Electronic Supplementary Material (ESI) for Chemical Communications

Chiral Guanidine-Catalyzed Asymmetric Direct Vinylogous Michael Reaction of α,β-Unsaturated γ-Butyrolactam with Alkylidene Malonates

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Supporting Information

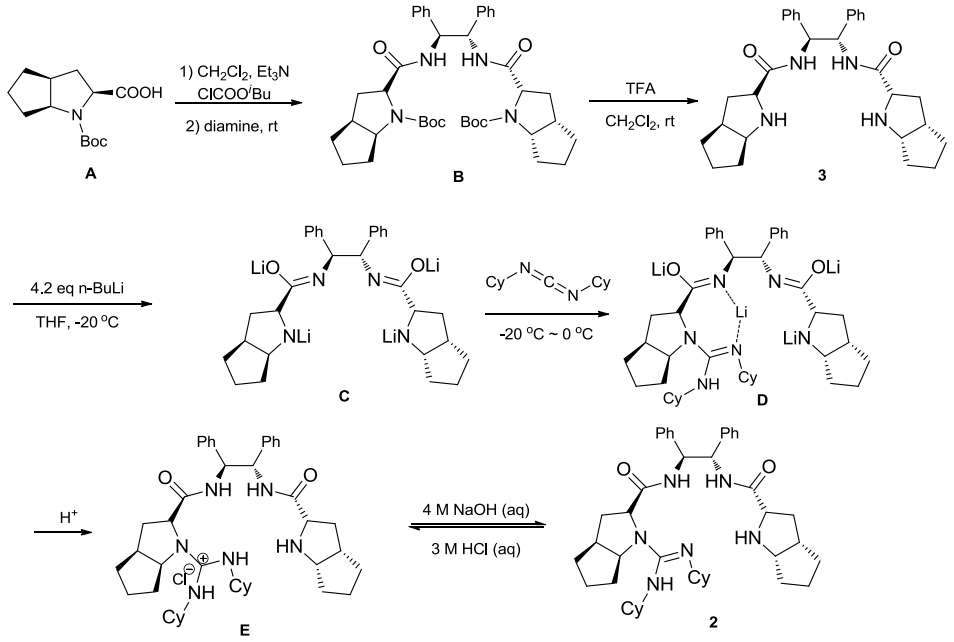
Contents of the supporting information:

1. General Remarks

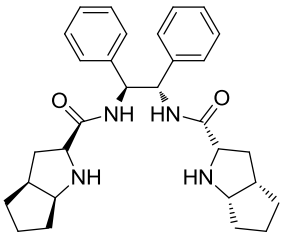
The ^{1}H NMR spectra were recorded at 300 MHz or 400 MHz. The chemical shifts are reported in ppm downfield to $CDCl_3$ (δ = 7.26) or d_6-DMSO (δ = 2.50) for ^{1}H NMR. Coupling constants in ^{1}H NMR were in Hz. ^{13}C NMR spectra were collected on commerical instruments (75 MHz or 100 MHz) with complete proton decoupling. Chemical shifts are reported in ppm with the solvent resonance as internal standard ($CDCl_3$, δ = 77.0 or d_6-DMSO, δ = 39.4). The enantiomeric excess (ee) of the products were determined by HPLC using Chiralpak AD-H or IA columns with hexane/isopropanol as eluent, and the retention times were compared to corresponding racemic samples. Optical rotations were measured on a commercial polarimeter and reported as follows: $[\alpha]_D^T$ (c = g/100 mL, in solvent). Melting points (m.p.) were measured on electrothermal digital melting point apparatus and were uncorrected.

α,β-Unsaturated γ-butyrolactam **4** was prepared according to the reported procedure.[1] The guanidines were prepared according to the methods mentioned in catalyst preparation section.[2]

2. Procedure and Characterization of the catalysts[2]



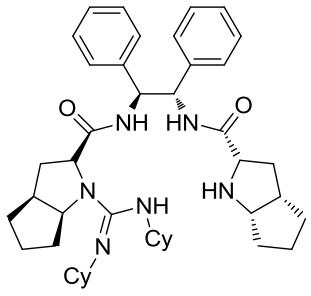
To a solution of **A** (2.4 g, 9.4 mmol) in CH_2Cl_2 (40 mL) was added Et_3N (1.31 mL, 9.4 mmol), isobutyl carbonochloridate (1.23 mL, 9.4 mmol) at 0 °C under stirring. After 10 min, (1*S*, 2*S*)-1,2-diphenylethane-1,2-diamine (0.951 g, 4.48 mmol) was added. The reaction was allowed to warm to room temperature and detected by TLC. Overnight, the mixture was washed with 1 N $KHSO_4$ solution, saturated $NaHCO_3$ solution, brine, dried over anhydrous Na_2SO_4 and concentrated and purified through flash chromatograph (EtOAc : petroleum ether = 1 : 3) as white solid. TFA (6 mL) was added to the CH_2Cl_2 (6 mL) solution of the amide, and stirred until reaction was finished (1 h). Then, the solvent was evaporated, and H_2O (10 mL) was added. The pH value of the mixture was brought into the range of 10–12 by the addition of 2 N NaOH solution. The aqueous phase was extracted with CH_2Cl_2 (3 × 30 mL). The combined organic phase was washed with brine, dried over anhydrous Na_2SO_4, and evaporated in vacuo to get a kind of white foam **3**.



(2*S*,3a*S*,6a*S*)-*N*-((1*S*,2*S*)-2-((2*R*,3a*S*,6a*S*)-octahydrocyclopenta[*b*]pyrrole-2-carboxamido)-1,2-diphenylethyl)-octahydrocyclopenta[*b*]pyrrole-2-carboxamide (**3**): $[\alpha]_D^{15} = -7.4$ (c = 0.20, in MeOH). m.p. 90 – 94 °C. ^{1}H NMR (400 MHz, d_6-DMSO) δ 8.53 (2 H, d, *J* = 8.3 Hz), 7.25 – 7.10 (10 H, m), 5.24

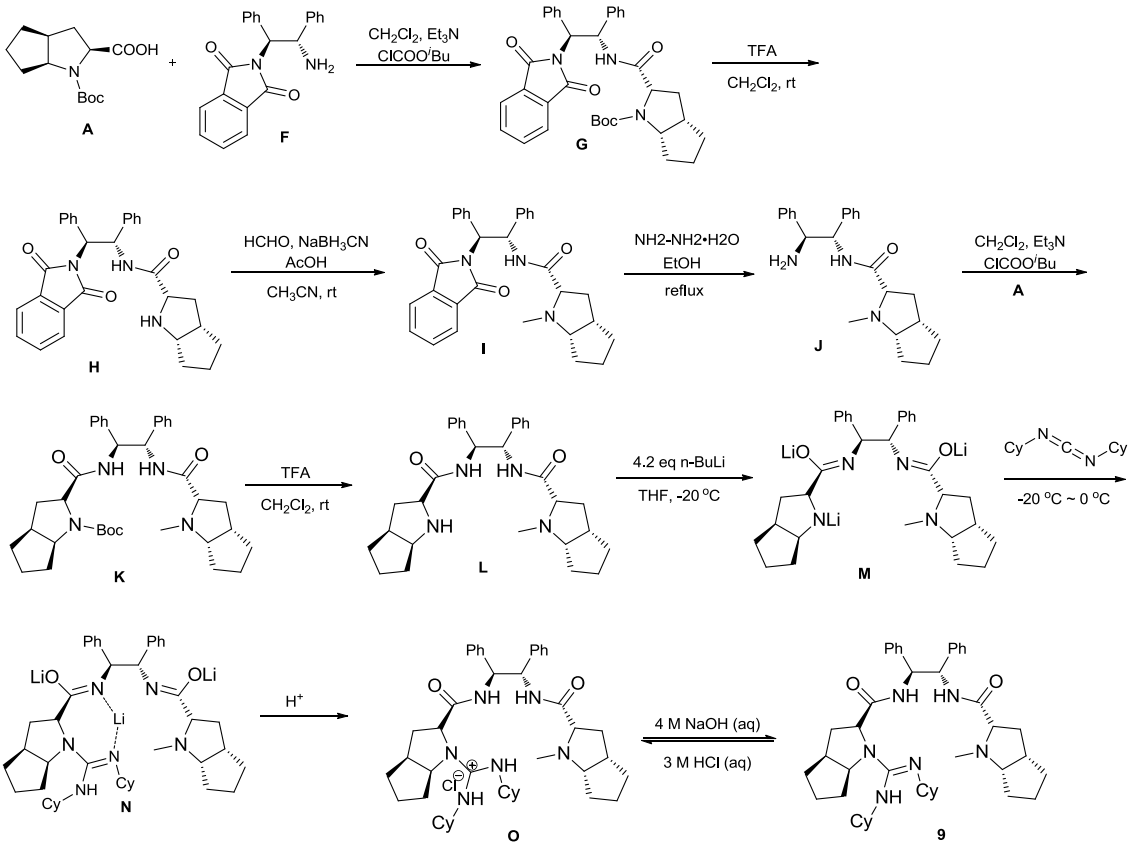
– 5.14 (2 H, m), 3.66 – 3.55 (2 H, m), 3.52 – 3.44 (4 H, m), 2.50 – 2.38 (2 H, m), 2.17 – 2.05 (2 H, m), 1.56 – 1.36 (10 H, m), 1.26 – 1.15 (2 H, m), 1.12 – 1.03 (2 H, m). ^{13}C NMR δ (100 MHz, d_6-DMSO): 172.66, 139.52, 127.85, 127.30, 127.01, 63.32, 61.96, 56.38, 42.49, 37.92, 34.06, 32.17, 23.54. HRMS (ESI): calcd for $C_{30}H_{38}N_4O_2$ [M+H$^+$] 487.3068, found 487.3075.

2.4 M *n*-BuLi in *n*-hexane (4.2 eq, 2.63 mL) was injected into a solution of **3** (730 mg, 1.5 mmol) in THF (40 mL) dropwise over 10 mins under nitrogen atmosphere at −20 °C with well stirring. For additional 10 mins, a solution of *N,N'*-dicyclohexylcarbodiimide (1.3 eq., 402 mg, 1.95 mmol) in 10 mL THF was added dropwise in 10 mins. The reaction was allowed to warm to room temperature, and detected by TLC. After 48 h, the mixture was evaporated under reduced pressure to get rid of THF, and the pH value of the mixture was brought into the range of 0–1 by the addition of 2 N HCl. The aqueous phase was extracted with CH_2Cl_2 (3 × 30 mL). The combined organic phase was washed with brine, dried over anhydrous $MgSO_4$, and evaporated in vacuum, and purified through flash chromatograph on silica gel (EtOAc : MeOH = 3:1) to produce **E**. The white foam **E** in CH_2Cl_2 (10 mL) was added 5 N NaOH (10 mL) and stirred until the basification was finished (10 mins). The pH value of the mixture was kept in the range of 11–12. The aqueous phase was extracted with CH_2Cl_2 (3 × 20 mL). The combined organic phase was washed with 3 N NaOH in birne, dried over anhydrous $NaSO_4$ and evaporated in vacuum. Finally, a white solid **2** was obtained. Then it was dissolved in CH_2Cl_2 and filtration through Celite to remove the silicone gel, concentrated to get a kind of white solid (540 mg, 52% yield).



(2*S*,3a*S*,6a*S*)-*N*-((1*S*,2*S*)-2-((2*R*,3a*S*,6a*S*)-1-(carbamimidoyl)-octahydrocyclopenta[*b*]pyrrole-2-carboxamido)-1,2-diphenylethyl)-octahydrocyclopenta[*b*]pyrrole-2-carboxamide（**2**）：$[\alpha]_D^{16}$ = −53.0 (c = 0.23, in CH_2Cl_2). m.p. 78 – 82 °C. ^{1}H NMR (400 MHz, $CDCl_3$) δ 7.24 – 6.97 (10 H, m), 5.15 (2 H, s), 4.68 (1 H, s), 4.03 (1 H, d, *J* = 4.8 Hz), 3.71 (1 H, t, *J* = 6.4 Hz), 3.58 (1 H, t, *J* = 8.4 Hz), 3.01 (2 H, s), 2.65 – 2.44 (2 H, m), 2.31 – 2.19 (1 H, m), 2.15-1.95 (2 H, m), 1.94 – 1.41 (20 H, m), 1.40 – 0.91 (15 H, m). ^{13}C NMR δ (75 MHz, $CDCl_3$): 174.60, 174.06, 171.75, 139.61, 138.89, 128.06, 127.98, 127.86, 127.83, 127.71, 127.28, 127.19, 127.05, 126.82, 126.23, 77.20, 66.65, 65.92, 64.94, 63.56, 62.56, 58.44, 58.03, 57.21, 43.35, 42.79,

42.62, 38.17, 35.06, 34.92, 33.38, 33.07, 32.50, 30.74, 29.58, 25.49, 25.31, 24.93, 24.63, 23.72. HRMS (ESI): calcd for $C_{43}H_{60}N_6O_2$ [M+H$^+$] 693.4851, found 693.4852.



To a solution of **A** (1.28 g, 5 mmol) in CH_2Cl_2 (40 mL) was added Et_3N (0.84 mL, 6 mmol), isobutyl carbonochloridate (0.84 mL, 6 mmol) at 0 ^oC under stirring. After 10 min, **F** (1.54 g, 4.5 mmol) was added. The reaction was allowed to warm to room temperature, and detected by TLC. After 3 hours, the mixture was washed with 1 N $KHSO_4$ solution, saturated $NaHCO_3$ solution, brine, dried over anhydrous Na_2SO_4 and concentrated and purified through flash chromatograph (EtOAc : petroleum ether = 1 : 2) as white solid. TFA (4 mL) was added to the CH_2Cl_2 (4 mL) solution of the amide and stirred until reaction was finished (1 h). Then, the solvent was evaporated, and H_2O (10 mL) was added. The pH value of the mixture was brought into the range of 10–12 by the addition of 2 N NaOH solution. The aqueous phase was extracted with CH_2Cl_2 (3 × 30 mL). The combined organic phase was washed with brine, dried over anhydrous Na_2SO_4 and evaporated in vacuo to get a kind of white foam **H**.

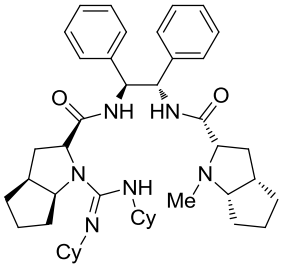
To a solution of **H** (1.811 g, 3.78 mmol) in CH_3CN (15 mL) was added paraformaldehyde $(CH_2O)_n$

(0.341 g, 11.34 mmol, 3 eq) at r.t. under stirring. After 10 min, $NaBH_3CN$ (0.275 g, 4.16 mmol, 1.1 eq) was added stirring for 15 min, then glacial acetic acid (0.65 mL, 11.34 mmol, 3.0 eq) was added. The reaction was detected by TLC. After 2 hours, the residue was filtered, the organic phase was concentrated and dissolved in CH_2Cl_2. The pH value of the mixture was brought into the range of 7–8 by the addition of sat. $NaHCO_3$ solution. The aqueous phase was extracted with CH_2Cl_2 (3 × 30 mL). The combined organic phase was washed with brine, dried over anhydrous Na_2SO_4, concentrated and purified through flash chromatograph (EtOAc : petroleum ether = 1 : 3) to get a white solid **I**. Then **I** and NH_2-NH_2 • H_2O was dissolved in EtOH, and the reaction was allowed to reflux, and detected by TLC. After 3 hours, the residue was filtered, the organic phase was concentrated and dissolved in CH_2Cl_2. This step was repeated third times, then the mixture was concentrated and purified through flash chromatograph (EtOAc : petroleum ether = 1 : 1) to get a kind of white foam **J**.

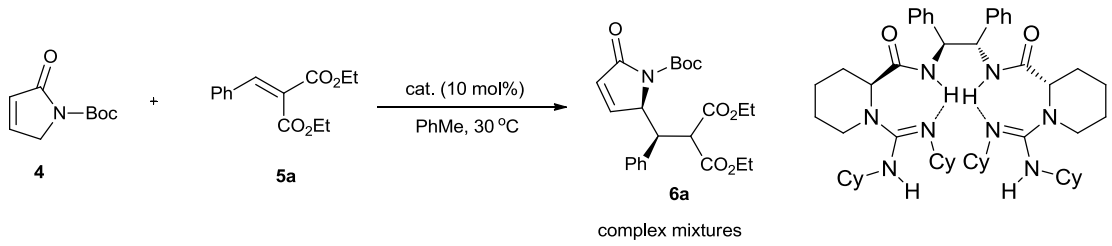
Synthesis of **L** from **J** was according to the procedure for **H** from **F**. The mixture was isolated by column chromatography on silica gel (EtOAc : petroleum ether = 4 : 1) to afford **L** as a white solid. ^{1}H NMR (400 MHz, $CDCl_3$) δ 8.28 (1 H, d, *J* = 8.0 Hz), 7.87 (1 H, d, *J* = 7.6 Hz),7.26 – 6.92 (10 H, m), 5.30 – 5.15 (2 H, m), 3.74 (1 H, t, *J* = 6.0 Hz), 3.62 (1 H, t, *J* = 8.0 Hz), 2.92 (2 H, t, *J* = 8.8 Hz), 2.74 (2 H, s), 2.55 – 2.42 (2 H, m), 2.37 – 2.20 (5 H, m), 1.75 – 1.65 (1 H, m), 1.65 – 1.55 (1 H, m), 1.55 – 1.35 (7 H, m), 1.35 – 1.17 (3 H, m), 1.17 – 1.05 (1 H, m). ^{13}C NMR δ (100 MHz, $CDCl_3$): 174.24, 174.04, 138.66, 128.36, 128.34 127.58, 127.54, 127.28, 127.27, 72.43, 71.38, 63.67, 62.47, 57.66, 57.64, 42.67, 41.20, 40.53, 38.36, 37.93, 35.13, 33.33, 32.82, 32.39, 24.00, 23.72.

2.4 M *n*-BuLi in *n*-hexane (3.5 eq, 1.45 mL) was injected into a solution of **L** (497 mg, 0.993 mmol) in THF (40 mL) dropwise over 10 mins under nitrogen atmosphere at −20 ^{o}C with well stirring. For additional 10 mins, a solution of *N,N'*-dicyclohexylcarbodiimide (1.5 eq., 307 mg, 1.49 mmol) in 10 mL THF was added dropwise in 10 mins. The reaction was allowed to warm to room temperature, and detected by TLC. After 48 h, the mixture was evaporated under reduced pressure to get rid of THF, and the pH value of the mixture was brought into the range of 0–1 by the addition of 2 N HCl. The aqueous phase was extracted with CH_2Cl_2 (3 × 30 mL). The combined organic phase was washed with brine, dried over anhydrous $MgSO_4$, evaporated in vacuum, and purified through flash chromatograph on silica gel (EtOAc : MeOH = 5:1) to produce **O**. The white foam **O** in CH_2Cl_2 (10 mL) was added 5

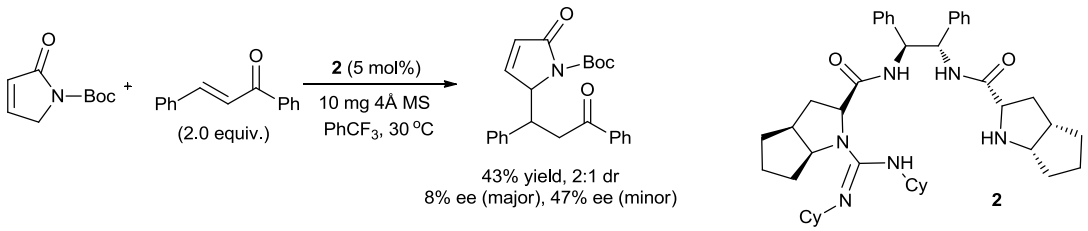
N NaOH (10 mL) and stirred until the basification was finished (10 mins). The pH value of the mixture was kept in the range of 11–12. The aqueous phase was extracted with CH_2Cl_2 (3 × 20 mL). The combined organic phase was washed with 3 N NaOH in birne, dried over anhydrous $NaSO_4$ and evaporated in vacuum. Finally, a white solid **9** was obtained. Then it was dissolved in CH_2Cl_2, and filtration through Celite to remove the silicone gel, concentrated to get a kind of white solid (442 mg, 63% yield).



(2*S*,3a*S*,6a*S*)-*N*-((1*S*,2*S*)-2-((2*R*,3a*S*,6a*S*)-1-(carbamimidoyl)-octahydrocyclopenta[*b*]pyrrole-2-carboxamido)-1,2-diphenylethyl)-1-methyl-octahydrocyclopenta[*b*]pyrrole-2-carboxamide (9): $[\alpha]_D^{15}$ = −119.5 (c = 0.23, in CH_2Cl_2). m.p. 58 – 62 °C. ^{1}H NMR (300 MHz, $CDCl_3$) δ 7.18 – 6.95 (10 H, m), 5.25 – 5.05 (2 H, m), 4.72 (1 H, s), 4.01 (1 H, d, *J* = 4.5 Hz), 3.05 – 2.93 (2 H, m), 2.93 – 2.80 (2 H, m), 2.60 – 2.40 (2 H, m), 2.31 – 2.21 (4 H, m), 2.10 – 1.87 (2 H, m), 1.62 (19 H, m), 1.41 – 1.07 (15 H, m). ^{13}C NMR δ (75 MHz, $CDCl_3$): 174.35, 173.34, 140.15, 138.77, 127.94, 127.83, 127.29, 127.19, 126.93, 77.20, 72.32, 71.44, 65.49, 62.07, 58.11, 57.90, 42.47, 41.14, 40.59, 38.21, 34.09, 33.45, 32.71, 31.87, 30.98, 30.24, 29.64, 25.54, 25.42, 25.32, 24.74, 24.13. HRMS (ESI): calcd for $C_{44}H_{64}N_6O_2$ [M+H$^+$] 707.5007, found 707.5001.



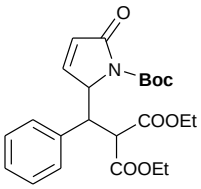
C_2-symmetric bisguanidine catalysts, perviously used in the catalytic asymmetric reactions of azlactone, afforded complex mixtures.



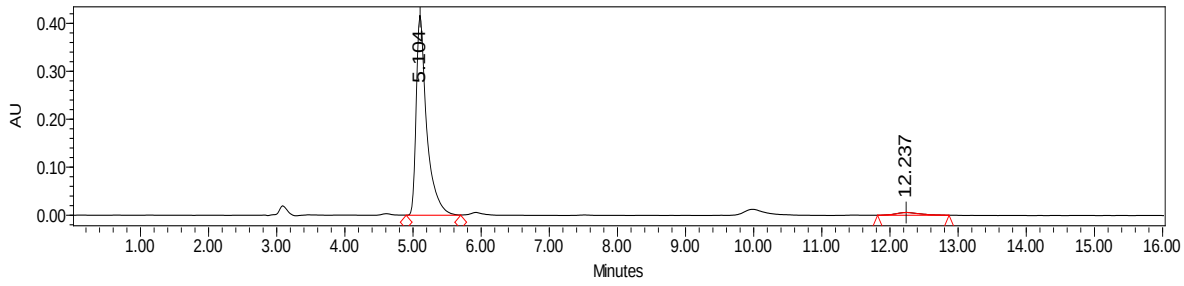
When α,β-unsaturated ketones, such as chalcone and cinnamone, were tested under the optimized conditions for this reaction, unsatisfied results were obtained. For chalcone, the corresponding product was obtained in 43% yield, 8% ee, 2:1 dr (47% ee for the minor isomer), although γ-butyrolactam was greatly consumed. For cinnamone, only trace amount of the desired product was obtained in 24 hours.

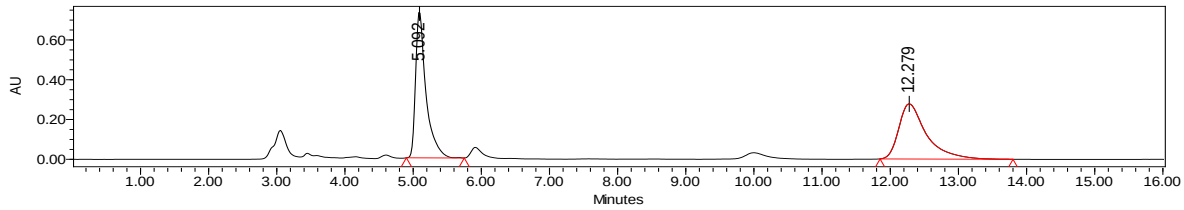
3. General procedure for the catalytic asymmetric vinylogous Michael reaction

α,β-Unsaturated γ-butyrolactam **4** (9.2 mg, 0.05 mmol) and the catalyst **2** (1.7 mg, 0.0025 mmol) were added into $PhCF_3$ (0.25 mL), then stirred for 15–30 mins at ambient temperature. Then the diethyl benzylidenemalonates **5a** (24.8 mg, 0.1 mmol) was added. The mixture was stirred at 30 ^{o}C for 18 hours. After that, the reaction mixture was purified directly by flash chromatography to give desired product **6a** in 82% yield. The *syn*/*anti* ratio of the product was determined by ^{1}H NMR analysis or HPLC.

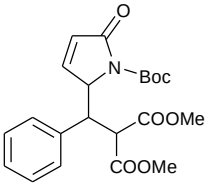


***tert*-butyl 2-(3-ethoxy-2-(ethoxycarbonyl)-3-oxo-1-phenylpropyl)-5-oxo-2*H*-pyrrole-1(5*H*)-carboxylate（6a）:** The reaction time is 18 hours. The mixture was isolated by column chromatography on silica gel (3:1 P.E./EtOAc) to afford **6a** (82% yield, 95:5 dr and 94% ee). ^{1}H NMR (300 MHz, $CDCl_3$) δ 7.36 – 7.27 (3H, m), 7.21 – 7.19 (2H, m), 7.08 – 7.06 (1H, m), 6.13 (1H, dd, *J* = 7.6, 1.4 Hz), 4.84 (1H, t, *J* = 1.7 Hz), 4.50 (1H, dd, *J* = 13.2, 3.6 Hz), 4.22 (2H, dd, *J* = 7.2, 1.5 Hz), 3.93 – 3.81 (3H, m), 1.65 (9H, s), 1.27 (3H, t, *J* = 7.1Hz), 0.88 (3H, t, *J* = 7.1 Hz) ppm. ^{13}C NMR δ (75 MHz, $CDCl_3$): 168.70, 167.81, 167.07, 149.29, 146.46, 137.11, 128.80, 128.43, 128.24, 127.78, 83.54, 65.52, 62.58, 61.48, 51.89, 45.69, 28.17, 13.82, 13.52. HRMS (ESI): calcd for $C_{23}H_{29}NO_7$ [M+Na^+] 454.1836, found 454.1837. The ee was determined by HPLC analysis using a Chiral ADH column (*n*-hexane/2-propanol 80: 20, 1.0 mL/min, λ = 210 nm; t_1 = 5.1 min, t_2 = 12.2 min).

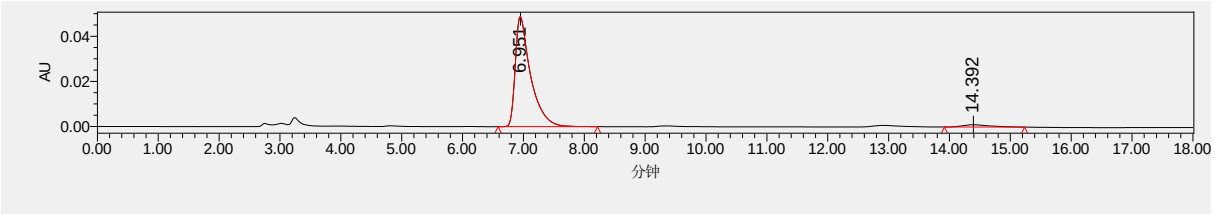


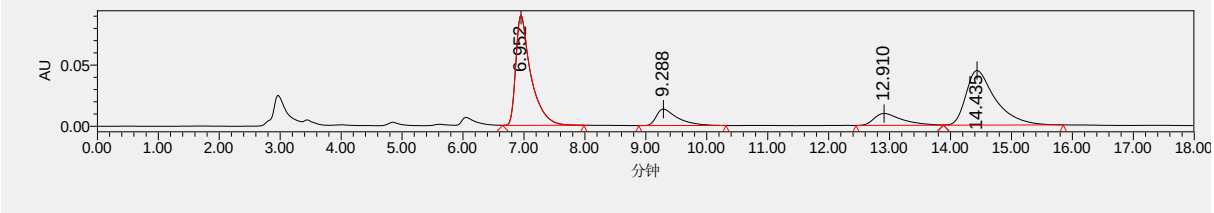


	Retention Time	Area	% Area	Height	% Height
1	5.104	4423774	91.48	416623	94.93
2	5.921	52436	1.08	4929	1.12
3	9.982	222066	4.59	11659	2.66
4	12.237	137633	2.85	5665	1.29

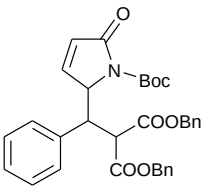


***tert*-butyl 2-(3-methoxy-2-(methoxycarbonyl)-3-oxo-1-phenylpropyl)-5-oxo-2*H*-pyrrole-1(5*H*)-carboxylate （6b）:** The reaction time is 18 hours. The mixture was isolated by column chromatography on silica gel (3:1 P.E./EtOAc) to afford **6b** (85% yield, 95:5 dr and 93% ee). ^{1}H NMR (300 MHz, $CDCl_3$) δ 7.36 – 7.27 (3H, m), 7.20 – 7.18 (2H, m), 7.04 (1H, dd, *J* = 6.2, 1.6 Hz), 6.15 (1H, dd, *J* = 6.2, 1.6 Hz), 4.81 (1H, dt, *J* = 3.6, 1.8 Hz), 4.53 (1 H, dd, *J* = 12.3, 3.5 Hz), 3.85 (1H, d, *J* = 12.3 Hz), 3.76 (3H, s), 3.43 (3H, s), 1.65 (9H, s) ppm. ^{13}C NMR δ (75 MHz, $CDCl_3$): 168.71, 168.04, 167.41, 149.13, 146.05, 137.03, 128.90, 128.54, 127.89, 127.81, 83.60, 65.56, 53.51, 52.61, 51.25, 45.50, 28.11. HRMS (ESI): calcd for $C_{21}H_{25}NO_7$ [M+Na^+] 426.1523, found 426.1537. The ee was determined by HPLC analysis using a Chiral ADH column (*n*-hexane/2-propanol 85: 15, 1.0 mL/min, λ = 210 nm; t_1 = 6.9 min, t_2 = 14.4 min).

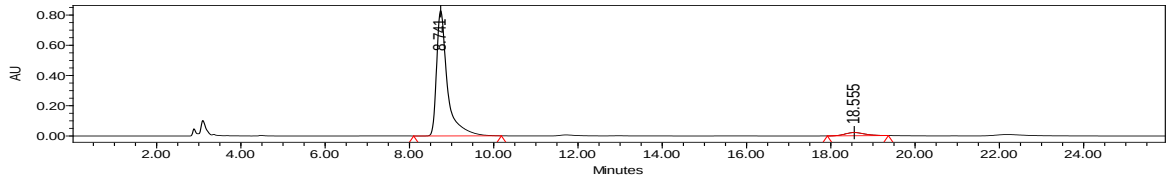


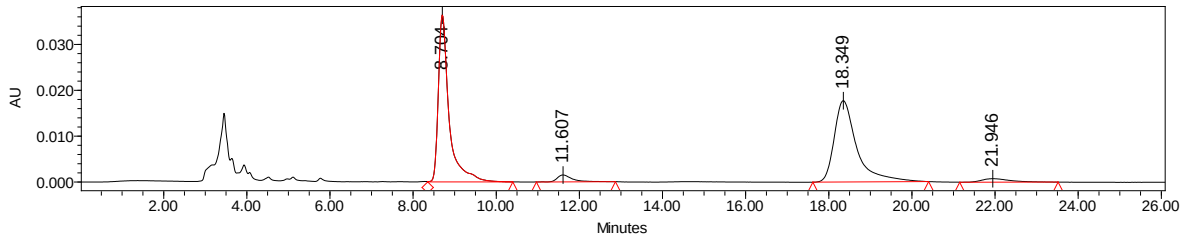


	Retention Time	Area	% Area	Height
1	6.942	11016297	92.74	631637
2	9.328	148584	1.25	6152
3	12.907	317180	2.67	10246
4	14.386	397264	3.34	12834

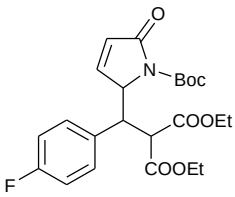


***tert*-butyl 2-(3-(benzyloxy)-2-(benzyloxycarbonyl)-3-oxo-1-phenylpropyl)-5-oxo-2*H*-pyrrole-1(5*H*)-carboxylate** （**6c**）: The reaction time is 18 hours. The mixture was isolated by column chromatography on silica gel (3:1 P.E./EtOAc) to afford **6c** (83% yield, 95: 5 dr and 91% ee). ^{1}H NMR (300 MHz, $CDCl_3$) δ 7.33 – 7.26 (7H, m), 7.25 – 7.11 (6H, m), 7.03 (1H, dd, *J* = 6.2, 2.0 Hz), 7.01 – 6.93 (2H, m), 6.11 (1H, dd, *J* = 6.2, 1.6 Hz), 5.29 (1H, d, *J* = 12.2 Hz), 5.11 (1H, d, *J* = 12.2 Hz), 4.91 – 4.86 (1H, m), 4.84 (2H, s), 4.55 (1H, dt, *J* = 8.8, 4.4 Hz), 3.98 (1H, d, *J* = 12.3 Hz), 1.65 (9H, s) ppm. ^{13}C NMR δ (75 MHz, $CDCl_3$): 168.79, 167.46, 166.75, 149.30, 146.48, 136.68, 135.11, 134.81, 128.88, 128.49, 128.43, 128.36, 128.26, 128.17, 128.07, 128.05, 127.92, 127.83, 83.64, 68.12, 67.24, 65.40, 51.75, 45.66, 28.14. HRMS (ESI): calcd for $C_{33}H_{33}NO_7$ [M+Na^+] 578.2149, found 578.2146. The ee was determined by HPLC analysis using a Chiral IA column (*n*-hexane/2-propanol 80: 20, 1.0 mL/min, λ = 210 nm; t_1 = 8.7 min, t_2 = 18.5 min).

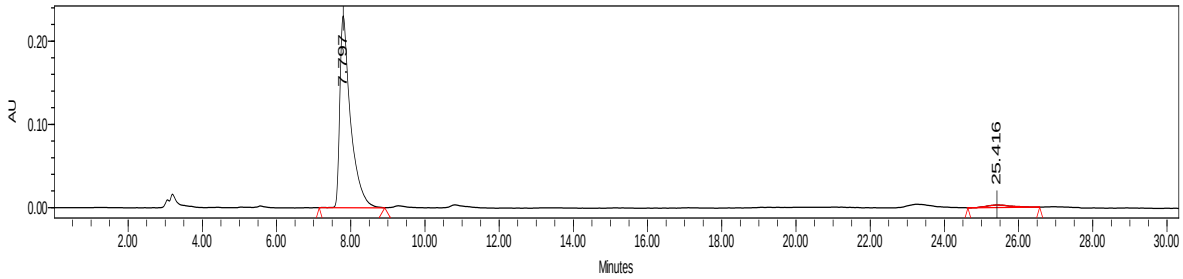


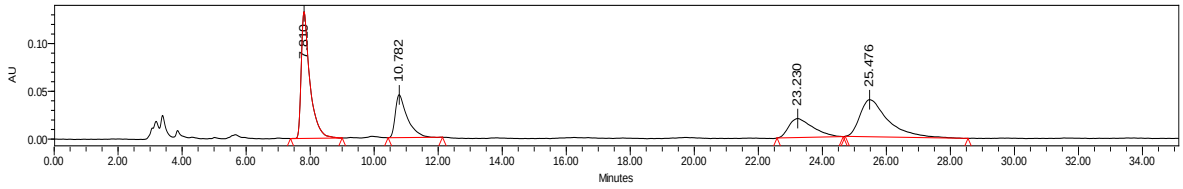


	Retention Time	Area	% Area	Height	% Height
1	8.741	14789268	92.15	830766	95.79
2	11.719	155708	0.97	6474	0.75
3	18.555	717051	4.47	21369	2.46
4	22.188	386808	2.41	8664	1.00

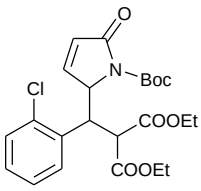


***tert*-butyl 2-(3-ethoxy-2-(ethoxycarbonyl)-1-(4-fluorophenyl)-3-oxopropyl)-5-oxo-2*H*-pyrrole-1(5*H*)-carboxylate （6d）**: The reaction time is 12 hours. The mixture was isolated by column chromatography on silica gel (3:1 P.E./EtOAc) to afford **6d** (78% yield, 95: 5 dr and 94% ee). ^{1}H NMR (300 MHz, $CDCl_3$) δ 7.20 – 7.12 (2 H, m), 7.07 – 6.95 (3 H, m), 6.10 (1 H, d, *J* = 6.1 Hz), 4.84 (1 H, s), 4.43 (1 H, dd, *J* = 12.2, 3.2 Hz), 4.19 (2 H, tt, *J* = 10.8, 5.3 Hz), 3.91 (2 H, dq, *J* = 11.0, 3.7 Hz), 3.82 (1 H, d, *J* = 12.2 Hz), 1.62 (9 H, s), 1.26 (3H, t, *J* = 7.0 Hz), 0.90 (3 H, t, *J* = 7.1 Hz). ^{13}C NMR δ (75 MHz, $CDCl_3$): 168.48, 167.64, 166.98, 163.67, 149.42, 146.44, 132.60, 129.88 (d, *J* = 8.0 Hz), 128.43, 115.83, 83.57, 65.09, 62.53, 61.52, 52.13, 45.07, 28.09, 13.77, 13.55. HRMS (ESI): calcd for $C_{23}H_{28}FNO_7$ [M+Na^+] 472.1742, found 472.1749. The ee was determined by HPLC analysis using a Chiral ADH column (*n*-hexane/2-propanol 90: 10, 1.0 mL/min, λ = 210 nm; t_1 = 7.8 min, t_2 = 25.4 min)

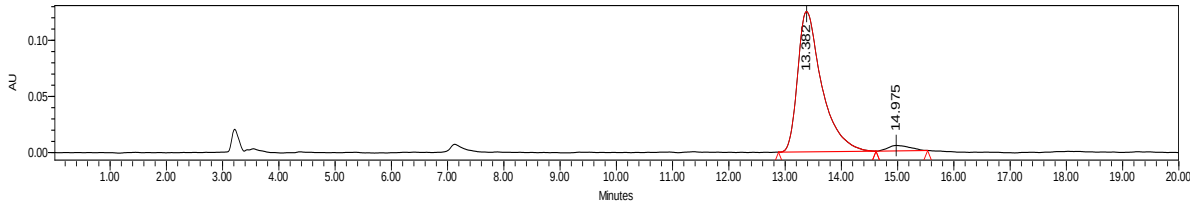


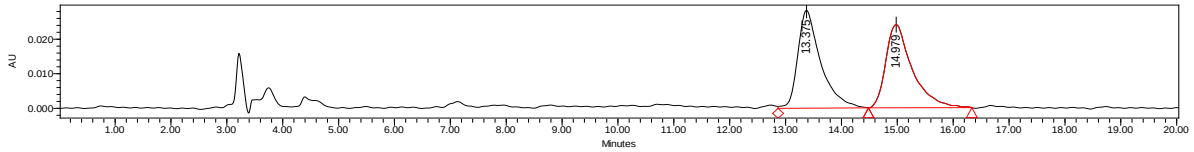


	Retention Time	Area	% Area	Height	% Height
1	7.797	4610041	92.30	230663	95.66
2	10.806	101335	2.03	3577	1.48
3	23.253	150777	3.02	3868	1.60
4	25.416	132576	2.65	3013	1.25

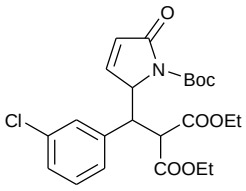


***tert*-butyl 2-(1-(2-chlorophenyl)-3-ethoxy-2-(ethoxycarbonyl)-3-oxopropyl)-5-oxo-2*H*-pyrrole-1(5*H*)-carboxylate （6e）:** The reaction time is 12 hours. The mixture was isolated by column chromatography on silica gel (3:1 P.E./EtOAc) to afford **6e** (75% yield, 95: 5 dr and 93% ee). ^{1}H NMR (300 MHz, $CDCl_3$) δ 7.43 – 7.34 (1 H, m), 7.24 – 7.16 (2 H, m), 7.13 – 7.03 (2 H, m), 6.02 (1 H, dd, *J* = 6.1, 1.5 Hz), 5.16 – 5.08 (1 H, m), 4.92 (1 H, dd, *J* = 12.2, 3.6 Hz), 4.33 – 4.21 (2 H, m), 4.01 – 3.93 (1 H, m), 3.93 – 3.80 (2 H, m), 1.62 (9 H, s), 1.29 (3 H, t, *J* = 7.2 Hz), 0.88 (3 H, t, *J* = 7.2 Hz) ppm. ^{13}C NMR δ (75 MHz, $CDCl_3$): 168.94, 167.75, 166.94, 149.96, 147.59, 134.91, 133.90, 130.19, 128.99, 128.92, 127.85, 126.79, 83.77, 62.74, 62.41, 61.55, 52.72, 42.34, 28.19, 13.87, 13.47. HRMS (ESI): calcd for $C_{23}H_{28}{}^{34.9689}ClNO_7$ [M+Na^+] 488.1447, found 488.1449. The ee was determined by HPLC analysis using a Chiral ADH column (*n*-hexane/2-propanol 95: 5, 1.0 mL/min, λ = 210 nm; t_1 = 13.4 min, t_2 = 15.0 min).

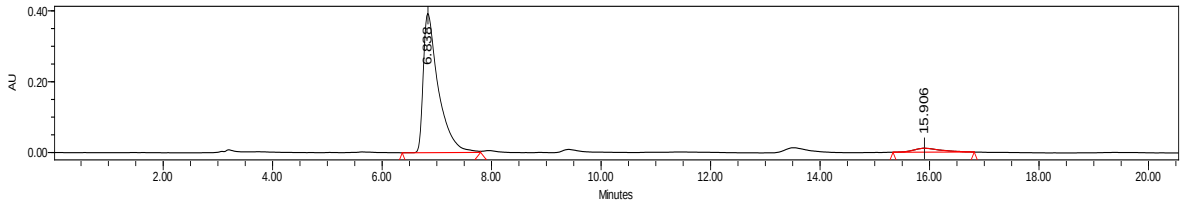


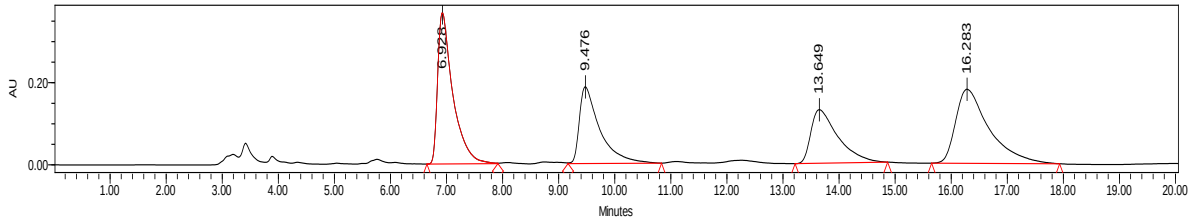


	Retention Time	Area	% Area	Height	% Height
1	13.382	3716516	96.56	125048	96.25
2	14.975	132556	3.44	4872	3.75

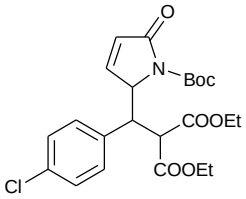


***tert*-butyl 2-(1-(3-chlorophenyl)-3-ethoxy-2-(ethoxycarbonyl)-3-oxopropyl)-5-oxo-2*H*-pyrrole-1(5*H*)-carboxylate （6f）**: The reaction time is 12 hours. The mixture was isolated by column chromatography on silica gel (3:1 P.E./EtOAc) to afford **6f** (80% yield, 94:6 dr and 90% ee). ^{1}H NMR (300 MHz, $CDCl_3$) δ 7.28 – 7.23 (2 H, m), 7.22 – 7.17 (1 H, m), 7.11 – 7.03 (2 H, m), 6.14 (1 H, dd, *J* = 6.2, 1.6 Hz), 4.86 – 4.79 (1 H, m), 4.45 (1 H, dd, *J* = 12.2, 3.3 Hz), 4.26 – 4.16 (2 H, m), 3.93 (2 H, qd, *J* = 7.1, 2.5 Hz), 3.83 (1 H, d, *J* = 12.2 Hz), 1.63 (9 H, s), 1.25 (3H, t, *J* = 7.1 Hz), 0.94 (3 H, t, *J* = 7.1 Hz) ppm. ^{13}C NMR δ (75 MHz, $CDCl_3$): 168.35, 167.54, 166.85, 149.34, 146.09, 139.07, 134.63, 130.03, 128.64, 128.46, 128.02, 126.31, 83.68, 65.04, 62.64, 61.63, 51.69, 45.36, 28.11, 13.77, 13.57. HRMS (ESI): calcd for $C_{23}H_{28}{}^{34.9689}ClNO_7$ [M+Na^+] 488.1447, found 488.1453. The ee was determined by HPLC analysis using a Chiral ADH column (*n*-hexane/2-propanol 90: 10, 1.0 mL/min, λ = 210 nm; t_1 = 6.8 min, t_2 = 15.9 min).

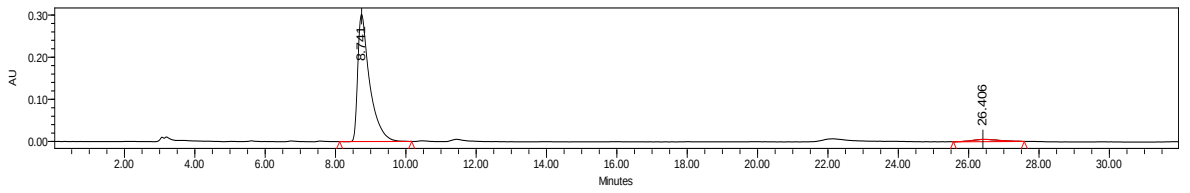


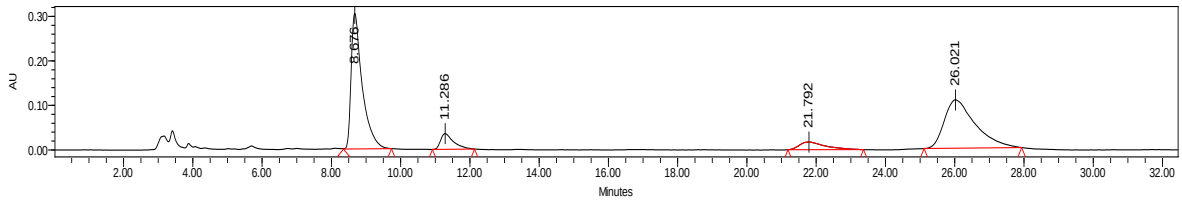


	Retention Time	Area	% Area	Height	% Height
1	6.838	7489721	89.61	393413	92.33
2	9.406	138472	1.66	8162	1.92
3	13.512	350351	4.19	13671	3.21
4	15.906	379209	4.54	10870	2.55

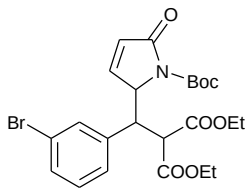


***tert*-butyl 2-(1-(4-chlorophenyl)-3-ethoxy-2-(ethoxycarbonyl)-3-oxopropyl)-5-oxo-2*H*-pyrrole-1(5*H*)-carboxylate （6g）**：The reaction time is 12 hours. The mixture was isolated by column chromatography on silica gel (3:1 P.E./EtOAc) to afford **6g** (85% yield, 95: 5 dr and 92% ee). ^{1}H NMR (300 MHz, $CDCl_3$) δ 7.31 – 7.26 (2 H, m), 7.17 – 7.11 (2 H, m), 7.02 (1 H, dd, *J* = 6.1, 1.9 Hz), 6.11 (1 H, dd, *J* = 6.3, 1.5 Hz), 4.83 (1 H, d, *J* = 1.5 Hz), 4.42 (1 H, dd, *J* = 12.1, 3.3 Hz), 4.28 – 4.15 (2 H, m), 3.91 (2 H, qd, *J* = 7.2, 3.6 Hz), 3.82 (1 H, d, *J* = 12.3 Hz), 1.62 (9 H, s), 1.26 (3 H, t, *J* = 6.4 Hz), 0.93 (3 H, t, *J* = 7.1 Hz) ppm. ^{13}C NMR δ (75 MHz, $CDCl_3$): 168.40, 167.58, 166.91, 149.41, 146.28, 135.41, 133.66, 129.56, 128.93, 128.52, 83.62, 64.97, 62.57, 61.59, 51.91, 45.16, 28.10, 13.77, 13.58. HRMS (ESI): calcd for $C_{23}H_{28}{}^{34.9689}ClNO_7$ [M+Na^+] 488.1447, found 488.1449. The ee was determined by HPLC analysis using a Chiral ADH column (*n*-hexane/2-propanol 90: 10, 1.0 mL/min, λ = 210 nm; t_1 = 8.7 min, t_2 = 26.4 min)

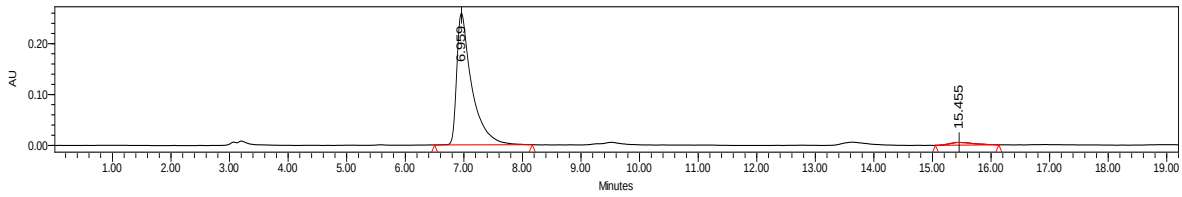


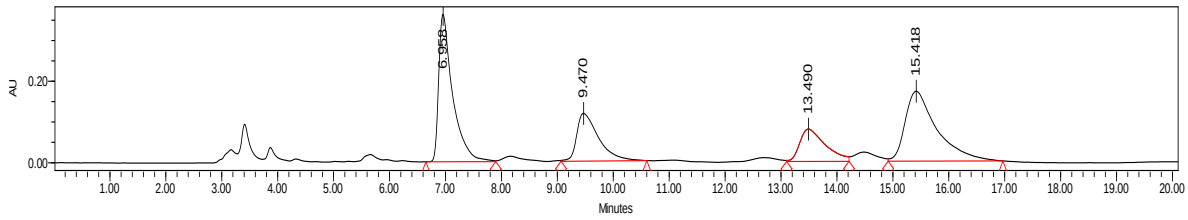


	Retention Time	Area	% Area	Height	% Height
1	8.741	7049617	90.70	302232	94.64
2	11.442	138381	1.78	5334	1.67
3	22.149	300553	3.87	6564	2.06
4	26.406	284103	3.66	5233	1.64

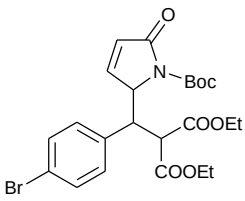


***tert*-butyl 2-(1-(3-bromophenyl)-3-ethoxy-2-(ethoxycarbonyl)-3-oxopropyl) -5-oxo-2*H*-pyrrole-1(5*H*)-carboxylate （6h）**: The reaction time is 12 hours. The mixture was isolated by column chromatography on silica gel (3:1 P.E./EtOAc) to afford **6h** (85% yield, 94:6 dr and 93% ee). ^{1}H NMR (300 MHz, $CDCl_3$) δ 7.45 – 7.30 (2 H, m), 7.22 – 7.17 (1 H, m), 7.15 – 7.10 (1 H, m), 7.04 (1 H, dd, *J* = 6.2, 1.8 Hz), 6.13 (1 H, dd, *J* = 6.1, 1.3 Hz), 4.85 – 4.78 (1 H, m), 4.43 (1 H, dd, *J* = 12.2, 3.3 Hz), 4.19 (2 H, q, *J* = 7.1 Hz), 3.92 (2 H, ddd, *J* = 14.1, 7.1, 2.0 Hz), 3.82 (1 H, d, *J* = 12.2 Hz), 1.62 (9 H, s), 1.25 (3 H, t, *J* = 7.1 Hz), 0.93 (3 H, t, *J* = 7.1 Hz). ^{13}C NMR δ (75 MHz, $CDCl_3$): 168.29, 167.48, 166.80, 149.29, 146.02, 139.32, 131.33, 130.90, 130.27, 128.62, 126.72, 122.75, 83.64, 65.02, 62.60, 61.60, 51.61, 45.29, 28.08, 13.73, 13.56. HRMS (ESI): calcd for $C_{23}H_{28}{}^{78.9183}BrNO_7$ [M+Na^+] 532.0941, found 532.0941. The ee was determined by HPLC analysis using a Chiral ADH column (*n*-hexane/2-propanol 90: 10, 1.0 mL/min, λ = 210 nm; t_1 = 6.9 min, t_2 = 15.4 min)

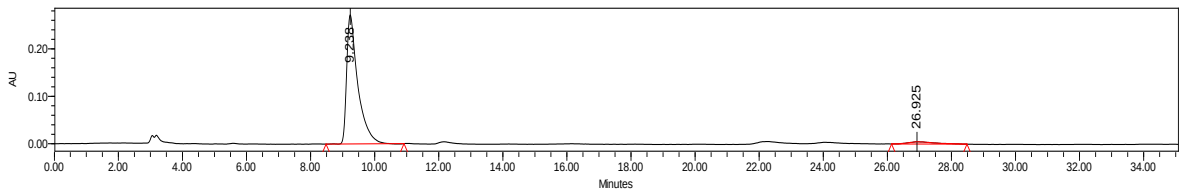


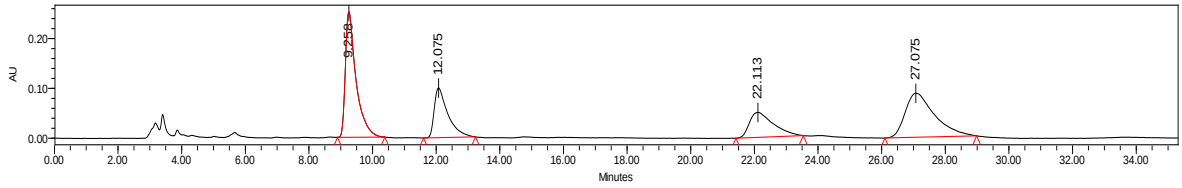


	Retention Time	Area	% Area	Height	% Height
1	6.959	4583960	91.12	259665	94.08
2	9.515	102729	2.04	4738	1.72
3	13.634	184210	3.66	6243	2.26
4	15.455	159824	3.18	5360	1.94

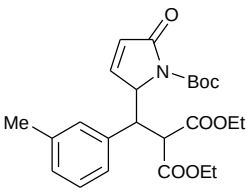


***tert*-butyl 2-(1-(4-bromophenyl)-3-ethoxy-2-(ethoxycarbonyl)-3-oxopropyl)-5-oxo-2*H*-pyrrole-1(5*H*)-carboxylate （6i）:** The reaction time is 12 hours. The mixture was isolated by column chromatography on silica gel (3:1 P.E./EtOAc) to afford **6i** (86% yield, 95: 5 dr and 93% ee). ^{1}H NMR (300 MHz, $CDCl_3$) δ 7.48 – 7.40 (2 H, m), 7.10 – 7.04 (2 H, m), 7.01 (1 H, dd, *J* = 6.2, 2.0 Hz), 6.10 (1 H, dd, *J* = 6.1, 1.5 Hz), 4.86 – 4.79 (1 H, m), 4.41 (1 H, dd, *J* = 12.2, 3.3 Hz), 4.25 – 4.15 (2 H, m), 3.91 (2 H, qd, *J* = 7.1, 3.5 Hz), 3.81 (1 H, d, *J* = 12.2 Hz), 1.61 (9 H, s), 1.25 (3 H, t, *J* = 6.3 Hz), 0.93 (3 H, t, *J* = 7.1 Hz). ^{13}C NMR δ (75 MHz, $CDCl_3$): 168.35, 167.54, 166.87, 149.38, 146.22, 135.95, 131.87, 129.86, 128.52, 121.72, 83.60, 64.88, 62.55, 61.58, 51.81, 45.20, 28.08, 13.75, 13.57. HRMS (ESI): calcd for $C_{23}H_{28}{}^{78.9183}BrNO_7$ [M+Na^+] 532.0941, found 532.0948. The ee was determined by HPLC analysis using a Chiral ADH column (*n*-hexane/2-propanol 90: 10, 1.0 mL/min, λ = 210 nm; t_1 = 9.2 min, t_2 = 26.9 min)

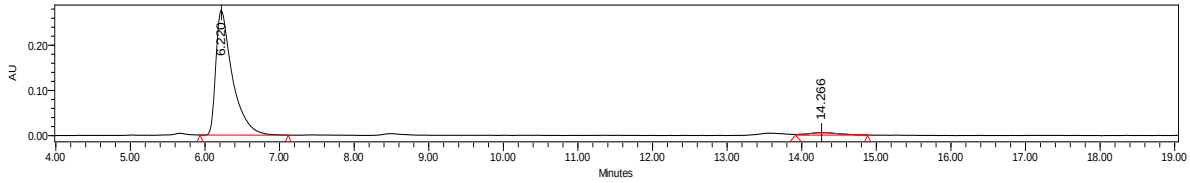


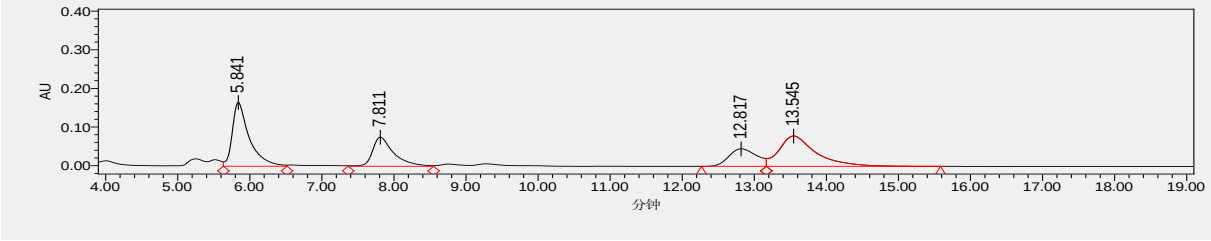


	Retention Time	Area	% Area	Height	% Height
1	9.238	6573578	90.91	272205	94.86
2	12.168	129194	1.79	4698	1.64
3	22.263	260003	3.60	5470	1.91
4	26.925	268317	3.71	4584	1.60

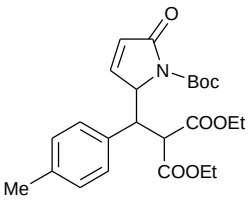


***tert*-butyl 2-(3-ethoxy-2-(ethoxycarbonyl)-3-oxo-1-*m*-tolylpropyl)-5-oxo-2*H*-pyrrole-1(5*H*)-carboxylate（6j）:** The reaction time is 18 hours. The mixture was isolated by column chromatography on silica gel (3:1 P.E./EtOAc) to afford **6j** (76% yield, 95: 5 dr and 93% ee). ^{1}H NMR (300 MHz, $CDCl_3$) δ 7.21 (1 H, t, *J* = 7.6 Hz), 7.11 – 7.01 (3 H, m), 6.98 (1 H, d, *J* = 7.7 Hz), 6.15 (1 H, dd, *J* = 6.2, 1.7 Hz), 4.81 (1 H, dt, *J* = 3.7, 1.9 Hz), 4.48 (1 H, dd, *J* = 12.2, 3.5 Hz), 4.25 – 4.15 (2 H, m), 3.98 – 3.84 (2 H, m), 3.80 (1 H, d, *J* = 12.2 Hz), 2.33 (3 H, s), 1.65 (9 H, s), 1.27 (3H, t, *J* = 6.4 Hz), 0.90 (3 H, t, *J* = 7.1 Hz). ^{13}C NMR δ (75 MHz, $CDCl_3$): 168.64, 167.83, 167.09, 149.31, 146.47, 138.45, 137.17, 129.20, 128.62, 128.48, 128.40, 125.01, 83.47, 65.68, 62.54, 61.41, 51.83, 45.54, 28.19, 21.41, 13.81, 13.55. HRMS (ESI): calcd for $C_{24}H_{31}NO_7$ [M+Na^+] 468.1993, found 468.2010. The ee was determined by HPLC analysis using a Chiral ADH column (*n*-hexane/2-propanol 90: 10, 1.0 mL/min, λ = 210 nm; t_1 = 6.2 min, t_2 = 14.2 min)

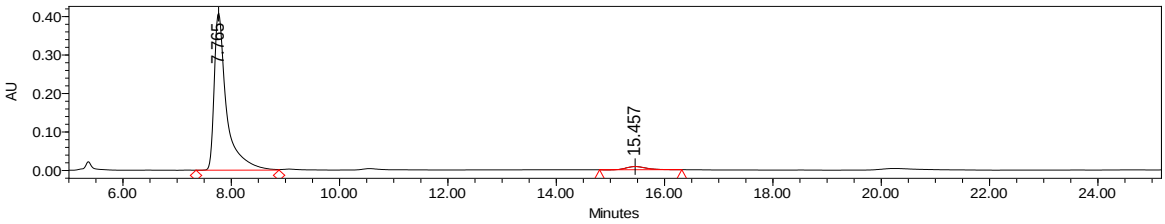


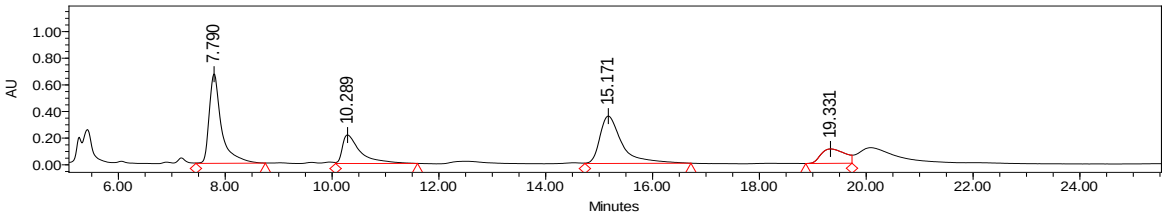


	Retention Time	Area	% Area	Height	% Height
1	6.220	4217125	92.45	276340	95.26
2	8.492	73018	1.60	3875	1.34
3	13.574	101911	2.23	4349	1.50
4	14.266	169532	3.72	5530	1.91

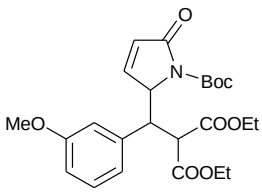


***tert*-butyl 2-(3-ethoxy-2-(ethoxycarbonyl)-3-oxo-1-*p*-tolylpropyl)-5-oxo-2*H*-pyrrole-1(5*H*)-carboxylate （6k）:** The reaction time is 18 hours. The mixture was isolated by column chromatography on silica gel (3:1 P.E./EtOAc) to afford **6k** (82% yield, 95: 5 dr and 93% ee). ^{1}H NMR (300 MHz, $CDCl_3$) δ 7.14 – 7.05 (5 H, m), 6.12 (1 H, dd, *J* = 6.2, 1.6 Hz), 4.85 – 4.78 (1 H, m), 4.46 (1 H, dd, *J* = 12.2, 3.5 Hz), 4.21 (2 H, tt, *J* = 7.1, 3.6 Hz), 3.97 – 3.83 (2 H, m), 3.81 (1 H, d, *J* = 12.2 Hz), 2.31 (3 H, s), 1.65 (9 H, s), 1.28 (3 H, t, *J* = 7.2 Hz), 0.92 (3 H, t, *J* = 7.1 Hz). ^{13}C NMR δ (75 MHz, $CDCl_3$): 168.80, 167.87, 167.12, 149.27, 146.60, 137.45, 133.98, 129.46, 128.35, 128.07, 83.49, 65.67, 62.55, 61.44, 51.90, 45.28, 28.17, 21.02, 13.81, 13.58. HRMS (ESI): calcd for $C_{24}H_{31}NO_7$ [M+Na^+] 468.1993, found 468.2004. The ee was determined by HPLC analysis using a Chiral IA column (*n*-hexane/2-propanol 90: 10, 1.0 mL/min, λ = 210 nm; t_1 = 7.8 min, t_2 = 15.4 min)

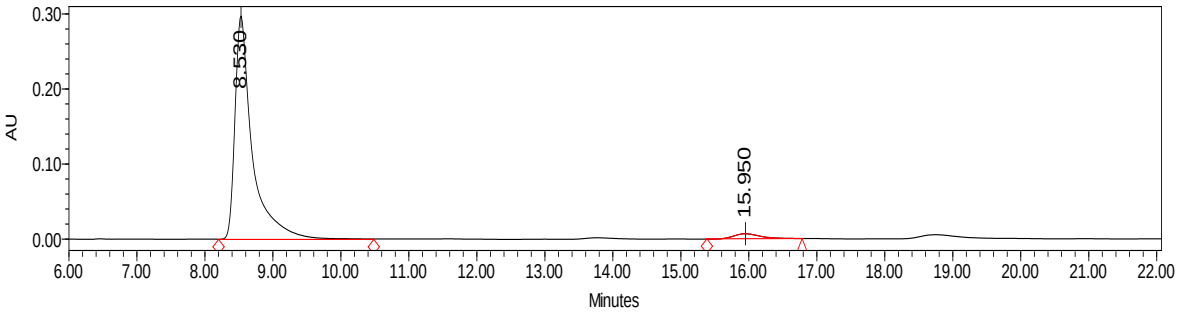


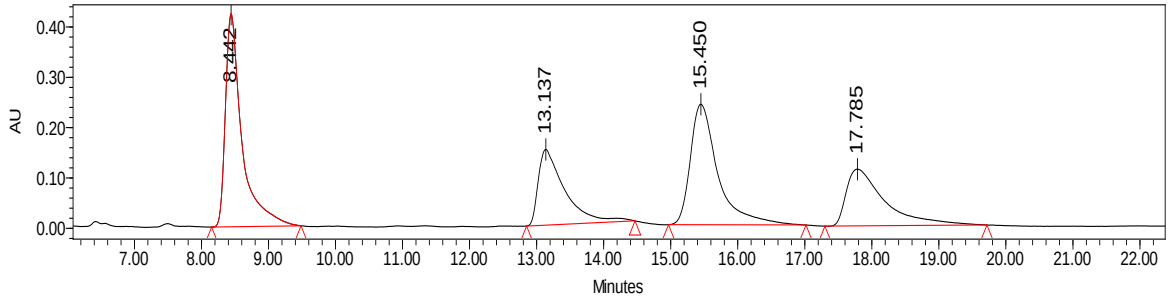


	Retention Time	Area	% Area	Height	% Height
1	7.765	6407496	93.56	408297	96.34
2	10.550	65914	0.96	3336	0.79
3	15.457	212502	3.10	8304	1.96
4	20.247	162445	2.37	3866	0.91

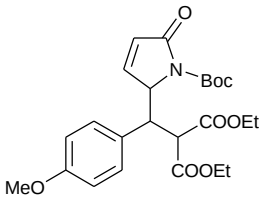


***tert*-butyl 2-(3-ethoxy-2-(ethoxycarbonyl)-1-(3-methoxyphenyl)-3-oxopropyl) -5-oxo-2*H*-pyrrole-1(5*H*)-carboxylate（6l）:** The reaction time is 18 hours. The mixture was isolated by column chromatography on silica gel (3:1 P.E./EtOAc) to afford **6l** (93% yield, 95: 5 dr and 93% ee). ^{1}H NMR (300 MHz, $CDCl_3$) δ 7.23 (1 H, d, *J* = 7.8 Hz), 7.07 (1 H, dd, *J* = 6.2, 2.0 Hz), 6.82 – 6.75 (3 H, m), 6.14 (1 H, dd, *J* 6.1, 1.6), 4.87 – 4.79 (1 H, m), 4.48 (1 H, dd, *J* = 12.5, 3.8 Hz), 4.25 – 4.15 (2 H, m), 3.99 – 3.85 (2 H, m), 3.78 (3 H, s), 1.65 (9 H, s), 1.27 (3 H, t, *J* = 7.2 Hz), 0.93 (3 H, t, *J* = 7.2 Hz). ^{13}C NMR δ (75 MHz, $CDCl_3$): 168.71, 167.75, 167.02, 159.80, 146.44, 138.78, 129.80, 128.80, 128.42, 120.23, 114.31, 112.98, 83.51, 65.55, 62.62, 61.49, 55.18, 51.77, 45.57, 29.66, 13.79, 13.56. HRMS (ESI): calcd for $C_{24}H_{31}NO_8$ [M+Na^+] 484.1942, found 484.1951. The ee was determined by HPLC analysis using a Chiral IA column (*n*-hexane/2-propanol 90: 10, 1.0 mL/min, λ = 210 nm; t_1 = 8.5 min, t_2 = 15.9 min)

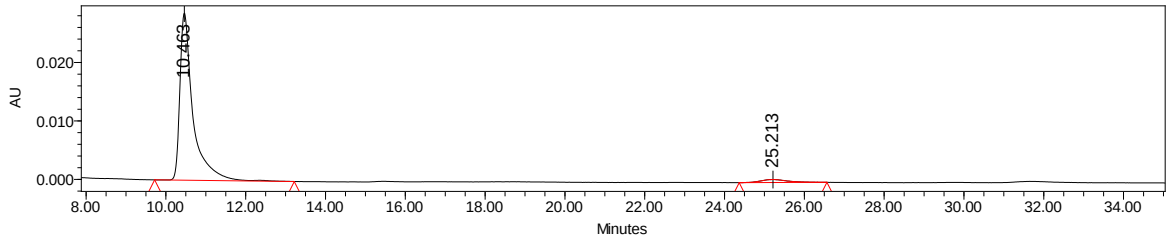


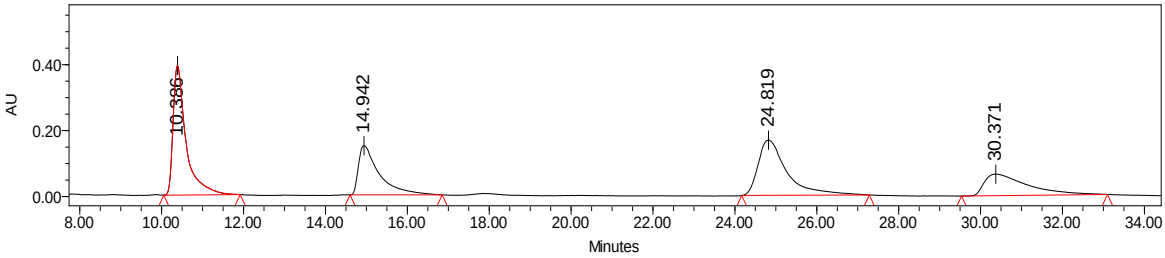


	Retention Time	Area	% Area	Height	% Height
1	8.530	5291488	92.73	297640	95.57
2	13.766	37434	0.66	1622	0.52
3	15.950	183525	3.22	6874	2.21
4	18.743	194124	3.40	5301	1.70

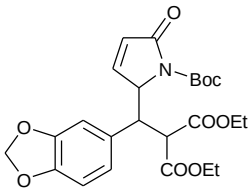


***tert*-butyl 2-(3-ethoxy-2-(ethoxycarbonyl)-1-(4-methoxyphenyl)-3-oxopropyl) -5-oxo-2*H*-pyrrole-1(5*H*)-carboxylate** （**6m**）: The reaction time is 24 hours. The mixture was isolated by column chromatography on silica gel (3:1 P.E./EtOAc) to afford **6m** (72% yield, 95: 5 dr and 93% ee). ^{1}H NMR (300 MHz, $CDCl_3$) δ 7.15 – 7.03 (3 H, m), 6.85 (2 H, d, *J* = 8.7 Hz), 6.12 (1 H, dd, *J* = 6.1, 1.6 Hz), 4.82 (1 H, dd, *J* = 3.5, 1.8 Hz), 4.42 (1 H, dd, *J* = 12.2, 3.4 Hz), 4.21 (2 H, qd, *J* = 7.1, 2.3 Hz), 3.97 – 3.84 (2 H, m), 3.78 (3 H, s), 1.64 (9 H, s), 1.26 (3 H, t, *J* = 7.2 Hz), 0.92 (3 H, t, *J* = 7.1 Hz). ^{13}C NMR δ (75 MHz, $CDCl_3$): 168.81, 167.86, 167.16, 158.96, 146.77, 132.06, 130.77, 129.35, 128.32, 114.12, 81.98, 65.61, 62.52, 61.46, 55.22, 52.16, 45.01, 28.16, 13.83, 13.63. HRMS (ESI): calcd for $C_{24}H_{31}NO_8$ [M+Na$^+$] 484.1942, found 484.1954. The ee was determined by HPLC analysis using a Chiral IA column (*n*-hexane/2-propanol 90: 10, 1.0 mL/min, λ = 210 nm; t_1 = 10.4 min, t_2 = 25.2 min)

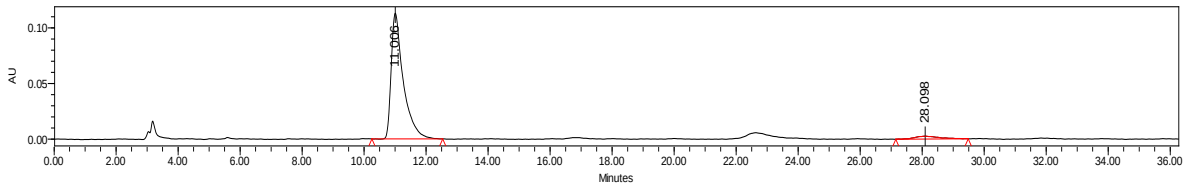


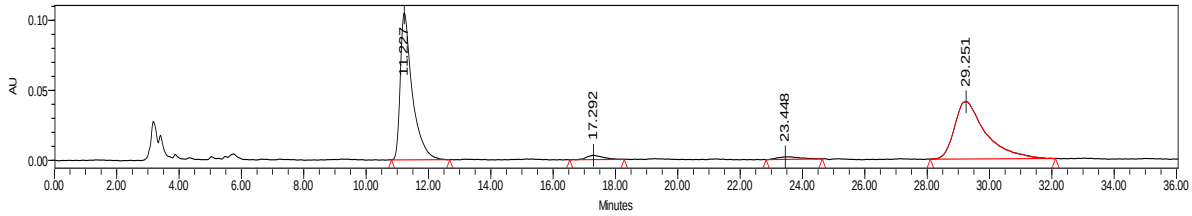


	Retention Time	Area	% Area	Height	% Height
1	10.463	651534	96.49	28625	98.23
2	25.213	23701	3.51	516	1.77

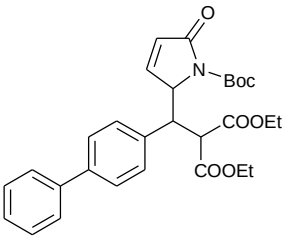


***tert*-butyl 2-(1-(benzo[*d*][1,3]dioxol-5-yl)-3-ethoxy-2-(ethoxycarbonyl)-3-oxopropyl)-5-oxo-2*H*-pyrrole-1(5*H*)-carboxylate（6n）:** The reaction time is 36 hours. The mixture was isolated by column chromatography on silica gel (3:1 P.E./EtOAc) to afford **6n** (64% yield, 90:10 dr and 91% ee). ^{1}H NMR (300 MHz, $CDCl_3$) δ 7.08 (1 H, dd, *J* = 6.1, 1.8 Hz), 6.74 (1 H, d, *J* = 8.0 Hz), 6.69 – 6.58 (2 H, m), 6.13 (1 H, d, *J* = 6.1 Hz), 5.94 (2 H, s), 4.81 (1 H, s), 4.38 (1 H, dd, *J* = 12.3, 3.3 Hz), 4.20 (2 H, q, *J* = 7.1 Hz), 4.01 – 3.87 (2 H, m), 3.77 (1 H, d, *J* = 12.2 Hz), 1.63 (9 H, s), 1.25 (3 H, t, *J* = 7.1 Hz), 0.97 (3 H, t, *J* = 7.1 Hz). ^{13}C NMR δ (75 MHz, $CDCl_3$): 168.66, 167.72, 167.04, 149.31, 147.87, 147.01, 146.64, 130.58, 128.35, 121.32, 108.72, 108.40, 101.18, 83.52, 65.48, 62.54, 61.48, 52.11, 45.35, 28.12, 13.79, 13.66. HRMS (ESI): calcd for $C_{24}H_{29}NO_9$ [M+Na^+] 498.1735, found 498.1734. The ee was determined by HPLC analysis using a Chiral ADH column (*n*-hexane/2-propanol 90: 10, 1.0 mL/min, λ = 210 nm; t_1 = 11.0 min, t_2 = 28.1 min)

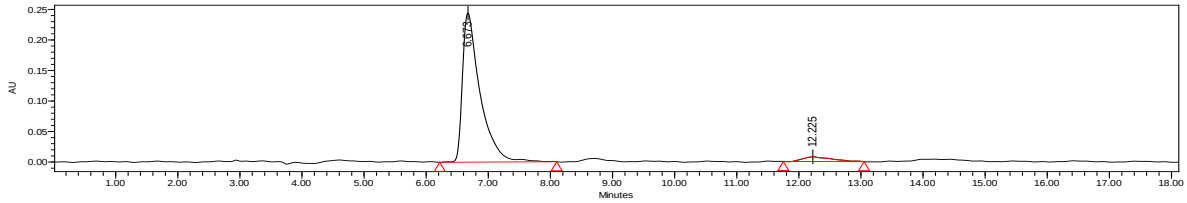


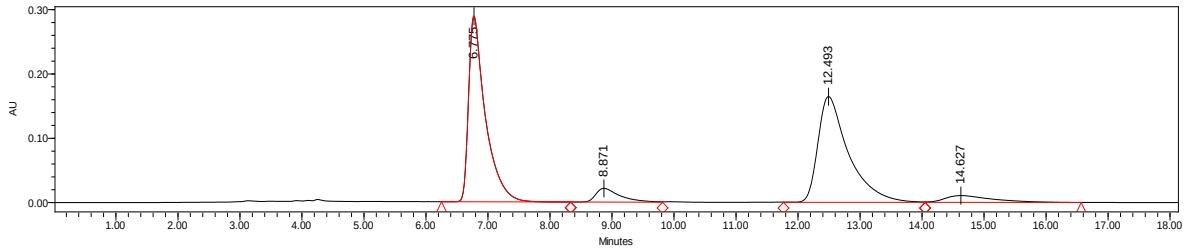


	Retention Time	Area	% Area	Height	% Height
1	11.006	3011949	86.09	112924	92.35
2	16.764	42036	1.20	1230	1.01
3	22.626	305299	8.73	5585	4.57
4	28.098	139380	3.98	2540	2.08

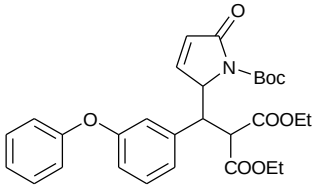


***tert*-butyl 2-(3-ethoxy-2-(ethoxycarbonyl)-1-(biphenyl-4-yl)-3-oxopropyl) -5-oxo-2*H*-pyrrole-1(5*H*)-carboxylate （6o）**: The reaction time is 18 hours. The mixture was isolated by column chromatography on silica gel (3:1 P.E./EtOAc) to afford **6o** (83% yield, 95: 5 dr and 90% ee). ^{1}H NMR (300 MHz, $CDCl_3$) δ 7.61 – 7.52 (4 H, m), 7.46 – 7.40 (2 H, m), 7.37 – 7.40 (1 H, m), 7.28 (2 H, d, *J* = 8.2 Hz), 7.11 (1 H, dd, *J* = 6.2, 1.9 Hz), 6.16 (1 H, dd, *J* = 6.1, 1.4 Hz), 4.87 (1 H, d, *J* = 1.5 Hz), 4.56 (1 H, dd, *J* = 12.2, 3.4 Hz), 4.28 – 4.16 (2 H, m), 4.00 – 3.88 (2 H, m), 3.88 – 3.81 (1 H, m), 1.66 (9 H, s), 1.28 (3 H, t, *J* = 7.2 Hz), 0.91 (3 H, t, *J* = 7.1 Hz). ^{13}C NMR δ (75 MHz, $CDCl_3$): 168.64, 167.71, 167.02, 149.21, 146.40, 140.53, 140.15, 136.06, 128.75, 128.57, 128.44, 127.44, 127.37, 126.89, 83.51, 65.47, 62.56, 61.48, 51.78, 45.29, 28.11, 13.76, 13.51. HRMS (ESI): calcd for $C_{29}H_{33}NO_7$ [M+Na^+] 530.2149, found 530.2155. The ee was determined by HPLC analysis using a Chiral ADH column (*n*-hexane/2-propanol 80: 20, 1.0 mL/min, λ = 210 nm; t_1 = 6.6 min, t_2 = 12.2 min)

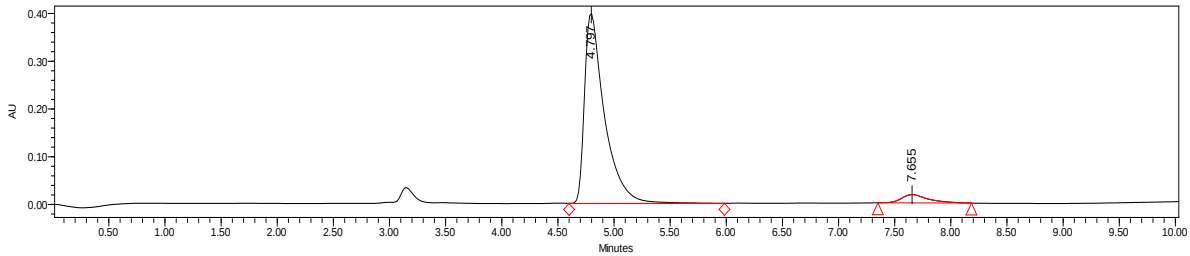


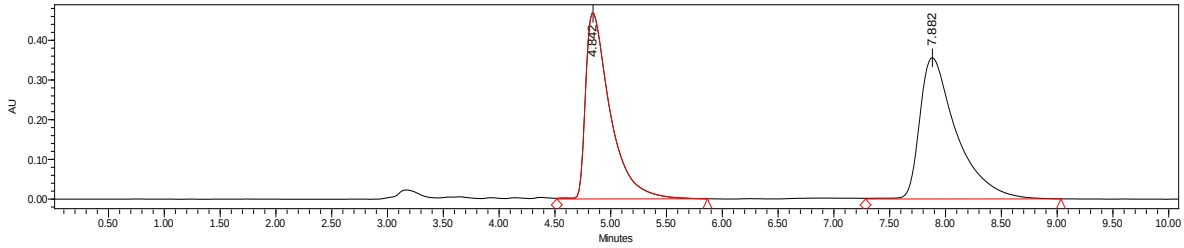


	Retention Time	Area	% Area	Height	% Height
1	6.673	4773444	90.02	244568	93.72
2	8.700	128219	2.42	5296	2.03
3	12.225	258583	4.88	7744	2.97
4	14.180	142553	2.69	3341	1.28

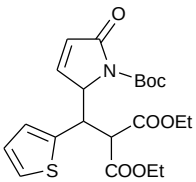


***tert*-butyl 2-(3-ethoxy-2-(ethoxycarbonyl)-3-oxo-1-(3-phenoxyphenyl) propyl)-5-oxo-2*H*-pyrrole-1(5*H*)-carboxylate （6p）:** The reaction time is 18 hours. The mixture was isolated by column chromatography on silica gel (3:1 P.E./EtOAc) to afford **6p** (89% yield, 95:5 dr and 89% ee). ^{1}H NMR (300 MHz, $CDCl_3$) δ 7.38 – 7.24 (3 H, m), 7.14 – 7.08 (1 H, m), 7.04 (1 H, dd, *J* = 6.2, 2.0 Hz), 6.98 – 6.88 (4 H, m), 6.83 (1 H, d, *J* = 1.8 Hz), 6.12 (1 H, dd, *J* = 6.2, 1.7 Hz), 4.82 (1 H, dt, *J* = 3.5, 1.9 Hz), 4.44 (1 H, dd, *J* = 12.2, 3.3 Hz), 4.24 – 4.14 (2 H, m), 4.00 – 3.87 (2 H, m), 3.79 (1 H, d, *J* = 12.2 Hz), 1.57 (9 H, s), 1.24 (3 H, t, *J* = 7.1 Hz), 0.96 (3 H, t, *J* = 7.1 Hz). ^{13}C NMR δ (75 MHz, $CDCl_3$): 168.59, 167.63, 166.88, 157.61, 156.59, 149.08, 146.28, 139.02, 130.05, 129.80, 128.44, 123.58, 122.71, 118.98, 118.40, 117.87, 83.48, 65.29, 62.57, 61.48, 51.68, 45.46, 28.03, 13.73, 13.59. HRMS (ESI): calcd for $C_{29}H_{33}NO_8$ [M+Na^+] 546.2098, found 546.2109. The ee was determined by HPLC analysis using a Chiral ADH column (*n*-hexane/2-propanol 80: 20, 1.0 mL/min, λ = 210 nm; t_1 = 4.5 min, t_2 = 7.6 min)

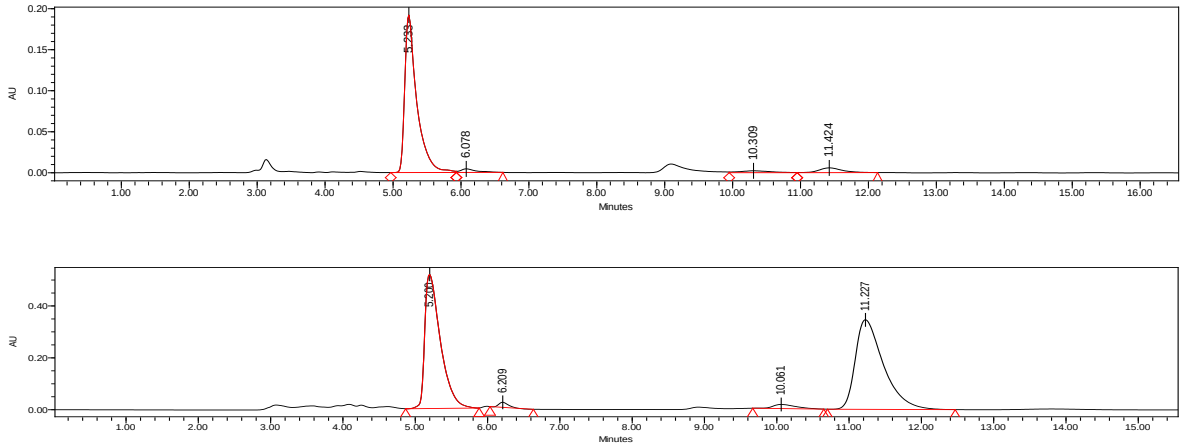




	Retention Time	Area	% Area	Height	% Height
1	4.797	4929559	94.55	397789	95.81
2	7.655	283991	5.45	17410	4.19

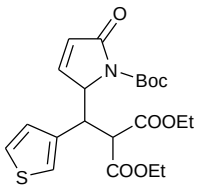


***tert*-butyl 2-(3-ethoxy-2-(ethoxycarbonyl)-3-oxo-1-(thiophen-2-yl)propyl)-5-oxo-2*H*-pyrrole-1(5*H*)-carboxylate（6q）:** The reaction time is 18 hours. The mixture was isolated by column chromatography on silica gel (3:1 P.E./EtOAc) to afford **6q** (72% yield, 95:5 dr and 90% ee). ^{1}H NMR (300 MHz, $CDCl_3$) δ7.23 – 7.13 (2 H, m), 6.95 – 6.91 (1 H, m), 6.86 (1 H, d, *J* = 3.4 Hz), 6.12 (1 H, dd, *J* = 6.1, 1.7 Hz), 4.92 (1 H, dt, *J* = 3.6, 1.9 Hz), 4.72 (1 H, dd, *J* = 11.9, 3.2 Hz), 4.28 – 4.11 (2 H, m), 4.00 – 3.86 (2 H, m), 3.73 (1 H, d, *J* = 11.9 Hz), 1.61 (9 H, s), 1.24 (3 H, t, *J* = 7.1 Hz), 0.96 (3 H, t, *J* = 7.1 Hz). ^{13}C NMR δ (75 MHz, $CDCl_3$): 168.64, 167.17, 166.77, 149.15, 146.79, 138.97, 128.43, 126.83, 126.18, 124.87, 83.57, 65.05, 62.51, 61.56, 53.60, 41.03, 28.06, 13.75, 13.54. HRMS (ESI): calcd for $C_{21}H_{27}NO_7S$ [M+Na^+] 460.1400, found 460.1404. The ee was determined by HPLC analysis using a Chiral ADH column (*n*-hexane/2-propanol 80: 20, 1.0 mL/min, λ = 210 nm; t_1 = 5.2 min, t_2 = 11.4 min)

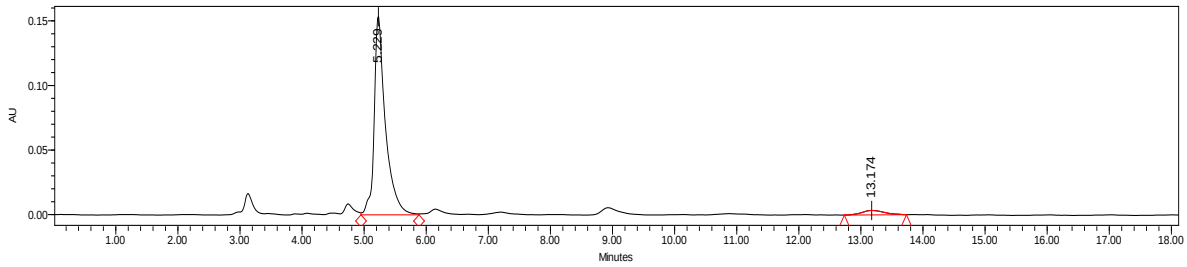


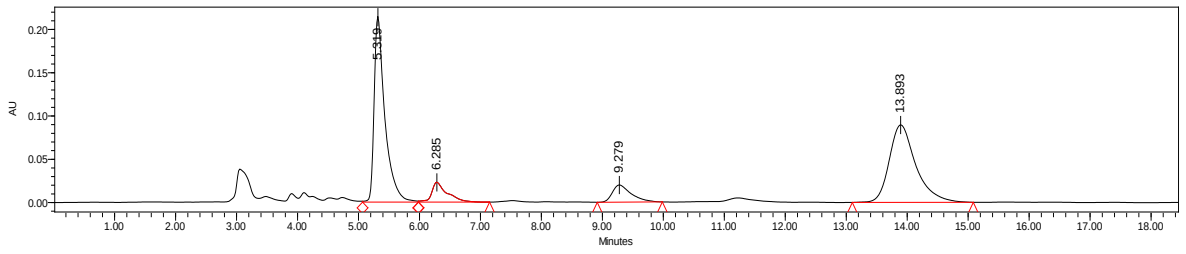
	Retention	Area	% Area	Height	% Height

	Time				
1	5.233	2373222	90.61	191995	94.19
2	6.078	80832	3.09	4621	2.27
3	10.309	42643	1.63	1692	0.83
4	11.424	122402	4.67	5538	2.72



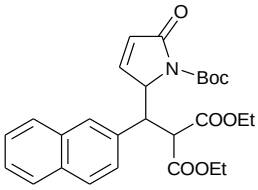
***tert*-butyl 2-(3-ethoxy-2-(ethoxycarbonyl)-3-oxo-1-(thiophen-3-yl)propyl)-5-oxo-2*H*-pyrrole-1(5*H*)-carboxylate （6r）**: The reaction time is 18 hours. The mixture was isolated by column chromatography on silica gel (3:1 P.E./EtOAc) to afford **6r** (70% yield, 93:7 dr and 91% ee). ^{1}H NMR (300 MHz, $CDCl_3$) δ 7.32 – 7.24 (1 H, m), 7.08 – 7.04 (2 H, m), 6.98 – 6.92 (1 H, m), 6.11 (1 H, dd, *J* = 6.1, 1.5 Hz), 4.89 – 4.82 (1 H, m), 4.58 (1 H, dd, *J* = 12.0, 3.3 Hz), 4.25 – 4.13 (2 H, m), 4.00 – 3.84 (2 H, m), 3.74 (1 H, d, *J* = 12.0 Hz), 1.61 (9 H, s), 1.24 (3 H, t, *J* = 7.1 Hz), 0.93 (3 H, t, *J* = 7.1 Hz). ^{13}C NMR δ (75 MHz, $CDCl_3$): 168.61, 167.53, 167.08, 149.29, 146.94, 137.28, 128.26, 127.41, 126.24, 122.60, 83.43, 64.79, 62.43, 61.48, 52.70, 41.30, 28.07, 13.76, 13.51. HRMS (ESI): calcd for $C_{21}H_{27}NO_7S$ [M+Na$^+$] 460.1400, found 460.1402. The ee was determined by HPLC analysis using a Chiral ADH column (*n*-hexane/2-propanol 80: 20, 1.0 mL/min, λ = 210 nm; t_1 = 5.2 min, t_2 = 13.2 min)



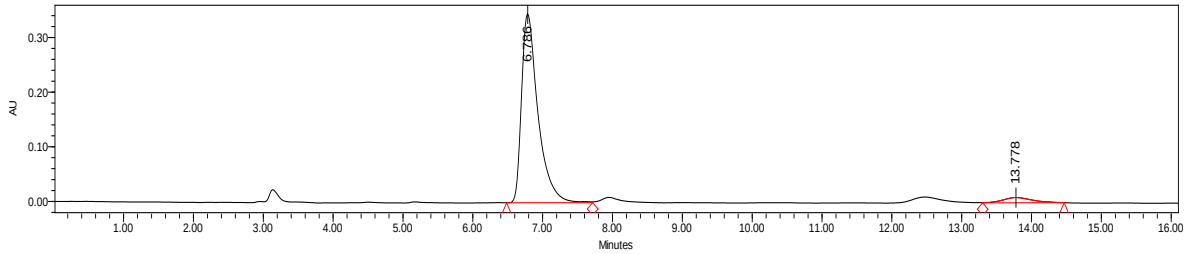


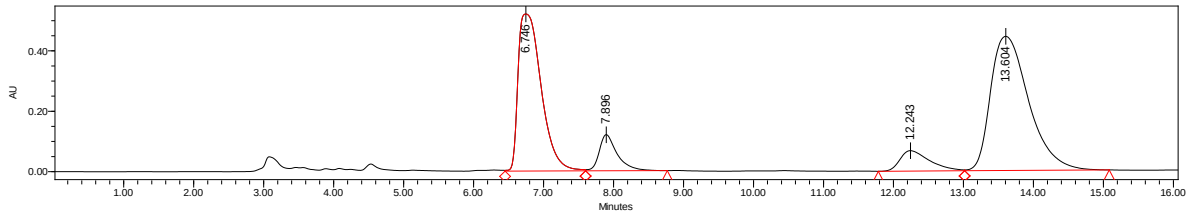
	Retention Time	Area	% Area	Height	% Height

1	5.229	1936932	88.93	153773	92.32
2	6.148	47449	2.18	3770	2.26
3	8.928	105376	4.84	5571	3.34
4	13.174	88289	4.05	3460	2.08



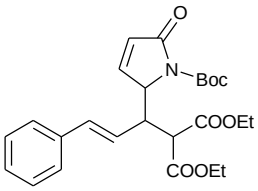
***tert*-butyl 2-(3-ethoxy-2-(ethoxycarbonyl)-1-(naphthalen-2-yl)-3-oxopropyl)-5-oxo-2*H*-pyrrole-1(5*H*)-carboxylate （6s）:** The reaction time is 18 hours. The mixture was isolated by column chromatography on silica gel (3:1 P.E./EtOAc) to afford **6s** (82% yield, 93:7 dr and 91% ee). ^{1}H NMR (300 MHz, $CDCl_3$) δ 7.88 – 7.73 (3 H, m), 7.64 (1 H, s), 7.53 – 7.43 (2 H, m), 7.36 (1 H, dd, *J* = 8.5, 1.6 Hz), 7.10 (1 H, dd, *J* = 6.2, 2.0 Hz), 6.15 (1 H, dd, *J* = 6.1, 1.6 Hz), 4.96 – 4.88 (1 H, m), 4.69 (1 H, dd, *J* = 12.2, 3.5 Hz), 4.30 – 4.18 (2 H, m), 3.97 (1 H, d, *J* = 12.2 Hz), 3.85 (2 H, dtt, *J* = 10.8, 7.1, 3.7 Hz), 1.68 (9 H, s), 1.28 (3 H, t, *J* = 7.1 Hz), 0.83 (3 H, t, *J* = 7.1 Hz). ^{13}C NMR δ (75 MHz, $CDCl_3$): 168.58, 167.75, 167.03, 149.28, 146.33, 134.71, 133.12, 132.61, 128.65, 128.48, 127.68, 127.62, 126.84, 126.46, 126.22, 126.20, 83.55, 65.50, 62.60, 61.46, 51.83, 45.61, 28.15, 13.78, 13.53. HRMS (ESI): calcd for $C_{27}H_{31}NO_7$ [M+Na$^+$] 504.1993, found 504.2006. The ee was determined by HPLC analysis using a Chiral ADH column (*n*-hexane/2-propanol 80: 20, 1.0 mL/min, λ = 210 nm; t_1 = 6.7 min, t_2 = 13.7 min)



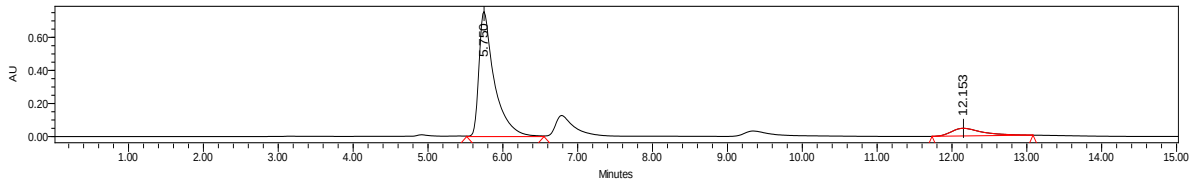


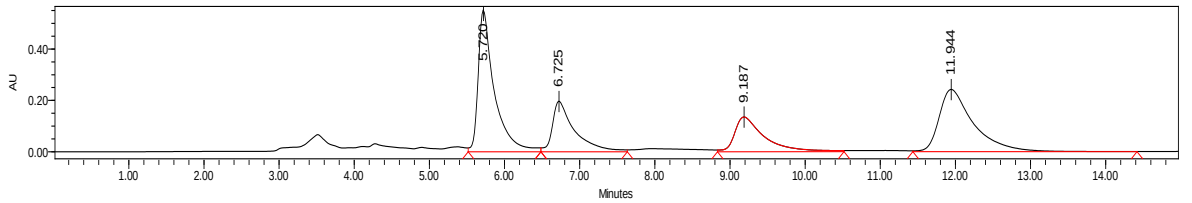
	Retention Time	Area	% Area	Height	% Height
1	6.786	5641332	88.82	346073	92.35
2	7.950	142983	2.25	8494	2.27

3	12.473	303210	4.77	10741	2.87
4	13.778	263644	4.15	9419	2.51

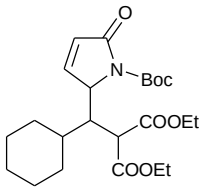


(*E*)-*tert*-butyl 2-(1-ethoxy-2-(ethoxycarbonyl)-1-oxo-5-phenylpent-4-en-3-yl)-5-oxo-2*H*-pyrrole-1(5*H*)-carboxylate （**6t**）: The reaction time is 12 hours. The mixture was isolated by column chromatography on silica gel (3:1 P.E./EtOAc) to afford **6t** (75% yield, 81:19 dr and 78% ee). ^{1}H NMR (300 MHz, $CDCl_3$) δ 7.34 – 7.30 (4 H, m), 7.27 – 7.18 (2 H, m), 6.60 (1 H, d, *J* = 15.7 Hz), 6.23 – 6.08 (2 H, m), 4.89 – 4.81 (1 H, m), 4.24 – 4.13 (2 H, m), 4.05 (2 H, dt, *J* = 7.1, 3.8 Hz), 3.95 (1 H, td, *J* = 9.5, 3.7 Hz), 3.46 (1 H, d, *J* = 9.2 Hz), 1.61 (9 H, s), 1.23 (3 H, t, *J* = 7.1 Hz), 1.13 (3 H, t, *J* = 7.1 Hz). ^{13}C NMR δ (75 MHz, $CDCl_3$): 168.78, 167.74, 167.68, 149.36, 147.59, 136.00, 135.45, 128.57, 128.07, 127.88, 126.42, 123.39, 83.55, 64.94, 62.06, 61.51, 51.69, 44.11, 28.02, 13.96, 13.88. HRMS (ESI): calcd for $C_{25}H_{31}NO_7$ [M+Na^+] 480.1993, found 480.1997. The ee was determined by HPLC analysis using a Chiral ADH column (*n*-hexane/2-propanol 80: 20, 1.0 mL/min, λ = 210 nm; t_1 = 5.7 min, t_2 = 12.1 min)

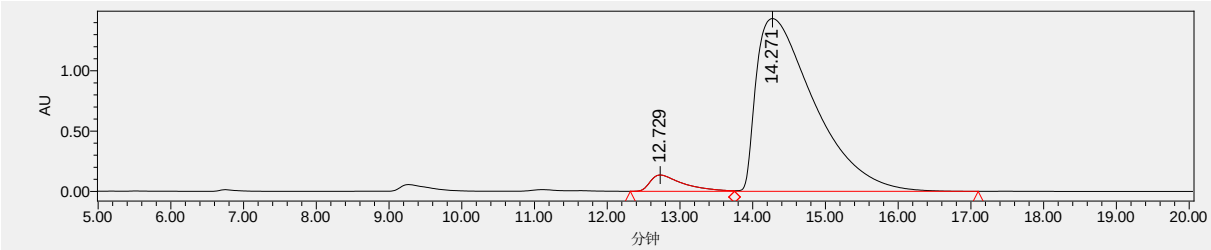


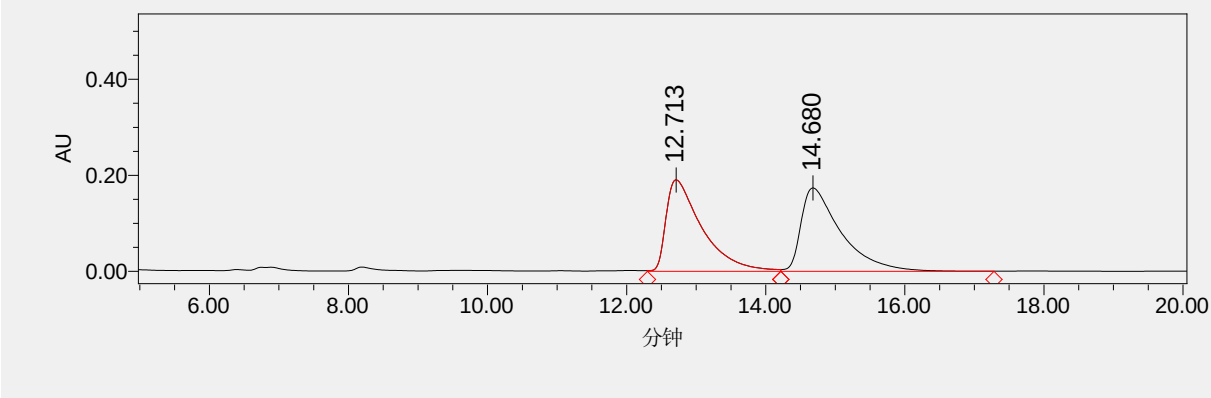


	Retention Time	Area	% Area	Height	% Height
1	5.750	10775343	72.53	756081	78.95
2	6.787	2098300	14.12	124296	12.98
3	9.348	621081	4.18	30501	3.18
4	12.153	1361889	9.17	46797	4.89



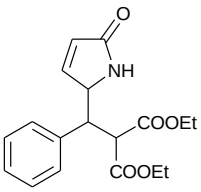
***tert*-butyl 2-(1-cyclohexyl-3-ethoxy-2-(ethoxycarbonyl)-3-oxopropyl)-5-oxo-2*H*-pyrrole-1(5*H*)-carboxylate （6u）：** The reaction time is 18 hours. The mixture was isolated by column chromatography on silica gel (3:1 P.E./EtOAc) to afford **6u** (70% yield, 95: 5 dr and 90% ee). ^{1}H NMR (300 MHz, $CDCl_3$) δ 7.15 (1 H, d, *J* = 6.2 Hz), 6.06 (1 H, d, *J* = 6.1 Hz), 4.96 (1 H, s), 4.11 (4 H, dt, *J* = 12.2, 6.1 Hz), 3.21 (1 H, d, *J* = 5.1 Hz), 3.17-3.12 (1 H, m), 1.99 – 1.62 (7 H, m), 1.56 (9 H, s), 1.29 – 1.14 (10 H, m). ^{13}C NMR δ (75 MHz, $CDCl_3$): 169.15, 169.09, 168.47, 147.88, 127.65, 83.44, 62.40, 61.90, 61.16, 48.90, 44.68, 37.72, 31.89, 31.15, 28.06, 26.42, 26.21, 13.90, 13.84. HRMS (ESI): calcd for $C_{23}H_{35}NO_7$ [M+Na$^+$] 460.2306, found 460.2314. The ee was determined by HPLC analysis using a Chiral ADH column (*n*-hexane/2-propanol 95: 5, 1.0 mL/min, λ = 210 nm; t_1 = 12.7 min, t_2 = 14.3 min)



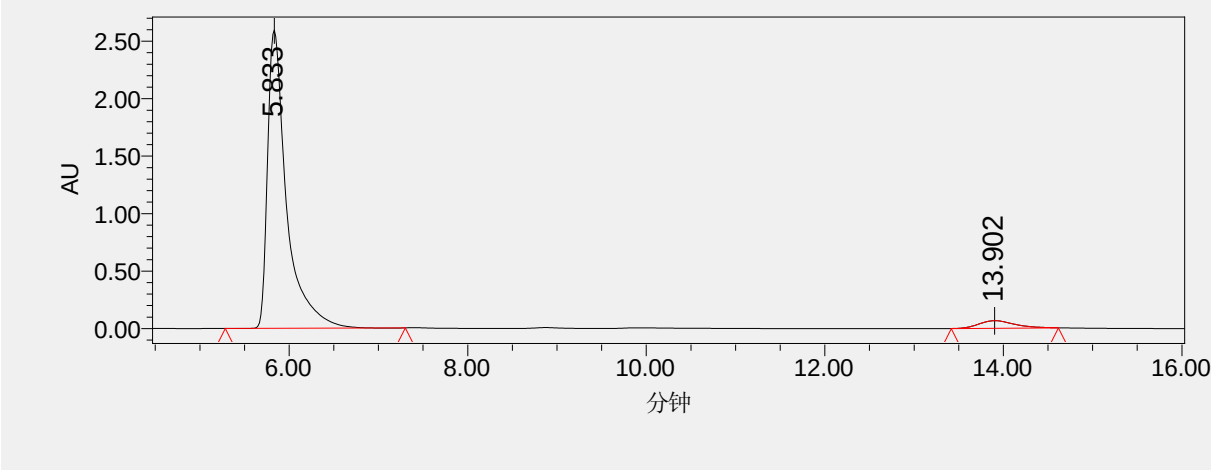


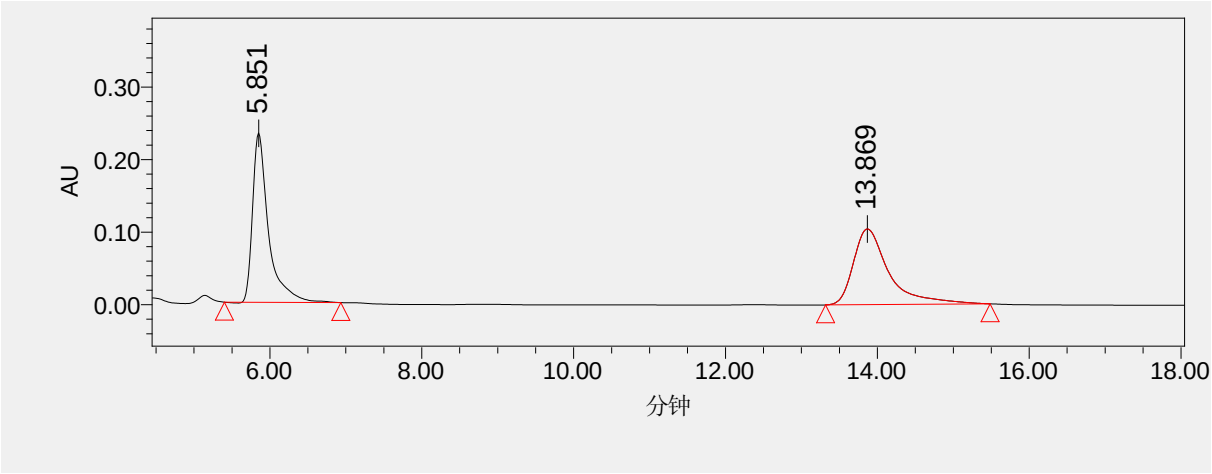
	Retention Time	Area	% Area	Height
1	12.729	4271128	5.09	135284
2	14.271	79650982	94.91	1432831

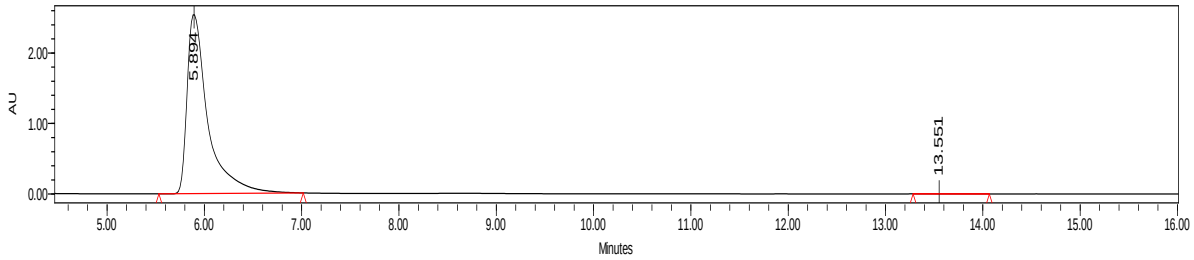
4. Transformation of the products 6 to 5-substituted pyrrolidin-2-one 8



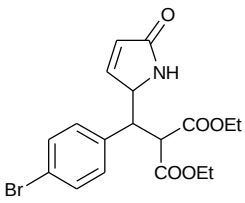
diethyl 2-((5-oxo-2,5-dihydro-1*H*-pyrrol-2-yl)(phenyl)methyl)malonate （7a）: To a solution of *syn*-**6a** (363 mg, 0.84 mmol, 1.0 equiv) in CH_2Cl_2 (10.0 mL), TFA (2 mL) was added at room temperature, then stirred for 20 mins. After checking the complete consumption of the starting material by TLC, a solution of 2 *N* NaOH was added to reaction solution until pH = 10 and extracted with CH_2Cl_2 (30 x 3 mL). The combined organic phase was washed with brine, and dried over anhydrous Na_2SO_4. After evaporation of solvent, the residue was isolated by column chromatography on silica gel (1:2 P.E./EtOAc) to afford **7a** (99% yield and 92% ee). The desired product was recrystallized in petroleum/CH_2Cl_2 to get the optical pure product as single isomer (73% yield, 99% ee). $[\alpha]_D^{15}$ = +126.7 (c = 0.18, in CH_2Cl_2). m.p. 118 – 120 ^oC. ^1H NMR (400 MHz, $CDCl_3$) δ 7.32-7.15 (5 H, m), 6.94 (1 H, d, *J* 5.0), 6.91 – 6.74 (1 H, m), 5.93 (1 H, d, *J* 5.2), 4.60 (1 H, s), 4.28 (2 H, q, *J* 6.7), 4.00-3.80 (4 H, m), 1.31 (3 H, t, *J* 7.0), 0.96 (3 H, t, *J* 6.6). ^{13}C NMR δ (100 MHz, $CDCl_3$): 174.01, 168.43, 167.09, 148.09, 135.95, 128.46, 128.45, 128.09, 127.89, 62.36, 61.67, 61.14, 54.56, 47.42, 14.05, 13.66. HRMS (ESI): calcd for $C_{18}H_{21}NO_5$ $[M+H^+]$ 332.1492, found 332.1504. The ee was determined by HPLC analysis using a Chiral IA column (*n*-hexane/2-propanol 70: 30, 1.0 mL/min, λ = 210 nm; t_1 = 5.8 min, t_2 = 13.9 min).



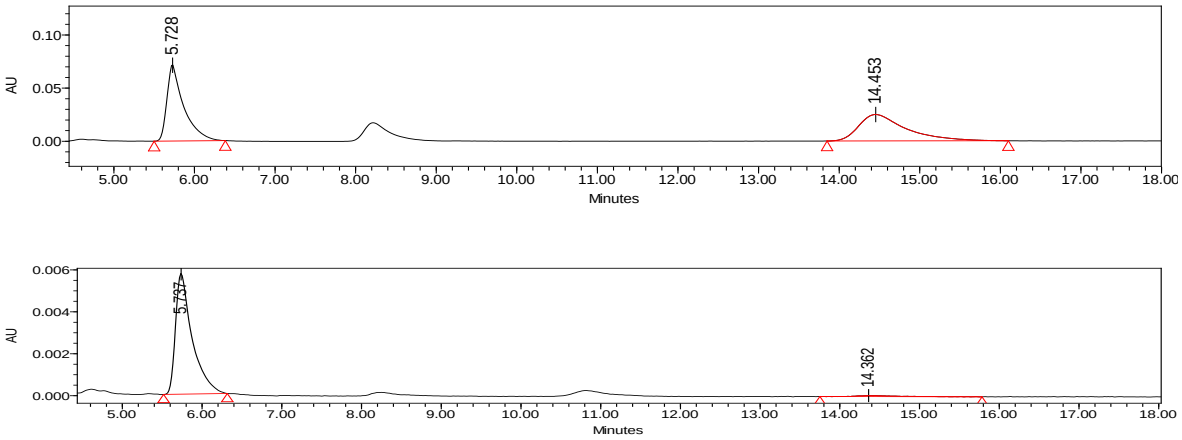


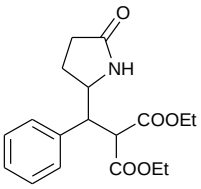


Data obtained after recrystalization

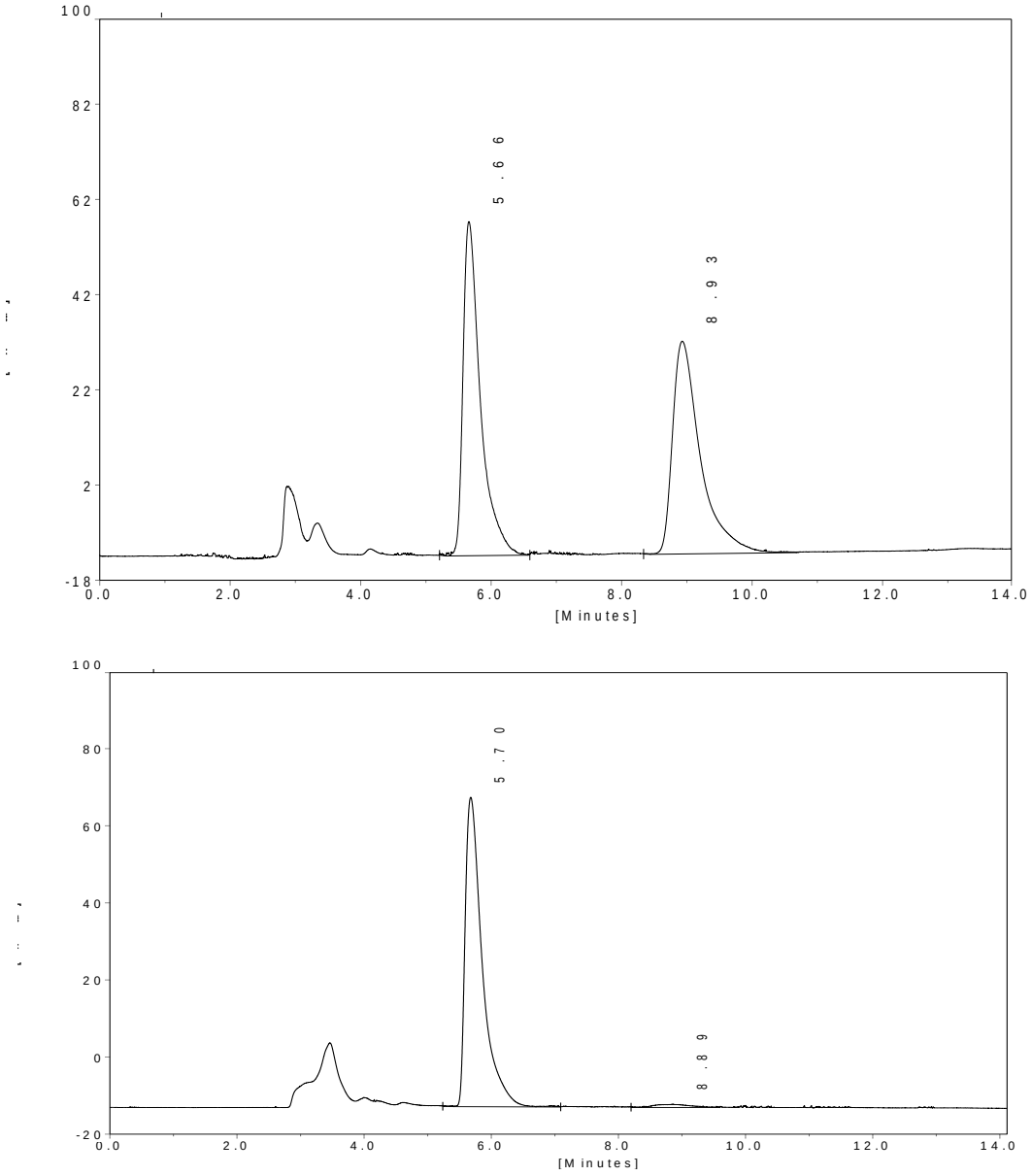


diethyl 2-((4-bromophenyl)(5-oxo-2,5-dihydro-1*H*-pyrrol-2-yl)methyl) malonate （7i）： Prepared according to the procedure for **7a**, from **6i** (423 mg, 0.83 mmol) and TFA for 20 mins to provide the crude product. The mixture was isolated by column chromatography on silica gel (1:2 P.E./EtOAc) to afford **7i** (99% yield and 93% ee). $[\alpha]_D^{15}$ = +140.5 (c = 0.22, in CH_2Cl_2). m.p. 144 – 146 ^oC. ^1H NMR (400 MHz, $CDCl_3$) δ 7.42-7.25 (3 H, m), 7.07 (2 H, d, *J* 7.8), 6.92 (1 H, d, *J* 3.8), 5.92 (1 H, d, *J* 4.3), 4.60 (1 H, s), 4.28 (2 H, q, *J* 6.8), 4.05 – 3.88 (3 H, m), 3.86-3.75 (1 H, m), 1.30 (3 H, t, *J* 6.9), 1.01 (3 H, t, *J* 6.8). ^{13}C NMR δ (100 MHz, $CDCl_3$): 174.34, 168.16, 166.96, 148.12, 134.67, 131.47, 130.21, 128.27, 121.90, 62.44, 61.80, 60.63, 54.46, 46.74, 14.04, 13.74. HRMS (ESI): calcd for $C_{18}H_{20}BrNO_5$ $[M+H^+]$ 410.0598, found 410.0631. The ee was determined by HPLC analysis using a Chiral ADH column (*n*-hexane/2-propanol 70: 30, 1.0 mL/min, λ = 210 nm; t_1 = 5.7 min, t_2 = 14.4 min).





diethyl 2-((5-oxopyrrolidin-2-yl)(phenyl)methyl)malonate（8a）： A suspension of **7a** (718mg, 2.17 mmol) and Pd/C (140 mg, 20 wt%) in 20 mL EtOAc is placed under hydrogen atmosphere at room temperature and stirred overnight. The solution is filtered and the solvent is removed under reduced pressure to give the mixture, which was isolated by column chromatography on silica gel (1:2 P.E./EtOAc) to afford **8a** (99% yield and 98% ee). $[\alpha]_D^{12}$ = +18.7 (c = 0.60, in CH_2Cl_2). ^{1}H NMR (400 MHz, $CDCl_3$) δ 7.38-7.18 (5 H, m), 6.81 (1 H, s), 4.26 (2 H, q, *J* 6.8), 4.06 (1 H, d, *J* 5.7), 3.99 – 3.83 (3 H, m), 3.51 (1 H, dd, *J* 10.9, 3.0), 2.29 – 2.13 (1 H, m), 2.04 – 1.92 (1 H, m), 1.83 (1 H, t, *J* 11.0), 1.48 (1 H, dt, *J* 17.7, 8.8), 1.29 (3 H, t, *J* 6.9), 0.94 (3 H, t, *J* 6.6). ^{13}C NMR δ (100 MHz, $CDCl_3$): 178.79, 168.39, 167.26, 136.22, 129.49, 128.48, 127.73, 62.02, 61.42, 55.62, 54.63, 50.02, 29.49, 25.04, 14.03, 13.63. HRMS (ESI): calcd for $C_{18}H_{23}NO_5$ $[M+H^+]$ 334.1649, found 334.1649. The ee was determined by HPLC analysis using a Chiral ADH column (*n*-hexane/2-propanol 70: 30, 1.0 mL/min, λ = 210 nm; t_1 = 5.7 min, t_2 = 8.9 min).

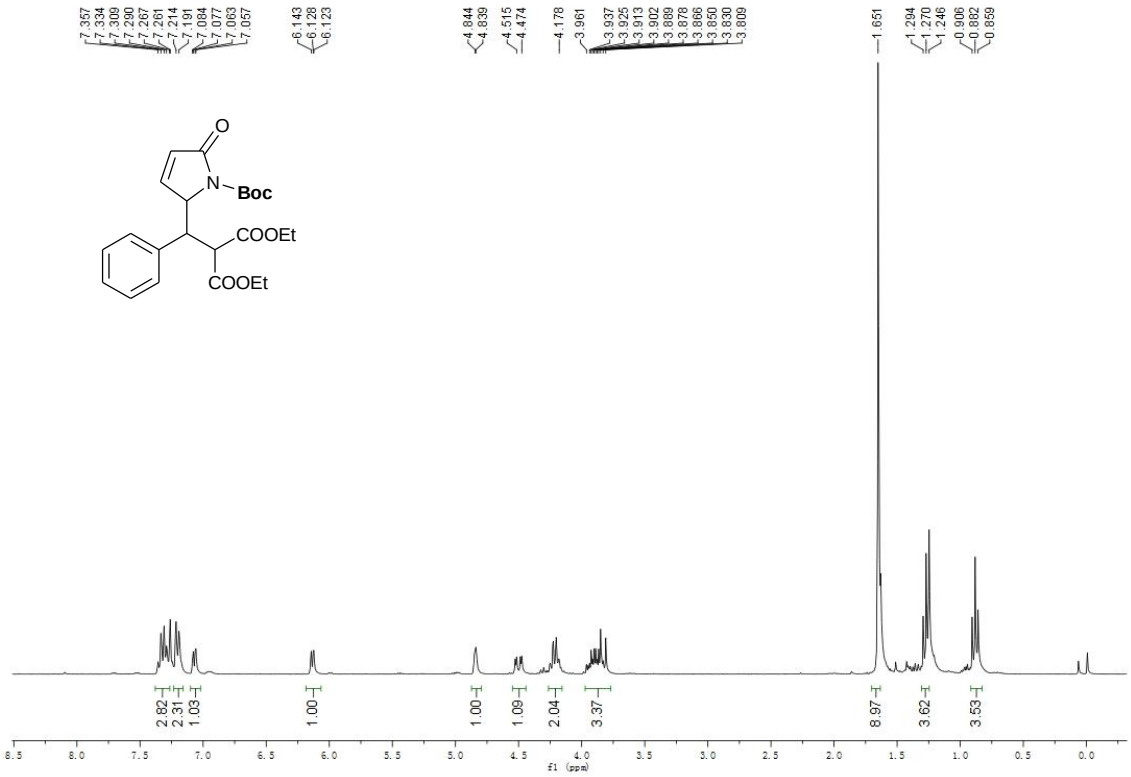


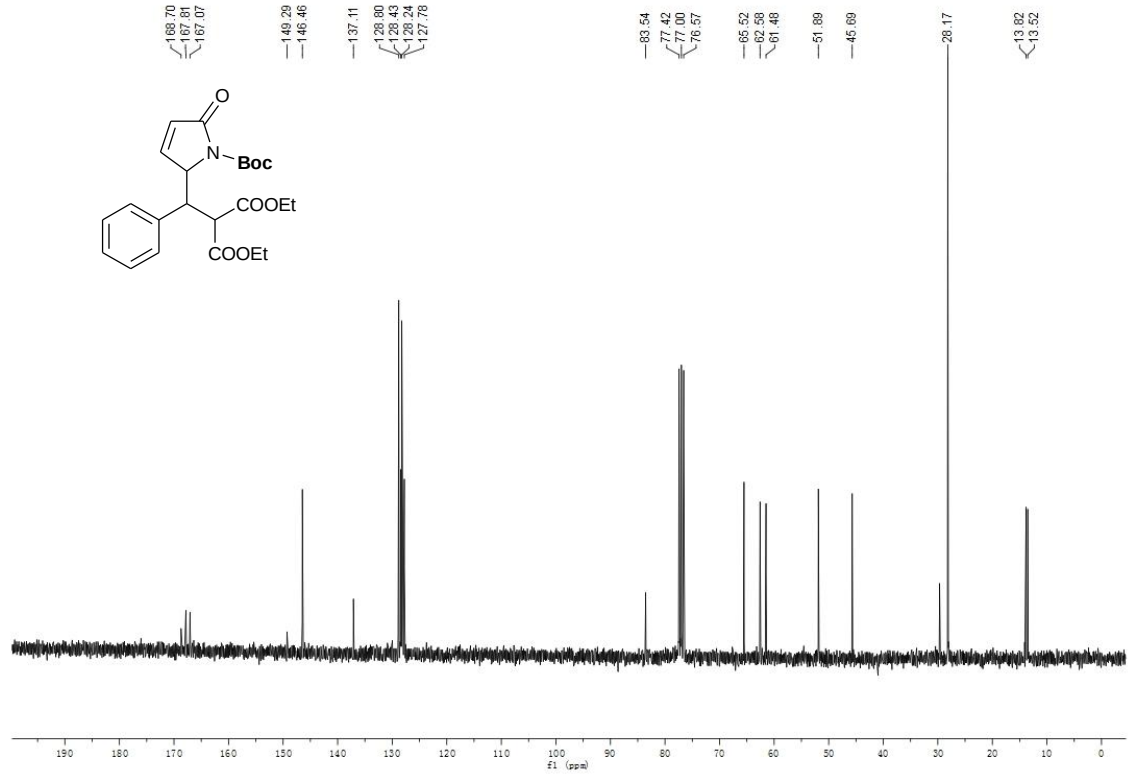
5. References

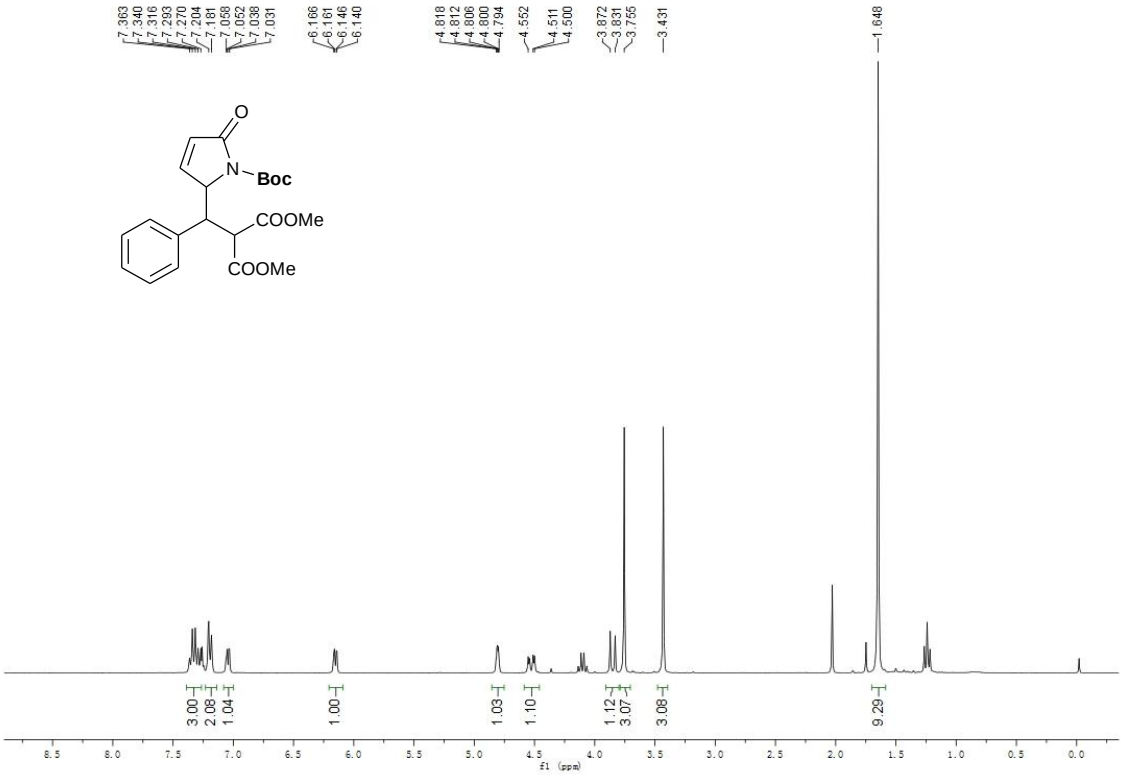
(1) C. Curti, A. Sartori, L. Battistini, G. Rassu, P. Burreddu, F. Zanardi and G. Casiraghi, *J. Org. Chem.* 2008, **73**, 5446.

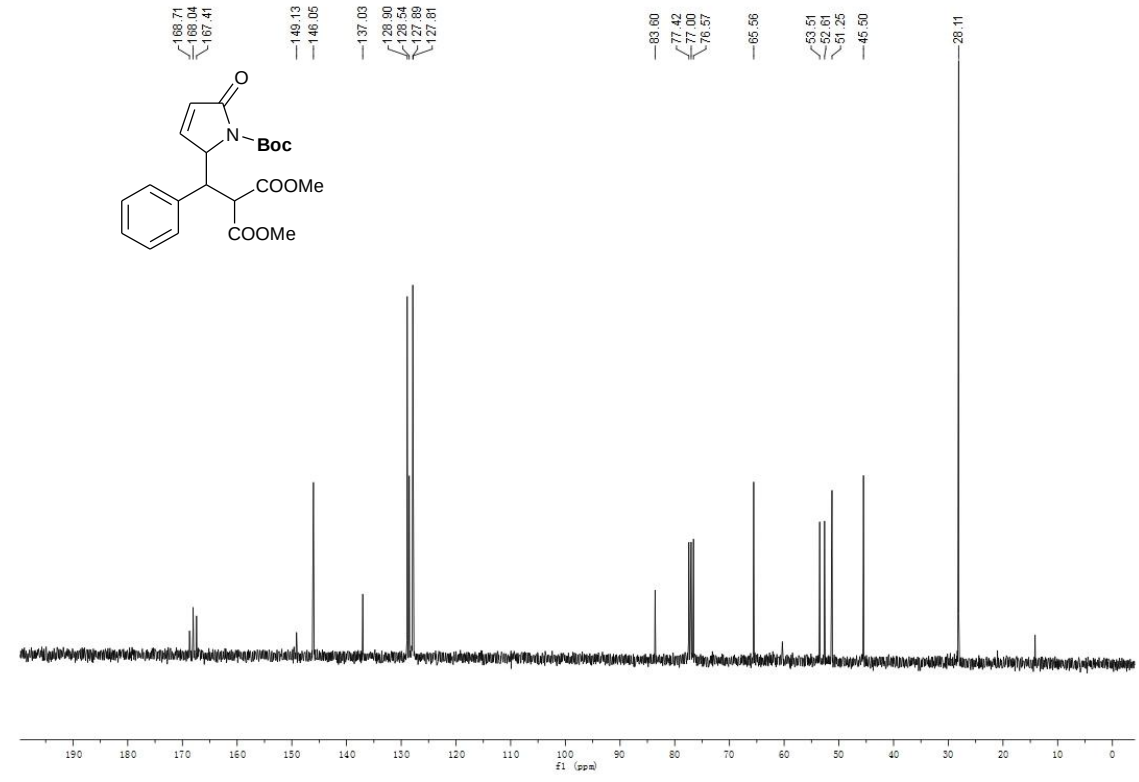
(2) (a) Z. Yu, X. Liu, L. Zhou, L. Lin and X. Feng, *Angew. Chem., Int. Ed.*, 2009, **48**, 5195; (b) S. Dong, X. Liu, X. Chen, F. Mei, Y. Zhang, B. Gao, L. Lin and X. Feng, *J. Am. Chem. Soc.* 2010, **132**, 10650.

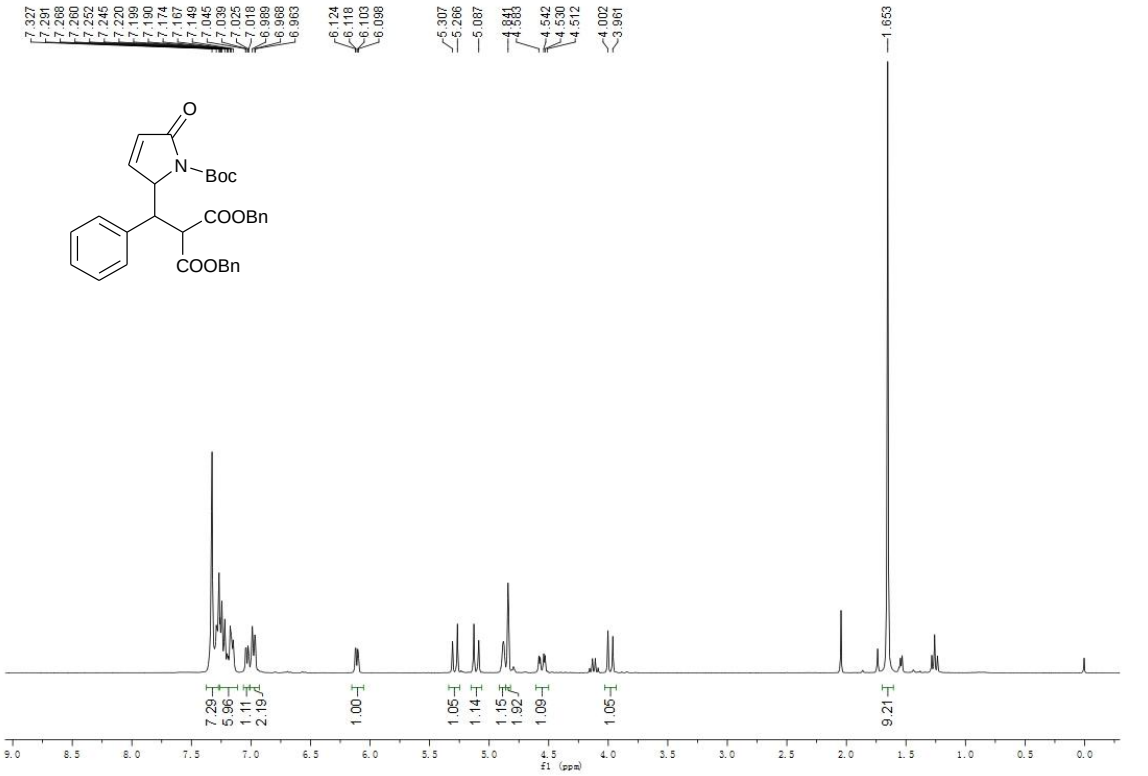
6. Copy of 1H NMR and 13C NMR spectra

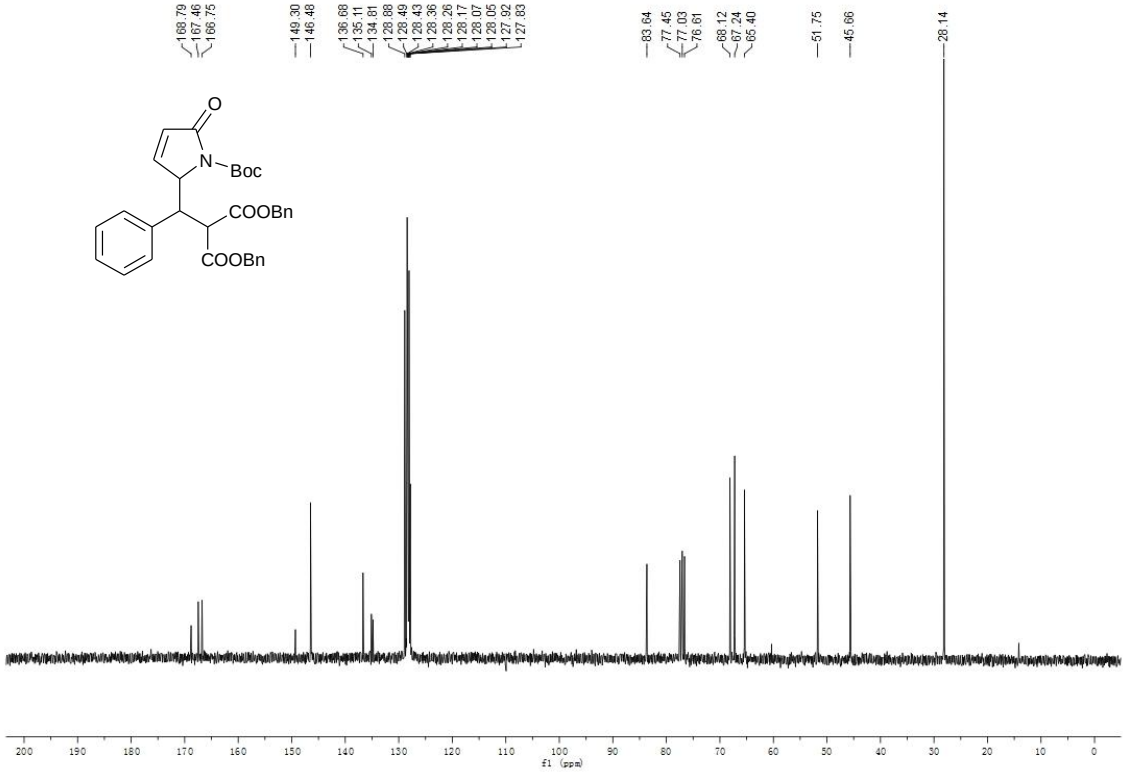


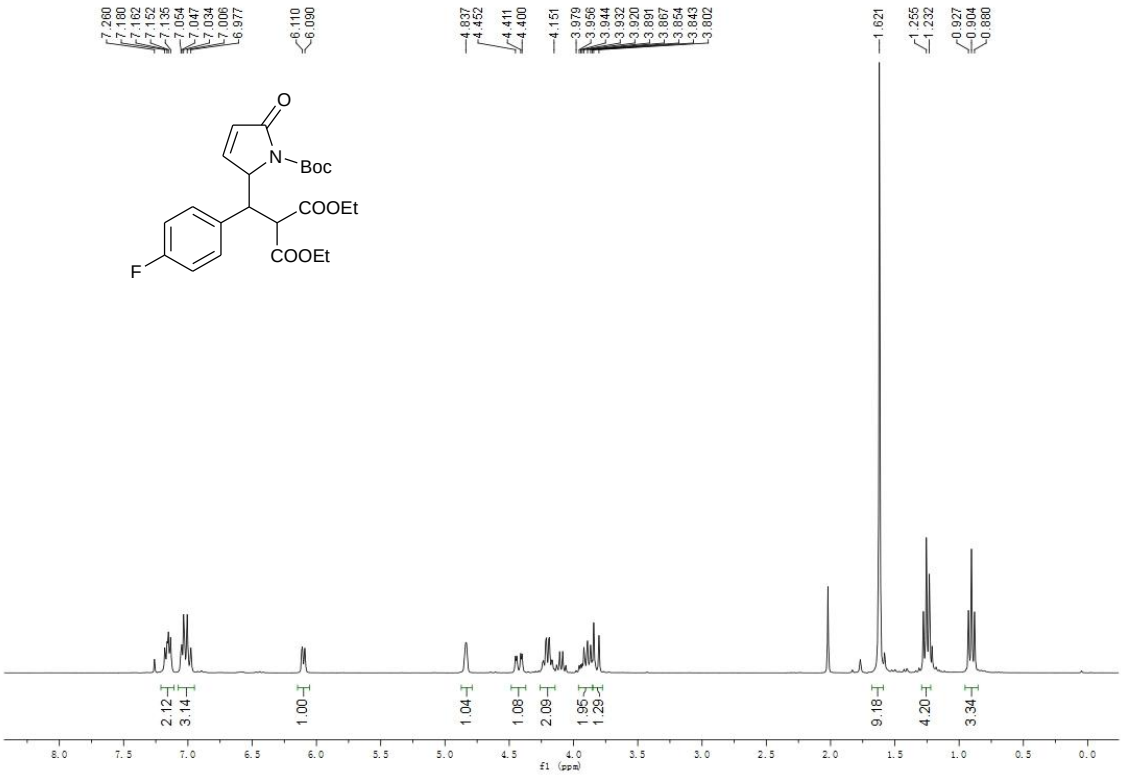


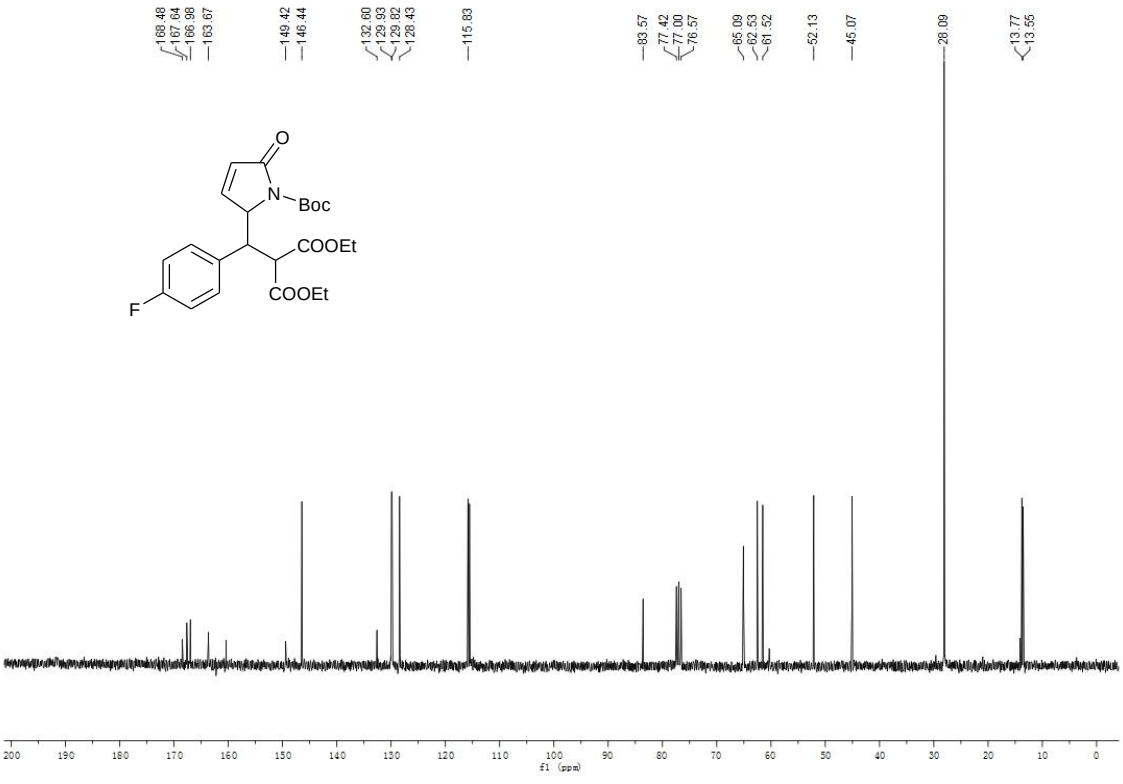


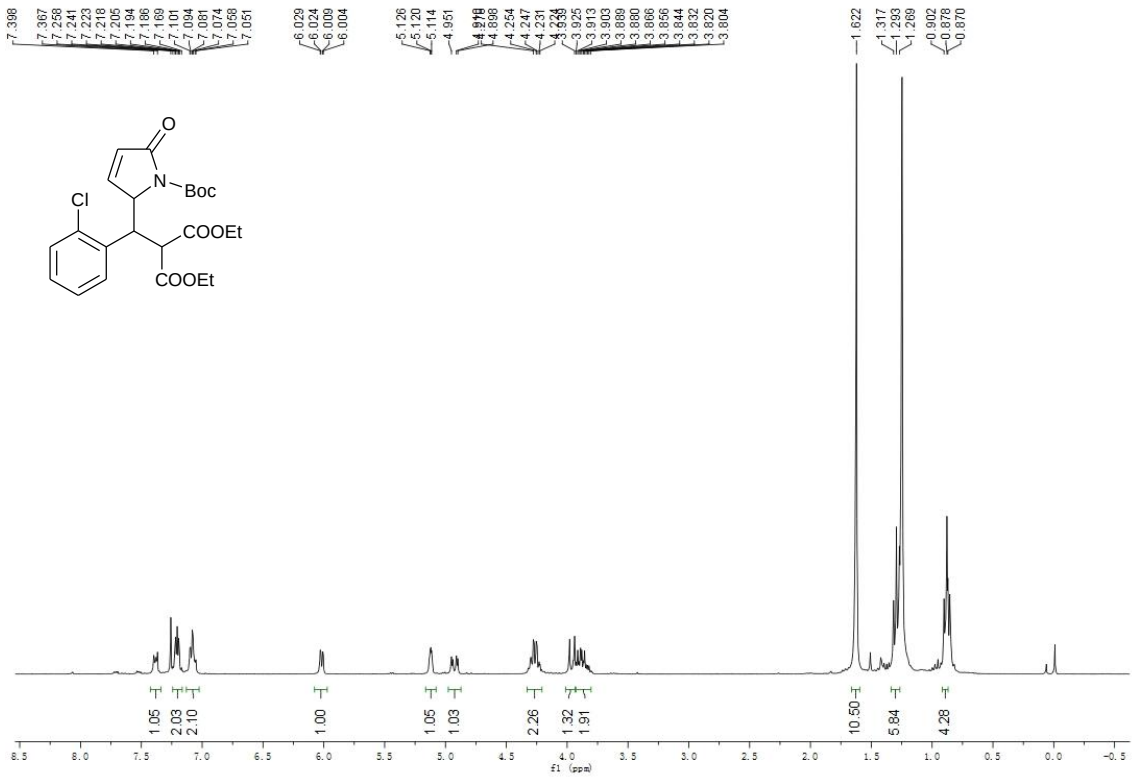


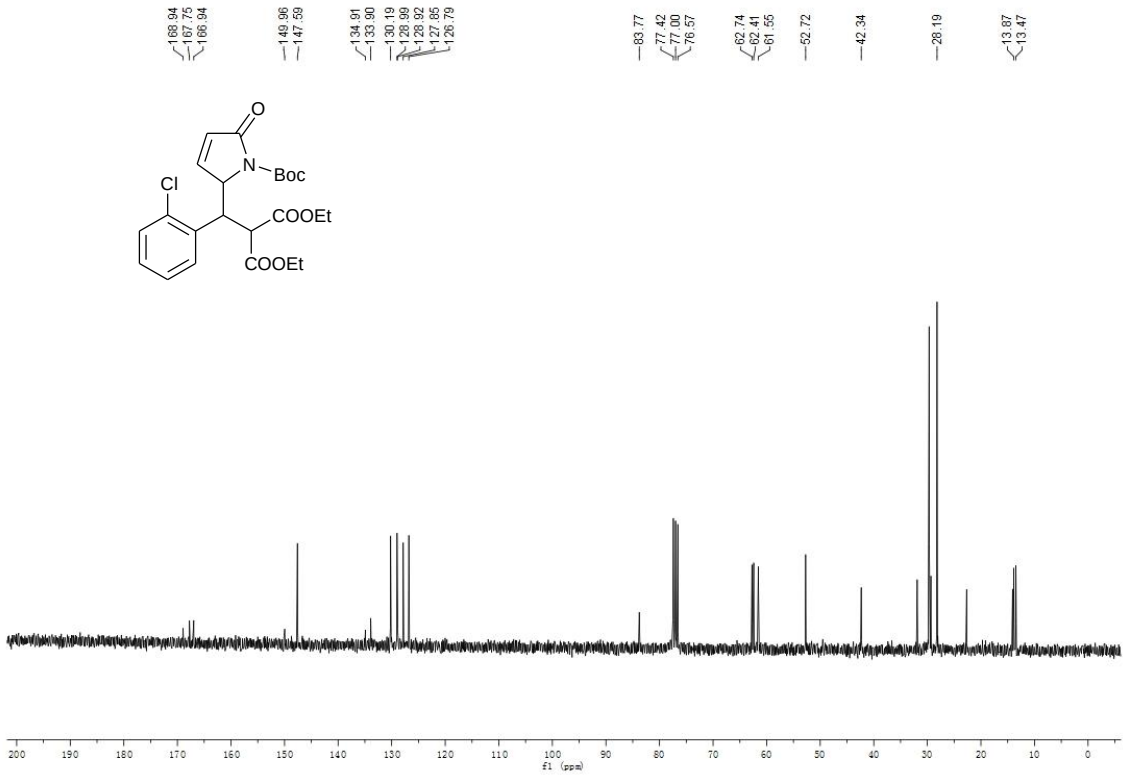


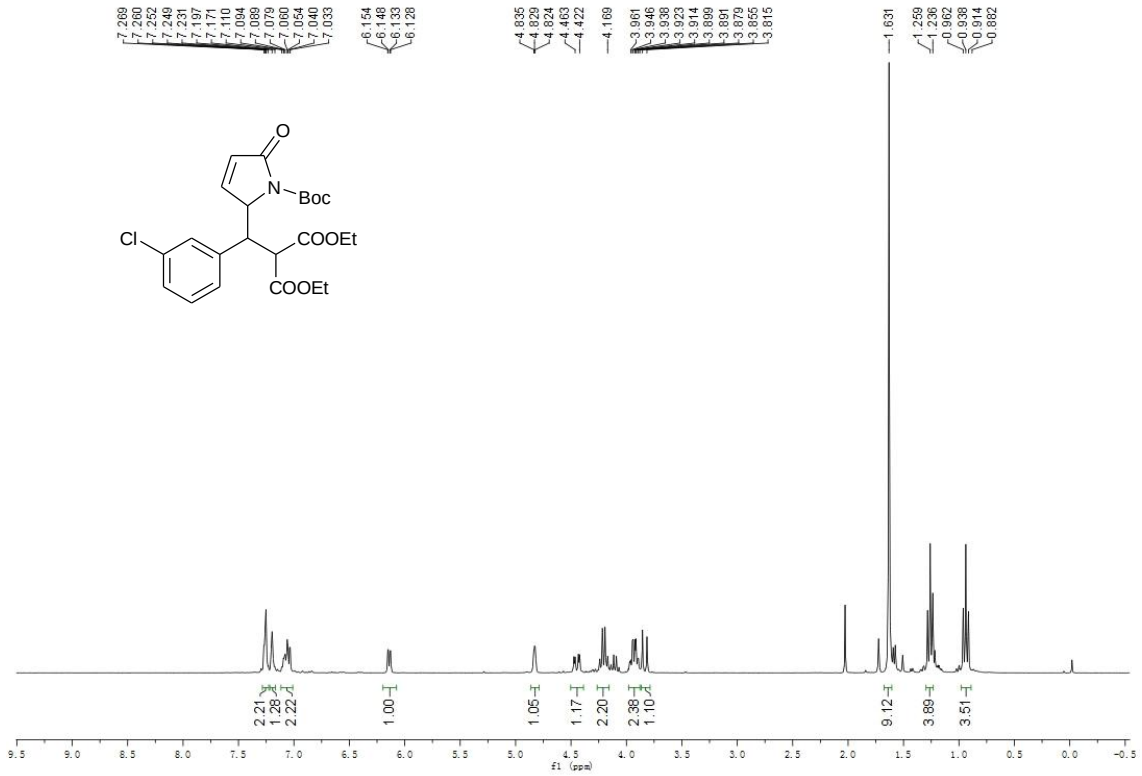


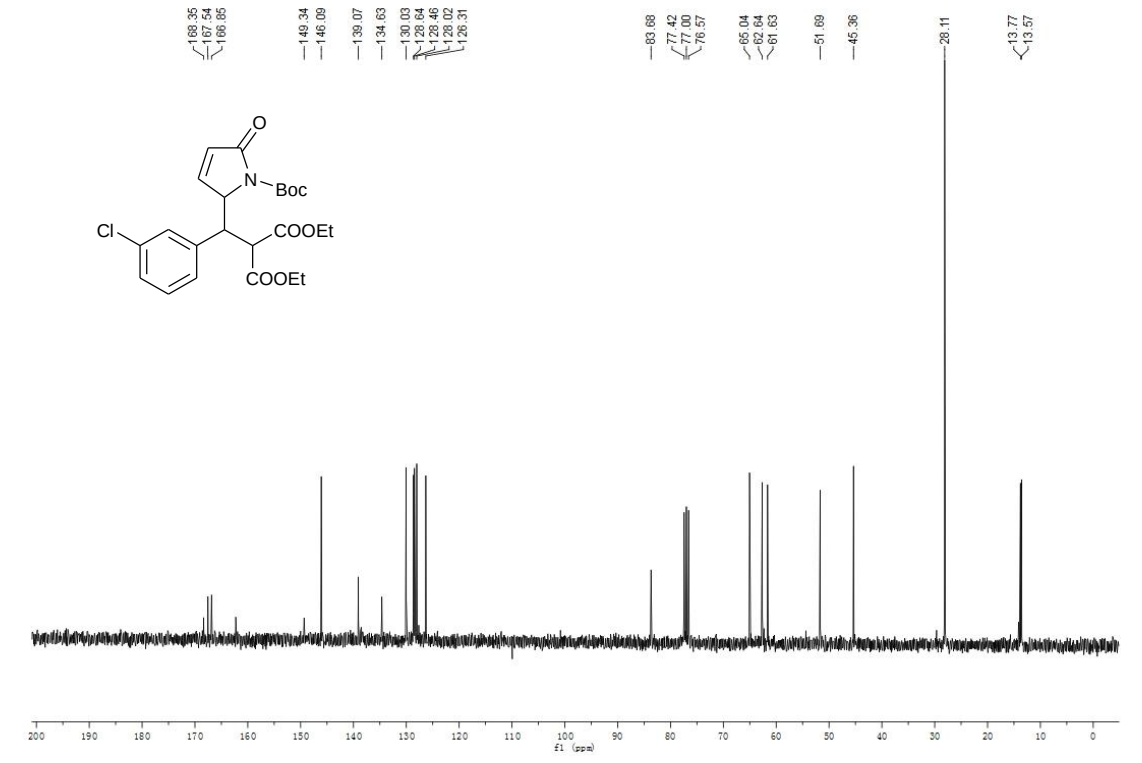


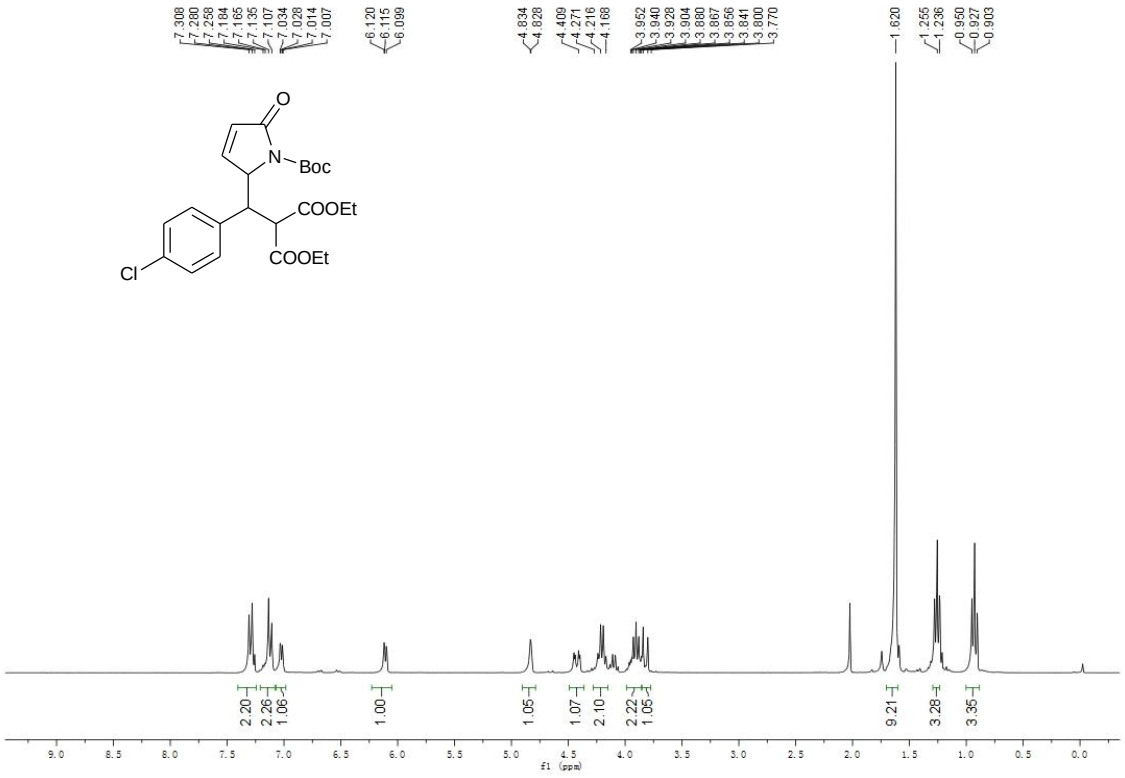


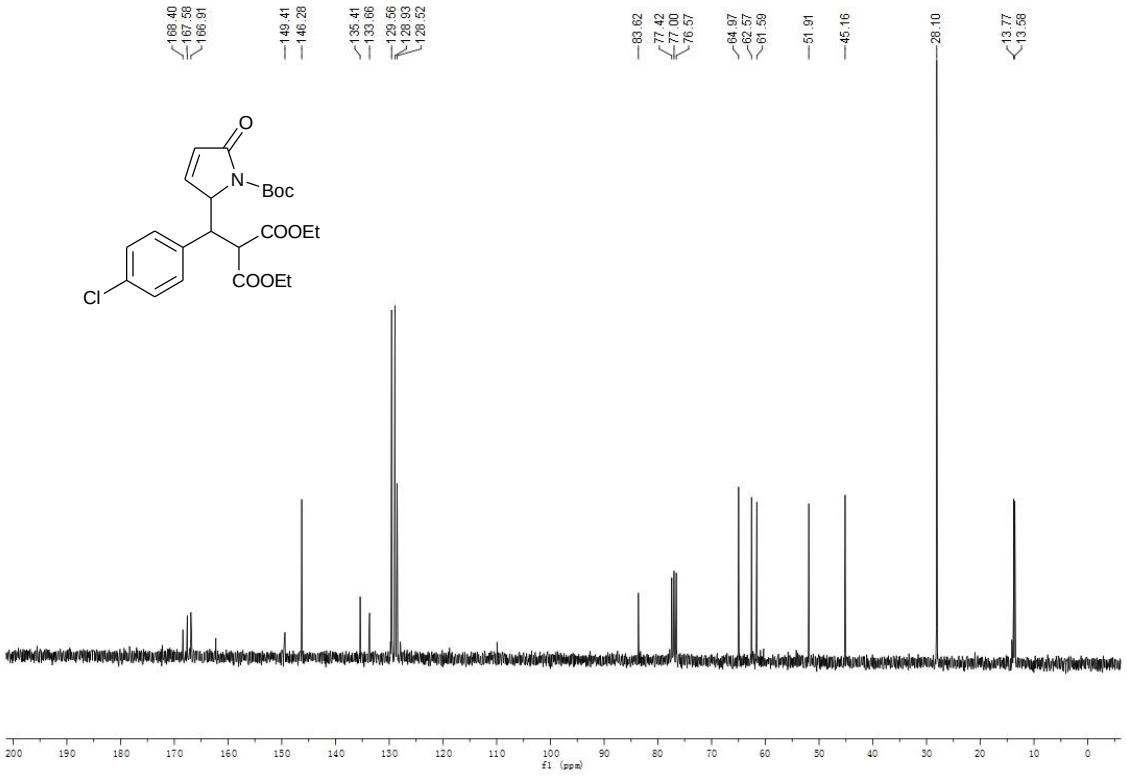


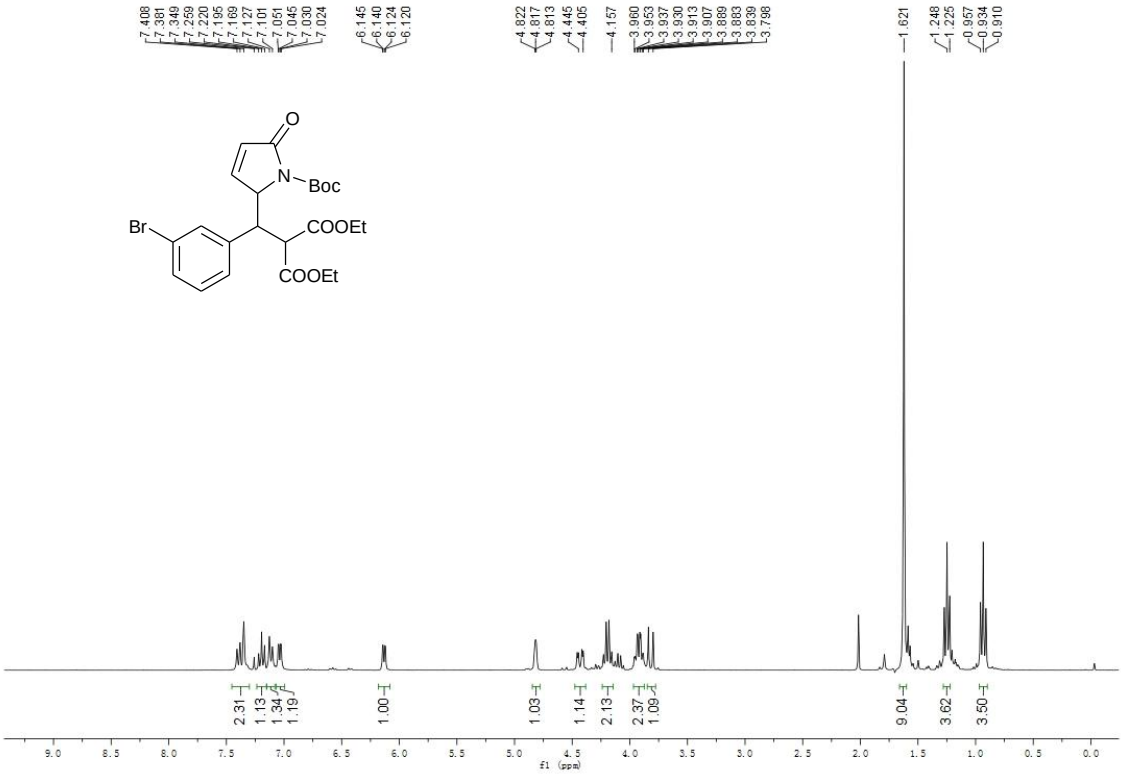


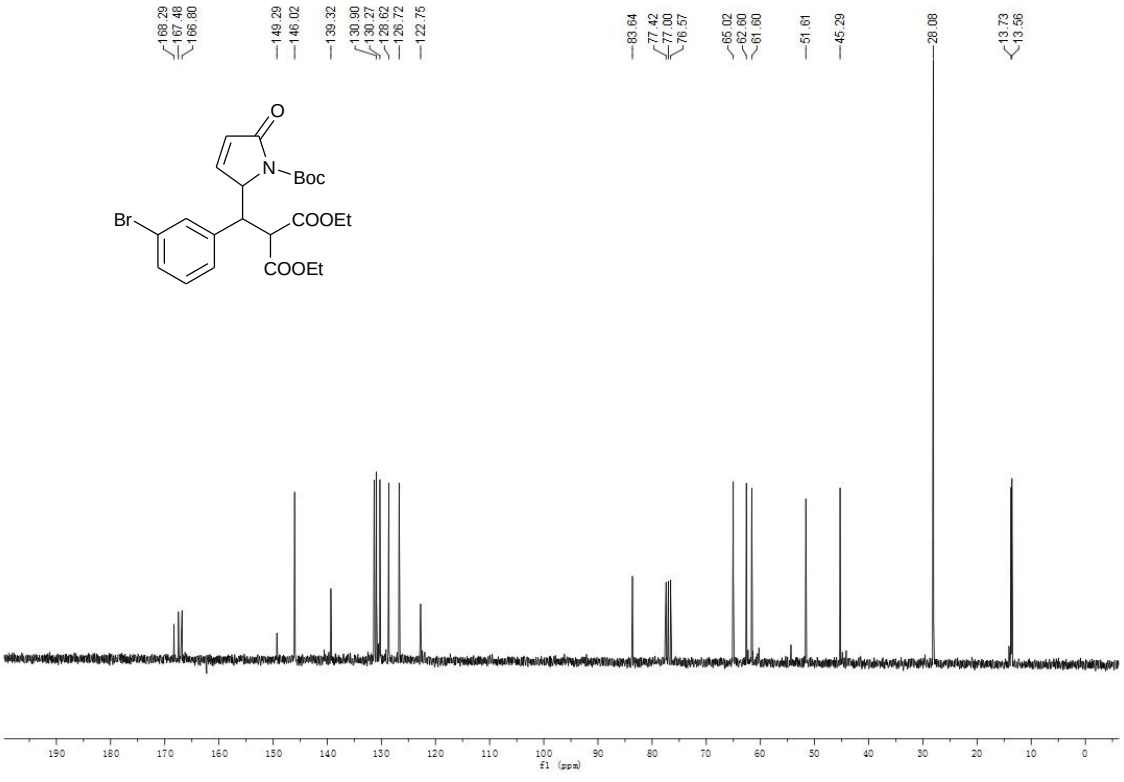


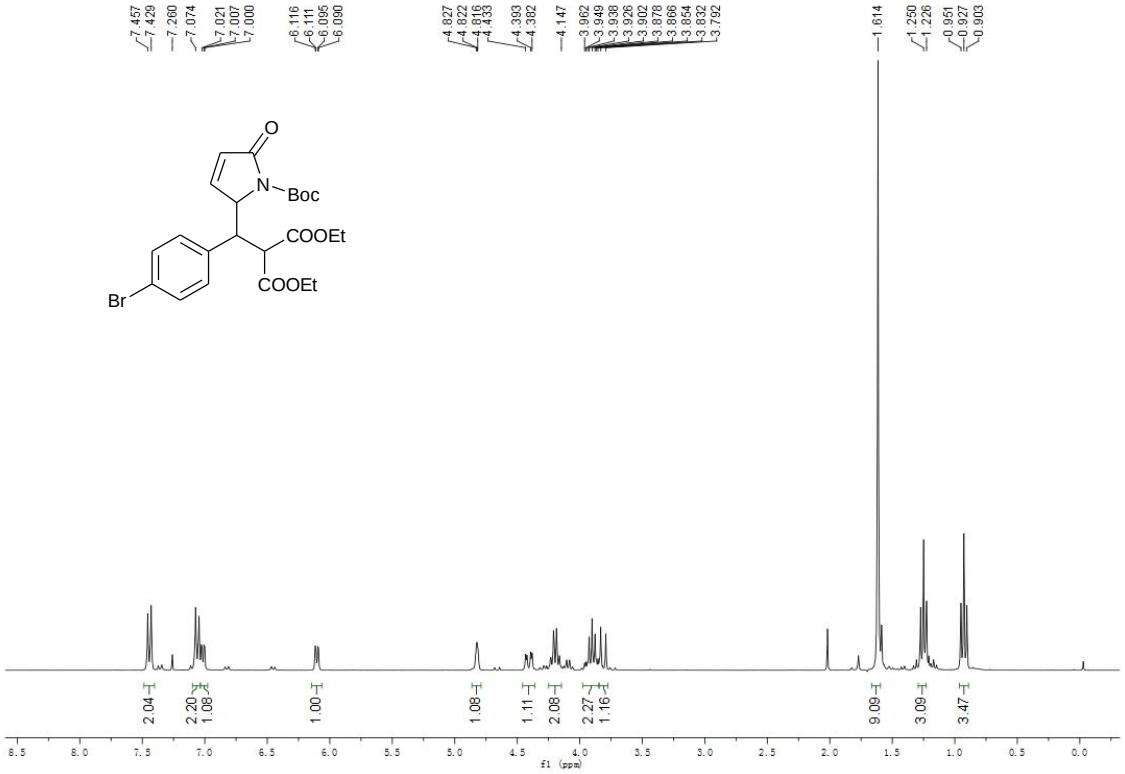


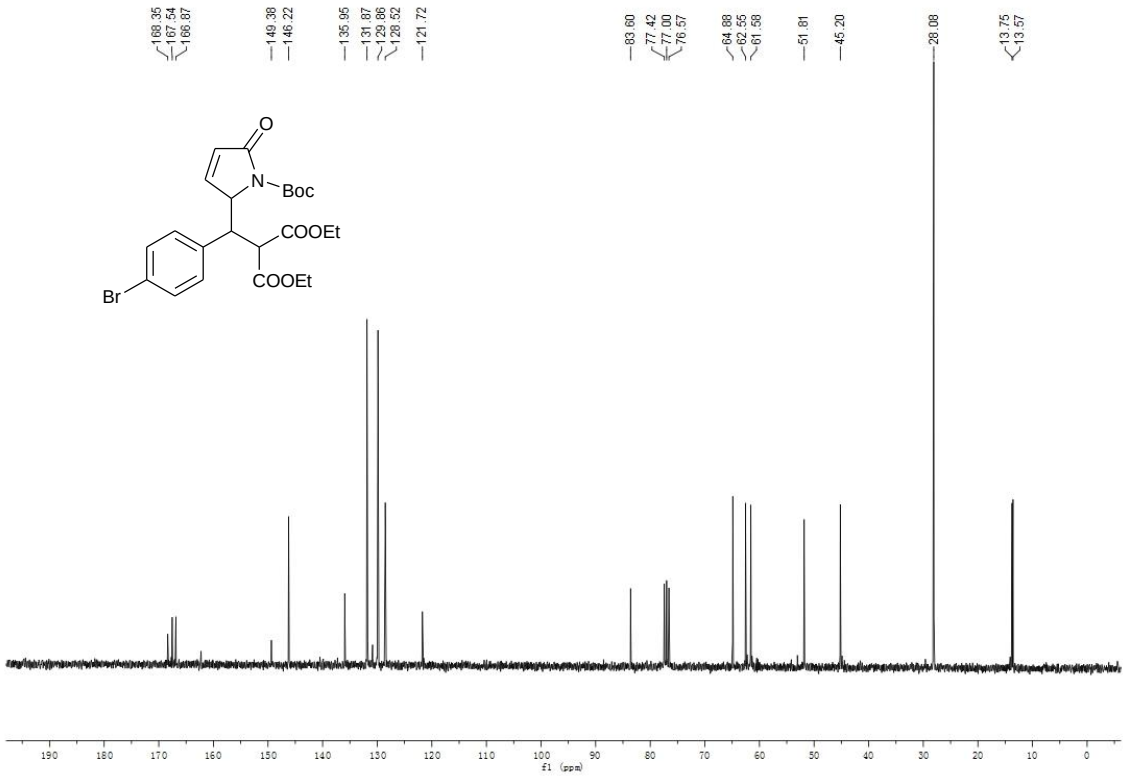


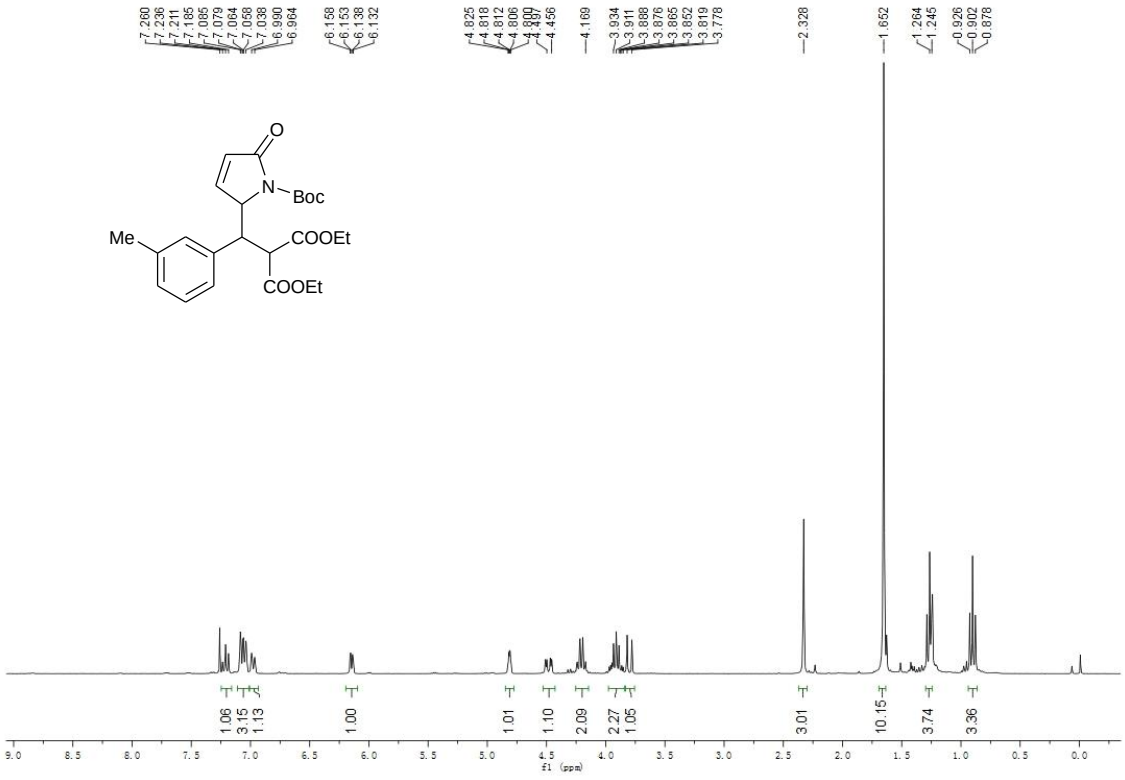


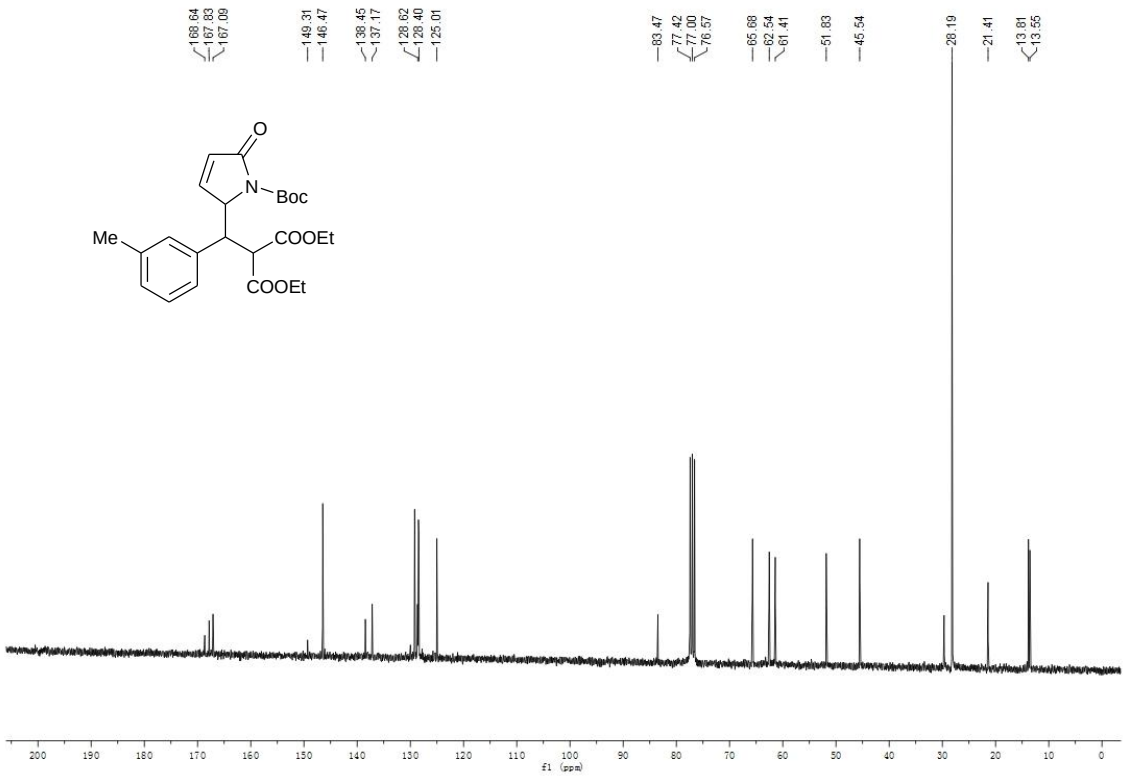


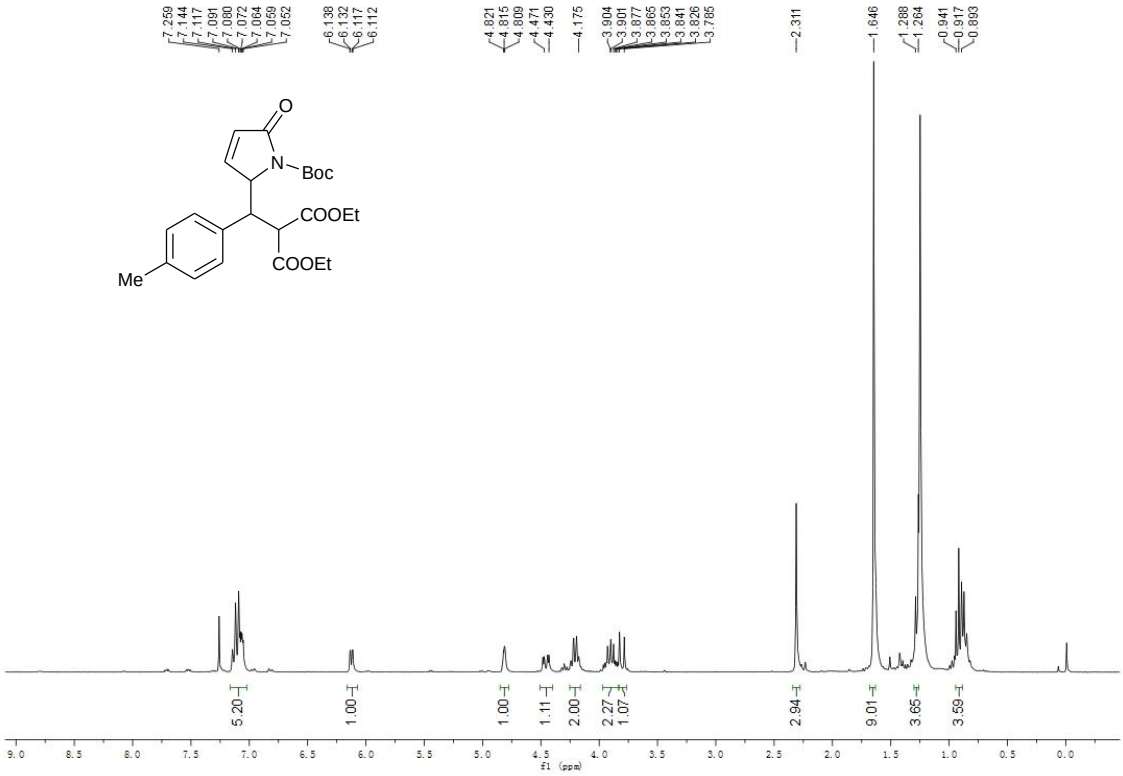








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4.430
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3.901
3.877
3.865
3.853
3.841
3.828
3.785
2.311
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1.288
1.264
0.941
0.917
0.893
O
N
Boc
COOEt
COOEt
Me
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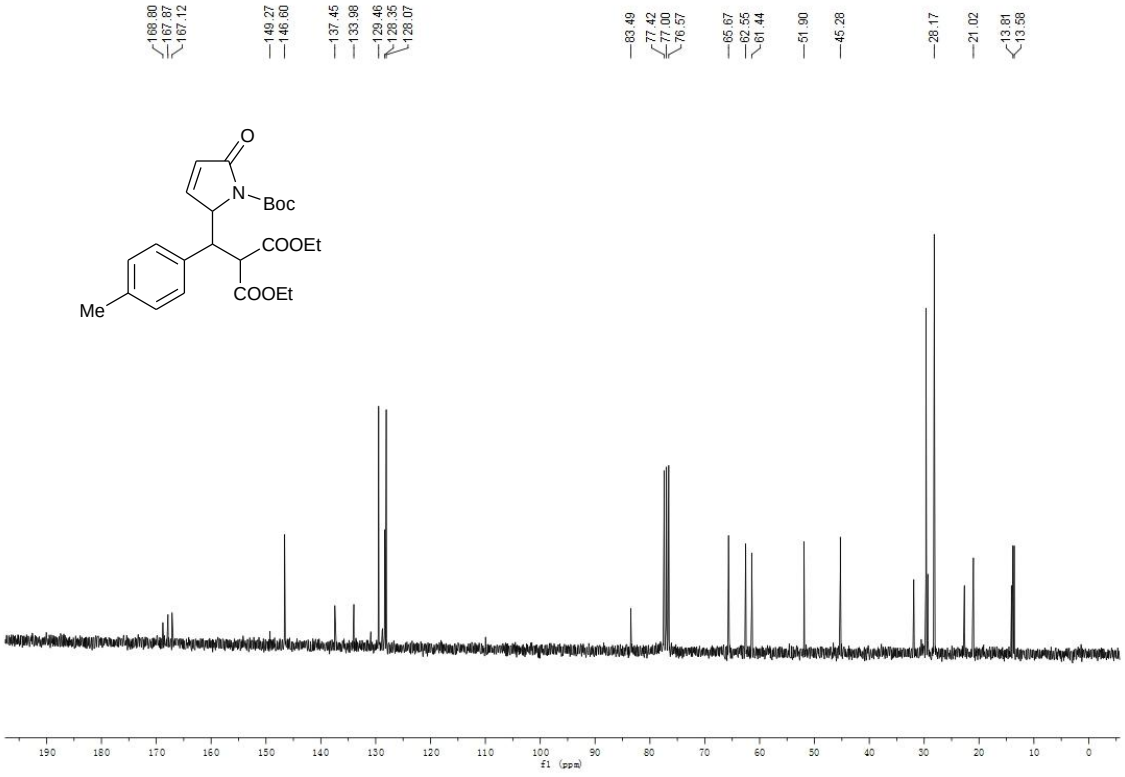
f1 (ppm)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Boc
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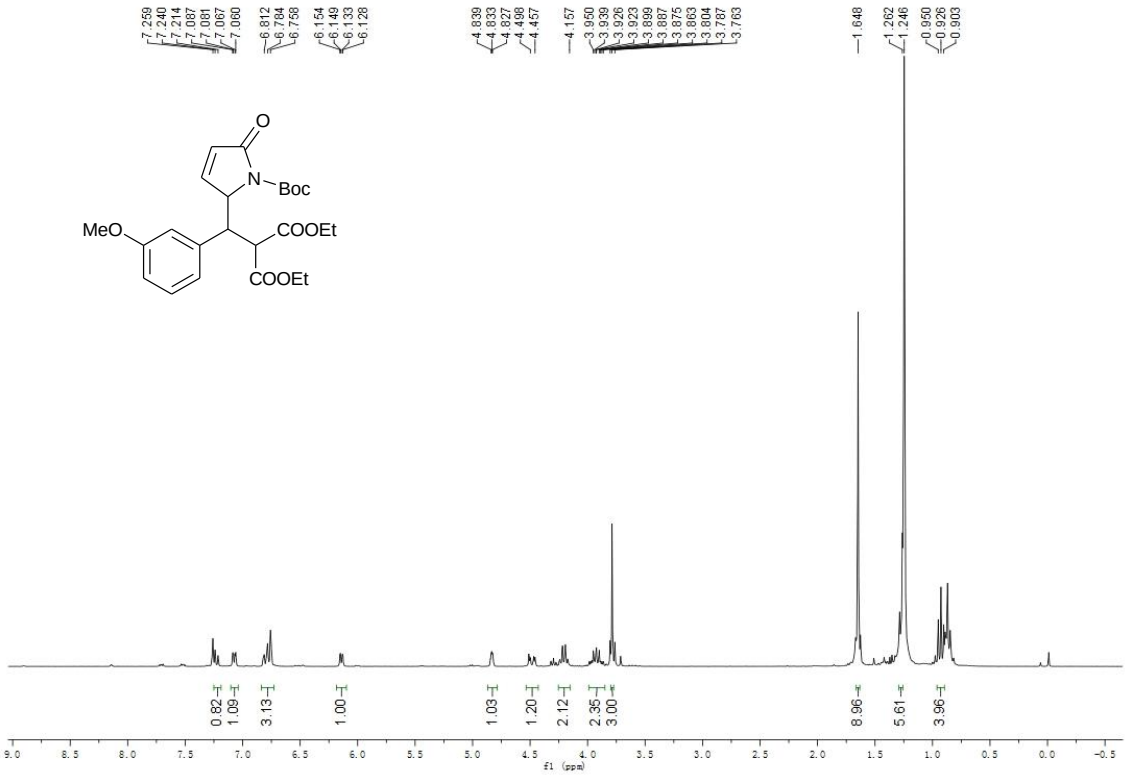
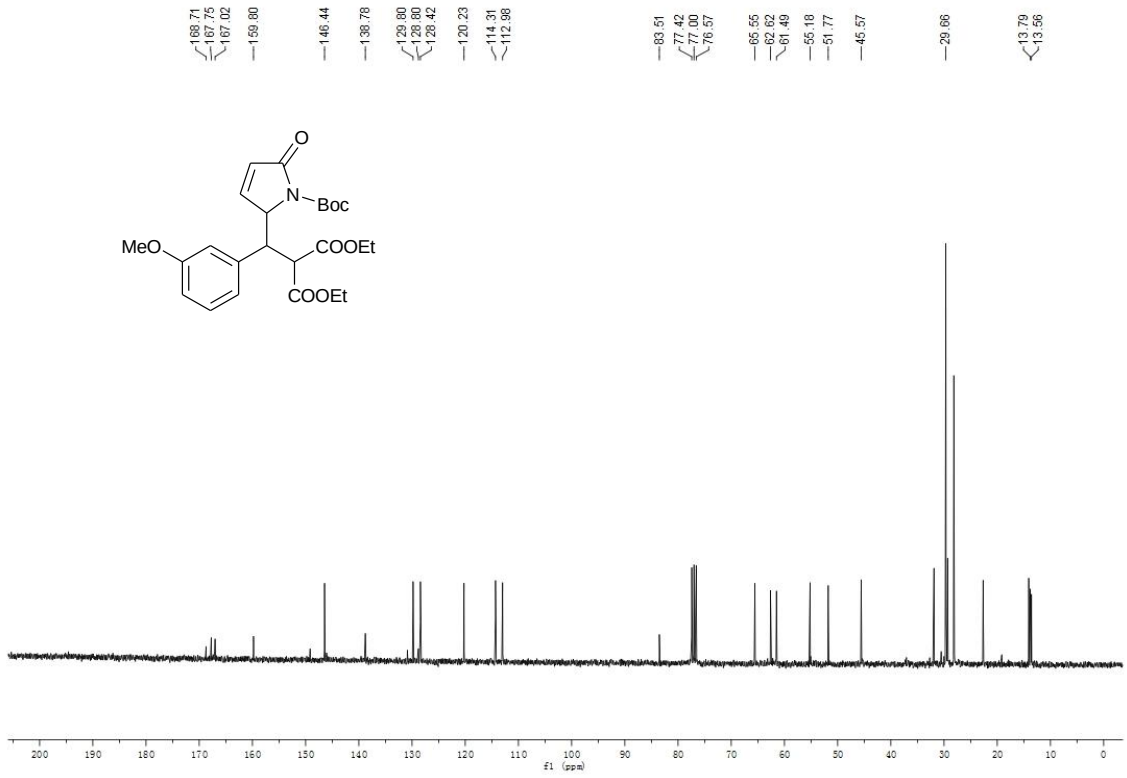
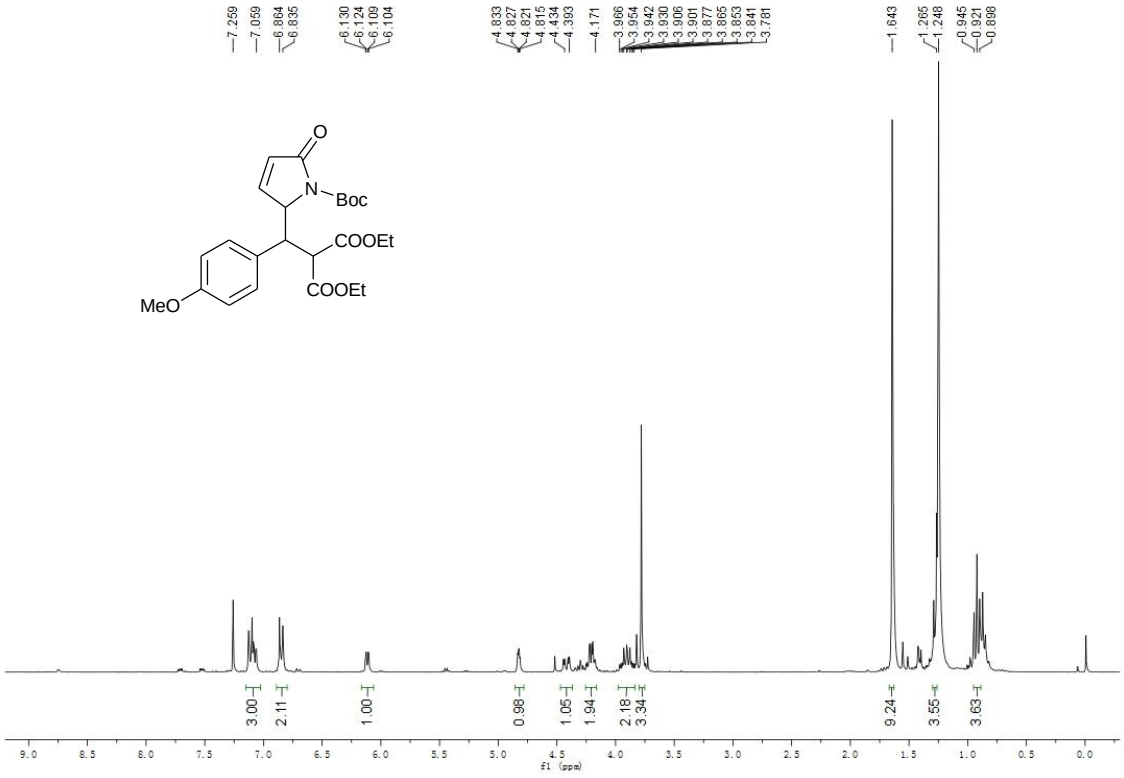
COOEt
Me
f1 (ppm)



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COOEt
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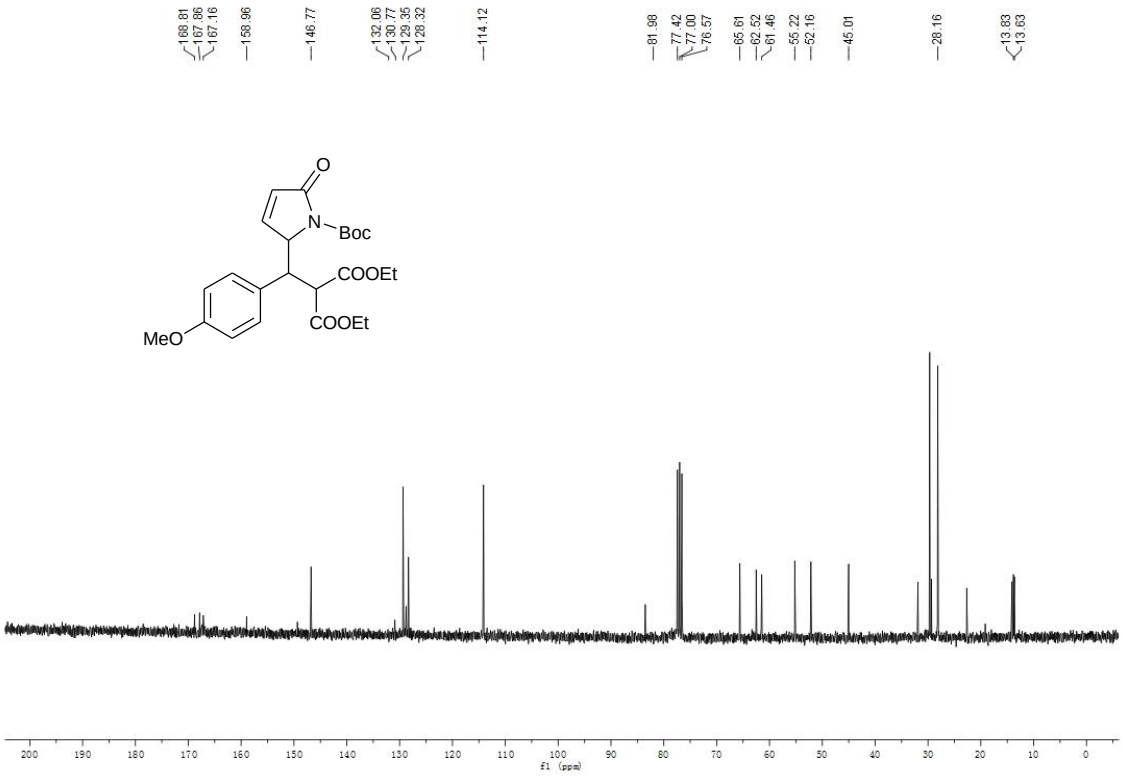
f1 (ppm)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76.57
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62.52
61.46
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Boc
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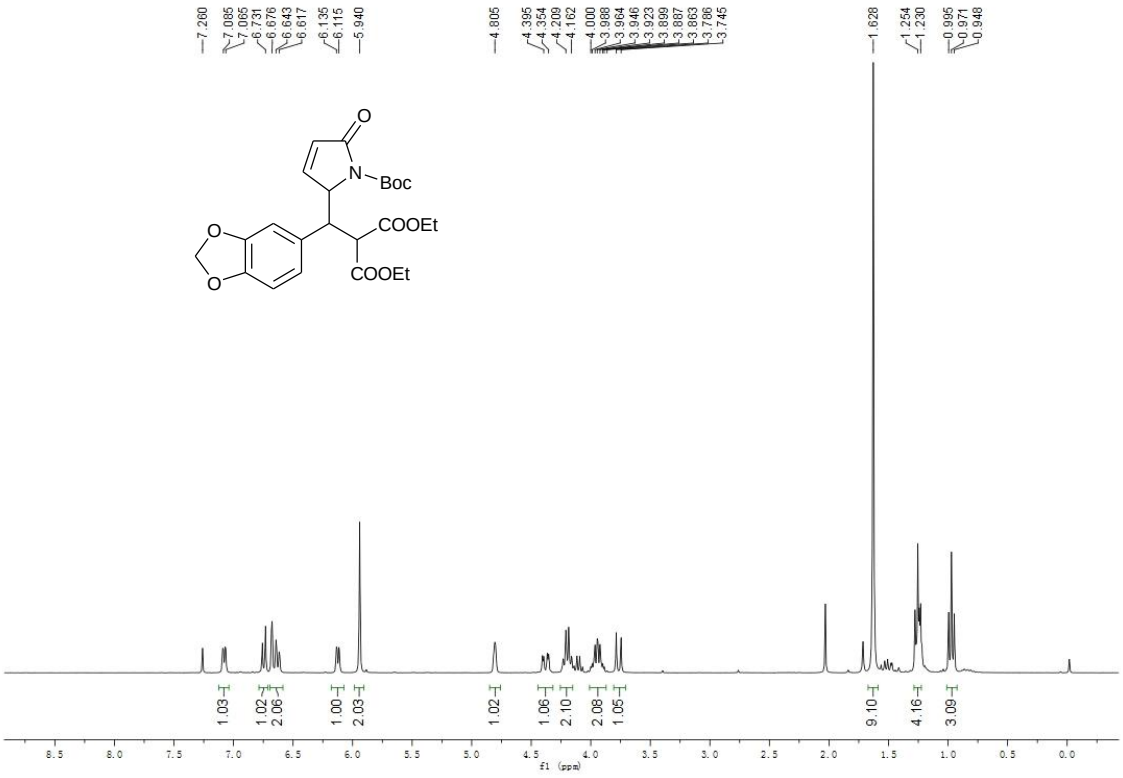
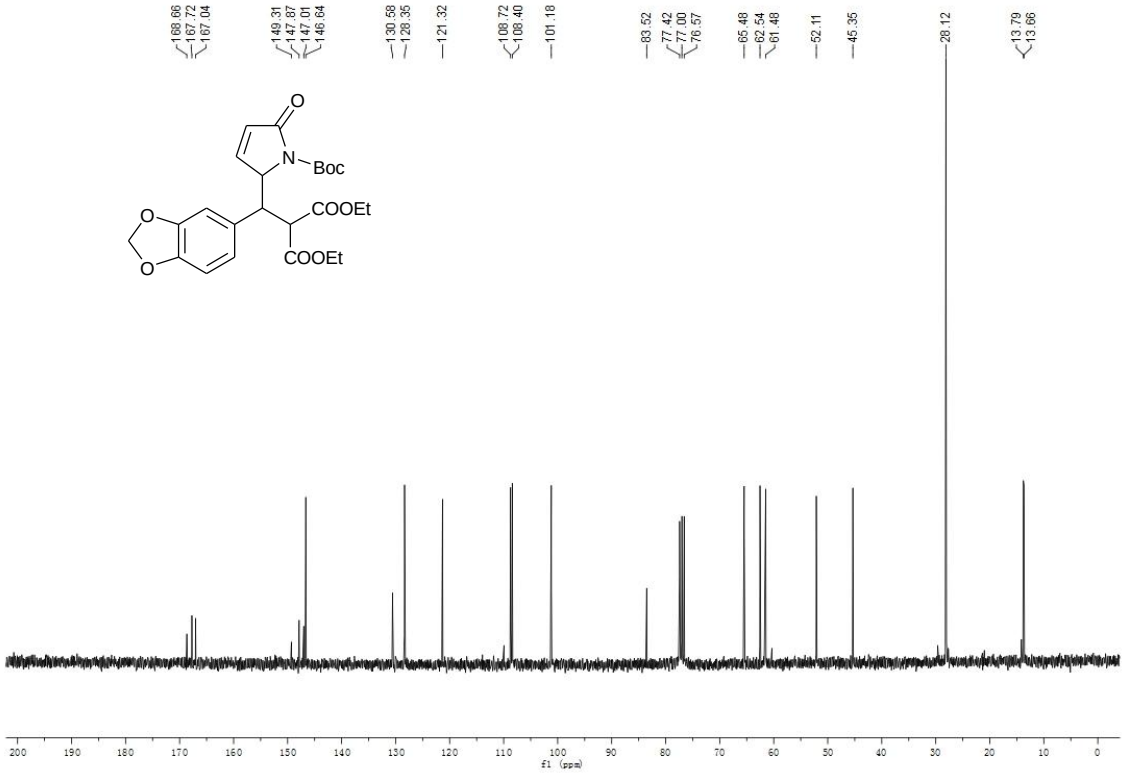
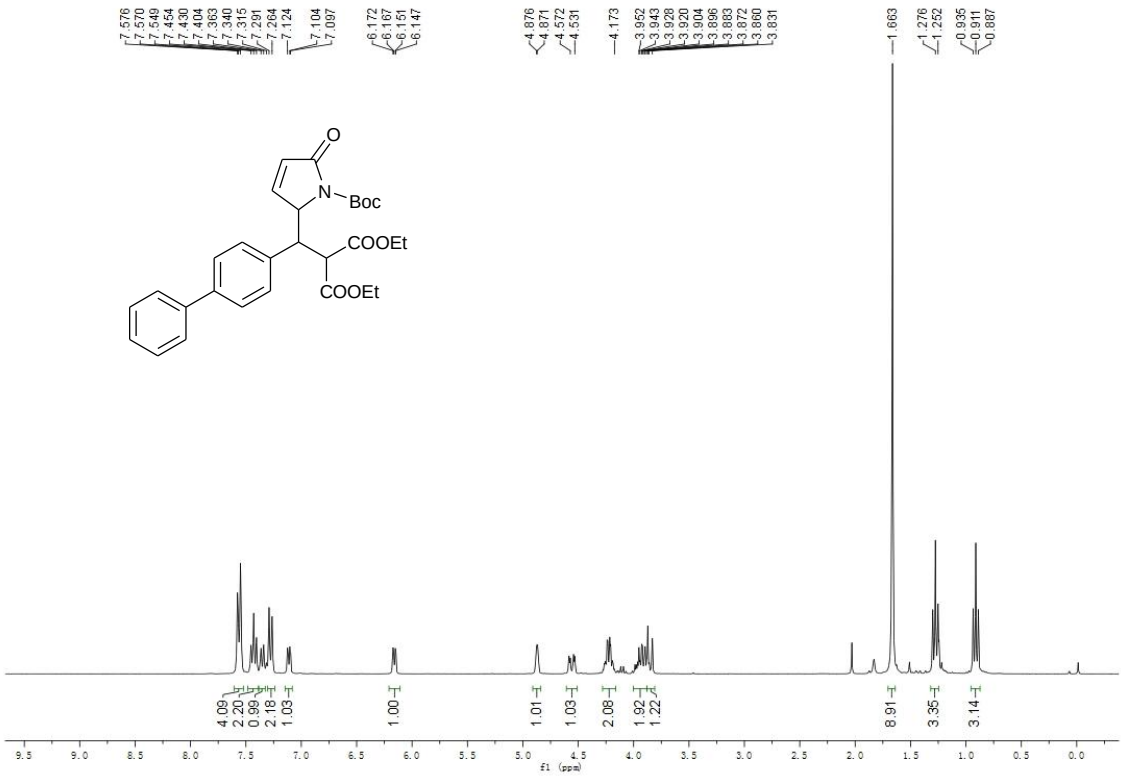
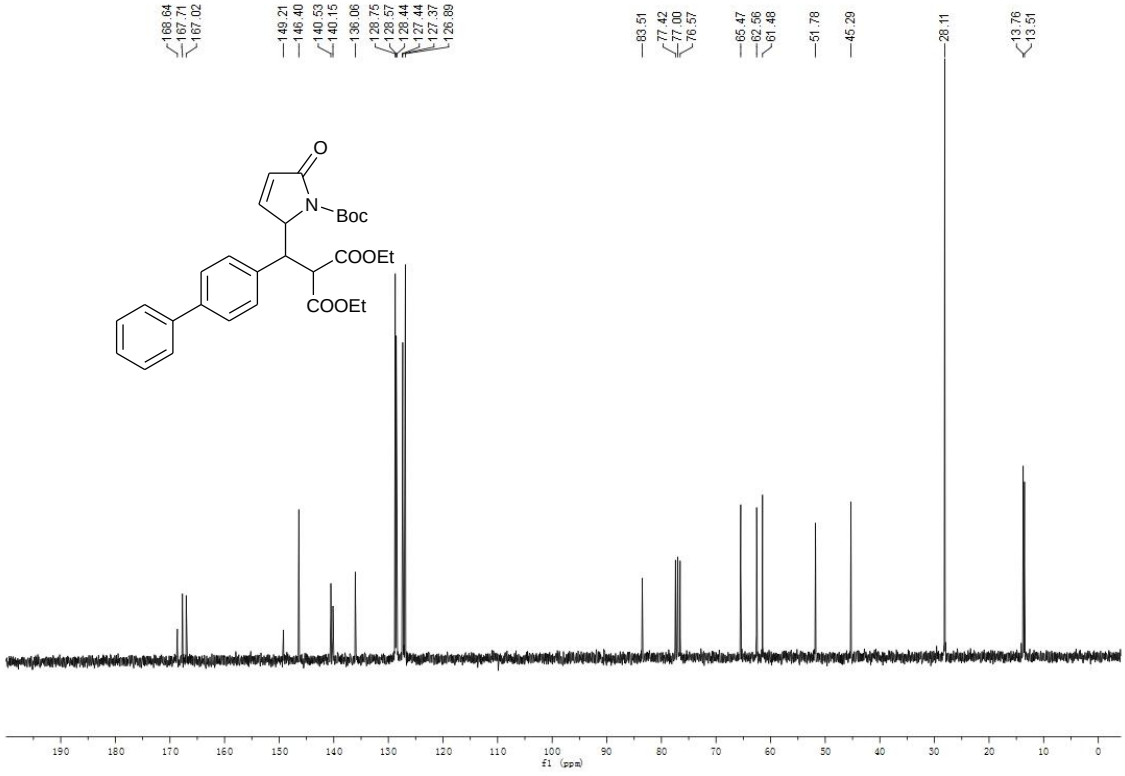
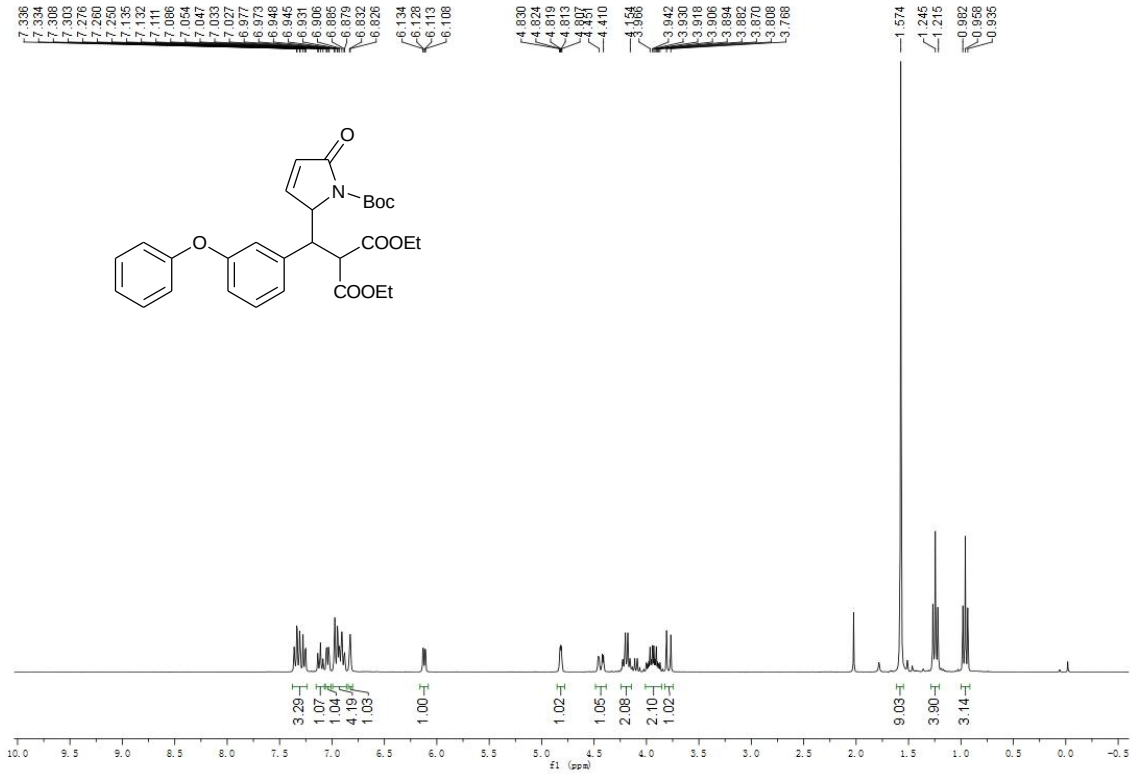
f1 (ppm)

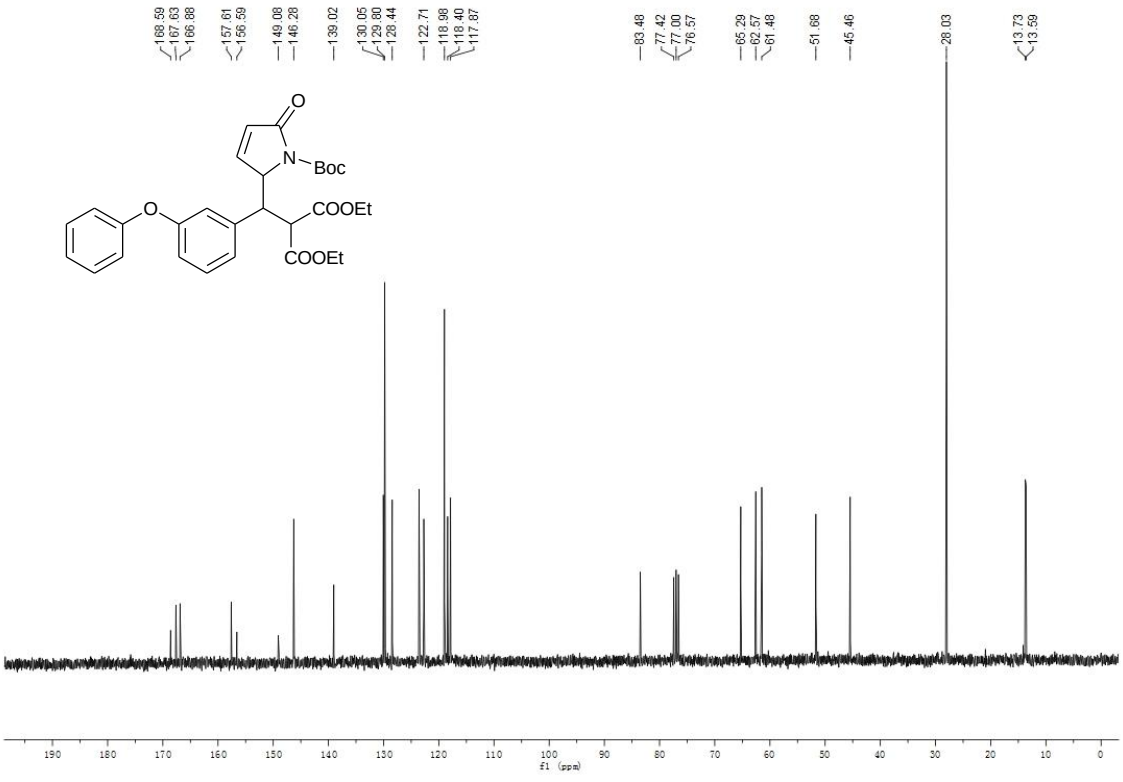


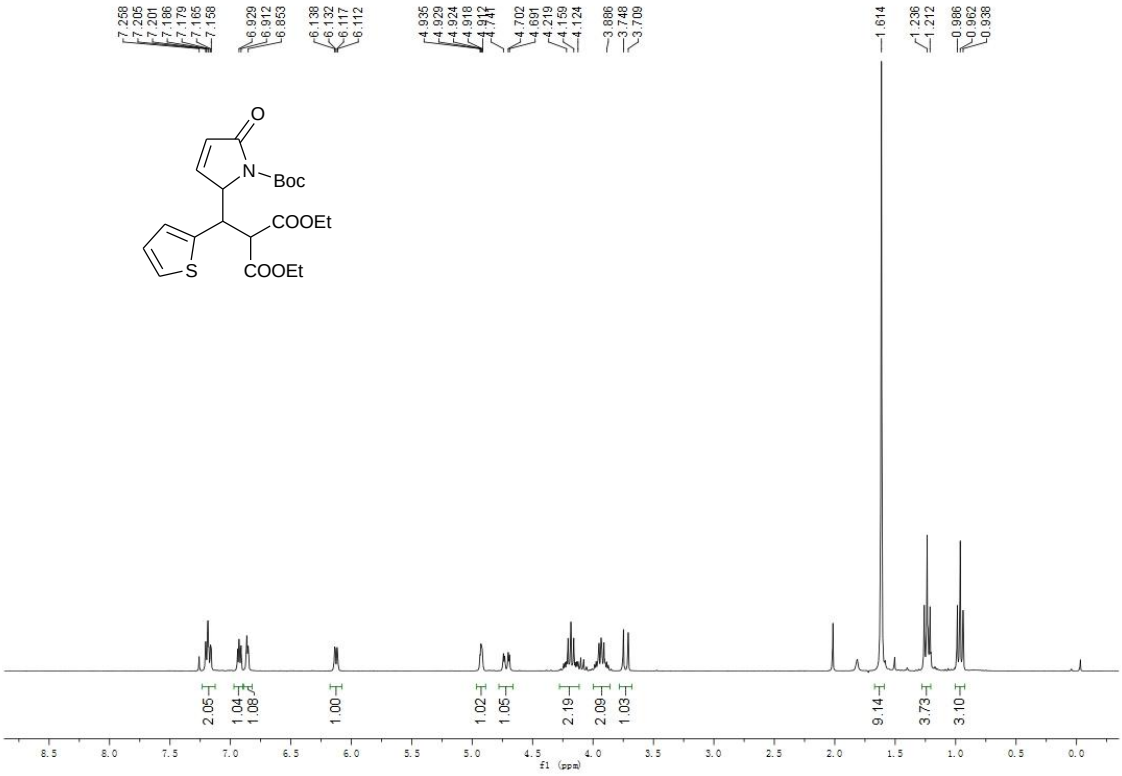


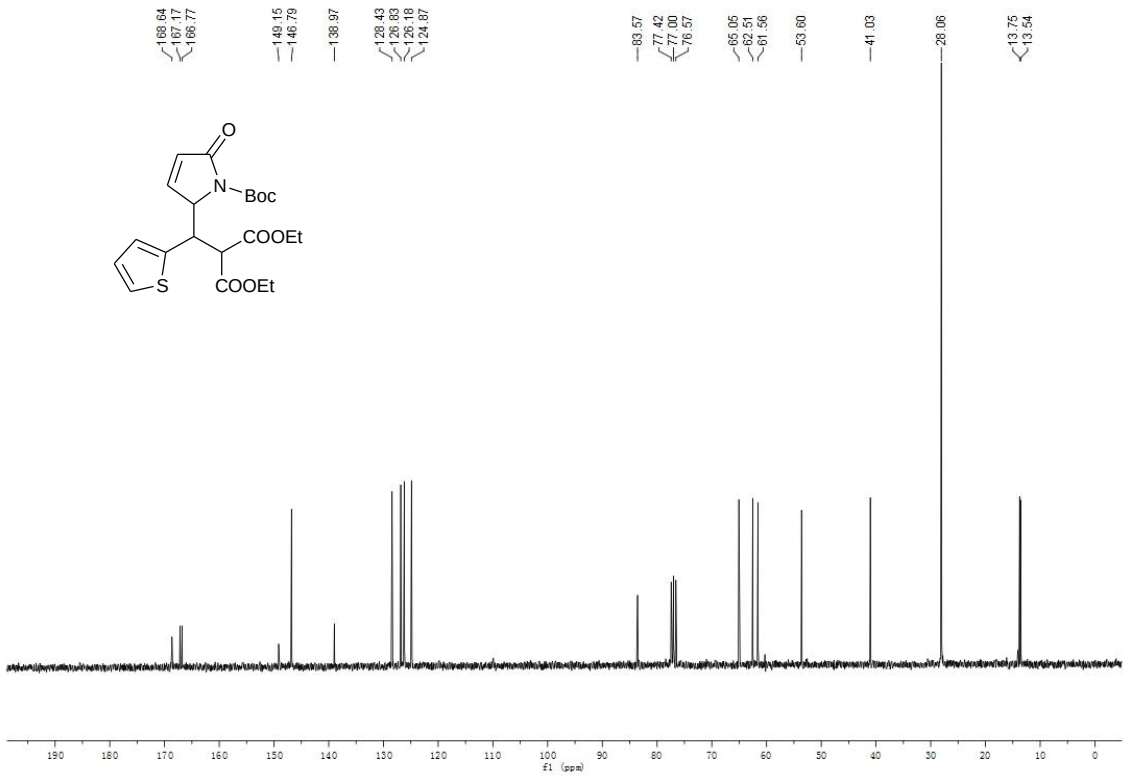


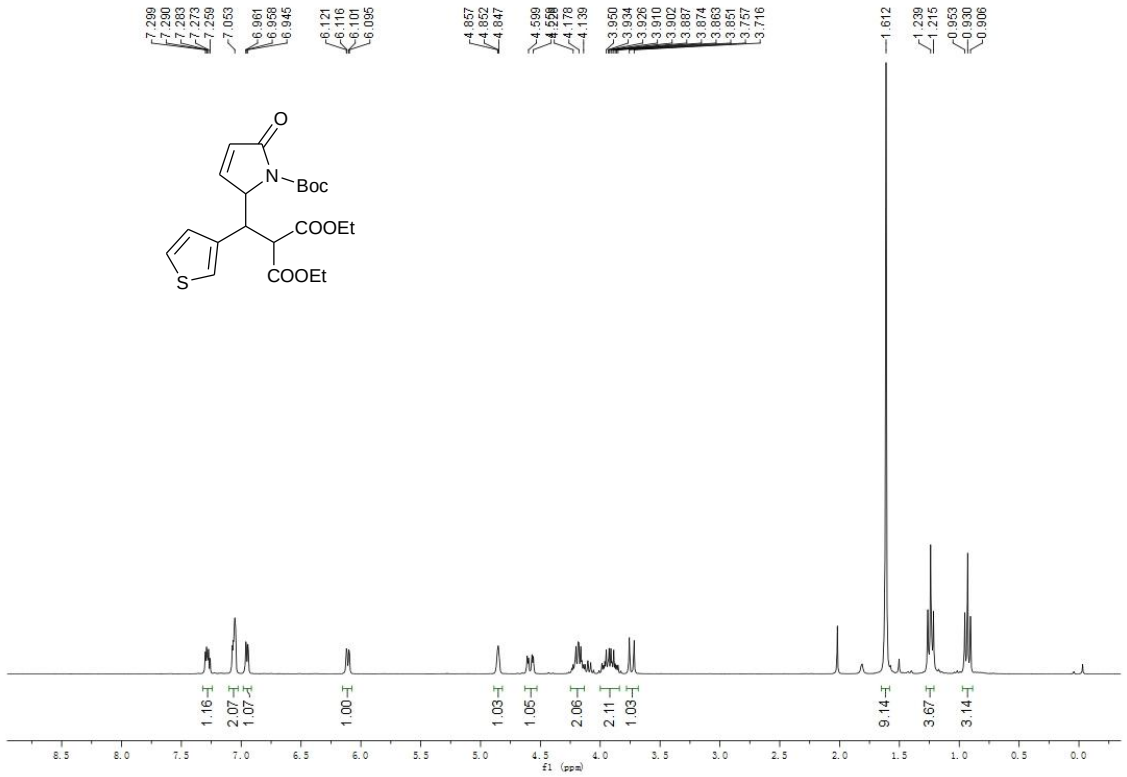


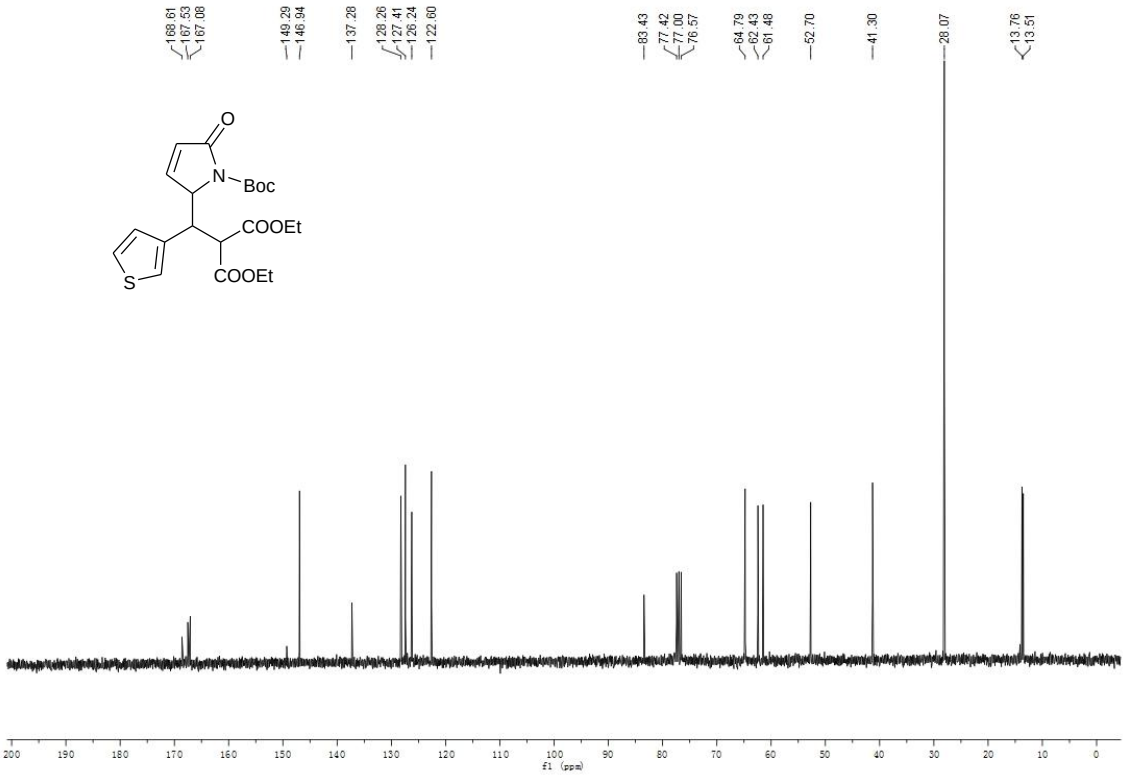


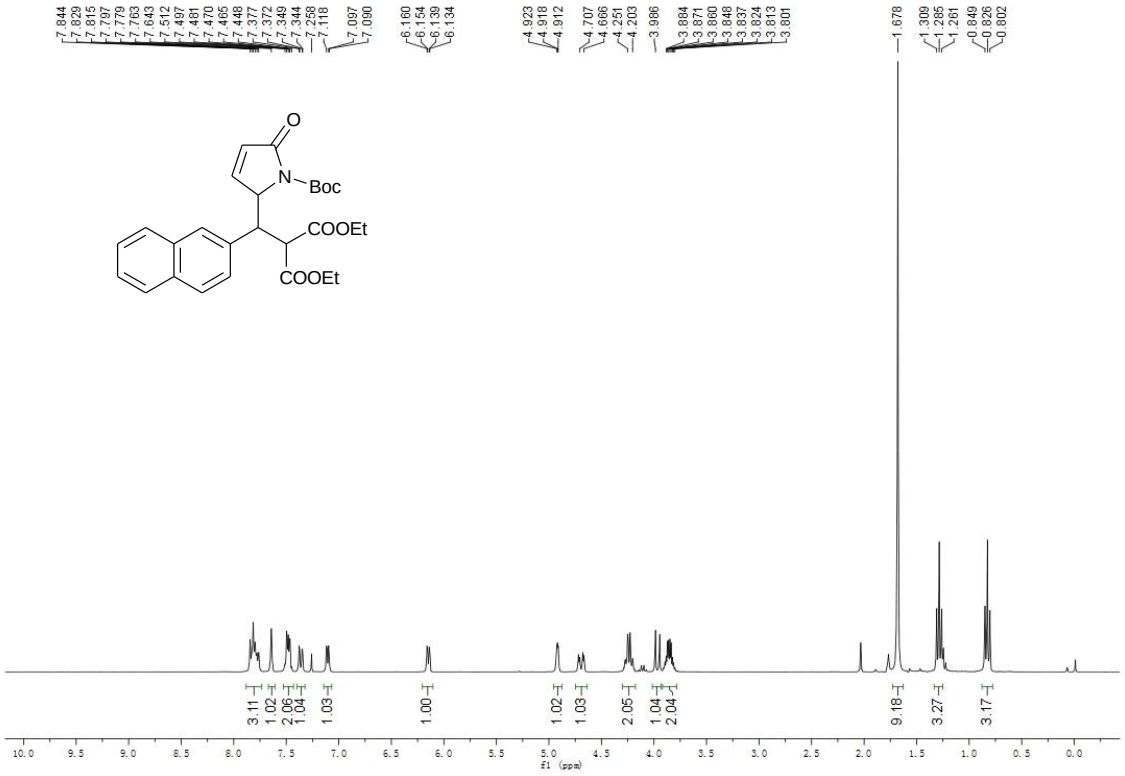








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COOEt
COOEt
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2.06
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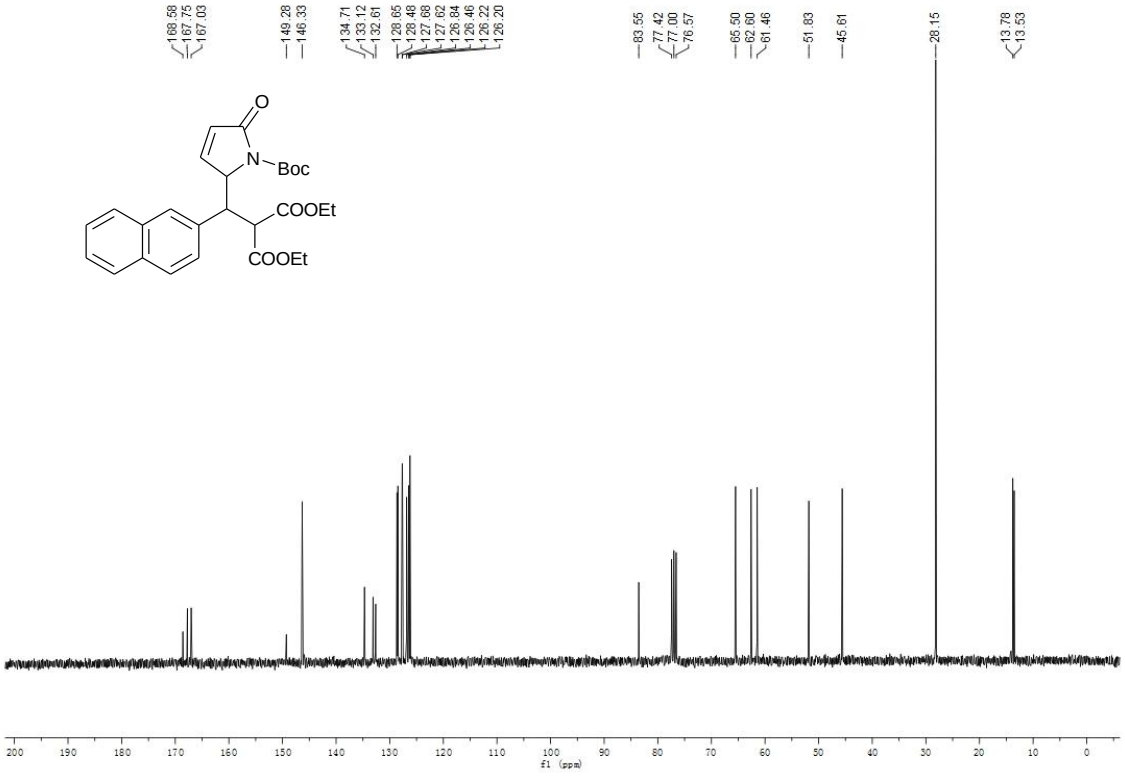
f1 (ppm)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77.00
76.57
65.50
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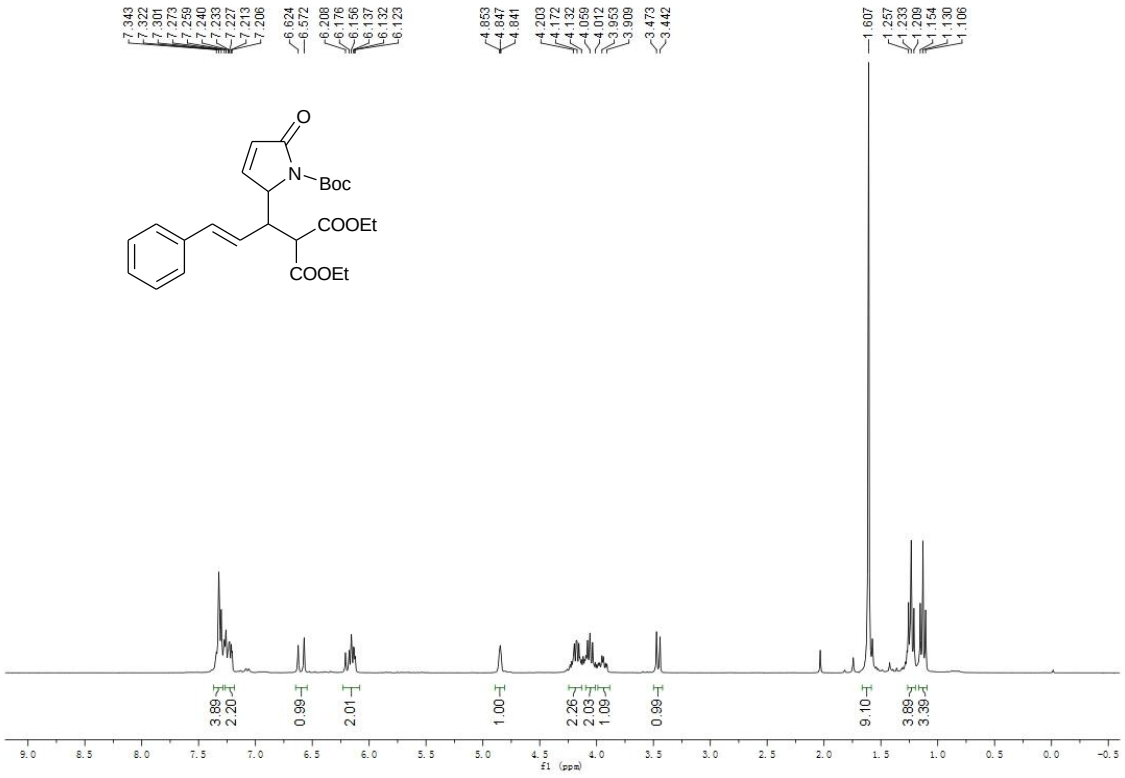
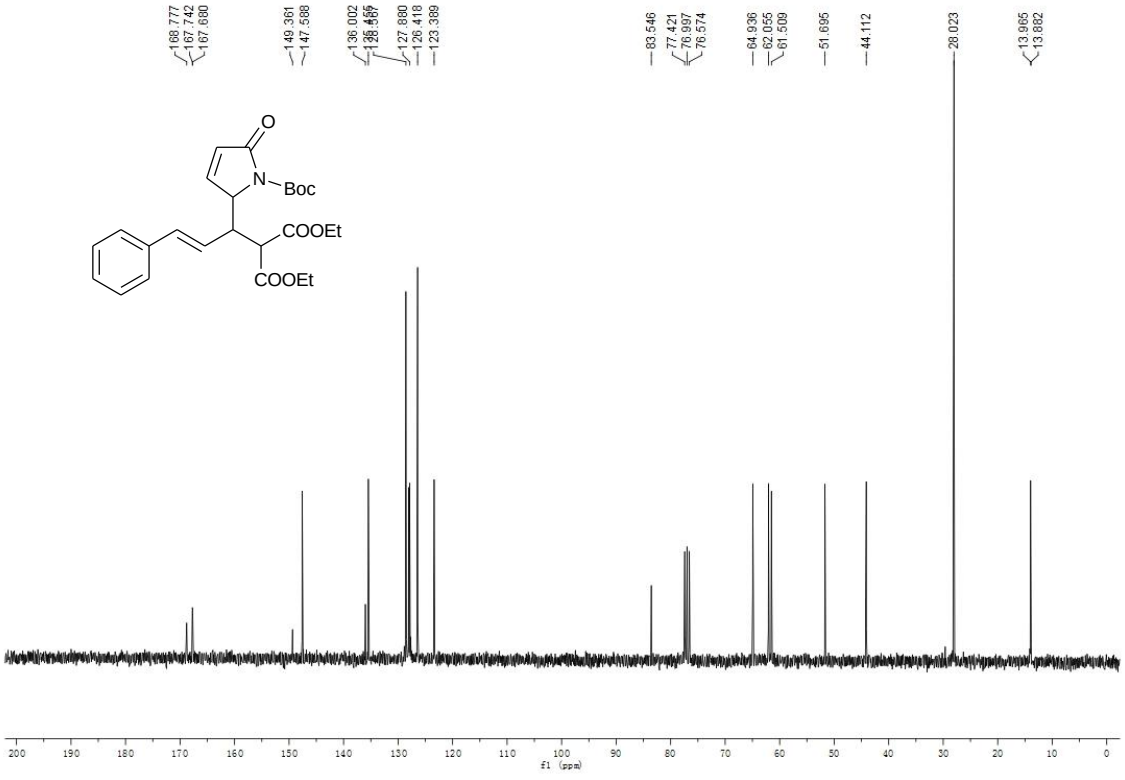
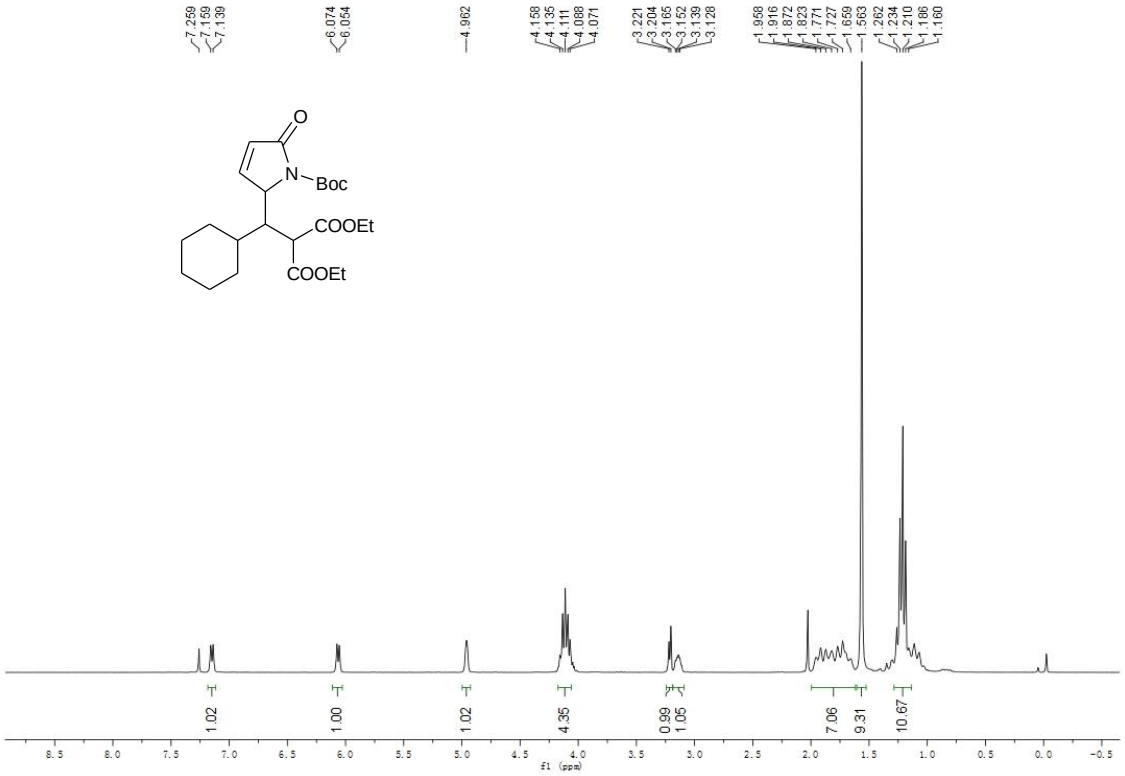
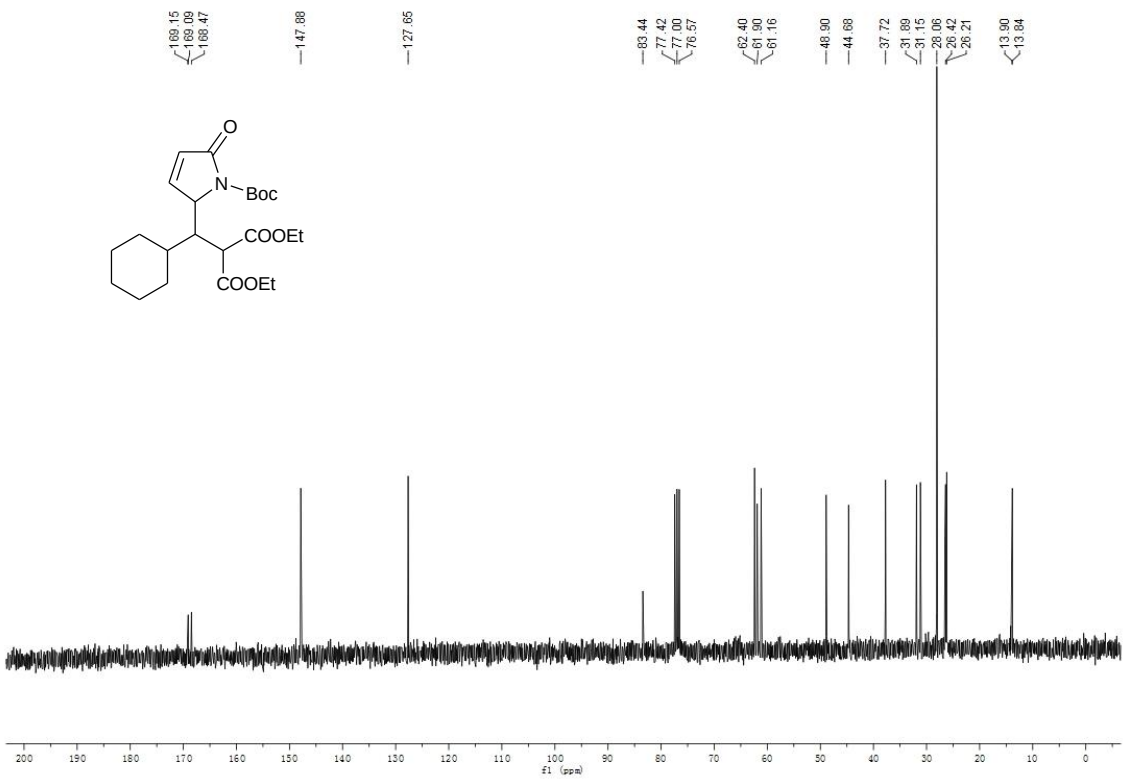
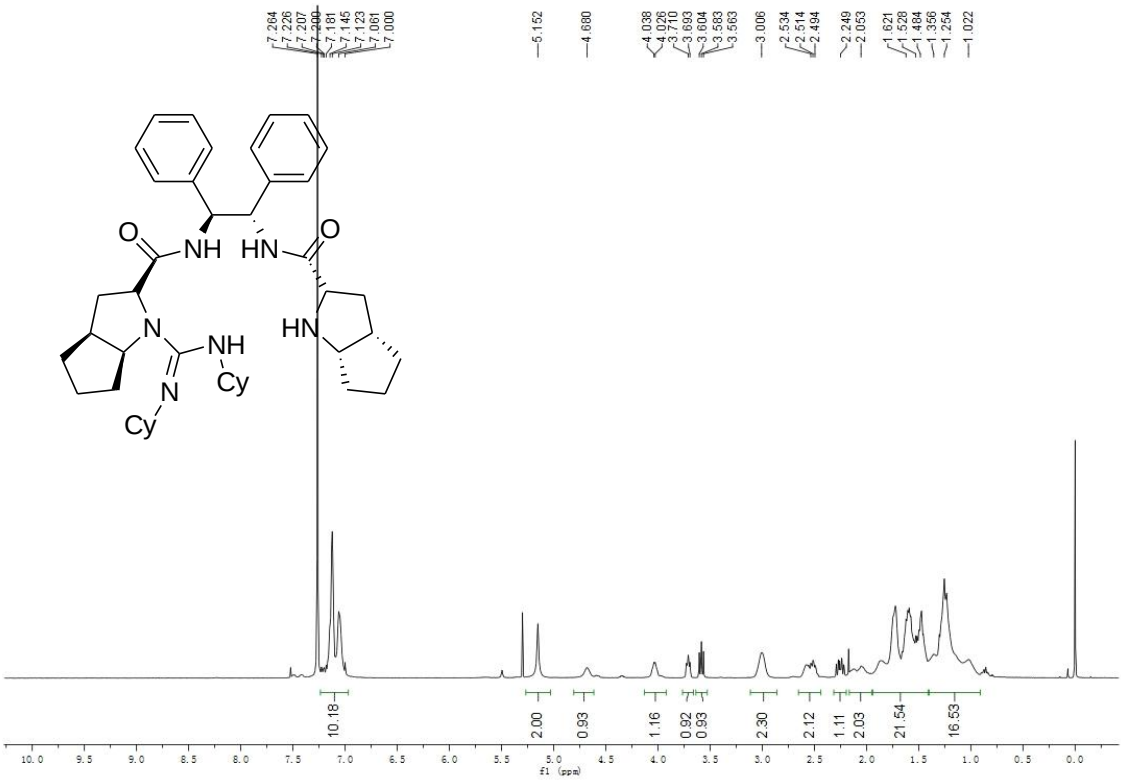
COOEt
COOEt
f1 (ppm)







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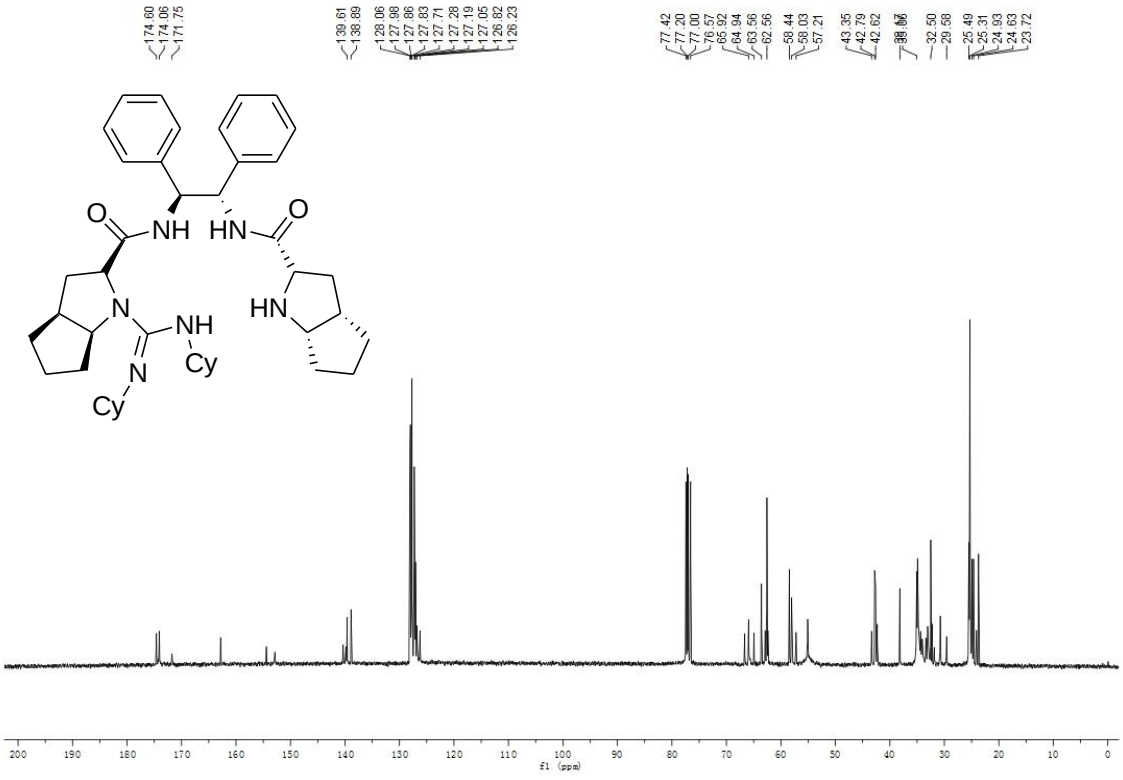
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127.71
127.28
127.19
127.05
126.82
126.23
77.42
77.20
77.00
76.57
65.92
64.94
63.56
62.56
58.44
58.03
57.21
43.35
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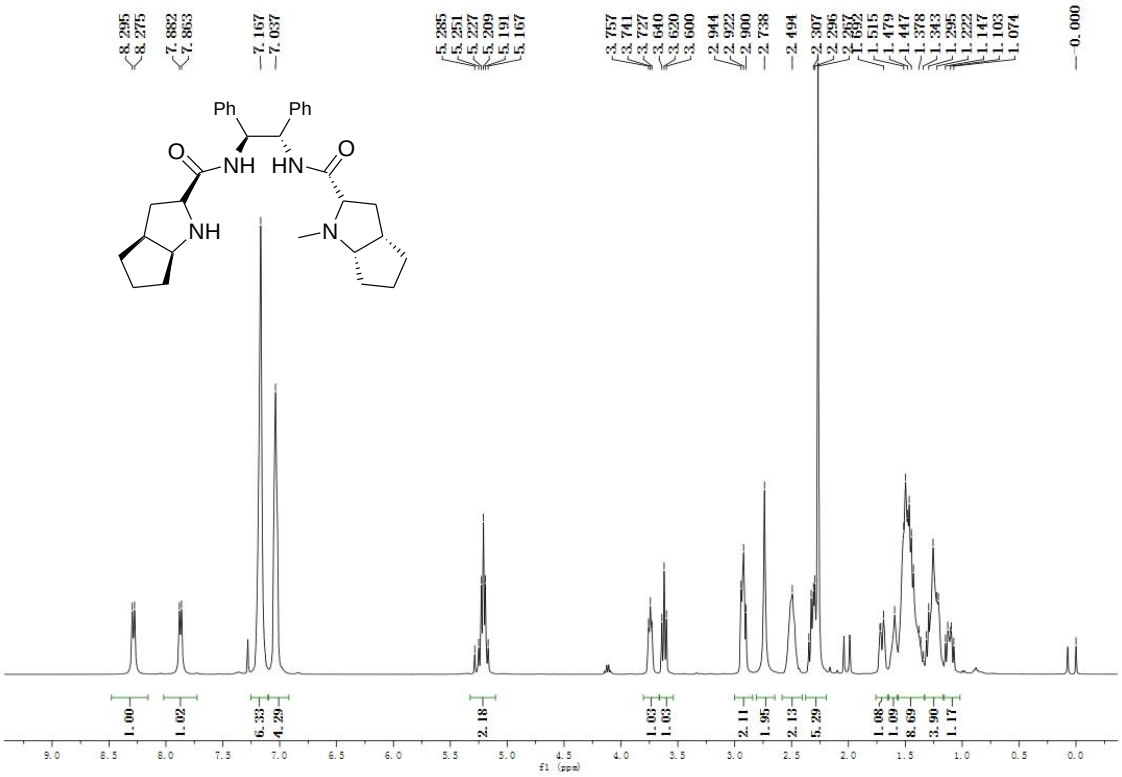
42.62
32.50
29.58
25.49
25.31
24.93
24.63
23.72
f1 (ppm)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7.167
7.037
5.285
5.251
5.227
5.209
5.191
5.167
3.757
3.741
3.727
3.640
3.620
3.600
2.944
2.922
2.900
2.738
2.494
2.307
2.296
2.257
2.232
1.515
1.479
1.447
1.378
1.343
1.295
1.222
1.147
1.103
1.074
0.000
Ph
Ph
O
NH
HN
O
NH
N
1.00
1.02
6.33
4.29
2.18
1.03
1.03
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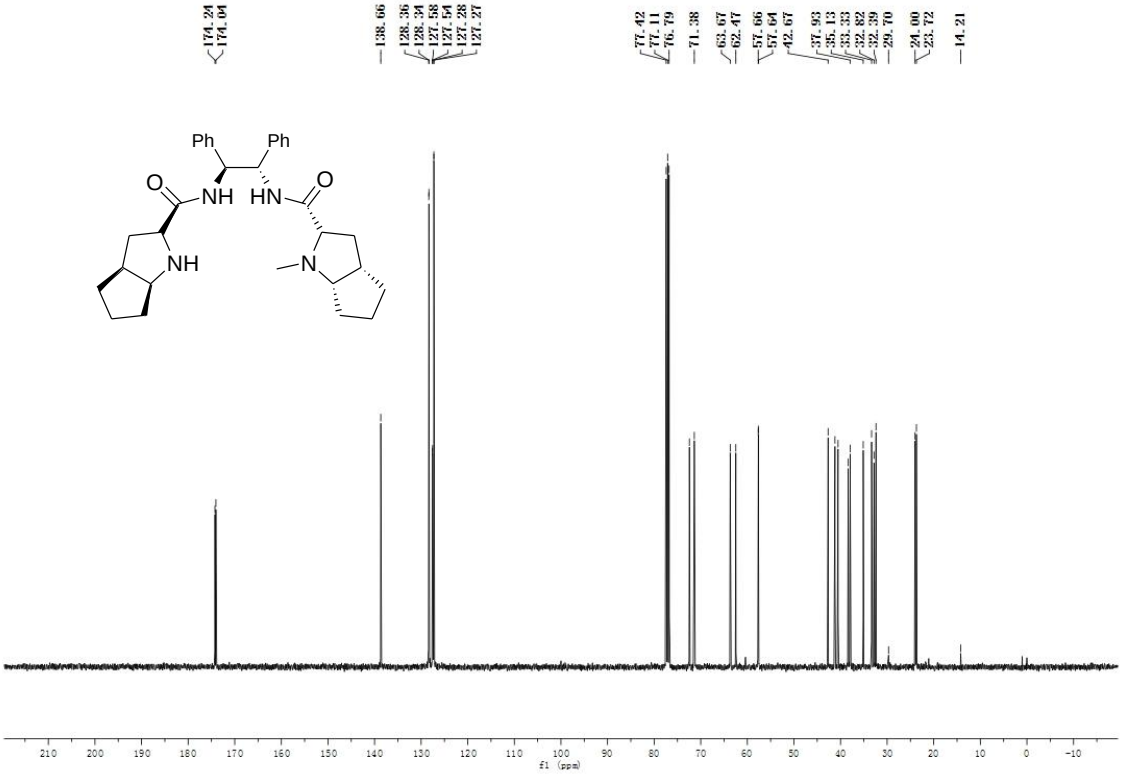
1.95
2.13
5.29
1.08
1.09
8.69
3.90
1.17
f1 (ppm)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128.36
128.34
127.58
127.54
127.28
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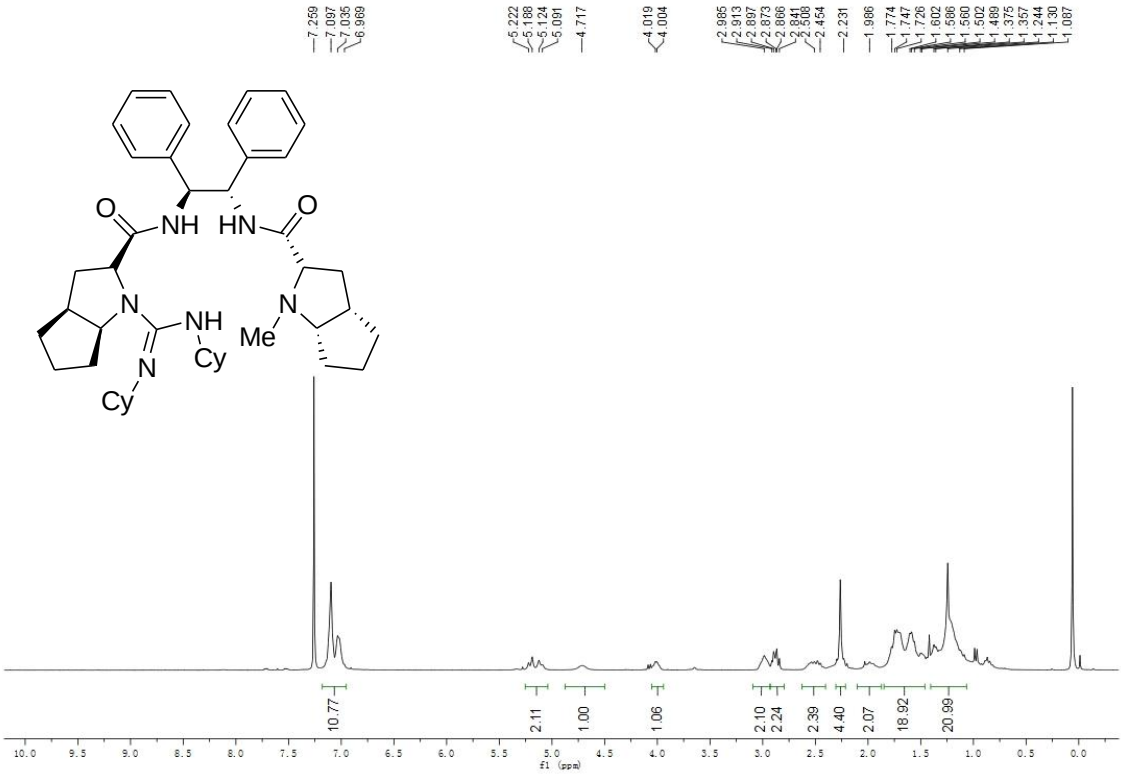
77.42
77.11
76.79
71.38
63.67
62.47
57.66
57.64
42.67
37.93
35.13
33.33
32.82
32.39
29.70
24.00
23.72
14.21
Ph
Ph
O
NH
HN
O
NH
N
f1 (ppm)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5.124
5.091
4.717
4.019
4.004
2.985
2.913
2.897
2.873
2.866
2.841
2.508
2.454
2.231
1.986
1.774
1.747
1.726
1.602
1.586
1.560
1.502
1.489
1.375
1.357
1.244
1.130
1.087
O
NH
HN
O
N
NH
N
Me
Cy
N
Cy
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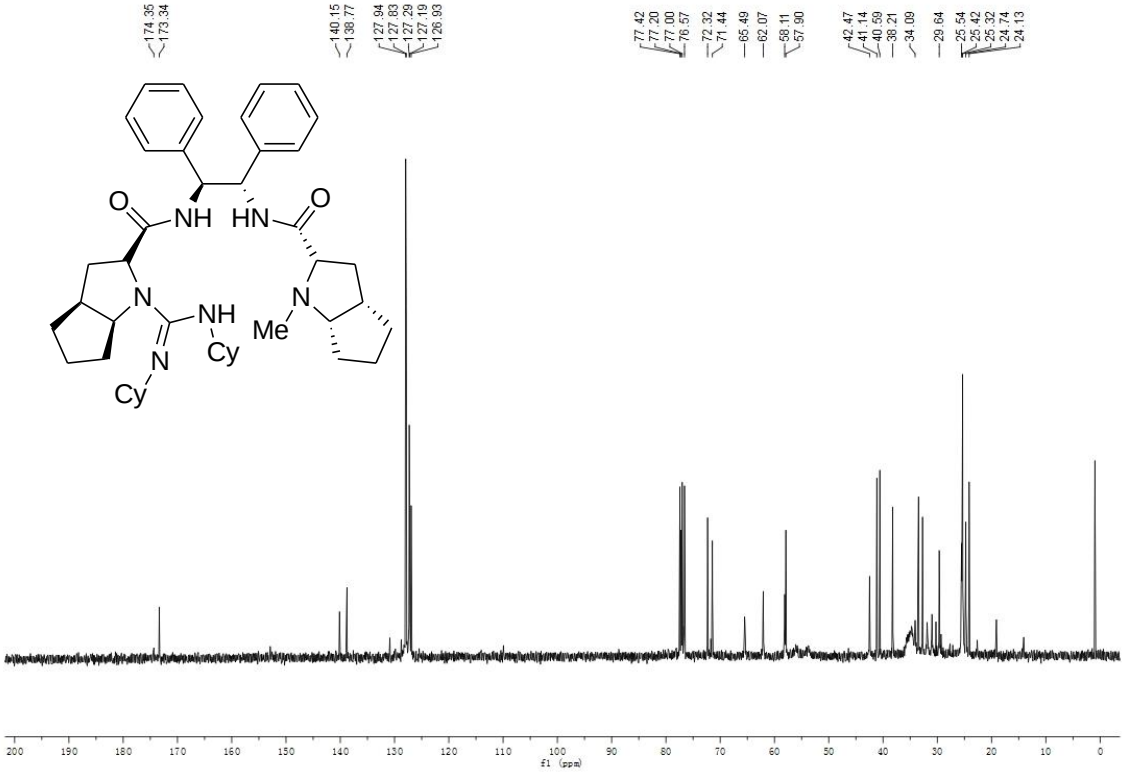
1.06
2.10
2.24
2.39
4.40
2.07
18.92
20.99
f1 (ppm)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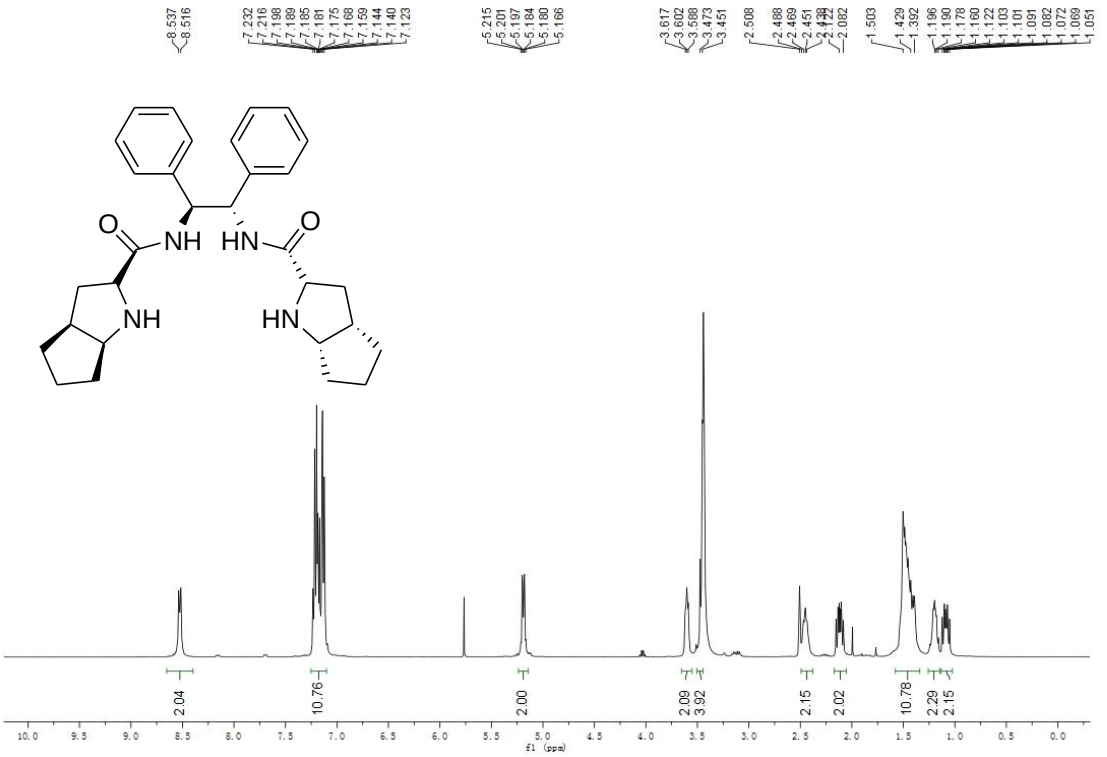
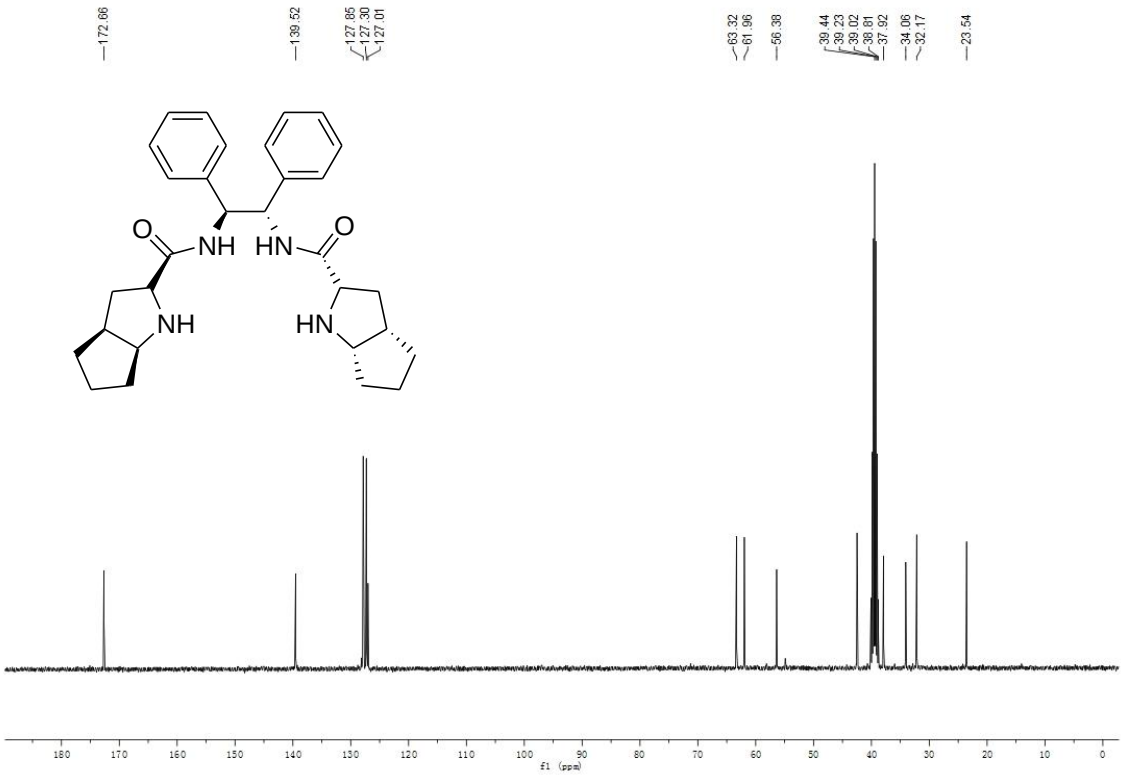
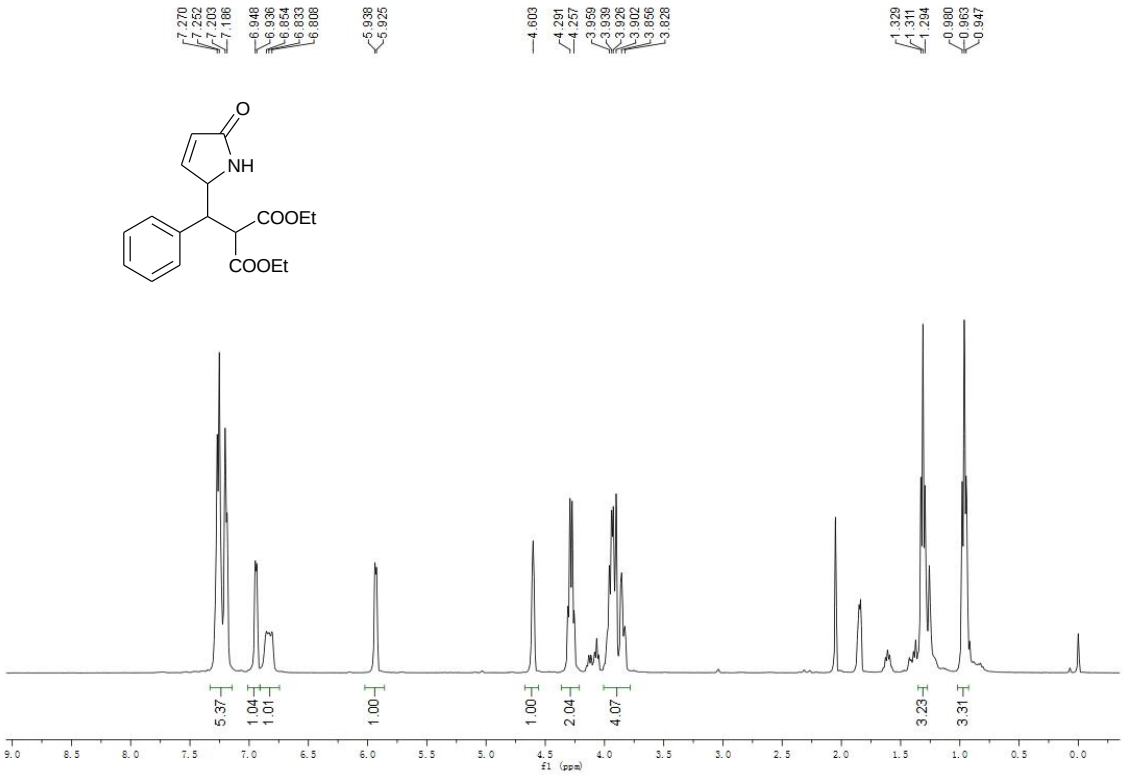
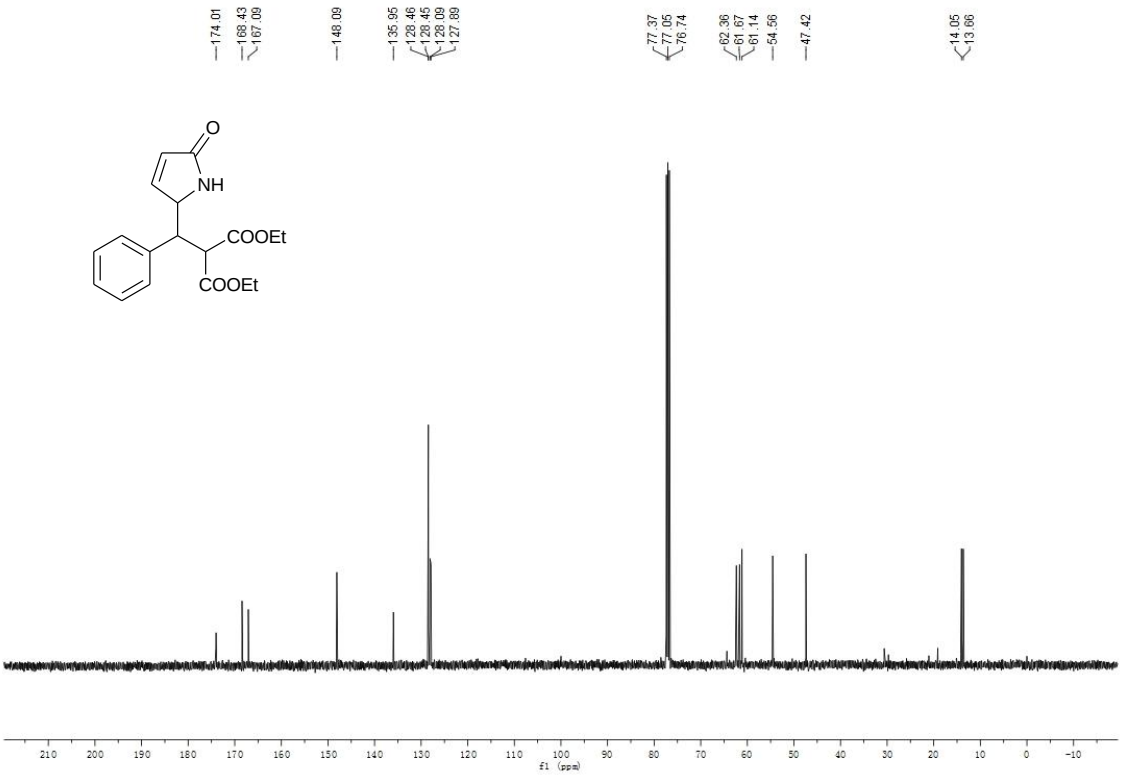
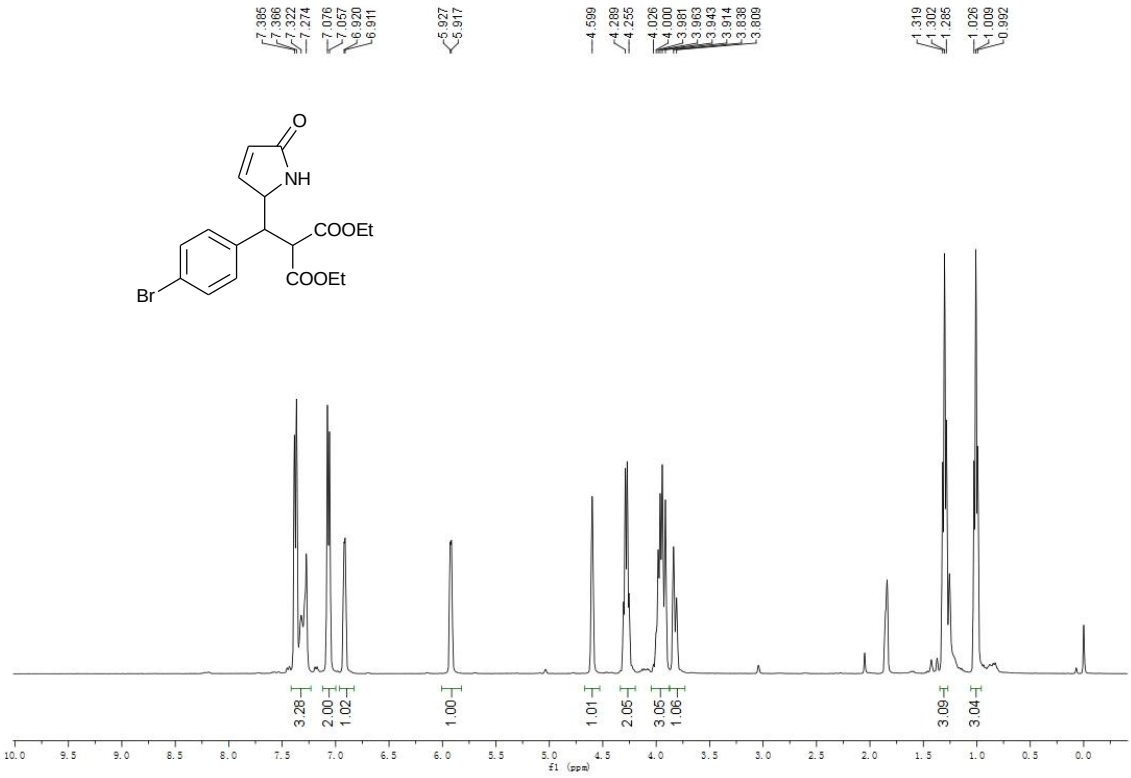
173.34
140.15
138.77
127.94
127.83
127.29
127.19
126.93
77.42
77.20
77.00
76.57
72.32
71.44
65.49
62.07
58.11
57.90
42.47
41.14
40.59
38.21
34.09
29.64
25.54
25.42
25.32
24.74
24.13
O
NH
HN
O
N
NH
N
Me
Cy
N
Cy
f1 (ppm)







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7.057
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6.911
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4.026
4.000
3.981
3.963
3.943
3.914
3.838
3.809
1.319
1.302
1.285
1.026
1.009
0.992
O
NH
COOEt
COOEt
Br
3.28
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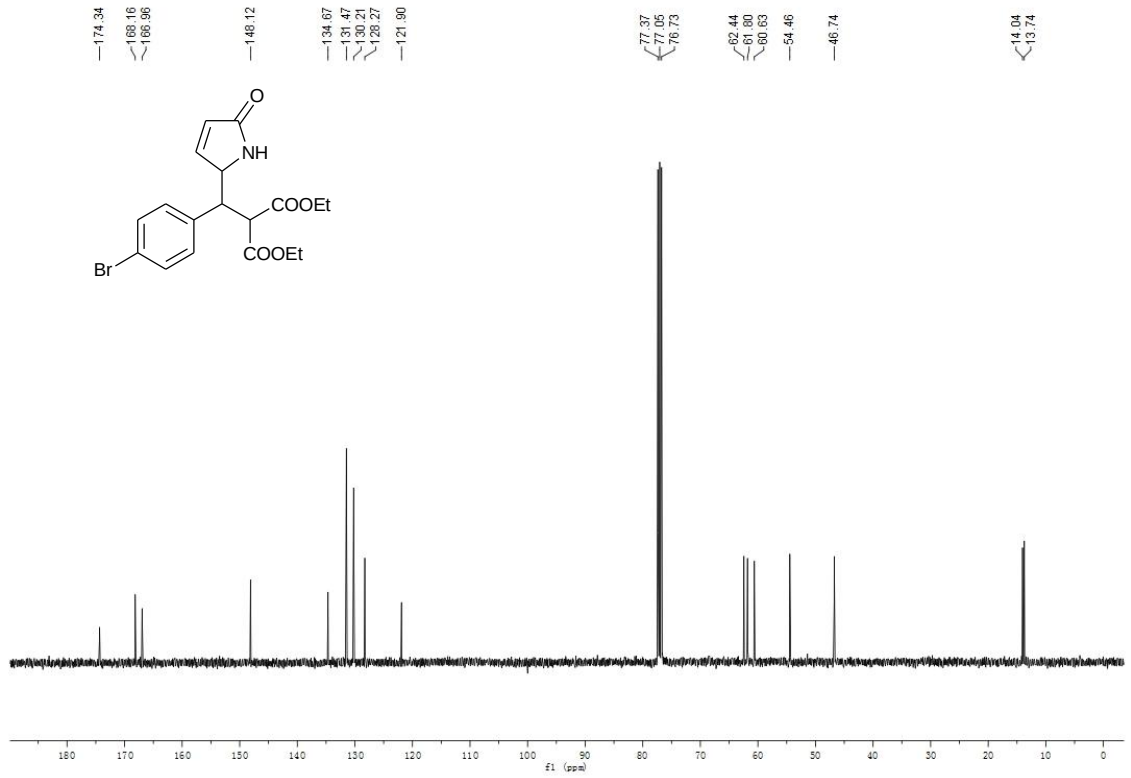
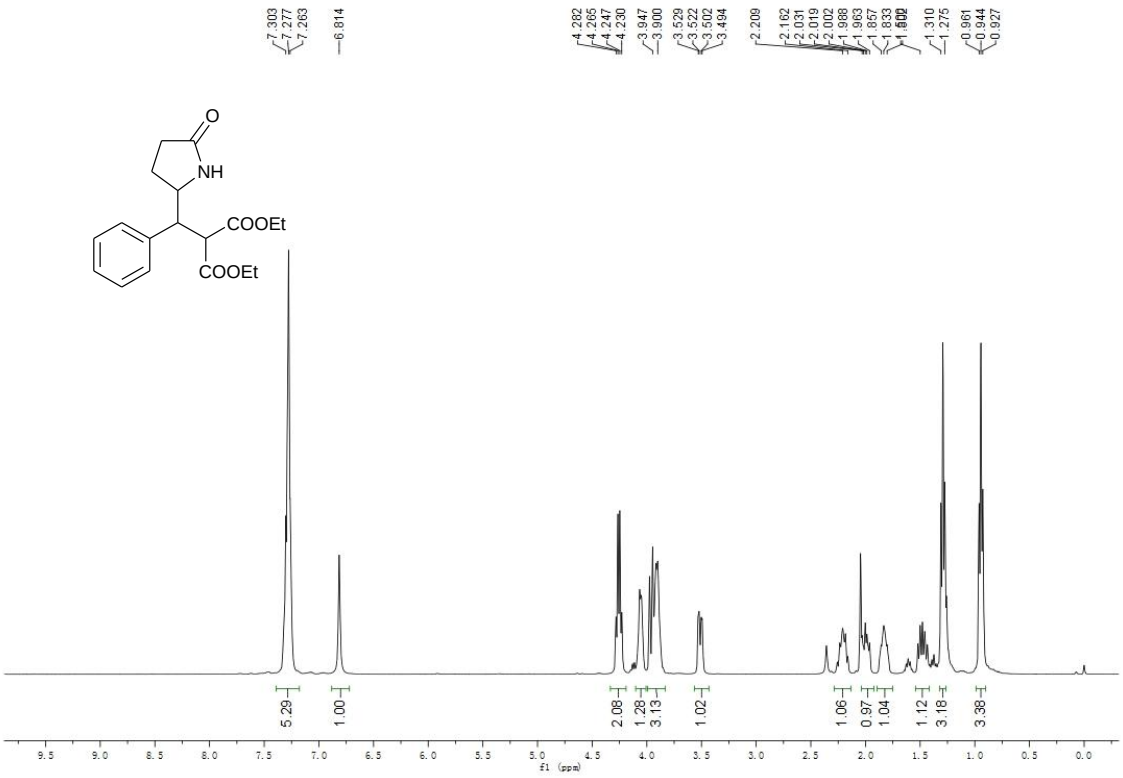
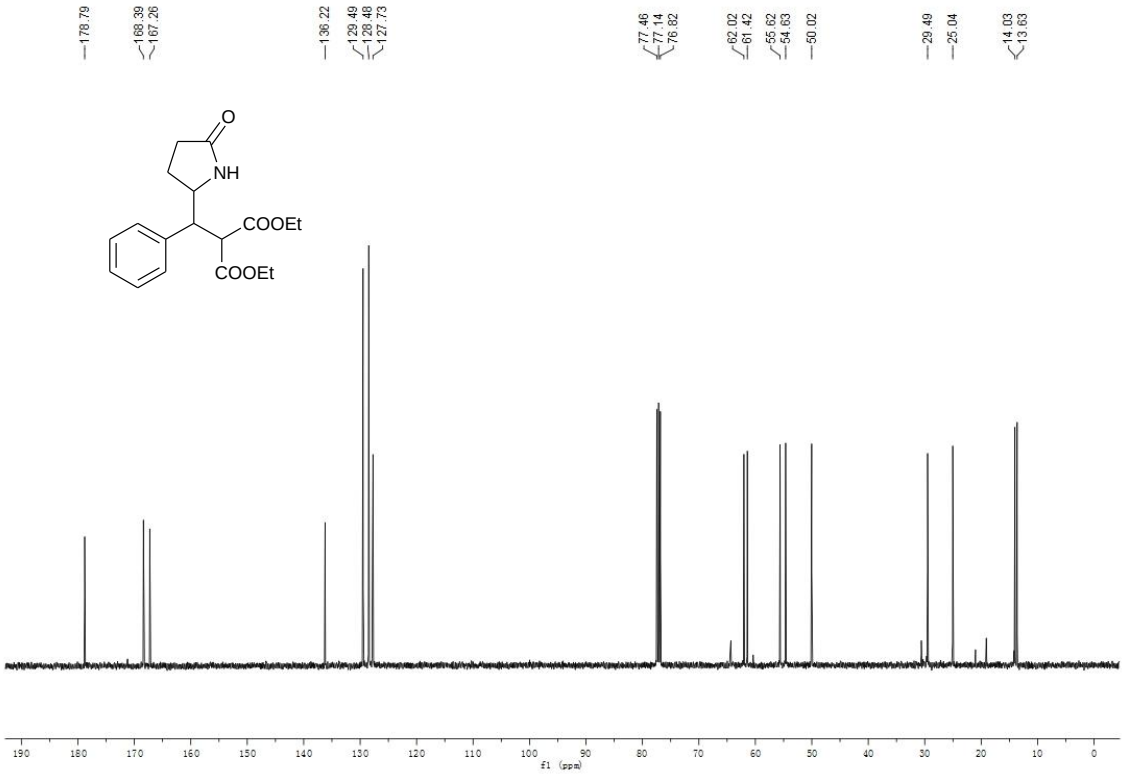
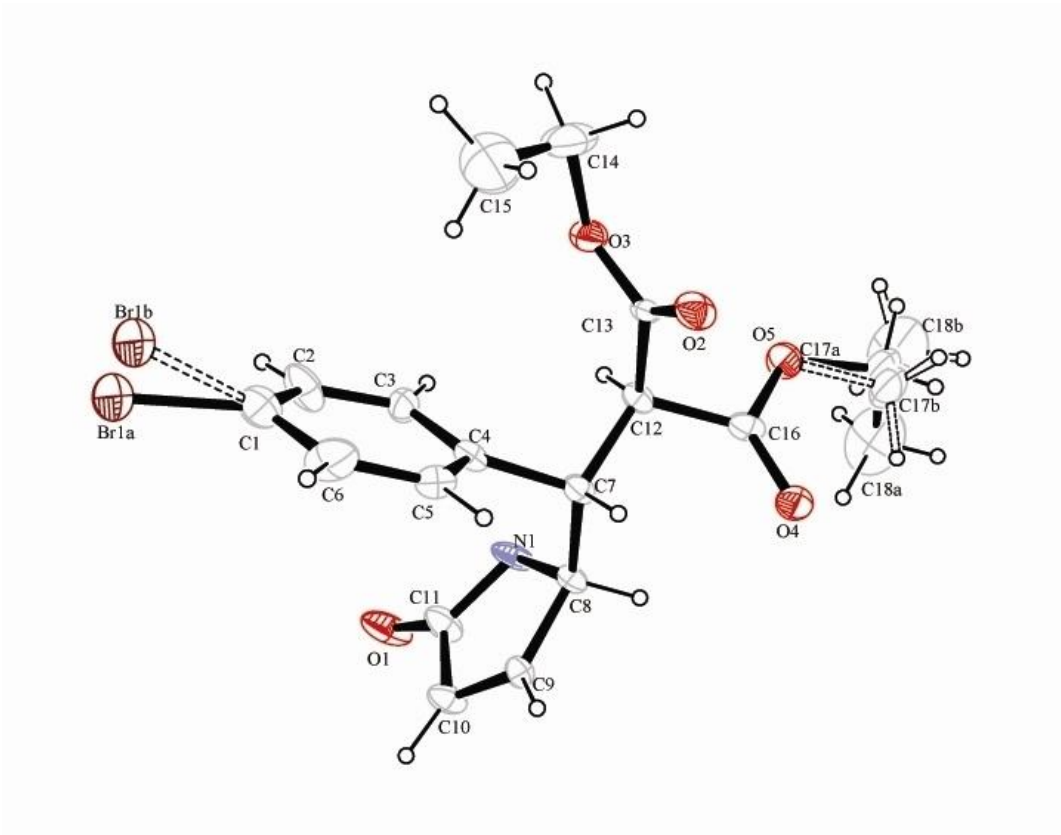
1.02
1.00
1.01
2.05
3.05
1.06
3.09
3.04
f1 (ppm)


174.34
168.16
166.96
148.12
134.67
131.47
130.21
128.27
121.90
77.37
77.05
76.73
62.44
61.80
60.63
54.46
46.74
14.04
13.74
O
NH
COOEt
COOEt
Br
f1 (ppm)





7. X-ray Structure of 7i



Empirical formula	$C_{18}H_{19}BrNO_5$
Formula weight	409.25
Temperature/K	135.05(10)
Crystal system	orthorhombic
Space group	$P2_12_12_1$
a/Å	8.3520(5)
b/Å	12.0788(10)
c/Å	21.7041(17)
α/°	90.00
β/°	90.00
γ/°	90.00
Volume/Å^3	2189.6(3)
Z	4

ρ_{calc}mg/mm^3	1.241
m/mm^{-1}	1.900
F(000)	836.0
Crystal size/mm^3	0.42 × 0.32 × 0.28
2Θ range for data collection	5.94 to 50.04°
Index ranges	-9 ≤ h ≤ 9, -11 ≤ k ≤ 14, -25 ≤ l ≤ 15
Reflections collected	8232
Independent reflections	3798[R(int) = 0.0542]
Data/restraints/parameters	3798/5/241
Goodness-of-fit on F^2	0.992
Final R indexes [I>=2σ (I)]	R_1 = 0.0958, wR_2 = 0.2459
Final R indexes [all data]	R_1 = 0.1340, wR_2 = 0.2810
Largest diff. peak/hole / e Å^{-3}	0.56/-0.43
Flack parameter	0.10(3)