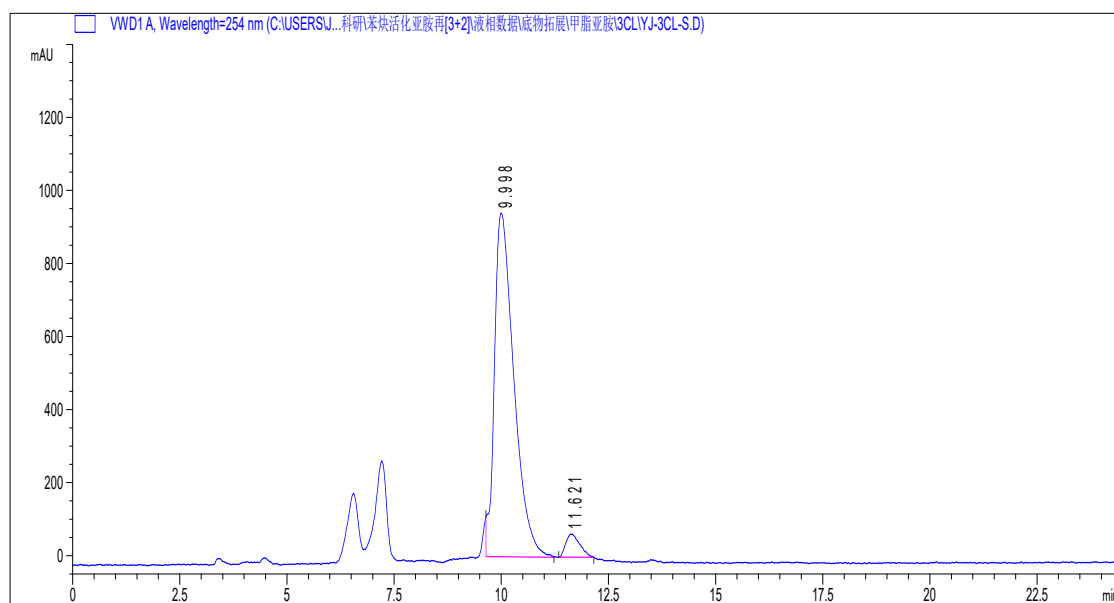
| Peak | RetTime/min | Type | Width/min | Area/mAU*s | Height/mAU | Area/% |
|------|-------------|------|-----------|------------|------------|----------|
| 1 | 5.308 | VB | 0.1353 | 2158.22998 | 250.84848 | 9.07801 |
| 2 | 6.822 | BB | 0.2138 | 2.16160e4 | 1562.44202 | 90.92199 |

HPLC chromatogram of racemic 3aI



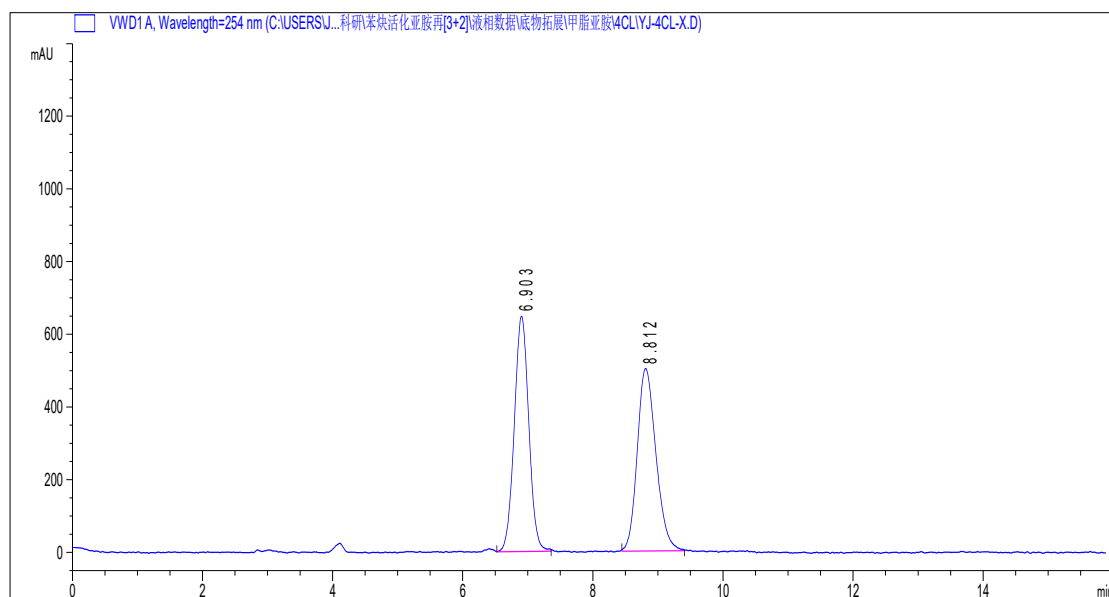
| Peak | RetTime/min | Type | Width/min | Area/mAU*s | Height/mAU | Area/% |
|------|-------------|------|-----------|------------|------------|----------|
| 1 | 10.319 | MF | 0.4954 | 1.19793e4 | 402.97836 | 49.82599 |
| 2 | 11.656 | FM | 0.5325 | 1.20630e4 | 377.52554 | 50.17401 |

HPLC chromatogram of chiral 3aI



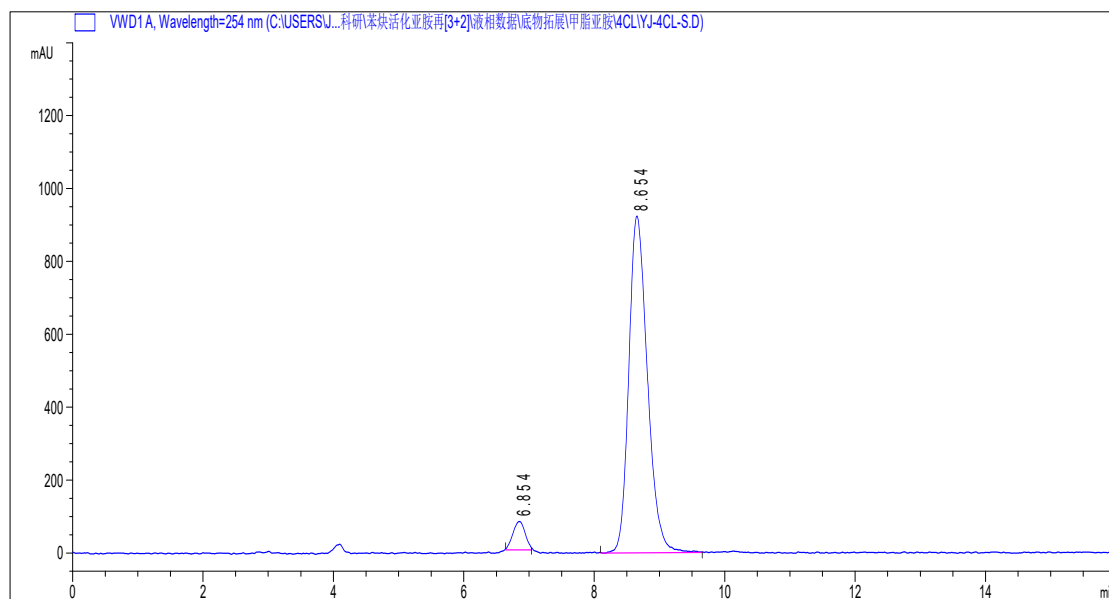
| Peak | RetTime/min | Type | Width/min | Area/mAU*s | Height/mAU | Area/% |
|------|-------------|------|-----------|------------|------------|----------|
| 1 | 9.998 | MM | 0.5254 | 2.96704e4 | 941.20343 | 95.38067 |
| 2 | 11.621 | MM | 0.3815 | 1436.95264 | 62.77784 | 4.61933 |

HPLC chromatogram of racemic 3am



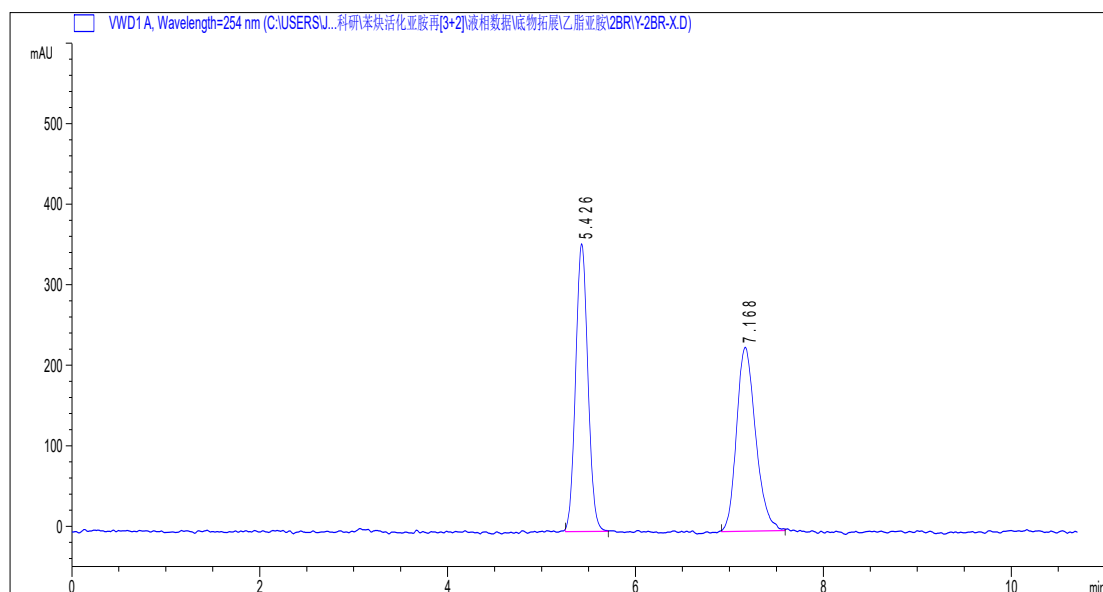
| Peak | RetTime/min | Type | Width/min | Area/mAU*s | Height/mAU | Area/% |
|------|-------------|------|-----------|------------|------------|----------|
| 1 | 6.903 | VB | 0.2358 | 1.00085e4 | 646.98254 | 49.93391 |
| 2 | 8.812 | BB | 0.3059 | 1.00350e4 | 502.20407 | 50.06609 |

HPLC chromatogram of chiral 3am



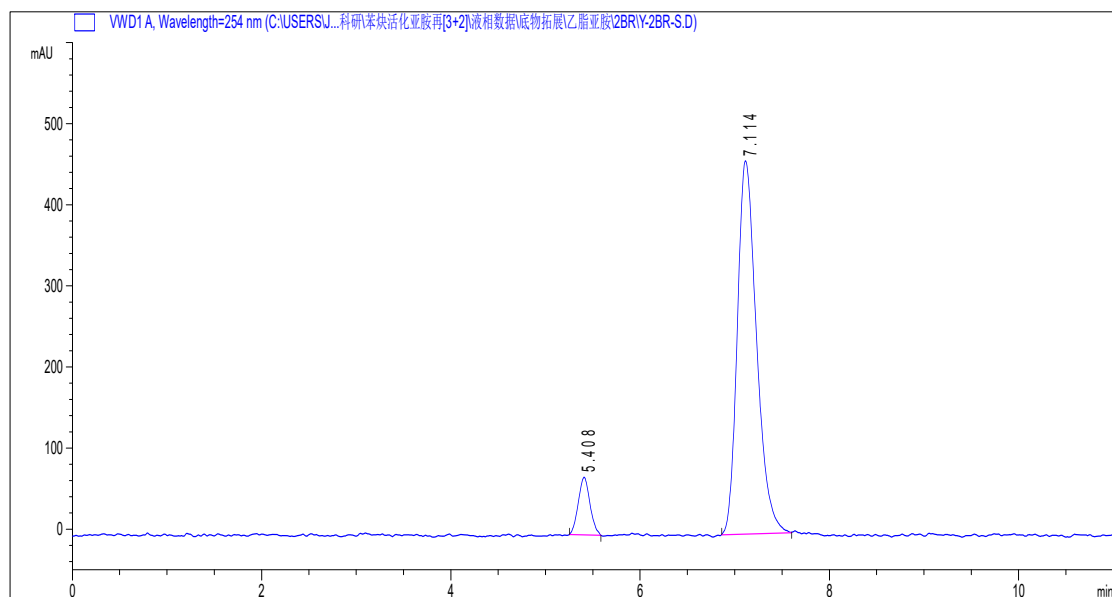
| Peak | RetTime/min | Type | Width/min | Area/mAU*s | Height/mAU | Area/% |
|------|-------------|------|-----------|------------|------------|----------|
| 1 | 6.854 | MM | 0.2168 | 1014.48260 | 77.97339 | 5.24057 |
| 2 | 8.654 | MM | 0.3307 | 1.83438e4 | 924.52594 | 94.75943 |

HPLC chromatogram of racemic 3an



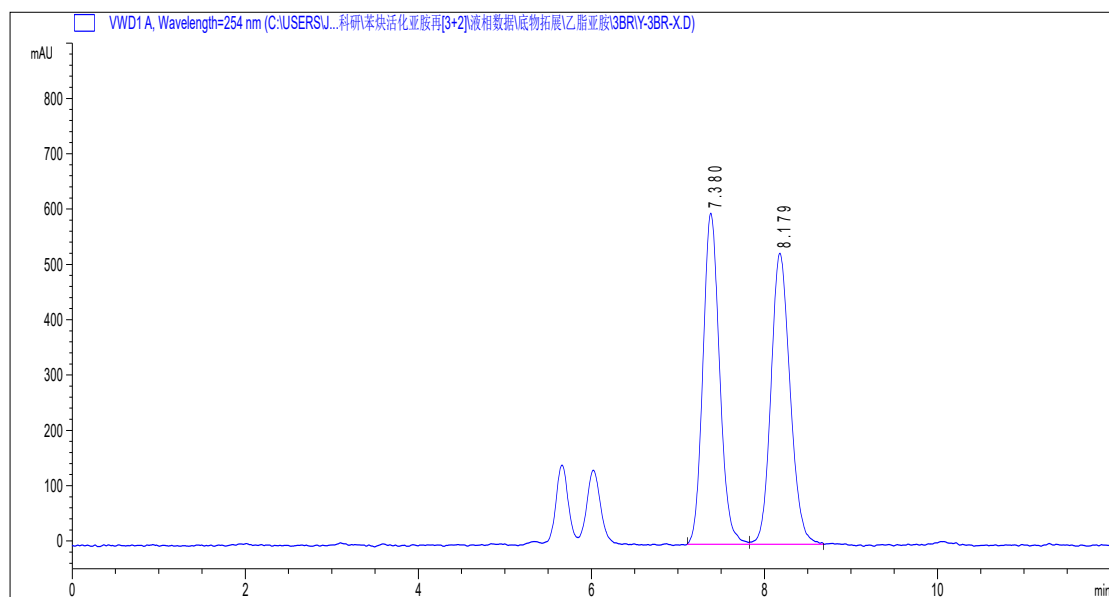
| Peak | RetTime/min | Type | Width/min | Area/mAU*s | Height/mAU | Area/% |
|------|-------------|------|-----------|------------|------------|----------|
| 1 | 5.426 | BB | 0.1410 | 3249.05249 | 357.43481 | 50.15414 |
| 2 | 7.168 | BB | 0.2145 | 3229.08203 | 228.30431 | 49.84586 |

HPLC chromatogram of chiral 3an



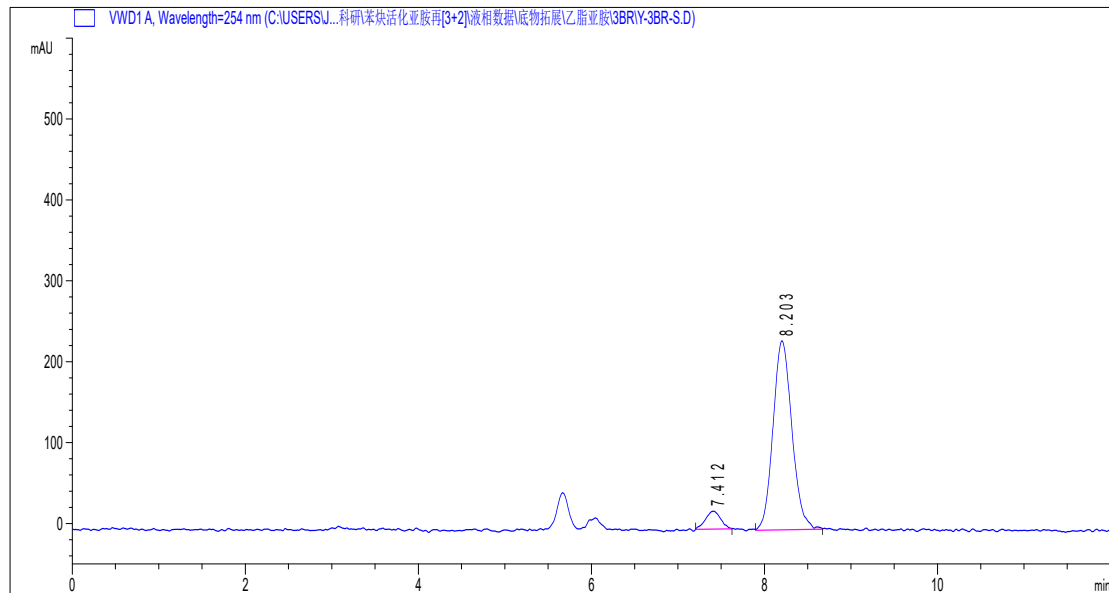
| Peak | RetTime/min | Type | Width/min | Area/mAU*s | Height/mAU | Area/% |
|------|-------------|------|-----------|------------|------------|----------|
| 1 | 5.408 | MM | 0.1425 | 609.28241 | 71.26005 | 8.56985 |
| 2 | 7.114 | BB | 0.2173 | 6500.32129 | 459.94644 | 91.43015 |

HPLC chromatogram of racemic 3ao



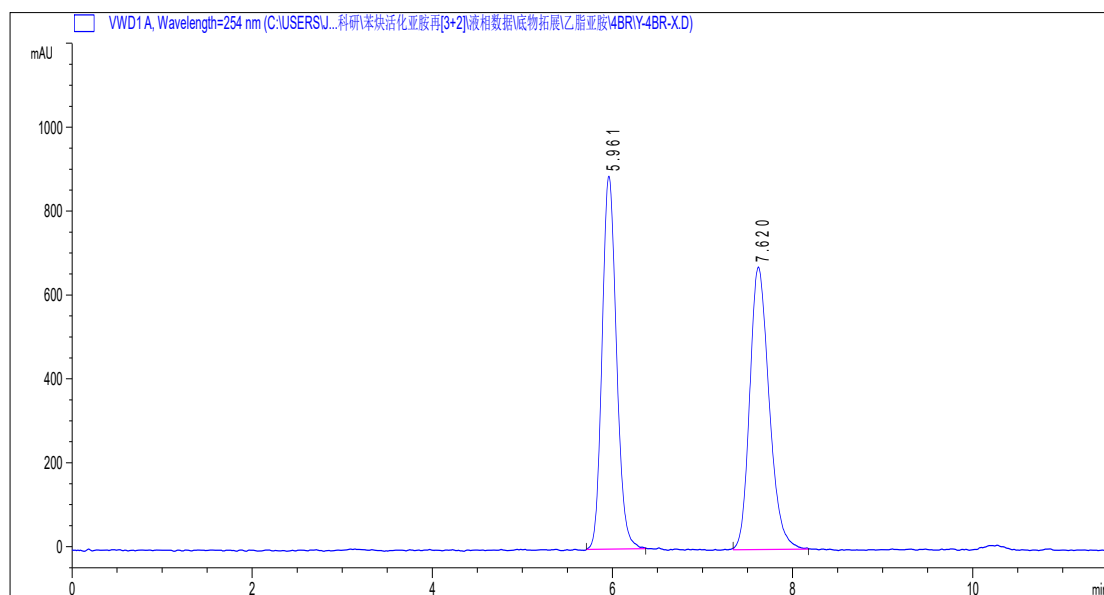
| Peak | RetTime/min | Type | Width/min | Area/mAU*s | Height/mAU | Area/% |
|------|-------------|------|-----------|------------|------------|----------|
| 1 | 7.380 | MM | 0.2226 | 7994.08105 | 598.61420 | 49.78434 |
| 2 | 8.719 | MM | 0.2554 | 8063.34131 | 526.18585 | 50.21566 |

HPLC chromatogram of chiral 3ao



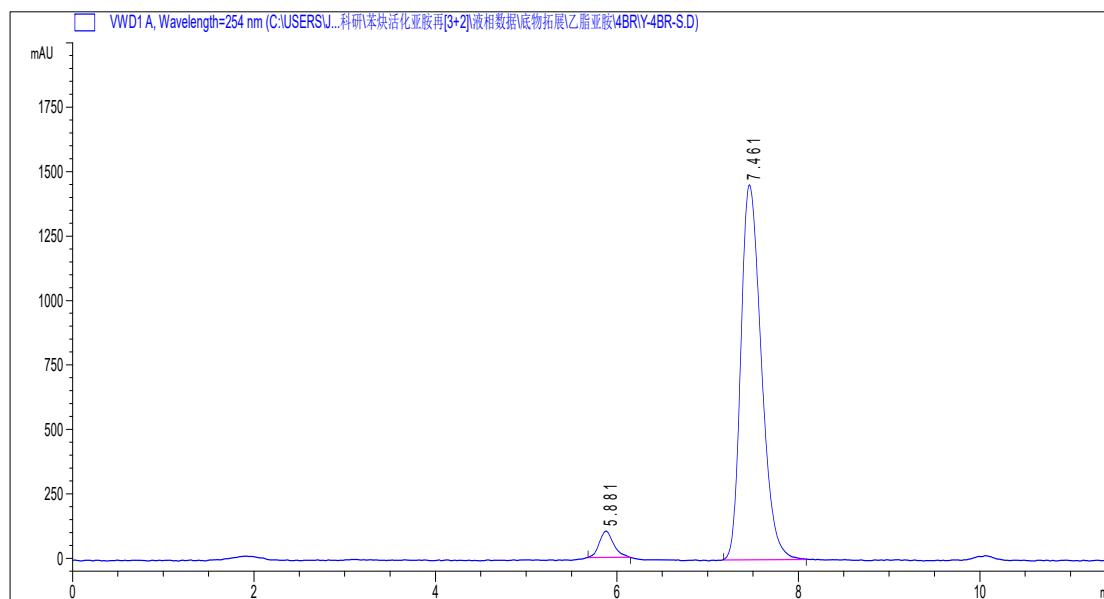
| Peak | RetTime/min | Type | Width/min | Area/mAU*s | Height/mAU | Area/% |
|------|-------------|------|-----------|------------|------------|----------|
| 1 | 7.412 | MM | 0.2039 | 273.27084 | 22.33444 | 7.16980 |
| 2 | 8.203 | MM | 0.2525 | 3538.14453 | 233.56857 | 92.83020 |

HPLC chromatogram of racemic 3ap



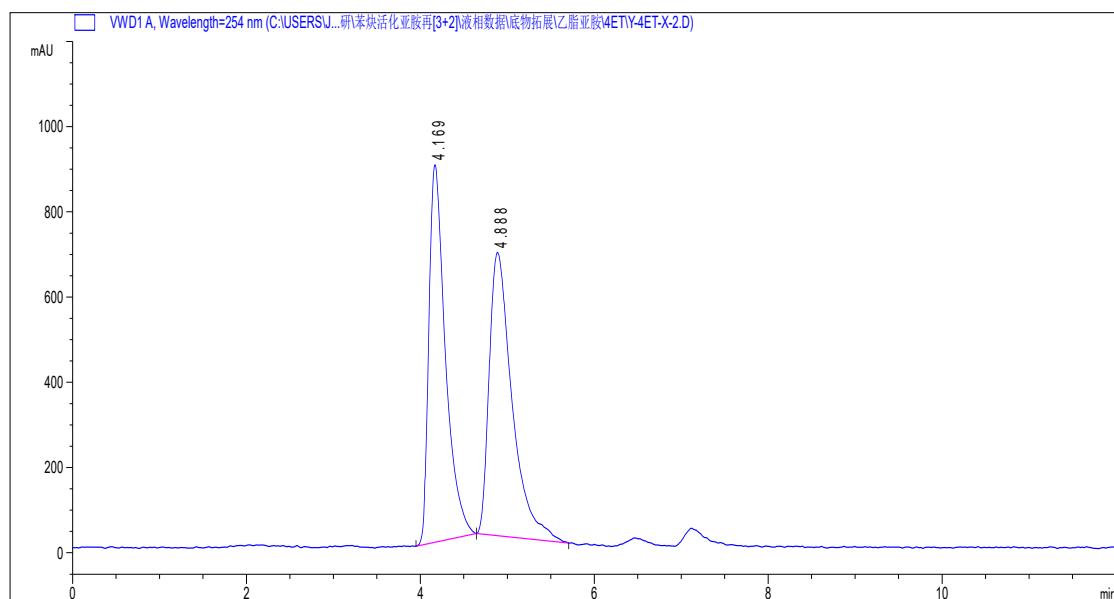
| Peak | RetTime/min | Type | Width/min | Area/mAU*s | Height/mAU | Area/% |
|------|-------------|------|-----------|------------|------------|----------|
| 1 | 5.961 | BB | 0.1736 | 9898.16211 | 889.12628 | 49.48386 |
| 2 | 7.620 | BB | 0.2304 | 1.01046e4 | 673.29724 | 50.51614 |

HPLC chromatogram of chiral 3ap



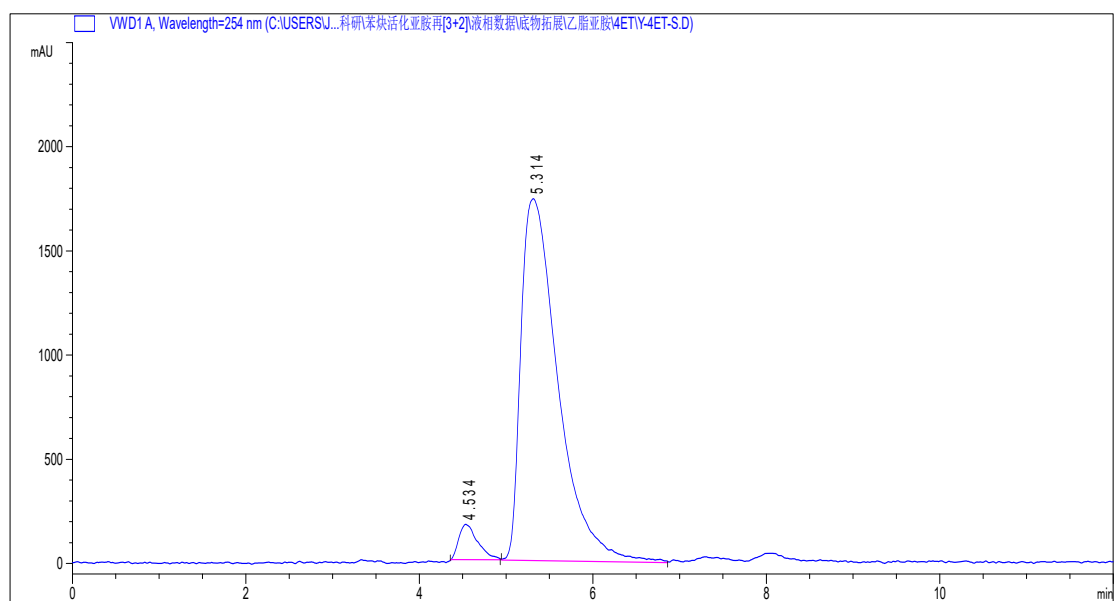
| Peak | RetTime/min | Type | Width/min | Area/mAU*s | Height/mAU | Area/% |
|------|-------------|------|-----------|------------|------------|----------|
| 1 | 5.881 | MM | 0.1837 | 1126.62012 | 102.22792 | 4.71162 |
| 2 | 7.461 | BB | 0.2439 | 2.27849e4 | 1454.91785 | 95.28838 |

HPLC chromatogram of racemic 3aq



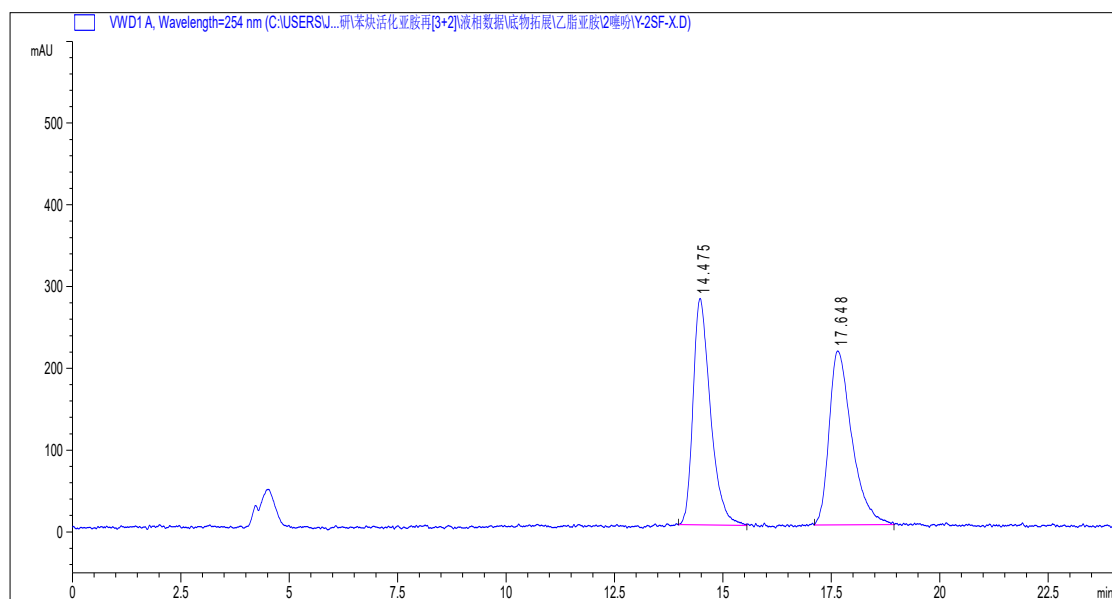
| Peak | RetTime/min | Type | Width/min | Area/mAU*s | Height/mAU | Area/% |
|------|-------------|------|-----------|------------|------------|---------|
| 1 | 4.169 | BB | 0.1978 | 1.16972e4 | 885.29675 | 49.0559 |
| 2 | 4.888 | BB | 0.2729 | 1.21475e4 | 664.74219 | 50.9441 |

HPLC chromatogram of chiral 3aq



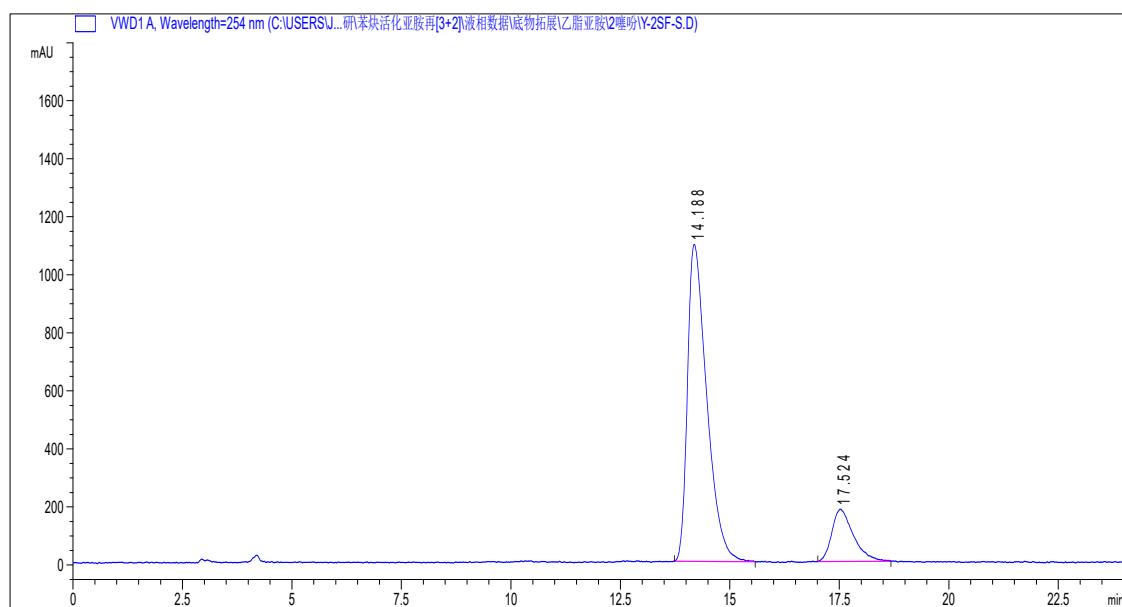
| Peak | RetTime/min | Type | Width/min | Area/mAU*s | Height/mAU | Area/% |
|------|-------------|------|-----------|------------|------------|----------|
| 1 | 4.534 | MM | 0.2527 | 2562.67554 | 169.03549 | 4.73203 |
| 2 | 5.314 | MM | 0.4953 | 5.15932e4 | 1735.96350 | 95.26797 |

HPLC chromatogram of racemic 3ar



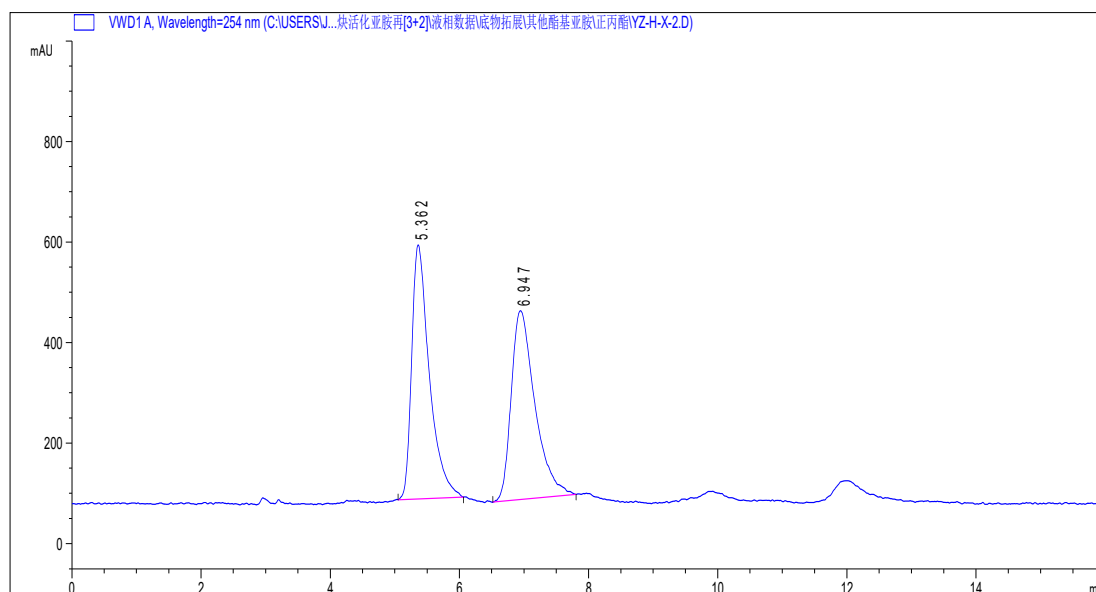
| Peak | RetTime/min | Type | Width/min | Area/mAU*s | Height/mAU | Area/% |
|------|-------------|------|-----------|------------|------------|---------|
| 1 | 14.475 | MM | 0.4636 | 7703.96777 | 276.95425 | 49.7772 |
| 2 | 17.648 | MM | 0.6093 | 7772.93945 | 212.62604 | 50.2228 |

HPLC chromatogram of chiral 3ar



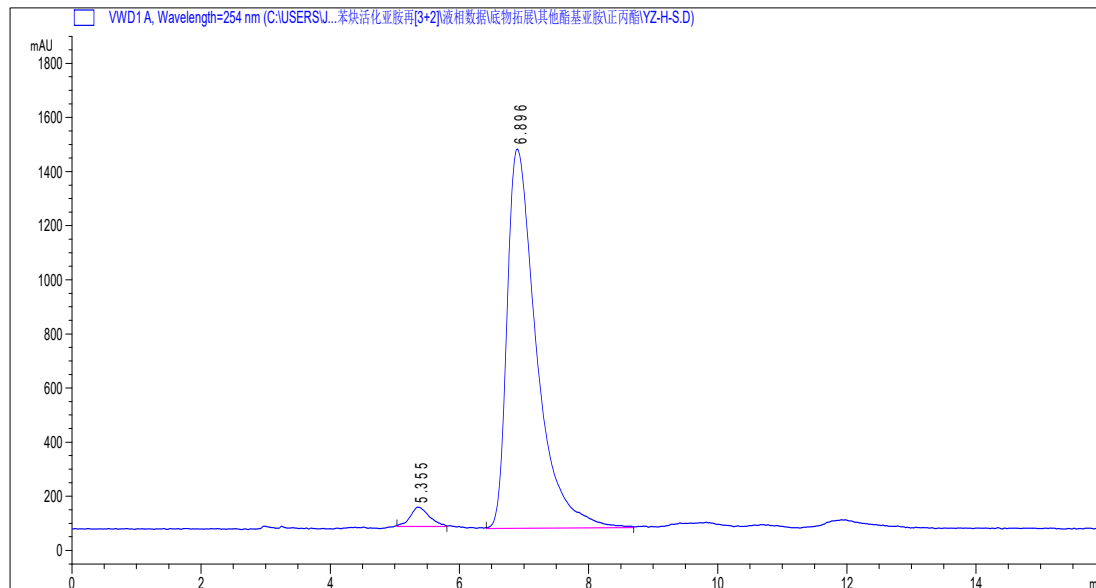
| Peak | RetTime/min | Type | Width/min | Area/mAU*s | Height/mAU | Area/% |
|------|-------------|------|-----------|------------|------------|---------|
| 1 | 14.188 | MM | 0.5103 | 3.34736e4 | 1093.35327 | 84.3990 |
| 2 | 17.524 | MM | 0.5712 | 6187.51855 | 180.55031 | 15.6010 |

HPLC chromatogram of racemic 3as



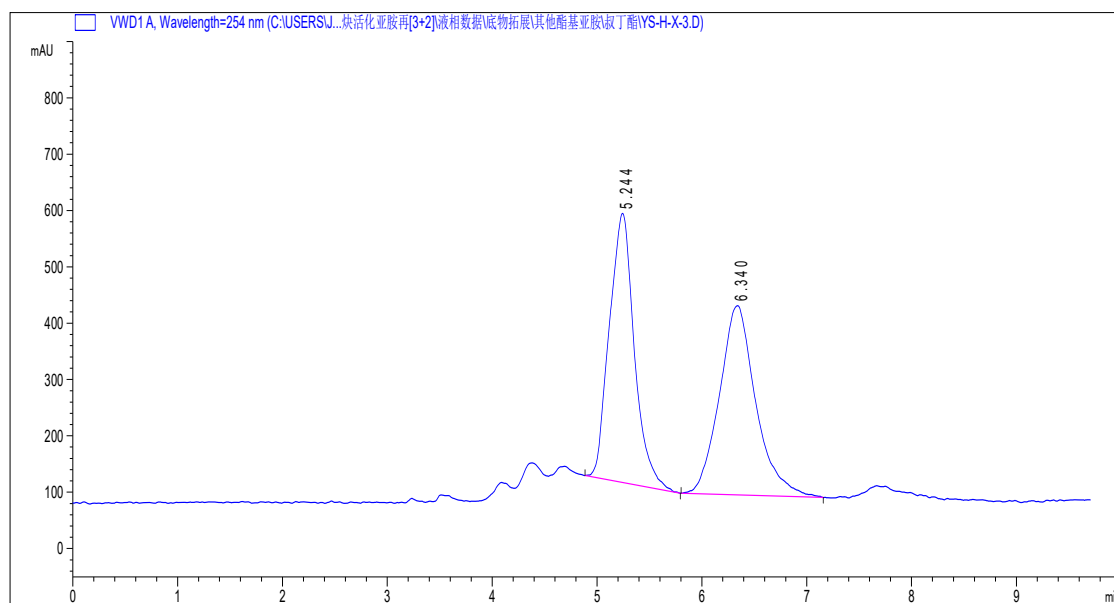
| Peak | RetTime/min | Type | Width/min | Area/mAU*s | Height/mAU | Area/% |
|------|-------------|------|-----------|------------|------------|---------|
| 1 | 5.362 | BB | 0.2743 | 9609.34570 | 505.23761 | 50.0894 |
| 2 | 6.947 | BB | 0.3672 | 9575.04004 | 375.74982 | 49.9106 |

HPLC chromatogram of chiral 3as



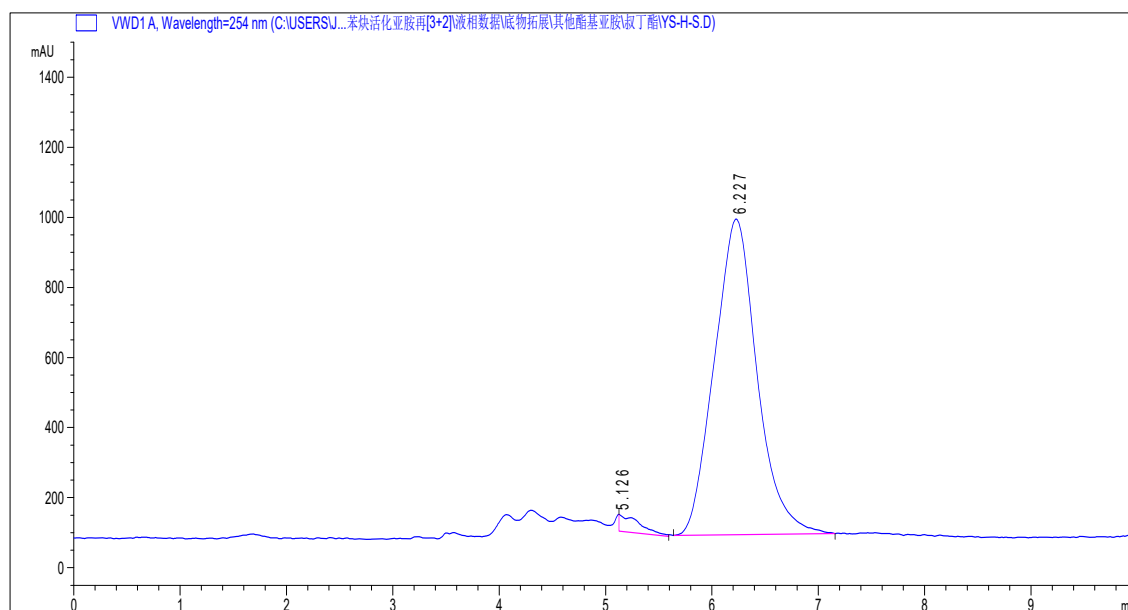
| Peak | RetTime/min | Type | Width/min | Area/mAU*s | Height/mAU | Area/% |
|------|-------------|------|-----------|------------|------------|---------|
| 1 | 5.355 | MM | 0.3447 | 1487.69666 | 71.92606 | 3.2547 |
| 2 | 6.896 | MM | 0.5256 | 4.42220e4 | 1402.17969 | 96.7453 |

HPLC chromatogram of racemic 3at



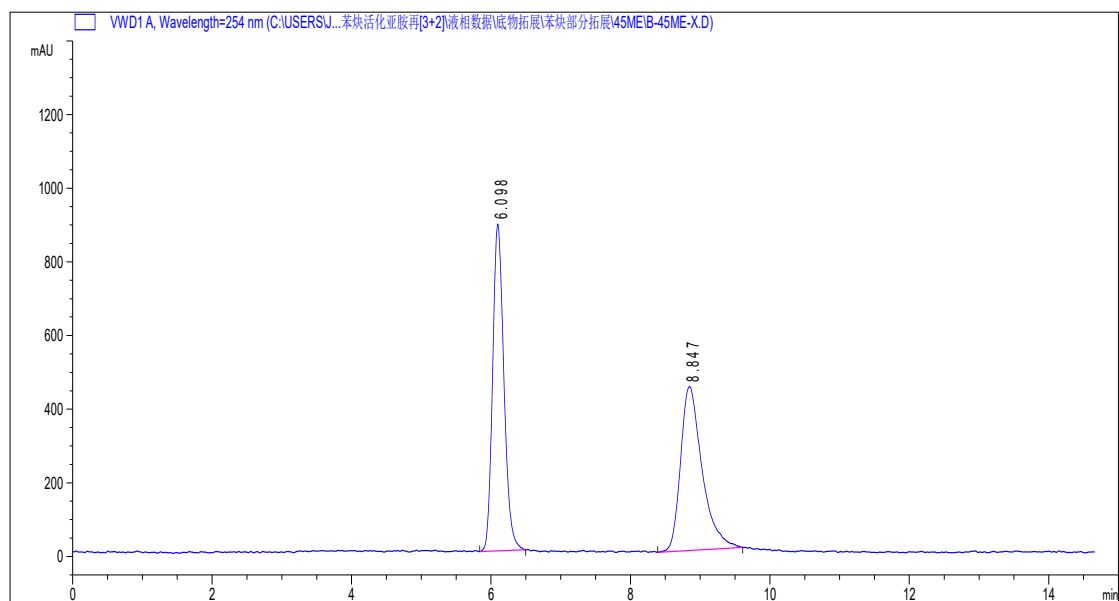
| Peak | RetTime/min | Type | Width/min | Area/mAU*s | Height/mAU | Area/% |
|------|-------------|------|-----------|------------|------------|---------|
| 1 | 5.244 | BB | 0.2308 | 7900.53076 | 477.75360 | 49.3600 |
| 2 | 6.340 | BB | 0.3425 | 8105.41553 | 336.08911 | 50.6400 |

HPLC chromatogram of chiral 3at



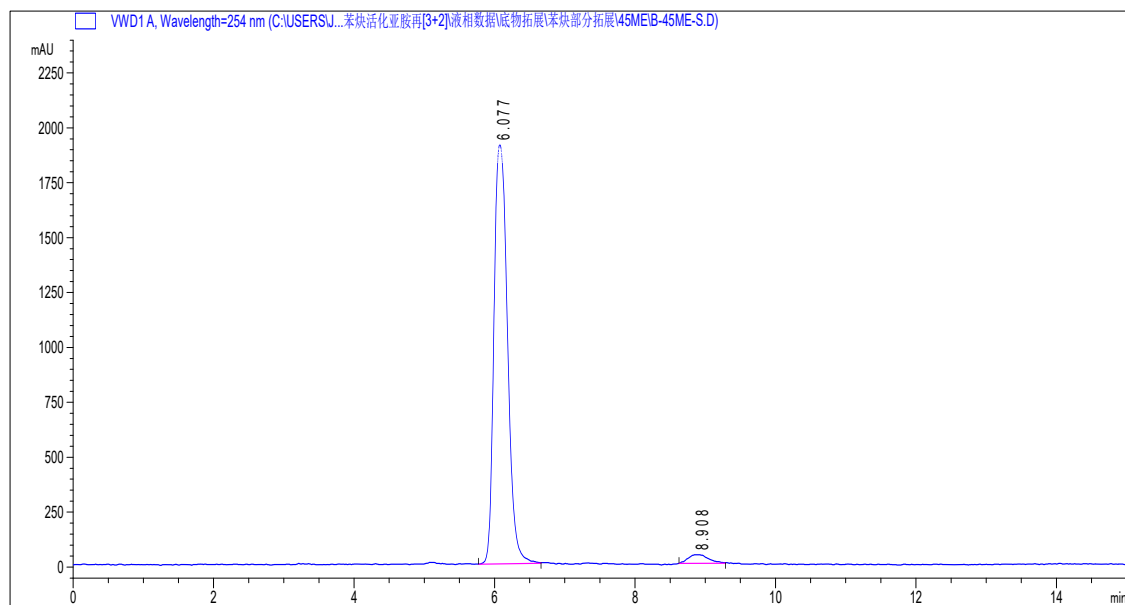
| Peak | RetTime/min | Type | Width/min | Area/mAU*s | Height/mAU | Area/% |
|------|-------------|------|-----------|------------|------------|---------|
| 1 | 5.126 | MM | 0.2260 | 648.95093 | 47.86767 | 2.5178 |
| 2 | 6.227 | BB | 0.4026 | 2.51259e4 | 900.61890 | 97.4822 |

HPLC chromatogram of racemic 3ba



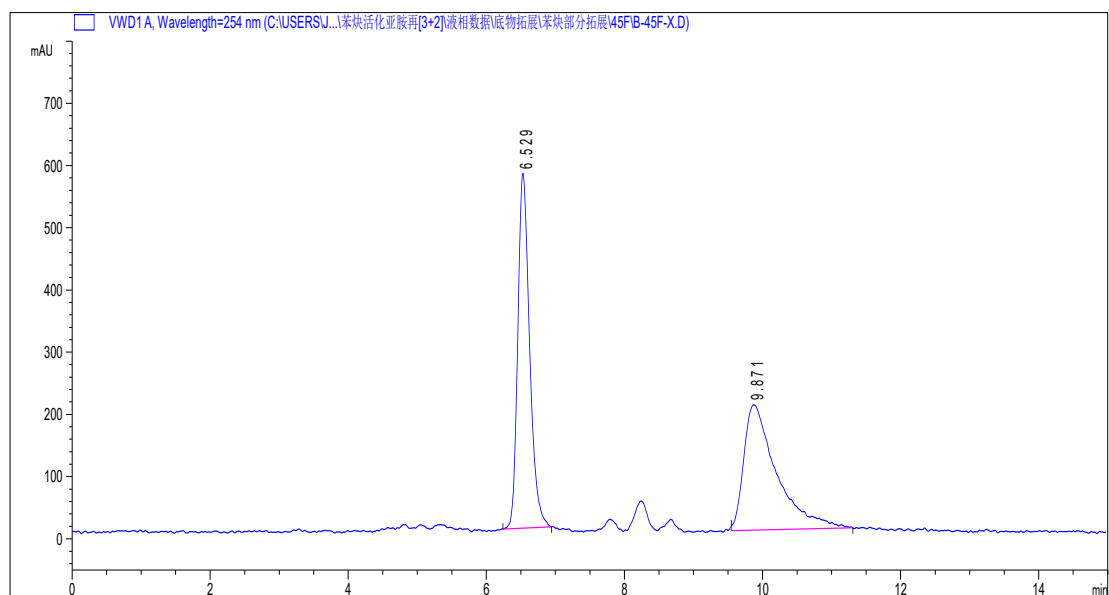
| Peak | RetTime/min | Type | Width/min | Area/mAU*s | Height/mAU | Area/% |
|------|-------------|------|-----------|------------|------------|---------|
| 1 | 6.098 | BB | 0.1729 | 9946.12402 | 888.04871 | 50.9414 |
| 2 | 8.847 | BB | 0.3135 | 9578.51074 | 445.42578 | 49.0586 |

HPLC chromatogram of chiral 3ba



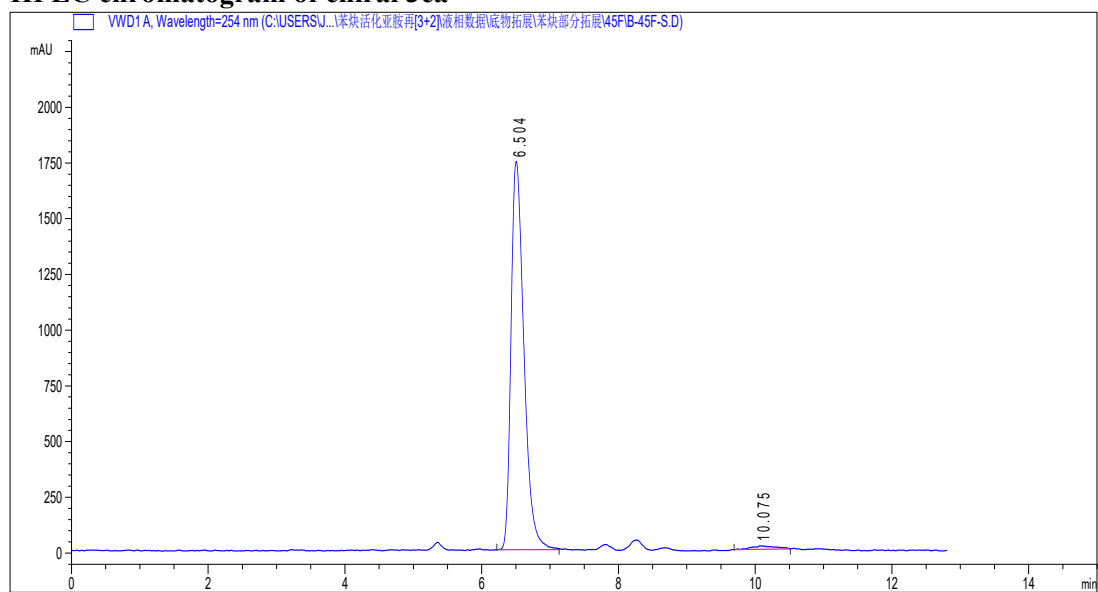
| Peak | RetTime/min | Type | Width/min | Area/mAU*s | Height/mAU | Area/% |
|------|-------------|------|-----------|------------|------------|---------|
| 1 | 6.077 | MM | 0.2222 | 2.54748e4 | 1910.45422 | 96.9424 |
| 2 | 8.908 | MM | 0.3391 | 803.47772 | 39.48487 | 3.0576 |

HPLC chromatogram of racemic 3ca



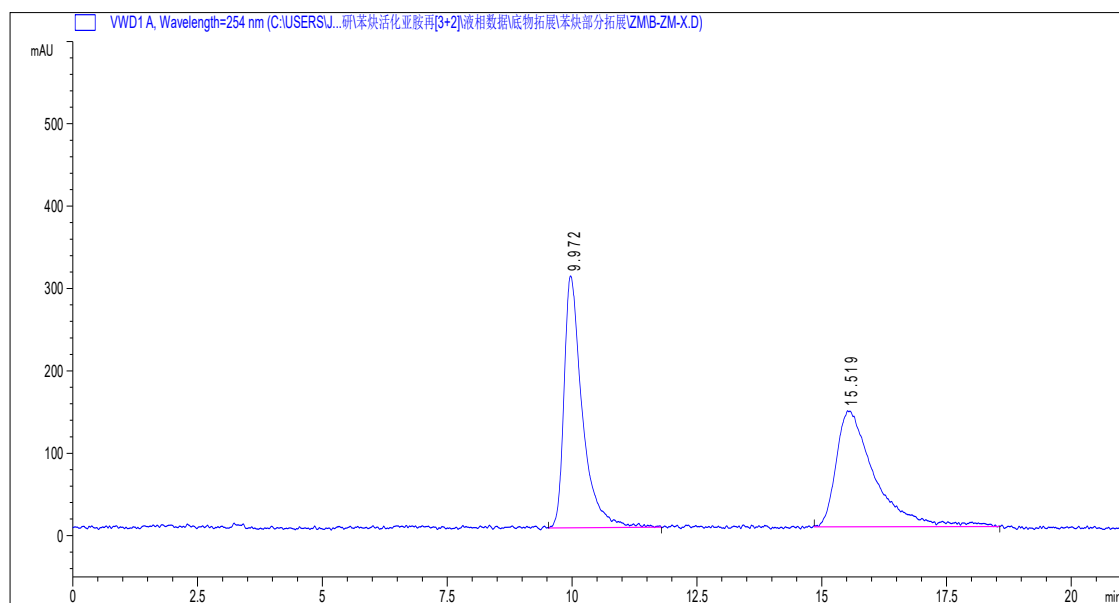
| Peak | RetTime/min | Type | Width/min | Area/mAU*s | Height/mAU | Area/% |
|------|-------------|------|-----------|------------|------------|---------|
| 1 | 6.529 | BB | 0.1833 | 6826.54297 | 570.35052 | 50.7186 |
| 2 | 9.871 | MM | 0.5497 | 6633.11377 | 201.09782 | 49.2814 |

HPLC chromatogram of chiral 3ca



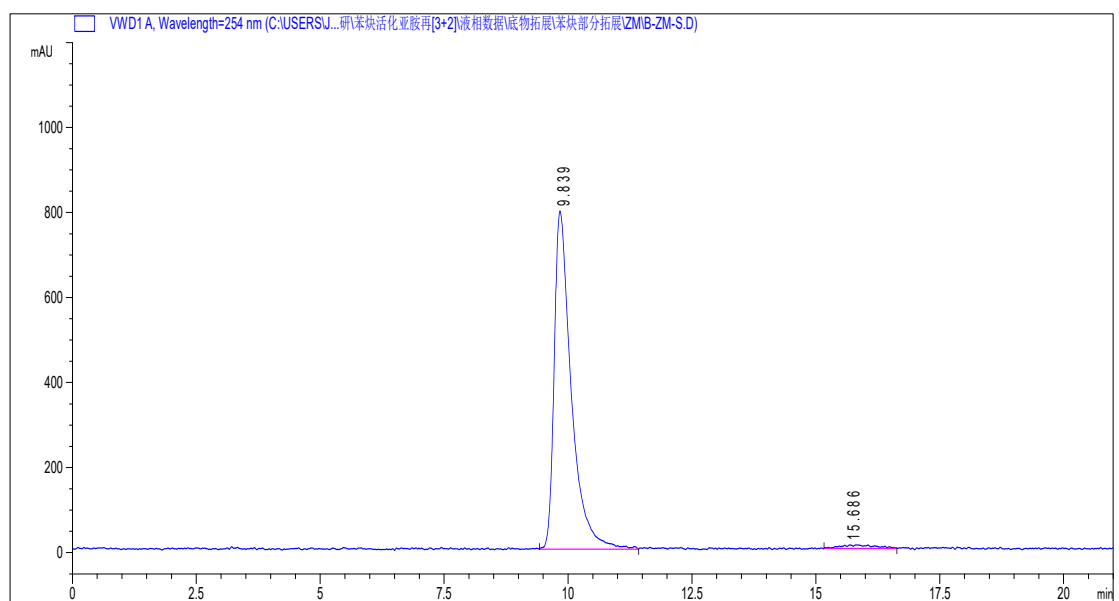
| Peak | RetTime/min | Type | Width/min | Area/mAU*s | Height/mAU | Area/% |
|------|-------------|------|-----------|------------|------------|---------|
| 1 | 6.504 | MM | 0.2199 | 2.30006e4 | 1743.51978 | 98.3491 |
| 2 | 10.075 | MM | 0.4104 | 386.09149 | 15.67957 | 1.6509 |

HPLC chromatogram of racemic 3da



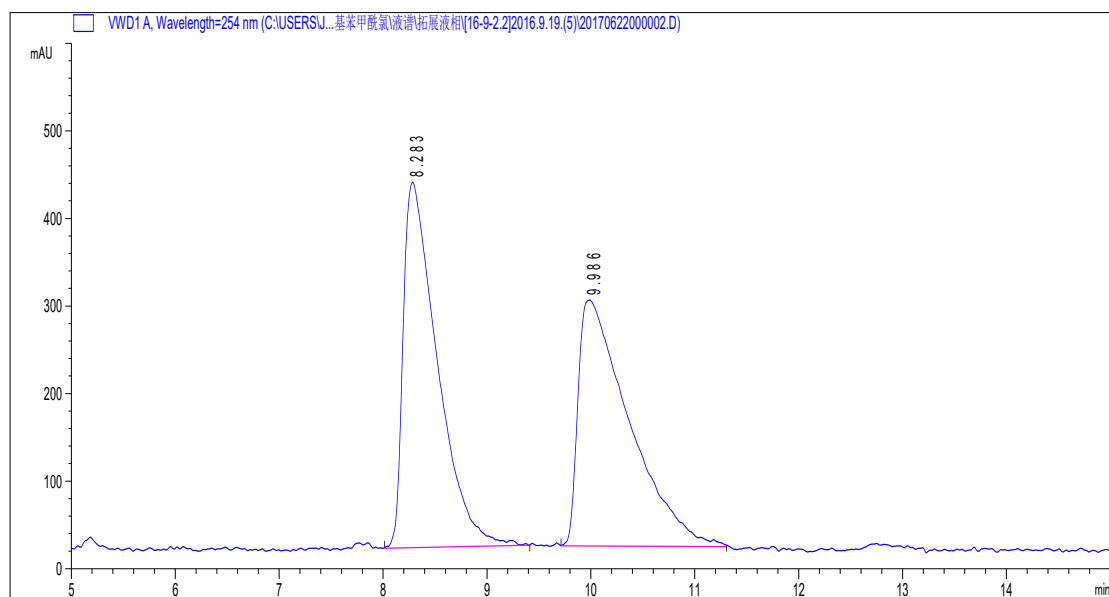
| Peak | RetTime/min | Type | Width/min | Area/mAU*s | Height/mAU | Area/% |
|------|-------------|------|-----------|------------|------------|---------|
| 1 | 9.972 | MM | 0.4251 | 7795.99316 | 305.65952 | 50.8181 |
| 2 | 15.519 | MM | 0.8920 | 7544.98438 | 140.97540 | 49.1819 |

HPLC chromatogram of chiral 3da



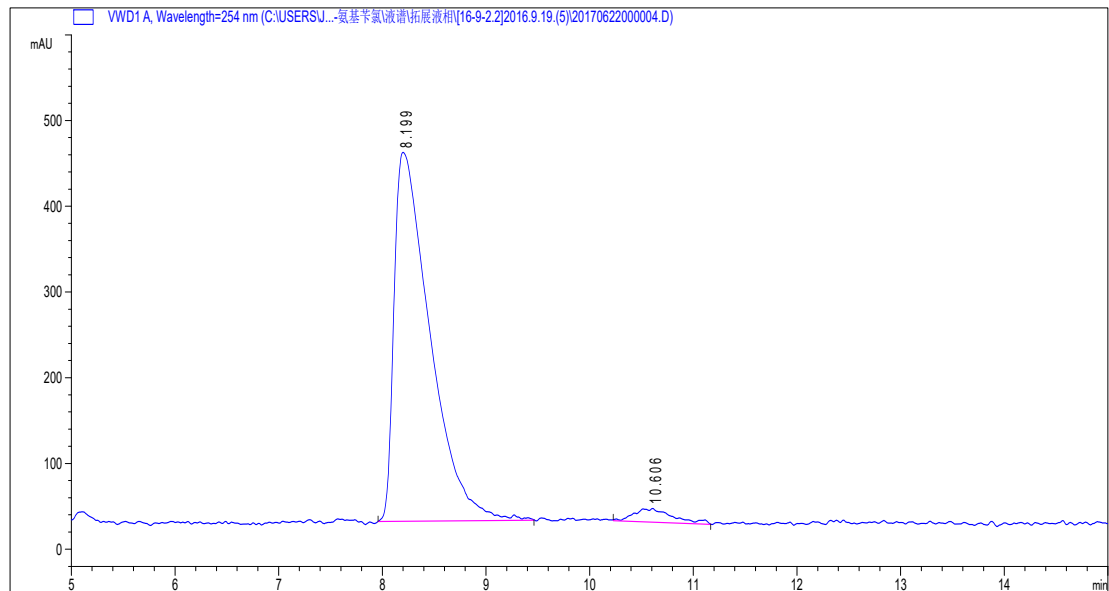
| Peak | RetTime/min | Type | Width/min | Area/mAU*s | Height/mAU | Area/% |
|------|-------------|------|-----------|------------|------------|---------|
| 1 | 9.839 | MM | 0.3997 | 1.90818e4 | 795.67645 | 97.9407 |
| 2 | 15.686 | MM | 0.8084 | 401.20746 | 8.27205 | 2.0593 |

HPLC chromatogram of racemic 4



| Peak | RetTime/min | Type | Width/min | Area/mAU*s | Height/mAU | Area/% |
|------|-------------|------|-----------|------------|------------|---------|
| 1 | 8.283 | MM | 0.3799 | 9510.80762 | 417.27222 | 49.8125 |
| 2 | 9.986 | MM | 0.5687 | 9582.41699 | 280.81998 | 50.1875 |

HPLC chromatogram of chiral 4



| Peak | RetTime/min | Type | Width/min | Area/mAU*s | Height/mAU | Area/% |
|------|-------------|------|-----------|------------|------------|----------|
| 1 | 8.199 | MM | 0.4008 | 1.03437e4 | 430.09491 | 96.19944 |
| 2 | 10.606 | MM | 0.4297 | 408.65103 | 15.84944 | 3.80056 |

X-Ray Crystallographic Data

Crystallographic data for **3ap** has been deposited with the Cambridge Crystallographic Data Centre as deposition number CCDC 1834725. 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.

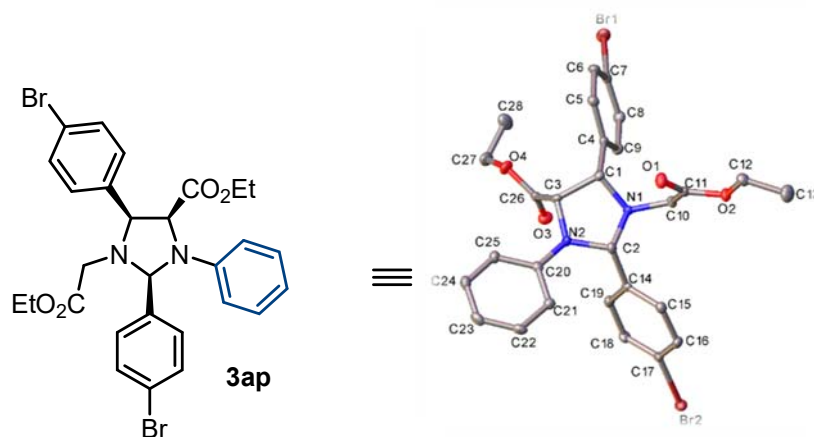


Table S1. Crystal data and structure refinement for **3ap**.

| | | |
|------------------------|---|--------|
| Identification code | sa5257 | |
| Empirical formula | C ₂₈ H ₂₈ Br ₂ N ₂ O ₄ | |
| Formula weight | 616.34 | |
| Temperature | 173.15 K | |
| Wavelength | 0.71073 Å | |
| Crystal system | Orthorhombic | |
| Space group | P2 ₁ 2 ₁ 2 ₁ | |
| Unit cell dimensions | a = 8.3572(3) Å | = 90°. |
| | b = 15.2648(5) Å | = 90°. |
| | c = 20.6156(6) Å | = 90°. |
| Volume | 2629.95(15) Å ³ | |
| Z | 4 | |
| Density (calculated) | 1.557 Mg/m ³ | |
| Absorption coefficient | 3.119 mm ⁻¹ | |

| | |
|-----------------------------------|---|
| F(000) | 1248 |
| Crystal size | 0.357 x 0.059 x 0.047 mm ³ |
| Theta range for data collection | 2.384 to 30.917°. |
| Index ranges | -12<=h<=11, -21<=k<=21, -28<=l<=29 |
| Reflections collected | 33718 |
| Independent reflections | 7669 [R(int) = 0.0778] |
| Completeness to theta = 25.242° | 99.9 % |
| Absorption correction | Semi-empirical from equivalents |
| Max. and min. transmission | 1.00000 and 0.62818 |
| Refinement method | Full-matrix least-squares on F ² |
| Data / restraints / parameters | 7669 / 0 / 327 |
| Goodness-of-fit on F ² | 1.022 |
| Final R indices [I>2sigma(I)] | R1 = 0.0520, wR2 = 0.0855 |
| R indices (all data) | R1 = 0.0837, wR2 = 0.0951 |
| Absolute structure parameter | -0.001(6) |
| Extinction coefficient | n/a |
| Largest diff. peak and hole | 0.773 and -0.453 e.Å ⁻³ |

Table S2. Atomic coordinates (x 10⁴) and equivalent isotropic displacement parameters (Å²x 10³) for **3ap**. U(eq) is defined as one third of the trace of the orthogonalized U^{ij} tensor.

| | x | y | z | U(eq) |
|-----|----------|---------|---------|-------|
| Br1 | 1368(1) | 6479(1) | 3984(1) | 36(1) |
| Br2 | 13184(1) | 8459(1) | 7209(1) | 30(1) |
| C1 | 5901(6) | 5193(3) | 6150(2) | 22(1) |
| C2 | 8230(6) | 5507(3) | 6777(2) | 21(1) |
| C3 | 7325(5) | 4670(3) | 5853(2) | 22(1) |
| C4 | 4742(6) | 5566(3) | 5653(2) | 20(1) |
| C5 | 3418(6) | 5071(3) | 5480(2) | 24(1) |

| | | | | |
|-----|----------|---------|---------|-------|
| C6 | 2382(6) | 5351(3) | 4998(2) | 26(1) |
| C7 | 2681(6) | 6146(3) | 4696(2) | 23(1) |
| C8 | 3939(6) | 6660(3) | 4879(2) | 27(1) |
| C9 | 4978(6) | 6368(3) | 5360(2) | 24(1) |
| C10 | 5809(5) | 6392(3) | 6957(2) | 23(1) |
| C11 | 5089(6) | 5910(3) | 7531(2) | 22(1) |
| C12 | 3669(7) | 6117(3) | 8518(2) | 30(1) |
| C13 | 3530(8) | 6802(4) | 9032(3) | 46(2) |
| C14 | 9478(5) | 6216(3) | 6859(2) | 21(1) |
| C15 | 9672(5) | 6593(3) | 7466(2) | 25(1) |
| C16 | 10754(6) | 7264(3) | 7570(2) | 26(1) |
| C17 | 11669(5) | 7544(3) | 7058(2) | 23(1) |
| C18 | 11504(6) | 7194(3) | 6445(2) | 26(1) |
| C19 | 10390(5) | 6530(3) | 6353(2) | 26(1) |
| C20 | 9883(6) | 4254(3) | 6367(2) | 22(1) |
| C21 | 10949(6) | 4312(3) | 6894(2) | 24(1) |
| C22 | 12204(6) | 3726(3) | 6955(3) | 29(1) |
| C23 | 12439(6) | 3070(3) | 6498(3) | 30(1) |
| C24 | 11397(6) | 3005(3) | 5982(2) | 29(1) |
| C25 | 10142(6) | 3584(3) | 5910(2) | 25(1) |
| C26 | 7713(6) | 4962(3) | 5165(2) | 26(1) |
| C27 | 7237(7) | 4621(4) | 4048(2) | 38(1) |
| C28 | 5715(7) | 5007(4) | 3823(3) | 46(2) |
| N1 | 6756(5) | 5881(2) | 6508(2) | 19(1) |
| N2 | 8627(5) | 4843(2) | 6292(2) | 23(1) |
| O1 | 4925(5) | 5131(2) | 7573(2) | 34(1) |
| O2 | 4608(4) | 6476(2) | 7988(2) | 27(1) |
| O3 | 8454(4) | 5603(2) | 5022(2) | 35(1) |
| O4 | 7102(4) | 4391(2) | 4733(2) | 36(1) |

Table S3. Bond lengths [\AA] and angles [$^\circ$] for **3ap**.

| | |
|----------|----------|
| Br1-C7 | 1.901(5) |
| Br2-C17 | 1.911(5) |
| C1-H1 | 1.0000 |
| C1-C3 | 1.558(7) |
| C1-C4 | 1.521(6) |
| C1-N1 | 1.469(6) |
| C2-H2 | 1.0000 |
| C2-C14 | 1.513(6) |
| C2-N1 | 1.467(6) |
| C2-N2 | 1.462(6) |
| C3-H3 | 1.0000 |
| C3-C26 | 1.523(7) |
| C3-N2 | 1.439(6) |
| C4-C5 | 1.386(7) |
| C4-C9 | 1.379(6) |
| C5-H5 | 0.9500 |
| C5-C6 | 1.385(6) |
| C6-H6 | 0.9500 |
| C6-C7 | 1.386(7) |
| C7-C8 | 1.366(7) |
| C8-H8 | 0.9500 |
| C8-C9 | 1.392(6) |
| C9-H9 | 0.9500 |
| C10-H10A | 0.9900 |
| C10-H10B | 0.9900 |
| C10-C11 | 1.517(7) |
| C10-N1 | 1.446(6) |
| C11-O1 | 1.200(6) |

| | |
|----------|----------|
| C11-O2 | 1.341(6) |
| C12-H12A | 0.9900 |
| C12-H12B | 0.9900 |
| C12-C13 | 1.493(7) |
| C12-O2 | 1.452(6) |
| C13-H13A | 0.9800 |
| C13-H13B | 0.9800 |
| C13-H13C | 0.9800 |
| C14-C15 | 1.387(6) |
| C14-C19 | 1.378(7) |
| C15-H15 | 0.9500 |
| C15-C16 | 1.383(7) |
| C16-H16 | 0.9500 |
| C16-C17 | 1.372(7) |
| C17-C18 | 1.377(6) |
| C18-H18 | 0.9500 |
| C18-C19 | 1.390(7) |
| C19-H19 | 0.9500 |
| C20-C21 | 1.406(7) |
| C20-C25 | 1.408(6) |
| C20-N2 | 1.392(6) |
| C21-H21 | 0.9500 |
| C21-C22 | 1.385(7) |
| C22-H22 | 0.9500 |
| C22-C23 | 1.388(7) |
| C23-H23 | 0.9500 |
| C23-C24 | 1.379(7) |
| C24-H24 | 0.9500 |
| C24-C25 | 1.380(7) |
| C25-H25 | 0.9500 |

| | |
|-----------|----------|
| C26-O3 | 1.195(6) |
| C26-O4 | 1.346(6) |
| C27-H27A | 0.9900 |
| C27-H27B | 0.9900 |
| C27-C28 | 1.476(8) |
| C27-O4 | 1.461(6) |
| C28-H28A | 0.9800 |
| C28-H28B | 0.9800 |
| C28-H28C | 0.9800 |
| C3-C1-H1 | 109.5 |
| C4-C1-H1 | 109.5 |
| C4-C1-C3 | 114.4(4) |
| N1-C1-H1 | 109.5 |
| N1-C1-C3 | 101.1(4) |
| N1-C1-C4 | 112.4(4) |
| C14-C2-H2 | 110.1 |
| N1-C2-H2 | 110.1 |
| N1-C2-C14 | 110.0(4) |
| N2-C2-H2 | 110.1 |
| N2-C2-C14 | 114.5(4) |
| N2-C2-N1 | 101.7(4) |
| C1-C3-H3 | 109.7 |
| C26-C3-C1 | 112.2(4) |
| C26-C3-H3 | 109.7 |
| N2-C3-C1 | 103.6(4) |
| N2-C3-H3 | 109.7 |
| N2-C3-C26 | 111.7(4) |
| C5-C4-C1 | 118.6(4) |
| C9-C4-C1 | 122.4(4) |

| | |
|---------------|----------|
| C9-C4-C5 | 119.0(4) |
| C4-C5-H5 | 119.5 |
| C6-C5-C4 | 121.0(5) |
| C6-C5-H5 | 119.5 |
| C5-C6-H6 | 120.7 |
| C5-C6-C7 | 118.7(5) |
| C7-C6-H6 | 120.7 |
| C6-C7-Br1 | 118.5(4) |
| C8-C7-Br1 | 120.3(4) |
| C8-C7-C6 | 121.2(5) |
| C7-C8-H8 | 120.2 |
| C7-C8-C9 | 119.5(5) |
| C9-C8-H8 | 120.2 |
| C4-C9-C8 | 120.5(5) |
| C4-C9-H9 | 119.8 |
| C8-C9-H9 | 119.8 |
| H10A-C10-H10B | 107.3 |
| C11-C10-H10A | 108.0 |
| C11-C10-H10B | 108.0 |
| N1-C10-H10A | 108.0 |
| N1-C10-H10B | 108.0 |
| N1-C10-C11 | 117.0(4) |
| O1-C11-C10 | 125.6(5) |
| O1-C11-O2 | 123.6(5) |
| O2-C11-C10 | 110.8(4) |
| H12A-C12-H12B | 108.4 |
| C13-C12-H12A | 110.1 |
| C13-C12-H12B | 110.1 |
| O2-C12-H12A | 110.1 |
| O2-C12-H12B | 110.1 |

| | |
|---------------|----------|
| O2-C12-C13 | 108.2(4) |
| C12-C13-H13A | 109.5 |
| C12-C13-H13B | 109.5 |
| C12-C13-H13C | 109.5 |
| H13A-C13-H13B | 109.5 |
| H13A-C13-H13C | 109.5 |
| H13B-C13-H13C | 109.5 |
| C15-C14-C2 | 118.5(4) |
| C19-C14-C2 | 123.1(4) |
| C19-C14-C15 | 118.3(4) |
| C14-C15-H15 | 119.2 |
| C16-C15-C14 | 121.6(4) |
| C16-C15-H15 | 119.2 |
| C15-C16-H16 | 120.8 |
| C17-C16-C15 | 118.3(4) |
| C17-C16-H16 | 120.8 |
| C16-C17-Br2 | 118.1(4) |
| C16-C17-C18 | 122.0(4) |
| C18-C17-Br2 | 119.9(4) |
| C17-C18-H18 | 120.8 |
| C17-C18-C19 | 118.4(4) |
| C19-C18-H18 | 120.8 |
| C14-C19-C18 | 121.3(5) |
| C14-C19-H19 | 119.3 |
| C18-C19-H19 | 119.3 |
| C21-C20-C25 | 117.7(4) |
| N2-C20-C21 | 121.6(4) |
| N2-C20-C25 | 120.7(4) |
| C20-C21-H21 | 119.7 |
| C22-C21-C20 | 120.6(5) |

| | |
|---------------|----------|
| C22-C21-H21 | 119.7 |
| C21-C22-H22 | 119.6 |
| C21-C22-C23 | 120.8(5) |
| C23-C22-H22 | 119.6 |
| C22-C23-H23 | 120.5 |
| C24-C23-C22 | 119.1(5) |
| C24-C23-H23 | 120.5 |
| C23-C24-H24 | 119.4 |
| C23-C24-C25 | 121.1(5) |
| C25-C24-H24 | 119.4 |
| C20-C25-H25 | 119.7 |
| C24-C25-C20 | 120.7(5) |
| C24-C25-H25 | 119.7 |
| O3-C26-C3 | 125.4(5) |
| O3-C26-O4 | 124.4(5) |
| O4-C26-C3 | 110.2(4) |
| H27A-C27-H27B | 108.2 |
| C28-C27-H27A | 109.8 |
| C28-C27-H27B | 109.8 |
| O4-C27-H27A | 109.8 |
| O4-C27-H27B | 109.8 |
| O4-C27-C28 | 109.5(4) |
| C27-C28-H28A | 109.5 |
| C27-C28-H28B | 109.5 |
| C27-C28-H28C | 109.5 |
| H28A-C28-H28B | 109.5 |
| H28A-C28-H28C | 109.5 |
| H28B-C28-H28C | 109.5 |
| C2-N1-C1 | 108.6(3) |
| C10-N1-C1 | 116.1(4) |

| | |
|------------|----------|
| C10-N1-C2 | 115.4(4) |
| C3-N2-C2 | 112.7(4) |
| C20-N2-C2 | 122.8(4) |
| C20-N2-C3 | 121.4(4) |
| C11-O2-C12 | 116.6(4) |
| C26-O4-C27 | 117.0(4) |

Symmetry transformations used to generate equivalent atoms:

Table S4. Anisotropic displacement parameters ($\text{\AA}^2 \times 10^3$) for **3ap**. The anisotropic displacement factor exponent takes the form: $-2 \left[h^2 a^{*2} U^{11} + \dots + 2 h k a^* b^* U^{12} \right]$

| | U^{11} | U^{22} | U^{33} | U^{23} | U^{13} | U^{12} |
|-----|----------|----------|----------|----------|----------|----------|
| Br1 | 42(1) | 36(1) | 30(1) | 3(1) | -13(1) | 8(1) |
| Br2 | 26(1) | 24(1) | 41(1) | -4(1) | 2(1) | -5(1) |
| C1 | 23(2) | 20(2) | 23(3) | 0(2) | 0(2) | -3(2) |
| C2 | 24(2) | 22(2) | 18(2) | 1(2) | 2(2) | 3(2) |
| C3 | 19(2) | 20(2) | 26(3) | 0(2) | -7(2) | -2(2) |
| C4 | 19(2) | 23(2) | 17(2) | -2(2) | -1(2) | 2(2) |
| C5 | 22(3) | 26(3) | 23(2) | 4(2) | 1(2) | 2(2) |
| C6 | 19(2) | 32(3) | 27(3) | -1(2) | -3(2) | -1(2) |
| C7 | 25(3) | 25(3) | 20(2) | -2(2) | -3(2) | 8(2) |
| C8 | 32(3) | 20(3) | 28(3) | 5(2) | 2(2) | -2(2) |
| C9 | 26(2) | 22(3) | 25(2) | 0(2) | 0(2) | -4(2) |
| C10 | 22(2) | 22(3) | 25(2) | 0(2) | 3(2) | 3(2) |
| C11 | 18(2) | 24(3) | 22(2) | -3(2) | -2(2) | 5(2) |
| C12 | 28(3) | 35(3) | 28(3) | 4(2) | 5(2) | 0(2) |
| C13 | 57(4) | 50(4) | 30(3) | -2(3) | 13(3) | 0(3) |
| C14 | 19(2) | 18(2) | 25(3) | 3(2) | -2(2) | 3(2) |

| | | | | | | |
|-----|-------|-------|-------|-------|-------|--------|
| C15 | 25(2) | 26(3) | 22(2) | 1(2) | 2(2) | 2(2) |
| C16 | 30(3) | 26(3) | 23(3) | -7(2) | 0(2) | -2(2) |
| C17 | 18(2) | 20(2) | 30(3) | -5(2) | -1(2) | 1(2) |
| C18 | 25(3) | 27(3) | 26(3) | 2(2) | 9(2) | -4(2) |
| C19 | 28(2) | 29(3) | 21(2) | -4(2) | 0(2) | 2(2) |
| C20 | 21(2) | 22(2) | 24(3) | 5(2) | 2(2) | 0(2) |
| C21 | 27(3) | 25(3) | 21(3) | 2(2) | 0(2) | -1(2) |
| C22 | 21(3) | 35(3) | 31(3) | 10(2) | -5(2) | 0(2) |
| C23 | 25(3) | 29(3) | 36(3) | 13(2) | 4(2) | 8(2) |
| C24 | 36(3) | 24(2) | 27(3) | -1(2) | 8(3) | 3(2) |
| C25 | 28(2) | 24(3) | 22(2) | 0(2) | 2(2) | 1(2) |
| C26 | 19(2) | 35(3) | 24(3) | -5(2) | -4(2) | 5(2) |
| C27 | 38(3) | 57(4) | 18(3) | -8(3) | 2(2) | -3(3) |
| C28 | 45(4) | 67(4) | 25(3) | 2(3) | 5(3) | 12(3) |
| N1 | 18(2) | 19(2) | 21(2) | 0(2) | -2(2) | 1(2) |
| N2 | 23(2) | 21(2) | 25(2) | -5(2) | -4(2) | 4(2) |
| O1 | 45(2) | 24(2) | 32(2) | 1(2) | 10(2) | 0(2) |
| O2 | 32(2) | 25(2) | 23(2) | -2(2) | 6(1) | 1(2) |
| O3 | 34(2) | 42(2) | 30(2) | 1(2) | 4(2) | -10(2) |
| O4 | 43(2) | 42(2) | 22(2) | -9(2) | -6(2) | -2(2) |

Table S5. Hydrogen coordinates ($\times 10^4$) and isotropic displacement parameters ($\text{\AA}^2 \times 10^3$) for **3ap**.

| | x | y | z | U(eq) |
|----|------|------|------|-------|
| H1 | 5306 | 4812 | 6462 | 27 |
| H2 | 8004 | 5222 | 7204 | 25 |
| H3 | 7071 | 4029 | 5856 | 26 |

| | | | | |
|------|-------|------|------|----|
| H5 | 3218 | 4532 | 5695 | 29 |
| H6 | 1484 | 5006 | 4878 | 31 |
| H8 | 4104 | 7214 | 4679 | 32 |
| H9 | 5855 | 6724 | 5488 | 29 |
| H10A | 4925 | 6667 | 6711 | 28 |
| H10B | 6489 | 6870 | 7127 | 28 |
| H12A | 4200 | 5589 | 8696 | 36 |
| H12B | 2593 | 5948 | 8361 | 36 |
| H13A | 3073 | 7336 | 8844 | 68 |
| H13B | 4592 | 6931 | 9209 | 68 |
| H13C | 2832 | 6589 | 9380 | 68 |
| H15 | 9046 | 6386 | 7818 | 30 |
| H16 | 10862 | 7525 | 7986 | 32 |
| H18 | 12138 | 7402 | 6095 | 31 |
| H19 | 10255 | 6287 | 5932 | 31 |
| H21 | 10805 | 4757 | 7210 | 29 |
| H22 | 12913 | 3773 | 7313 | 35 |
| H23 | 13306 | 2671 | 6541 | 36 |
| H24 | 11545 | 2553 | 5670 | 35 |
| H25 | 9447 | 3531 | 5547 | 30 |
| H27A | 7485 | 4091 | 3790 | 45 |
| H27B | 8117 | 5047 | 3987 | 45 |
| H28A | 5803 | 5157 | 3362 | 69 |
| H28B | 5484 | 5537 | 4074 | 69 |
| H28C | 4848 | 4583 | 3883 | 69 |

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

| | |
|-----------------|-----------|
| Br1-C7-C8-C9 | -174.0(4) |
| Br2-C17-C18-C19 | -180.0(3) |
| C1-C3-C26-O3 | 78.7(6) |
| C1-C3-C26-O4 | -101.4(5) |
| C1-C3-N2-C2 | -7.6(5) |
| C1-C3-N2-C20 | 153.3(4) |
| C1-C4-C5-C6 | -175.6(4) |
| C1-C4-C9-C8 | 176.1(4) |
| C2-C14-C15-C16 | -177.9(4) |
| C2-C14-C19-C18 | 178.8(4) |
| C3-C1-C4-C5 | 92.3(5) |
| C3-C1-C4-C9 | -86.6(5) |
| C3-C1-N1-C2 | -35.8(4) |
| C3-C1-N1-C10 | -167.8(4) |
| C3-C26-O4-C27 | 174.3(4) |
| C4-C1-C3-C26 | 25.9(6) |
| C4-C1-C3-N2 | 146.6(4) |
| C4-C1-N1-C2 | -158.2(4) |
| C4-C1-N1-C10 | 69.8(5) |
| C4-C5-C6-C7 | -0.9(7) |
| C5-C4-C9-C8 | -2.7(7) |
| C5-C6-C7-Br1 | 174.5(4) |
| C5-C6-C7-C8 | -2.0(7) |
| C6-C7-C8-C9 | 2.5(7) |
| C7-C8-C9-C4 | -0.1(7) |
| C9-C4-C5-C6 | 3.2(7) |
| C10-C11-O2-C12 | 170.6(4) |
| C11-C10-N1-C1 | 64.2(5) |

| | |
|-----------------|-----------|
| C11-C10-N1-C2 | -64.6(5) |
| C13-C12-O2-C11 | 169.1(4) |
| C14-C2-N1-C1 | 153.0(4) |
| C14-C2-N1-C10 | -74.6(5) |
| C14-C2-N2-C3 | -132.1(4) |
| C14-C2-N2-C20 | 67.3(6) |
| C14-C15-C16-C17 | -1.2(7) |
| C15-C14-C19-C18 | 1.3(7) |
| C15-C16-C17-Br2 | -179.1(3) |
| C15-C16-C17-C18 | 1.8(7) |
| C16-C17-C18-C19 | -0.9(7) |
| C17-C18-C19-C14 | -0.7(7) |
| C19-C14-C15-C16 | -0.4(7) |
| C20-C21-C22-C23 | 0.1(7) |
| C21-C20-C25-C24 | 0.4(7) |
| C21-C20-N2-C2 | -5.9(7) |
| C21-C20-N2-C3 | -164.9(4) |
| C21-C22-C23-C24 | -0.4(7) |
| C22-C23-C24-C25 | 0.7(7) |
| C23-C24-C25-C20 | -0.7(7) |
| C25-C20-C21-C22 | -0.1(7) |
| C25-C20-N2-C2 | 175.1(4) |
| C25-C20-N2-C3 | 16.2(7) |
| C26-C3-N2-C2 | 113.4(4) |
| C26-C3-N2-C20 | -85.7(5) |
| C28-C27-O4-C26 | -98.6(6) |
| N1-C1-C3-C26 | -95.2(4) |
| N1-C1-C3-N2 | 25.5(4) |
| N1-C1-C4-C5 | -153.1(4) |
| N1-C1-C4-C9 | 28.1(6) |

| | |
|----------------|-----------|
| N1-C2-C14-C15 | 97.9(5) |
| N1-C2-C14-C19 | -79.5(5) |
| N1-C2-N2-C3 | -13.5(5) |
| N1-C2-N2-C20 | -174.2(4) |
| N1-C10-C11-O1 | -17.7(7) |
| N1-C10-C11-O2 | 164.0(4) |
| N2-C2-C14-C15 | -148.3(4) |
| N2-C2-C14-C19 | 34.2(6) |
| N2-C2-N1-C1 | 31.2(4) |
| N2-C2-N1-C10 | 163.6(4) |
| N2-C3-C26-O3 | -37.2(7) |
| N2-C3-C26-O4 | 142.7(4) |
| N2-C20-C21-C22 | -179.1(5) |
| N2-C20-C25-C24 | 179.4(4) |
| O1-C11-O2-C12 | -7.8(7) |
| O3-C26-O4-C27 | -5.8(7) |

Symmetry transformations used to generate equivalent atoms:

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

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