Electronic Supplementary Material (ESI) for Organic Chemistry Frontiers.

Catalytic Asymmetric Ring-Opening of Aminocyclopropanes with Oxygen Nucleophiles: Access to Chiral γ-Amino Acid Derivatives

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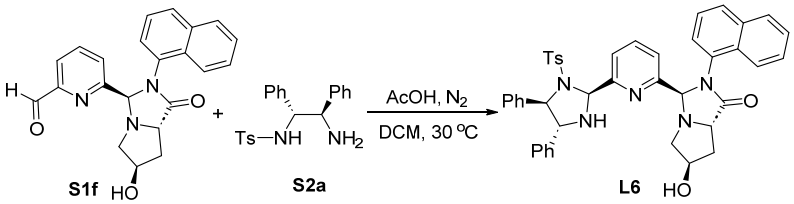
General information

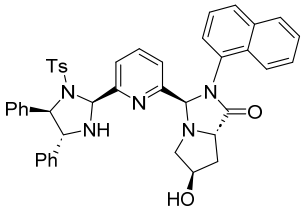
^{1}H NMR spectra were recorded on Bruker Avance III HD 600 or Avance 400 MHz spectrometer. Chemical shifts are recorded in ppm relative to tetramethylsilane and with the solvent resonance as the internal standard. Data are reported as follows: chemical shift, multiplicity (s = singlet, d = doublet; t = triplet; q = quartet; sept = septet; m = multiplet; br = broad), coupling constants (Hz), integration. ^{13}C NMR data were collected on Bruker Avance III HD 150 or Avance 100 MHz spectrometer. Chemical shifts are reported in ppm from the tetramethylsilane with the solvent resonance as internal standard. Enantiomer excesses were determined by chiral HPLC analysis on Chiralcel OD-H/IA/IG/AD-H in comparison with the authentic racemates. Chiral HPLC analysis recorded on Thermo scientific Dionex Ultimate 3000 and Agilent Technologies 1260 Infinity. Optical rotations were reported as follows: $[\alpha]_D^T$ (c: g/100 mL, in solvent). Optical rotations recorded on Autopol Automatic Polarimeter. HRMS was recorded on an ABI/Sciex QStar Mass Spectrometer (ESI-TOF). CH_2Cl_2 and MeOH were purchased extra dry solvents. Other solvents used for work-up and purification purposes were purchased in technical grade quality and distilled by rotary evaporator before use. These ligands **L1-5** and **L7-9** were prepared by previous reported methods.[1-3] Aminocyclopropanes **1a-1e** were prepared according to literature precedents.[4-7]

Synthesis of chiral L6



In a round-bottomed flask containing a stir bar, compound **S1f** (1.0 mmol, 373.1 mg), (*R*,*R*)-TsDPEN **S2a** (1.0 mmol, 366.1 mg), AcOH (1.5 mmol, 85.8 μL), and dichloromethane (10.0 mL) were added. Then, the reaction was stirred at 30 °C under N_2 for 6 h. After that, the reaction mixture was quenched by aqueous $NaHCO_3$. The organic layer was extracted with dichloromethane for 3 times, and the collected organic layer was dried over Na_2SO_4. After removing the solvent under reduced pressure. Chiral tridentate ligand **L6** can be obtained by recrystallization (recrystallization solvent: Pet / EtOAc) as a white solid.

(3*R*,6*R*,7a*S*)-3-(6-((2*S*,4*R*,5*R*)-4,5-diphenyl-1-tosylimidazolidin-2-yl)pyridin-2-yl)-6-hydroxy-2-(naphthalen-1-yl)hexahydro-1*H*-pyrrolo[1,2-*c*]imidazol-1-one (L6)



White solid: 569.6 mg, 79% yield; m.p.: 122.0-123.3 °C; R_f= 0.70 (CH_2Cl_2/MeOH, 25/1, v/v); $[\alpha]_D^{25}$ = -27.33 (c = 1.10, $CHCl_3$);

^{1}H NMR (600 MHz, $CDCl_3$) δ 7.88 (d, *J* = 7.2 Hz, 1H), 7.77 (t, *J* = 7.8 Hz, 1H), 7.73 (d, *J* = 7.8 Hz, 1H), 7.60 (t, *J* = 8.4 Hz, 4H), 7.39 - 7.31 (m, 3H), 7.23 - 7.14 (m, 8H), 7.10 - 7.07 (m, 3H), 6.86 (d, *J* = 7.2 Hz, 3H), 5.70 (s, 1H), 5.62 (s, 1H), 4.62 (dd, *J* = 8.4, 6.0 Hz, 2H), 4.52 (d, *J* = 6.0 Hz, 1H), 4.07 (s, 1H), 3.58 (d, *J* = 9.6 Hz, 3H), 3.34 (d, *J* = 10.2 Hz, 1H), 2.53 - 2.48 (m, 1H), 2.44 (s, 3H), 2.33 (dd, *J* = 13.8, 9.6 Hz, 1H), 2.24 (s, 1H).

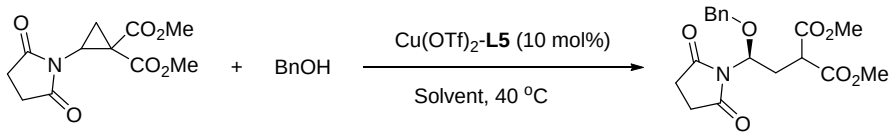
^{13}C NMR (150 MHz, $CDCl_3$) δ 159.0, 157.4, 143.9, 139.6, 139.0, 138.1, 134.4, 133.9, 130.0, 129.6, 128.7, 128.6, 128.4, 128.3, 128.0, 127.6, 127.5, 127.0, 126.94, 126.89, 126.3, 125.5, 123.8, 121.3, 85.7, 77.8, 72.0, 71.8, 69.6, 63.4, 63.2, 37.4, 29.7, 21.6.

HRMS (ESI): exact mass calcd for $C_{43}H_{40}N_5O_4S^+$ $(M+H)^+$ requires m/z 722.2796, found m/z 722.2800 (Δ = +4 ppm).

IR (neat) 3062, 2924, 1698, 1451, 1406, 1344, 1161, 1090, 909, 726, 664, 538 cm^{-1}.

General procedure for optimization study

Table S1. Screening of solvents

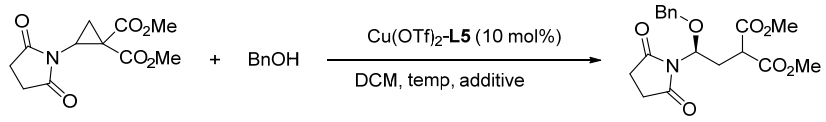


(±)-**1a** **2a** **3aa**

Entry[a]	Solvent	Yield [%][b]	ee [%][c]
1	DCE	32	95
2	EtOAc	24	88
3	THF	N.R.	
4	MTBE	13	75
5	Toluene	46	78
6	CH_3OH	N.R.	
7	CH_3CN	N.R.	

[a]Unless otherwise noted, reactions were carried out with $Cu(OTf)_2$ (10 mol%), **L5** (11 mol%), **1a** (0.11 mmol), **2a** (0.05 mmol) in solvent (1.0 mL) at 40 °C for 24 h. [b]The yield was determined by ^1H NMR spectra of the crude product. [c]Determined by chiral HPLC analysis. N.R. = No Reaction.

Table S2. Screening of other conditions.

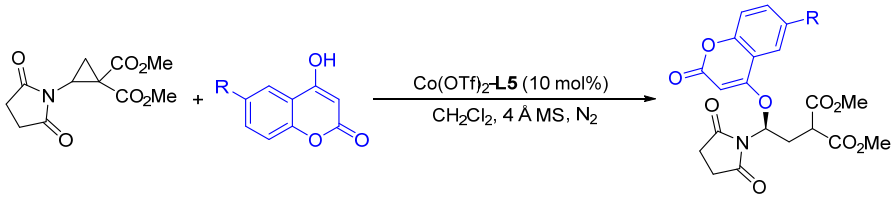


(±)-**1a** **2a** **3aa**

Entry[a]	Temp [°C]	Additive	Yield [%][c]	ee [%][d]
1	30	/	45	90
2	40	/	86	93
3	50	/	88	88
4[b]	40	3 Å MS	36	95
5[b]	40	4 Å MS	94	94
6[b]	40	5 Å MS	67	87

[a]Unless otherwise noted, reactions were carried out with $Cu(OTf)_2$ (10 mol%), **L5** (11 mol%), **1a** (0.11 mmol), **2a** (0.05 mmol), MS (5 mg) in solvent (1.0 mL) for 24 h. b With MS under N_2. [c]The yield was determined by ^1H NMR spectra of the crude product. [d]Determined by chiral HPLC analysis.

Table S3. Effect of temperature on **Scheme 4b**

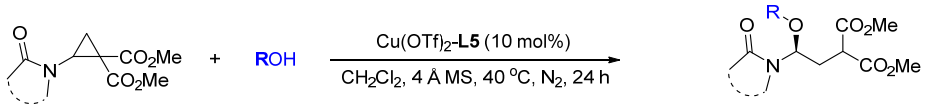


(±)-**1a** **8a-8c** R = H, Me, Br

Entry[a]	**8**	Temp [°C]	Time (h)	Yield [%][b]	ee [%][c]
1	**8a**	25	72	21	96
2	**8a**	40	24	95	96
3	**8a**	60	3	95	93
4	**8b**	40	72	33	98
5	**8b**	60	12	82	96
6	**8b**	80	10	88	94
7	**8c**	40	72	32	99
8	**8c**	60	72	60	97
9	**8c**	80	8	76	97
10	**8c**	100	8	88	88

[a]Unless otherwise noted, reactions were carried out with $Co(OTf)_2$ (10 mol%), **L5** (11 mol%), **1a** (0.22 mmol), **2a** (0.10 mmol), 4 Å MS (10 mg) in DCM (2.0 mL) . [b]Isolated yields were reported. [c]Determined by chiral HPLC analysis.

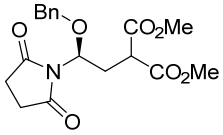
Catalytic asymmetric ring-opening of aminocyclopropanes with alcohols



(±)-**1a-1e** **2a-2v** **3aa-3av, 3ba-3ea**

General method A - In a dry reaction tube, a mixture of $Cu(OTf)_2$ (3.6 mg, 0.01 mmol, 10 mol%), ligand **L5** (7.8 mg, 0.011 mmol, 11 mol%), 4 Å MS (10mg), and aminocyclopropane **1** (0.22 mmol) in DCM (1.0 mL) were stirred at 30 °C for 30 minutes under the atmosphere of nitrogen. Then oxygen nucleophiles substrate **2** (0.1 mmol) in DCM (1.0 mL) was added to the mixture of catalyst via a syringe. Subsequently, the reaction was stirred at -40 °C or 0 °C or 40 °C for 24-240 h. After the reaction was complete (monitored by TLC), the reaction was filtered through a glass funnel within layer of silica gel (100-200 mesh) and purified by flash column chromatography (Pet/EtOAc/MeOH, v/v/v, 10:1:0.1-5:1:0.1; Pet/EtOAc/DCM/MeOH, v/v/v/v, 10:1:1:0.1-5:1:1:0.1; DCM:MeOH, v/v, 100:1-20:1) to give the product **3**.

Dimethyl (*S*)-2-(2-(benzyloxy)-2-(2,5-dioxopyrrolidin-1-yl)ethyl)malonate (3aa)



Colorless oil: 33.8 mg, 93% yield, 94% ee; R_f = 0.75 (Pet/EtOAc/MeOH, 1/1/0.1, v/v/v); **$[\alpha]_D^{25}$** = -1.17 (c = 0.60, $CHCl_3$); reaction time: 24 h; reaction temperature: 40 °C.

HPLC CHIRALPAK IA, n-hexane/2-propanol = 60/40, flow rate 1.0 mL/min, λ = 254 nm, retention time: 8.100 min (major), 9.440 min (minor).

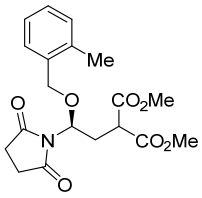
^{1}H NMR (400 MHz, $CDCl_3$) δ 7.35 - 7.26 (m, 5H), 5.39 (dd, *J* = 8.8, 4.8 Hz, 1H), 4.64 (d, *J* = 12.8 Hz, 1H), 4.42 (d, *J* = 12.8 Hz, 1H), 3.70 (s, 3H), 3.69 (s, 3H), 3.52 (dd, *J* = 8.8, 6.0 Hz, 1H), 3.05 - 2.97 (m, 1H), 2.41 - 2.34 (m, 5H).

^{13}C NMR (100 MHz, $CDCl_3$) δ 176.7, 169.1, 169.0, 137.2, 128.5, 128.13, 128.07, 80.3, 72.5, 52.8, 48.3, 31.3, 28.0.

HRMS (ESI): exact mass calcd for $C_{18}H_{21}NNaO_7^+$ $(M+Na)^+$ requires m/z 386.1210, found m/z 386.1207 (Δ = -3 ppm).

IR (neat): 2919, 1731, 1704, 1436, 1350, 1250, 1199, 1168, 1095, 744, 700, 664 cm^{-1}.

Dimethyl (*S*)-2-(2-(2,5-dioxopyrrolidin-1-yl)-2-((2-methylbenzyl)oxy)ethyl)malonate (3ab)



Colorless oil: 35.1 mg, 93% yield, 94% ee; R_f = 0.70 (Pet/EtOAc/MeOH, 1/1/0.1, v/v/v); **[α]$_D^{25}$** = -8.71 (c = 0.96, $CHCl_3$); reaction time: 24 h; reaction temperature: 40 ºC.

HPLC CHIRALPAK IA, n-hexane/2-propanol = 70/30, flow rate 0.8 mL/min, λ = 254 nm, retention time: 10.165 min (major), 11.340 min (minor).

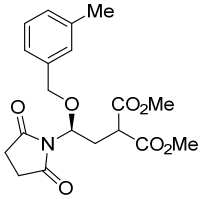
^{1}H NMR (400 MHz, $CDCl_3$) δ 7.22 - 7.10 (m, 4H), 5.40 (dd, *J* = 8.8, 4.8 Hz, 1H), 4.62 (d, *J* = 12.4 Hz, 1H), 4.45 (d, *J* = 12.4 Hz, 1H), 3.68 (s, 3H), 3.67 (s, 3H), 3.49 (dd, *J* = 8.8, 6.0 Hz, 1H), 3.01 - 2.93 (m, 1H), 2.44 - 2.33 (m, 5H), 2.31 (s, 3H).

^{13}C NMR (100 MHz, $CDCl_3$) δ 176.7, 169.1, 169.0, 137.5, 135.0, 130.5, 128.4, 125.7, 80.2, 71.1, 52.8, 48.2, 31.3, 28.0, 19.0.

HRMS (ESI): exact mass calcd for $C_{19}H_{23}NNaO_7^+$ $(M+Na)^+$ requires m/z 400.1367, found m/z 400.1369 (Δ = +2 ppm).

IR (neat): 2922, 2852, 1728, 1706, 1463, 1376, 1260, 1163, 1092, 1018, 797, 720 cm^{-1}.

Dimethyl (*S*)-2-(2-(2,5-dioxopyrrolidin-1-yl)-2-((3-methylbenzyl)oxy)ethyl)malonate (3ac)



Colorless oil: 30.2 mg, 80% yield, 91% ee; R_f = 0.66 (Pet/EtOAc/MeOH, 1/1/0.1, v/v/v); **[α]$_D^{25}$** = -1.08 (*c* = 1.30, $CHCl_3$); reaction time: 24 h; reaction temperature: 40 °C.

HPLC CHIRALPAK IA, n-hexane/2-propanol = 60/40, flow rate 1.0 mL/min, λ = 254 nm, retention time: 7.382 min (major), 8.415 min (minor).

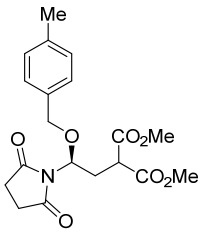
^{1}H NMR (400 MHz, $CDCl_3$) δ 7.19 (t, *J* = 7.6 Hz, 1H), 7.09 - 7.05 (m, 3H), 5.37 (dd, *J* = 8.8, 4.8 Hz, 1H), 4.59 (d, *J* = 12.4 Hz, 1H), 4.37 (d, *J* = 12.4 Hz, 1H), 3.70 (s, 3H), 3.68 (s, 3H), 3.52 (dd, *J* = 8.8, 6.0 Hz, 1H), 3.03 - 2.96 (m, 1H), 2.42 - 2.34 (m, 5H), 2.33 (s, 3H).

^{13}C NMR (100 MHz, $CDCl_3$) δ 176.7, 169.1, 169.0, 138.1, 137.0, 128.8, 128.4, 125.1, 80.3, 72.6, 52.8, 48.3, 31.3, 28.0, 21.4.

HRMS (ESI): exact mass calcd for $C_{19}H_{23}NNaO_7^+$ $(M+Na)^+$ requires m/z 400.1367, found m/z 400.1364 (Δ = -3 ppm).

IR (neat): 2954, 1732, 1704, 1435, 1349, 1250, 1160, 1094, 787, 735, 698 cm^{-1}.

Dimethyl (*S*)-2-(2-(2,5-dioxopyrrolidin-1-yl)-2-((4-methylbenzyl)oxy)ethyl)malonate (3ad)



Colorless oil: 30.9 mg, 82% yield, 93% ee; R_f = 0.60 (Pet/EtOAc/MeOH, 1/1/0.1, v/v/v); $[\alpha]_D^{25}$ = -15.18 (*c* = 0.65, $CHCl_3$); reaction time: 24 h; reaction temperature: 40 °C.

HPLC CHIRALPAK IA, n-hexane/2-propanol = 60/40, flow rate 1.0 mL/min, λ = 254 nm, retention time: 7.655 min (major), 8.822 min (minor).

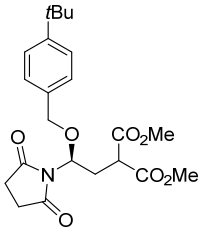
^{1}H NMR (600 MHz, $CDCl_3$) δ 7.35 (dd, *J* = 7.8 Hz, 1.8 Hz, 1H), 7.07 (td, *J* = 7.2 Hz, 1.2 Hz, 1H), 6.68 (t, *J* = 7.8 Hz, 1H), 6.33 (d, *J* = 7.8 Hz, 1H), 6.06 – 6.03 (m, 2H), 5.86 (d, *J* = 3.0 Hz, 1H), 3.81 (s, 3H), 3.64 (s, 3H), 2.88 (dd, *J* = 13.8, 8.4 Hz, 1H), 2.72 (s, 4H), 2.40 (dd, *J* = 13.2, 6.0 Hz, 1H).

^{13}C NMR (150 MHz, $CDCl_3$) δ 176.7, 169.1, 169.0, 137.8, 134.0, 129.1, 128.2, 78.0, 72.2, 52.79, 52.75, 48.2, 31.3, 28.0, 21.2.

HRMS (ESI): exact mass calcd for $C_{19}H_{23}NNaO_7^+$ $(M+Na)^+$ requires m/z 400.1367, found m/z 400.1363 (Δ = -4 ppm).

IR (neat): 2958, 1740, 1703, 1437, 1348, 1262, 1160, 1005, 811, 665, 639 cm^{-1}.

Dimethyl (*S*)-2-(2-((4-(tert-butyl)benzyl)oxy)-2-(2,5-dioxopyrrolidin-1-yl)ethyl)malonate (3ae)



Colorless oil: 36.9 mg, 88% yield, 95% ee; R_f = 0.71 (Pet/EtOAc/MeOH, 1/1/0.1, v/v/v); **[α]$_D^{25}$** = +3.60 (*c* = 1.24, $CHCl_3$); reaction time: 24 h; reaction temperature: 40 °C.

HPLC CHIRALPAK IA, n-hexane/2-propanol = 60/40, flow rate 1.0 mL/min, λ = 254 nm, retention time: 6.673 min (major), 7.995 min (minor).

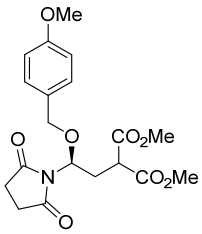
^{1}H NMR (600 MHz, $CDCl_3$) δ 7.33 (d, *J* = 7.8 Hz, 2H), 7.22 (d, *J* = 8.4 Hz, 2H), 5.37 (dd, *J* = 9.0, 4.8 Hz, 1H), 4.65 (d, *J* = 12.6 Hz, 1H), 4.37 (d, *J* = 12.6 Hz, 1H), 3.704 (s, 3H), 3.697 (s, 3H), 3.53 (dd, *J* = 9.0, 6.0 Hz, 1H), 3.01 - 2.96 (m, 1H), 2.39 - 2.35 (m, 1H), 2.30 (s, 4H), 1.29 (s, 9H).

^{13}C NMR (150 MHz, $CDCl_3$) δ 176.6, 169.1, 151.2, 134.2, 127.9, 125.4, 80.5, 72.6, 52.8, 48.3, 34.7, 31.42, 31.39, 28.0.

HRMS (ESI): exact mass calcd for $C_{22}H_{29}NNaO_7^+$ $(M+Na)^+$ requires m/z 442.1836, found m/z 442.1840 (Δ = +4 ppm).

IR (neat): 2956, 1733, 1705, 1436, 1349, 1250, 1167, 1094, 819, 734, 671 cm^{-1}.

Dimethyl (*S*)-2-(2-(2,5-dioxopyrrolidin-1-yl)-2-((4-methoxybenzyl)oxy)ethyl)malonate (3af)



White solid: 32.2 mg, 82% yield, 94% ee; m.p.: 95.2 - 96.6 °C; R_f = 0.65 (Pet/EtOAc/MeOH, 1/1/0.1, v/v/v); $[\alpha]_D^{25}$ = -6.93 (*c* = 1.95, $CHCl_3$); reaction time: 24 h; reaction temperature: 40 °C.

HPLC CHIRALPAK IA, n-hexane/2-propanol = 60/40, flow rate 1.0 mL/min, λ = 254 nm, retention time: 9.363 min (major), 11.120 min (minor).

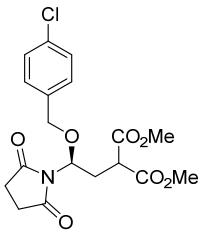
^{1}H NMR (600 MHz, $CDCl_3$) δ 7.21 (d, *J* = 8.4 Hz, 2H), 6.84 (d, *J* = 9.0 Hz, 2H), 5.35 (dd, *J* = 9.0, 4.8 Hz, 1H), 4.51 (d, *J* = 12.6 Hz, 1H), 4.37 (d, *J* = 12.0 Hz, 1H), 3.78 (s, 3H), 3.69 (s, 3H), 3.67 (s, 3H), 3.49 (dd, *J* = 9.0, 6.0 Hz, 1H), 2.99 - 2.94 (m, 1H), 2.44 (s, 4H), 2.36 - 2.31 (m, 1H).

^{13}C NMR (150 MHz, $CDCl_3$) δ 176.7, 169.1, 169.0, 159.6, 129.7, 129.2, 113.9, 79.8, 72.0, 55.4, 52.83, 52.80, 48.2, 31.3, 28.1.

HRMS (ESI): exact mass calcd for $C_{19}H_{23}NNaO_8^+$ $(M+K)^+$ requires m/z 416.1316, found m/z 416.1312 (Δ = -4 ppm).

IR (neat): 2954, 1731, 1703, 1436, 1349, 1247, 1170, 1094, 817, 733, 635 cm^{-1}.

Dimethyl (*S*)-2-(2-((4-chlorobenzyl)oxy)-2-(2,5-dioxopyrrolidin-1-yl)ethyl)malonate (3ag)



Colorless oil: 29.4 mg, 74% yield, 93% ee; R_f = 0.60 (Pet/EtOAc/MeOH, 1/1/0.1, v/v/v); **[α]$_D^{25}$** = -17.2 (*c* = 1.05, $CHCl_3$); reaction time: 24 h; reaction temperature: 40 °C.

HPLC CHIRALPAK IA, n-hexane/2-propanol = 70/30, flow rate 0.8 mL/min, λ = 254 nm, retention time: 11.843 min (major), 15.030 min (minor).

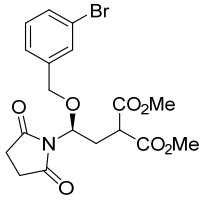
^{1}H NMR (600 MHz, $CDCl_3$) δ 7.29 (s, 1H), 7.27 - 7.26 (m, 2H), 7.19 - 7.16 (m, 1H), 5.39 (dd, *J* = 9.0, 4.8 Hz, 1H), 4.56 (d, *J* = 12.6 Hz, 1H), 4.41 (d, *J* = 12.6 Hz, 1H), 3.712 (s, 3H), 3.705 (s, 3H), 3.52 (dd, *J* = 8.4, 6.0 Hz, 1H), 3.06 - 3.01 (m, 1H), 2.50 (s, 4H), 2.43 - 2.38 (m, 1H).

^{13}C NMR (150 MHz, $CDCl_3$) δ 176.6, 169.1, 169.0, 139.2, 134.4, 129.9, 128.2, 127.9, 126.1, 80.3, 71.4, 52.9, 48.3, 31.1, 28.0.

HRMS (ESI): exact mass calcd for $C_{18}H_{20}ClNNaO_7^+$ $(M+Na)^+$ requires m/z 420.0821, found m/z 420.0824 (Δ = +3 ppm).

IR (neat): 2922, 1734, 1708, 1458, 1259, 1087, 1015, 864, 794, 702, 662 cm^{-1}.

Dimethyl (*S*)-2-(2-((3-bromobenzyl)oxy)-2-(2,5-dioxopyrrolidin-1-yl)ethyl)malonate (3ah)



Colorless oil: 31.3 mg, 71% yield, 94% ee; R_f = 0.60 (Pet/EtOAc/MeOH, 1/1/0.1, v/v/v); $[\alpha]_D^{25}$ = -1.45 (*c* = 2.90, $CHCl_3$); reaction time: 24 h; reaction temperature: 40 °C.

HPLC CHIRALPAK IA, n-hexane/2-propanol = 60/40, flow rate 1.0 mL/min, λ = 254 nm, retention time: 8.925 min (major), 11.693 min (minor).

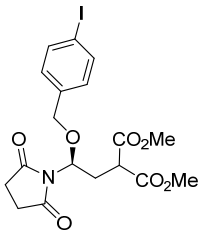
^{1}H NMR (600 MHz, $CDCl_3$) δ 7.41 (s, 1H), 7.38 (dt, *J* = 7.2, 1.8 Hz, 1H), 7.39 – 7.37 (m, 2H), 5.35 (dd, *J* = 9.0, 4.8 Hz, 1H), 4.53 (d, *J* = 12.6 Hz, 1H), 4.35 (d, *J* = 12.6 Hz, 1H), 3.68 (s, 3H), 3.67 (s, 3H), 3.49 (dd, *J* = 8.4, 6.0 Hz , 1H), 3.02 - 2.96 (m, 1H), 2.46 (s, 4H), 2.39 - 2.34 (m, 1H).

^{13}C NMR (150 MHz, $CDCl_3$) δ 176.6, 169.0, 168.9, 139.4, 131.1, 130.7, 130.1, 126.5, 122.4, 80.2, 71.3, 52.8,48.2, 31.1, 27.9.

HRMS (ESI): exact mass calcd for $C_{18}H_{20}BrNNaO_7^+$ $(M+Na)^+$ requires m/z 464.0315, found m/z 464.0314 (Δ = -1 ppm).

IR (neat): 2873, 1693, 1597, 1570, 1428, 1200, 1069, 1031, 773, 695, 683, 666 cm^{-1}.

Dimethyl (*S*)-2-(2-(2,5-dioxopyrrolidin-1-yl)-2-((4-iodobenzyl)oxy)ethyl)malonate (3ai)



White solid: 40.0 mg, 82% yield, 96% ee; m.p.: 136.5 - 138.2 °C; R_f = 0.60 (Pet/EtOAc/MeOH, 1/1/0.1, v/v/v); $[\alpha]_D^{25}$ = -1.40 (*c* = 0.60, $CHCl_3$); reaction time: 24 h; reaction temperature: 40 °C.

HPLC CHIRALPAK IA, n-hexane/2-propanol = 60/40, flow rate 1.0 mL/min, λ = 254 nm, retention time: 10.555 min (major), 13.165 min (minor).

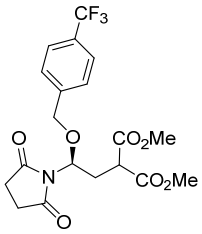
^{1}H NMR (600 MHz, $CDCl_3$) δ 7.62 (d, *J* = 7.8 Hz, 2H), 7.01 (d, *J* = 8.4 Hz, 2H), 5.31 (dd, *J* = 9.0, 4.2 Hz , 1H), 4.45 (d, *J* = 12.6 Hz, 1H), 4.35 (d, *J* = 12.6 Hz, 1H), 3.66 (s, 3H), 3.64 (s, 3H), 3.45 (dd, *J* = 9.0, 6.0 Hz , 1H), 2.98 - 2.94 (m, 1H), 2.46 (s, 4H), 2.35 - 2.30 (m, 1H).

^{13}C NMR (150 MHz, $CDCl_3$) δ 176.6, 168.9, 168.8, 137.5, 136.7, 129.9, 93.6, 79.8, 71.3, 52.81, 52.78, 48.1, 31.0, 28.0.

HRMS (ESI): exact mass calcd for $C_{18}H_{20}INNaO_7^+$ $(M+Na)^+$ requires m/z 512.0177, found m/z 512.0177 (Δ = 0 ppm).

IR (neat): 2955, 1734, 1702, 1436, 1349, 1197, 1159, 1004, 818, 795, 665 cm^{-1}.

Dimethyl (*S*)-2-(2-(2,5-dioxopyrrolidin-1-yl)-2-((4-(trifluoromethyl)benzyl)oxy)ethyl) malonate (3aj)



Colorless oil: 38.8 mg, 90% yield, 94% ee; R_f = 0.67 (Pet/EtOAc/MeOH, 10/10/1, v/v/v); **[α]$_D^{25}$** = -6.00 (c = 1.62, $CHCl_3$); reaction time: 24 h; reaction temperature: 40 ºC.

HPLC CHIRALPAK IA, n-hexane/2-propanol = 60/40, flow rate 1.0 mL/min, λ = 254 nm, retention time:8.110 min (major), 9.625 min (minor).

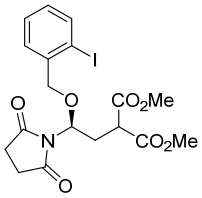
^{1}H NMR (600 MHz, $CDCl_3$) δ 7.59 (d, *J* = 7.8 Hz, 2H), 7.42 (d, *J* = 8.4 Hz, 2H), 5.39 (dd, *J* = 8.4, 4.8 Hz , 1H), 4.61 (d, *J* = 13.2 Hz, 1H), 4.49 (d, *J* = 12.6 Hz, 1H), 3.70 (s, 3H), 3.67 (s, 3H), 3.50 (dd, *J* = 9.0, 6.0 Hz , 1H), 3.06 - 3.01 (m, 1H), 2.49 (s, 4H), 2.43 - 2.39 (m, 1H).

^{13}C NMR (150 MHz, $CDCl_3$) δ 176.7, 169.02, 168.96, 130.4 (q, J_{C-F} = 33.0 Hz), 128.2, 125.4 (q, J_{C-F} = 3.0 Hz), 124.1 (q, J_{C-F} = 120.0 Hz), 80.2, 71.2, 52.89, 52.86, 48.3, 31.1, 28.0.

HRMS (ESI): exact mass calcd for $C_{19}H_{20}F_3NNaO_7^+$ $(M+Na)^+$ requires m/z 454.1084, found m/z 454.1086 (Δ = +2 ppm).

IR (neat): 2921, 1732, 1705, 1436, 1324, 1251, 1161, 1064, 1017, 734, 664, 633 cm^{-1}.

Dimethyl (*S*)-2-(2-(2,5-dioxopyrrolidin-1-yl)-2-((2-iodobenzyl)oxy)ethyl)malonate (3ak)



White solid: 41.1 mg, 84% yield, 93% ee; m.p.: 131.2 - 133.5 °C; R_f = 0.75 (Pet/EtOAc/MeOH, 10/10/1, v/v/v); $[\alpha]_D^{25}$ = -9.77 (c = 1.60, $CHCl_3$); reaction time: 24 h; reaction temperature: 40 °C.

HPLC CHIRALPAK IA, n-hexane/2-propanol = 60/40, flow rate 1.0 mL/min, λ = 254 nm, retention time: 9.208 min (major), 10.617 min (minor).

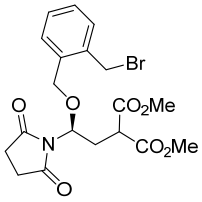
^{1}H NMR (400 MHz, $CDCl_3$) δ 7.80 (dd, *J* = 8.0, 1.2 Hz, 1H), 7.40 (dd, *J* = 7.6, 2.0 Hz, 1H), 7.34 (td, *J* = 7.6, 1.2 Hz, 1H), 6.98 (td, *J* = 7.6, 1.6 Hz, 1H), 5.46 (dd, *J* = 8.8, 4.8 Hz, 1H), 4.49 (dd, *J* = 16.8, 12.4 Hz, 2H), 3.70 (s, 6H), 3.58 (dd, *J* = 8.8, 6.0 Hz, 1H), 3.10 - 3.03 (m, 1H), 2.64 (s, 4H), 2.49 - 2.42 (m, 5H).

^{13}C NMR (100 MHz, $CDCl_3$) δ 176.7, 169.1, 169.0, 139.5, 139.2, 129.80, 129.77, 128.4, 98.4, 80.0, 75.4, 52.9, 48.4, 31.1, 28.2.

HRMS (ESI): exact mass calcd for $C_{18}H_{20}INNaO_7^+$ $(M+Na)^+$ requires m/z 512.0177, found m/z 512.0173 (Δ = -4 ppm).

IR (neat): 2922, 1730, 1703, 1435, 1347, 1250, 1164, 1012, 754, 733, 662, 635cm^{-1}.

Dimethyl (*S*)-2-(2-((2-(bromomethyl)benzyl)oxy)-2-(2,5-dioxopyrrolidin-1-yl)ethyl) malonate (3al)



Colorless oil: 39.1 mg, 86% yield, 93% ee; R_f = 0.75 (Pet/EtOAc/MeOH, 1/1/0.1, v/v/v); **$[\alpha]_D^{25}$** = -23.34 (c = 0.80, $CHCl_3$); reaction time: 24 h; reaction temperature: 40 ºC.

HPLC CHIRALPAK IA, n-hexane/2-propanol = 60/40, flow rate 1.0 mL/min, λ = 254 nm, retention time: 8.248 min (major), 11.425 min (minor).

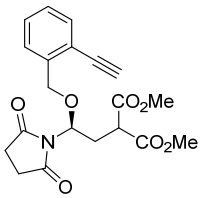
^{1}H NMR (600 MHz, $CDCl_3$) δ 7.34 - 7.32 (m, 1H), 7.30 - 7.25 (m, 3H), 5.44 (dd, *J* = 9.0, 4.8 Hz , 1H), 4.67 (t, *J* = 5.4 Hz, 3H), 7.01 (d, *J* = 10.2 Hz, 1H), 3.69 (s, 3H), 3.67 (s, 3H), 3.51 (dd, *J* = 8.4, 6.6 Hz , 1H), 3.03 - 2.98 (m, 1H), 2.52 - 2.49 (m, 4H), 2.42 - 2.37 (m, 1H).

^{13}C NMR (150 MHz, $CDCl_3$) δ 176.9, 169.02, 168.98, 136.9, 135.7, 130.9, 129.1, 128.9, 80.3, 70.2, 52.84, 52.80, 48.3, 31.7, 31.2, 28.1.

HRMS (ESI): exact mass calcd for $C_{19}H_{22}BrNNaO_7^+$ $(M+Na)^+$ requires m/z 478.0472, found m/z 478.0476 (Δ = +4 ppm).

IR (neat): 2953, 1731, 1703, 1435, 1348, 1167, 1094, 763, 728, 664, 601 cm^{-1}.

Dimethyl (*S*)-2-(2-(2,5-dioxopyrrolidin-1-yl)-2-((2-ethynylbenzyl)oxy)ethyl)malonate (3am)



Colorless oil: 30.9 mg, 80% yield, 90% ee; R_f = 0.60 (Pet/EtOAc/MeOH, 1/1/0.1, v/v/v); **[α]$_D^{25}$** = -20.06 (c = 1.86, $CHCl_3$); reaction time: 24 h; reaction temperature: 40 °C.

HPLC CHIRALPAK IA, n-hexane/2-propanol = 60/40, flow rate 1.0 mL/min, λ = 254 nm, retention time: 8.192 min (major), 9.472 min (minor).

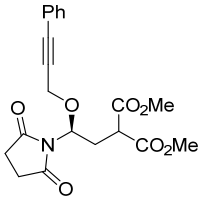
^{1}H NMR (400 MHz, $CDCl_3$) δ 7.46 (dd, *J* = 7.6, 1.2 Hz, 1H), 7.42 (dd, *J* = 8.0, 1.6 Hz, 1H), 7.33 (td, *J* = 8.0, 1.6 Hz, 1H), 7.23 (td, *J* = 7.6, 1.6 Hz, 1H), 5.43 (dd, *J* = 8.8, 4.8 Hz, 1H), 4.66 (s, 2H), 3.681 (s, 3H), 3.679 (s, 3H), 3.57 (dd, *J* = 8.4, 6.0 Hz , 1H), 3.29 (s, 1H), 3.07 - 2.97 (m, 1H), 2.59 (s, 4H), 2.45 - 2.38 (m, 1H).

^{13}C NMR (100 MHz, $CDCl_3$) δ 176.6, 169.1, 169.0, 139.2, 132.9, 129.0, 128.4, 127.8, 121.0, 82.2, 81.1, 80.1, 69.7, 52.8, 48.3, 31.2, 28.1.

HRMS (ESI): exact mass calcd for $C_{20}H_{21}NNaO_7^+$ $(M+Na)^+$ requires m/z 410.1210, found m/z 410.1209 (Δ = -1 ppm).

IR (neat): 2954, 2359, 2348, 1779, 1705, 1436, 1349, 1291, 1170, 819, 764, 664, 636 cm^{-1}.

Dimethyl (*S*)-2-(2-(2,5-dioxopyrrolidin-1-yl)-2-((3-phenylprop-2-yn-1-yl)oxy)ethyl) malonate (3an)



Colorless oil: 33.7 mg, 87% yield, 93% ee; R_f = 0.80 (Pet/EtOAc/MeOH, 1/1/0.1, v/v/v); **[α]$_D^{25}$** = -11.40 (c = 3.32, $CHCl_3$); reaction time: 24 h; reaction temperature: 40 °C.

HPLC CHIRALPAK IA, n-hexane/2-propanol = 60/40, flow rate 1.0 mL/min, λ = 254 nm, retention time: 8.865 min (major), 11.398 min (minor).

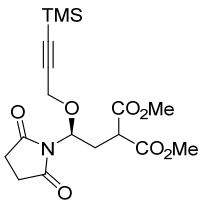
^{1}H NMR (600 MHz, $CDCl_3$) δ 7.44 - 7.42 (m, 2H), 7.33 - 7.29 (m, 3H), 5.54 (dd, *J* = 9.0, 4.8 Hz, 1H), 4.45 (d, *J* = 16.2 Hz, 1H), 4.33 (d, *J* = 16.2 Hz, 1H), 3.73 (s, 3H), 3.67 (s, 3H), 3.59 (dd, *J* = 9.0, 6.0 Hz, 1H), 3.05 - 3.00(m, 1H), 2.60 (s, 4H), 2.45 - 2.41 (m, 1H).

^{13}C NMR (150 MHz, $CDCl_3$) δ 176.9, 169.13, 169.06, 131.8, 128.6, 122.3, 86.6, 84.2, 80.1, 58.4, 52.91, 52.87, 48.2, 31.2, 28.1.

HRMS (ESI): exact mass calcd for $C_{20}H_{21}NNaO_7^+$ $(M+Na)^+$ requires m/z 410.1210, found m/z 410.1206 (Δ = -4 ppm).

IR (neat): 2962, 1776, 1703, 1257, 1009, 788, 691, 661 cm^{-1}.

Dimethyl (*S*)-2-(2-(2,5-dioxopyrrolidin-1-yl)-2-((3-(trimethylsilyl)prop-2-yn-1-yl)oxy)ethyl) malonate (3ao)



Colorless oli: 32.9 mg, 86% yield, 95% ee; R_f = 0.80 (Pet/EtOAc/MeOH, 1/1/0.1, v/v/v); **[α]$_D^{25}$** = -11.67 (c = 0.56, $CHCl_3$); reaction time: 24 h; reaction temperature: 40 °C.

HPLC CHIRALPAK IA, n-hexane/2-propanol = 70/30, flow rate 0.8 mL/min, λ = 254 nm, retention time: 7.418 min (major), 8.997 min (minor).

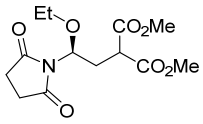
^{1}H NMR (600 MHz, $CDCl_3$) δ 5.44 - 5.41 (m, 1H), 4.19 (d, *J* = 16.2 Hz, 1H), 4.08 (d, *J* = 16.2 Hz, 1H), 3.73 (s, 3H), 3.72 (s, 3H), 3.54 - 3.51 (m, 1H), 2.98 - 2.93 (m, 1H), 2.68 (s, 4H), 2.45 - 2.40 (m, 1H), 0.15 (s, 9H).

^{13}C NMR (150 MHz, $CDCl_3$) δ 176.6, 169.1, 100.0, 92.0, 80.1, 58.2, 52.91, 52.88, 48.2, 31.1, 28.1, -0.2.

HRMS (ESI): exact mass calcd for $C_{17}H_{25}NNaO_7Si^+$ $(M+Na)^+$ requires m/z 406.1292, found m/z 406.1291 (Δ = -1 ppm).

IR (neat): 2957, 1731, 1708, 1436, 1348, 1249, 1167, 1093, 842, 760, 731, 664, 634 cm^{-1}.

Dimethyl (*S*)-2-(2-(2,5-dioxopyrrolidin-1-yl)-2-ethoxyethyl)malonate (3ap)



Colorless oli: 26.4 mg, 89% yield, 99% ee; R_f = 0.43 (Pet/EtOAc/MeOH, 2/1/0.1, v/v/v); **$[\alpha]_D^{25}$** = -8.59 (c = 0.85, $CHCl_3$); reaction time: 24 h; reaction temperature: 40 °C.

HPLC CHIRALPAK IG, n-hexane/2-propanol = 70/30, flow rate 0.8 mL/min, λ = 254 nm, retention time: 17.087 min (major), 26.753 min (minor).

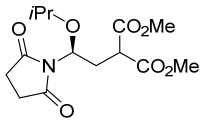
^{1}H NMR (600 MHz, $CDCl_3$) δ 5.27 (dd, *J* = 8.4, 4.8 Hz, 1H), 3.73 (s, 3H), 3.71 (s, 3H), 3.52 (dd, *J* = 8.4, 6.6 Hz, 1H), 3.50 - 3.45 (m, 1H), 3.41 - 3.36 (m, 1H), 2.97 - 2.93 (m, 1H), 2.69 (s, 4H), 2.39 - 2.95 (m, 1H), 1.14 (t, *J* = 7.2 Hz, 3H).

^{13}C NMR (150 MHz, $CDCl_3$) δ 176.8, 169.1, 80.0, 65.1, 52.83, 52.81, 48.4, 31.1, 28.1, 14.8.

HRMS (ESI): exact mass calcd for $C_{13}H_{19}NNaO_7^+$ $(M+Na)^+$ requires m/z 324.1054, found m/z 324.1056 (Δ = +2 ppm).

IR (neat): 2955, 1731, 1703, 1436, 1348, 1250, 1164 , 915, 729, 664, 634 cm^{-1}.

Dimethyl (S)-2-(2-(2,5-dioxopyrrolidin-1-yl)-2-isopropoxyethyl)malonate (3aq)



Colorless oli: 27.4 mg, 87% yield, 96% ee; R_f = 0.43 (Pet/EtOAc/MeOH, 2/1/0.1, v/v/v); $[\alpha]_D^{25}$ = -35.78 (c = 1.05, $CHCl_3$); reaction time: 24 h; reaction temperature: 40 °C.

HPLC CHIRALPAK IG, n-hexane/2-propanol = 60/40, flow rate 0.8 mL/min, λ = 254 nm, retention time: 10.605 min (major), 13.145 min (minor).

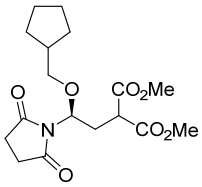
^{1}H NMR (600 MHz, $CDCl_3$) δ 5.37 (dd, *J* = 9.0, 4.8 Hz, 1H), 3.74 (s, 3H), 3.72 (s, 3H), 3.57 (t, *J* = 6.0 Hz, 1H), 3.53 (dd, *J* = 9.0, 5.4 Hz, 1H), 2.94 - 2.90 (m, 1H), 2.68 (s, 4H), 2.36 - 2.31 (m, 1H), 1.13 (d, *J* = 6.6 Hz, 3H), 1.07 (d, *J* = 6.0 Hz, 3H).

^{13}C NMR (150 MHz, $CDCl_3$) δ 176.8, 169.2, 169.1, 77.9, 70.8, 52.8, 48.4, 31.3, 28.1, 23.0, 21.2.

HRMS (ESI): exact mass calcd for $C_{14}H_{21}NNaO_7^+$ $(M+Na)^+$ requires m/z 338.1210, found m/z 338.1208 (Δ = -2 ppm).

IR (neat): 2955, 1732, 1704, 1436, 1344, 1250, 1165, 1094, 914, 818, 729, 665, 635 cm^{-1}.

Dimethyl (*S*)-2-(2-(cyclopentylmethoxy)-2-(2,5-dioxopyrrolidin-1-yl)ethyl)malonate (3ar)



Colorless oli: 25.6 mg, 72% yield, 93% ee; R_f = 0.57 (Pet/EtOAc/MeOH, 2/1/0.1, v/v/v); **$[\alpha]_D^{25}$** = -28.25 (c = 0.80, $CHCl_3$); reaction time: 24 h; reaction temperature: 40 °C.

HPLC CHIRALPAK IG, n-hexane/2-propanol = 70/30, flow rate 0.8 mL/min, λ = 254 nm, retention time: 13.460 min (major), 15.005 min (minor).

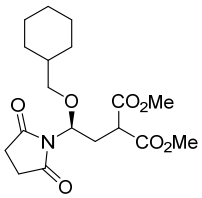
^{1}H NMR (600 MHz, $CDCl_3$) δ 5.27 (dd, *J* = 9.0, 5.4 Hz, 1H), 3.74 (s, 3H), 3.72 (s, 3H), 3.56 (dd, *J* = 9.0, 5.4 Hz, 1H), 3.27 - 3.19 (m, 2H), 2.98 - 2.93 (m, 1H), 2.70 (s, 4H), 2.40 - 2.35 (m, 1H), 2.12 - 2.05 (m, 1H), 1.70 - 1.65 (m, 2H), 1.58 - 1.54 (m, 4H), 1.19 - 1.09 (m, 2H).

^{13}C NMR (150 MHz, $CDCl_3$) δ 176.8, 169.2, 169.1, 80.3, 74.1, 52.9, 48.4, 39.1, 31.0, 29.54, 29.49, 28.1, 25.44, 25.41.

HRMS (ESI): exact mass calcd for $C_{17}H_{25}NNaO_7^+$ $(M+Na)^+$ requires m/z 378.1523, found m/z 378.1525 (Δ = +2 ppm).

IR (neat): 2954, 1732, 1704, 1436, 1345, 1250, 1165, 1118, 819, 732, 664, 635 cm^{-1}.

Dimethyl (*S*)-2-(2-(cyclohexylmethoxy)-2-(2,5-dioxopyrrolidin-1-yl)ethyl)malonate (3as)



Colorless oli: 25.1 mg, 68% yield, 93% ee; R_f = 0.57 (Pet/EtOAc/MeOH, 1/1/0.1, v/v/v); **$[\alpha]_D^{25}$** = -15.27 (c = 1.10, $CHCl_3$); reaction time: 24 h; reaction temperature: 40 °C.

HPLC CHIRALPAK IG, n-hexane/2-propanol = 60/40, flow rate 0.8 mL/min, λ = 254 nm, retention time: 11.587 min (major), 13.405 min (minor).

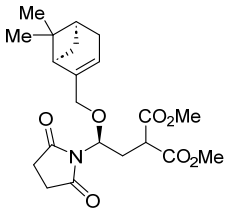
^{1}H NMR (600 MHz, $CDCl_3$) δ 5.22 (dd, *J* = 9.0, 5.4 Hz, 1H), 3.72 (s, 3H), 3.70 (s, 3H), 3.54 (dd, *J* = 9.0, 6.0 Hz, 1H), 3.15 - 3.10 (m, 2H), 2.96 - 2.91 (m, 1H), 2.68 (s, 4H), 2.38 - 2.33 (m, 1H), 1.68 - 1.59 (m, 5H), 1.53 - 1.45 (m, 1H), 1.24 - 1.06 (m, 3H), 0.88 - 0.77 (m, 2H).

^{13}C NMR (150 MHz, $CDCl_3$) δ 176.8, 169.09, 169.07, 80.3, 75.3, 52.8, 48.3, 37.7, 31.0, 29.90, 29.86, 28.1, 26.5, 25.8.

HRMS (ESI): exact mass calcd for $C_{18}H_{27}NNaO_7^+$ $(M+Na)^+$ requires m/z 392.1680, found m/z 392.1679 (Δ = -1 ppm).

IR (neat): 2956, 1732, 1704, 1436, 1348, 1257, 1167, 1095, 1015, 799, 672, 663, 635 cm^{-1}.

Dimethyl 2-((*S*)-2-(((1*R*,5*S*)-6,6-dimethylbicyclo[3.1.1]hept-2-en-2-yl)methoxy)-2-(2,5-dioxopyrrolidin-1-yl)ethyl)malonate (3at)



Colorless oli: 28.4 mg, 70% yield, >20:1 dr; R_f = 0.60 (Pet/EtOAc/MeOH, 1/1/0.1, v/v/v); **[α]$_D^{25}$** = 8.90 (c = 1.15, $CHCl_3$); reaction time: 24 h; reaction temperature: 40 °C.

HPLC CHIRALPAK AD-H, n-hexane/2-propanol = 70/30, flow rate 1.0 mL/min, λ = 210 nm, retention time: 7.003 min (major), 8.007 min (minor).

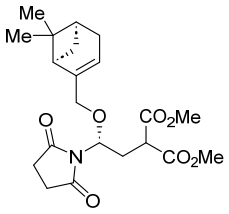
^{1}H NMR (600 MHz, $CDCl_3$) δ 5.43 - 5.42 (m, 1H), 5.27 (dd, *J* = 7.8, 2.4 Hz, 1H), 3.79 - 3.73 (m, 2H), 3.71 (s, 3H), 3.69 (s, 3H), 3.46 (dd, *J* = 8.4, 2.4 Hz , 1H), 2.89 - 2.84 (m, 1H), 2.66 (s, 4H), 2.47 - 2.42 (m, 1H), 2.36 - 2.32 (m, 1H), 2.23 (d, *J* = 18.0, 1H), 2.18 (d, *J* = 18.0, 1H), 2.04 (d, *J* = 4.8, 1H), 1.28 (s, 3H), 1.03 (d, *J* = 9.0, 1H), 0.76 (s, 3H).

^{13}C NMR (150 MHz, $CDCl_3$) δ 176.7, 169.1, 169.0, 144.2, 120.8, 80.1, 72.8, 52.8, 48.3, 43.4, 40.7, 38.0, 31.5, 31.4, 30.9, 28.1, 26.2, 21.0.

HRMS (ESI): exact mass calcd for $C_{21}H_{29}NNaO_7^+$ $(M+Na)^+$ requires m/z 430.1836, found m/z 430.1833 (Δ = -3 ppm).

IR (neat): 2918, 1733, 1705, 1435, 1347, 1250, 1165, 1097, 913, 818, 729, 663, 648 cm^{-1}.

Dimethyl 2-((*R*)-2-(((1*R*,5*S*)-6,6-dimethylbicyclo[3.1.1]hept-2-en-2-yl)methoxy)-2-(2,5-dioxopyrrolidin-1-yl)ethyl)malonate (3at')



Colorless oli: 26.5 mg, 65% yield, >20:1 dr; R_f = 0.60 (Pet/EtOAc/MeOH, 1/1/0.1, v/v/v); **[α]D^{25}** = -16.23 (c = 1.15, $CHCl_3$); reaction time: 24 h; reaction temperature: 40 °C.

HPLC CHIRALPAK AD-H, n-hexane/2-propanol = 70/30, flow rate 1.0 mL/min, λ = 210 nm, retention time: 7.045 min (minor), 8.103 min (major).

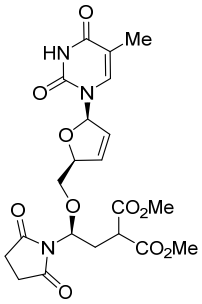
^{1}H NMR (400 MHz, $CDCl_3$) δ 5.46 - 5.45 (m, 1H), 5.28 (dd, *J* = 8.0, 5.6 Hz, 1H), 3.81 - 3.77 (m, 2H), 3.71 (s, 3H), 3.70 (s, 3H), 3.37 (d, *J* = 12.8 Hz, 1H), 3.45 (dd, *J* = 8.8, 6.4 Hz, 1H), 2.89 - 2.82 (m, 1H), 2.68 (t, *J* = 8.0 Hz, 4H), 2.48 - 2.41 (m, 1H), 2.38 - 2.31 (m, 1H), 2.29 (d, *J* = 18.0, 1H), 2.17 (d, *J* = 18.0, 1H), 2.05 (d, *J* = 4.8, 1H), 1.25 (s, 3H), 1.12 (d, *J* = 8.4, 1H), 0.76 (s, 3H).

^{13}C NMR (100 MHz, $CDCl_3$) δ 176.8, 169.1, 169.0, 143.6, 121.7, 79.0, 72.1, 52.8, 48.2, 43.4, 40.8, 38.1, 31.44, 31.38, 31.0, 28.1, 26.2, 21.0.

HRMS (ESI): exact mass calcd for $C_{21}H_{29}NNaO_7^+$ $(M+Na)^+$ requires m/z 430.1836, found m/z 430.1833 (Δ = -3 ppm).

IR (neat): 2917, 1750, 1733, 1705, 1435, 1347, 1250, 1166, 1095, 914, 818, 731, 664 cm^{-1}.

Dimethyl 2-((*S*)-2-(2,5-dioxopyrrolidin-1-yl)-2-(((2*S*,5*R*)-5-(5-methyl-2,4-dioxo-3,4-dihydropyrimidin-1(2*H*)-yl)-2,5-dihydrofuran-2-yl)methoxy)ethyl)malonate (3au)



Colorless oli: 34.0 mg, 71% yield, >20:1 dr; R_f = 0.44 (DCM/MeOH, 20/1, v/v); **[α]$_D^{25}$** = 16.62 (c = 0.64, $CHCl_3$); reaction time: 24 h; reaction temperature: 40 °C.

HPLC CHIRALPAK AD-H, n-hexane/2-propanol = 70/30, flow rate 1.0 mL/min, λ = 254 nm, retention time: 36.582 min (major), 40.400 min (minor).

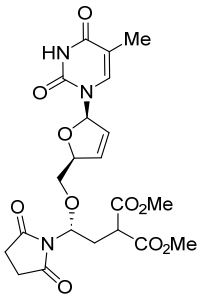
^{1}H NMR (400 MHz, $CDCl_3$) δ 8.76 (s, 1H), 7.33 (s, 1H), 6.96 (s, 1H), 6.24 (d, *J* = 6.0 Hz, 1H), 5.84 (d, *J* = 5.4 Hz, 1H), 5.29 (dd, *J* = 8.4, 5.4 Hz, 1H), 4.89 (s, 1H), 3.74 (s, 3H), 3.72 (s, 3H), 3.70 (s, 1H), 3.56 (dd, *J* = 10.8, 3.0 Hz, 1H), 3.44 (t, *J* = 7.2 Hz, 1H), 3.03 - 2.98 (m, 1H), 2.69 (s, 4H), 2.49 - 2.44 (m, 1H), 1.99 (s, 3H).

^{13}C NMR (150 MHz, $CDCl_3$) δ 175.6, 168.9, 168.8, 164.1, 151.0, 136.3, 133.4, 127.3, 111.6, 89.7, 84.9, 80.6, 69.9, 53.00, 52.97, 48.5, 30.7, 28.0, 12.3.

HRMS (ESI): exact mass calcd for $C_{21}H_{25}N_3NaO_{10}^+$ $(M+Na)^+$ requires m/z 502.1432, found m/z 502.1434 (Δ = +2 ppm).

IR (neat): 2923, 1779, 1685, 1436, 1353, 1249, 1168, 1054, 906, 794, 775, 732, 699, 671, 664, 545 cm^{-1}.

Dimethyl 2-((*R*)-2-(2,5-dioxopyrrolidin-1-yl)-2-(((2*S*,5*R*)-5-(5-methyl-2,4-dioxo-3,4-dihydropyrimidin-1(2*H*)-yl)-2,5-dihydrofuran-2-yl)methoxy)ethyl)malonate (3au')



Colorless oli: 33.5 mg, 70% yield, >20:1 dr; R_f = 0.44 (DCM/MeOH, 20/1, v/v); **[α]$_D^{25}$** = -13.73 (c = 1.25, $CHCl_3$); reaction time: 24 h; reaction temperature: 40 °C.

HPLC CHIRALPAK AD-H, n-hexane/2-propanol = 70/30, flow rate 1.0 mL/min, λ = 254 nm, retention time: 36.390 min (major), 41.173 min (minor).

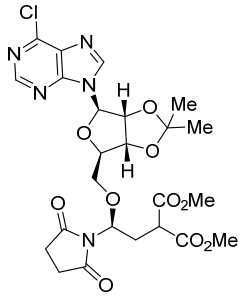
^{1}H NMR (400 MHz, $CDCl_3$) δ 8.90 (s, 1H), 7.28 (s, 1H), 7.00 (s, 1H), 6.15 (d, *J* = 5.4 Hz, 1H), 5.81 (d, *J* = 5.4 Hz, 1H), 5.31 (t, *J* = 6.6 Hz, 1H), 4.87 (s, 1H), 3.84 (d, *J* = 11.4 Hz, 1H), 3.73 (s, 3H), 3.71 (s, 3H), 3.53 (d, *J* =11.4 Hz, 1H), 3.41 (t, *J* = 8.4 Hz, 1H), 2.85 - 2.80 (m, 1H), 2.71 (s, 4H), 2.51 - 2.46 (m, 1H), 1.96 (s, 3H).

^{13}C NMR (150 MHz, $CDCl_3$) δ 176.8, 168.9, 168.8, 163.9, 151.2, 136.4, 134.0, 126.7, 111.3, 89.8, 85.2, 80.8, 70.9, 53.01, 52.95, 48.1, 30.9, 28.1, 12.3.

HRMS (ESI): exact mass calcd for $C_{21}H_{25}N_3NaO_{10}^+$ $(M+Na)^+$ requires m/z 502.1432, found m/z 502.1428 (Δ = -4 ppm).

IR (neat): 2923, 1776, 1698, 1685, 1436, 1351, 1248, 1169, 1053, 906, 798, 733, 699, 671, 664, 578 cm^{-1}.

Dimethyl 2-((*S*)-2-(((3a*R*,4*R*,6*R*,6a*R*)-6-(6-chloro-9*H*-purin-9-yl)-2,2-dimethyltetrahy drofuro[3,4-*d*][1,3]dioxol-4-yl)methoxy)-2-(2,5-dioxopyrrolidin-1-yl)ethyl) malonate (3av)



White solid: 47.6 mg, 82% yield, >20:1 dr; m.p.: 111.0 - 112.5 °C; R_f = 0.43 (Pet/EtOAc/DCM/MeOH, 1/1/1/0.1, v/v/v/v); $[\alpha]_D^{25}$ = 53.99 (c = 0.56, $CHCl_3$); reaction time: 24 h; reaction temperature: 40 °C.

HPLC CHIRALPAK AD-H, n-hexane/2-propanol = 60/40, flow rate 1.0 mL/min, λ = 210 nm, retention time: 13.775 min (major), 35.393 min (minor).

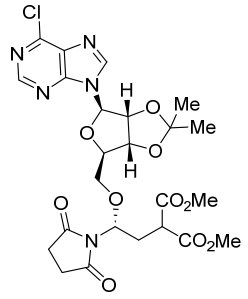
^{1}H NMR (400 MHz, $CDCl_3$) δ 7.87 (s, 1H), 6.36 (s, 1H), 6.23 (dd, *J* = 8.4, 7.2 Hz, 1H), 5.59 (d, *J* = 4.8 Hz, 1H), 5.57 (d, *J* = 9.6 Hz, 1H), 5.24 (dd, *J* = 6.6, 4.8 Hz, 1H), 4.89 (dd, *J* = 6.6, 3.0 Hz, 1H), 4.18 (dd, *J* = 5.4, 2.4 Hz, 1H), 4.14 (dd, *J* = 10.2, 2.4 Hz, 1H), 3.79 (s, 3H), 3.75 (dt, *J* = 12.6, 2.4 Hz, 1H), 3.64 (s, 3H), 3.63 - 3.60 (m, 1H), 2.88 (dd, *J* = 13.8, 8.4 Hz, 1H), 2.75 - 2.65 (m, 4H), 2.49 (dd, *J* = 13.8, 7.2 Hz, 1H), 1.53 (s, 3H), 1.32 (s, 3H).

^{13}C NMR (150 MHz, $CDCl_3$) δ 175.9, 169.0, 168.4, 159.1, 149.7, 133.9, 129.6, 113.7, 91.7, 86.5, 84.1, 80.9, 80.7, 67.3, 66.1, 63.5, 53.4, 53.3, 36.2, 28.3, 27.5, 25.7.

HRMS (ESI): exact mass calcd for $C_{24}H_{28}ClN_5NaO_{10}^+$ $(M+Na)^+$ requires m/z 604.1417, found m/z 604.1413 (Δ = -4 ppm).

IR (neat): 2933, 1732, 1702, 1597, 1497, 1366, 1277, 1179, 1065, 854, 813, 732, 700, 630, 577, 562 cm^{-1}.

Dimethyl 2-((*R*)-2-(((3a*R*,4*R*,6*R*,6a*R*)-6-(6-chloro-9*H*-purin-9-yl)-2,2-dimethyltetrahy drofuro[3,4-*d*][1,3]dioxol-4-yl)methoxy)-2-(2,5-dioxopyrrolidin-1-yl)ethyl)malonate (3av')



White solid: 34.9 mg, 60% yield, >20:1 dr; m.p.: 113.4 - 115.0 °C; R_f = 0.43 (Pet/EtOAc/DCM/MeOH, 1/1/1/0.1, v/v/v/v); **[α]D^{25}** = -123.63 (c = 0.90, $CHCl_3$); reaction time: 24 h; reaction temperature: 40 °C.

HPLC CHIRALPAK AD-H, n-hexane/2-propanol = 60/40, flow rate 1.0 mL/min, λ = 210 nm, retention time: 13.462 min (minor), 35.583 min (major).

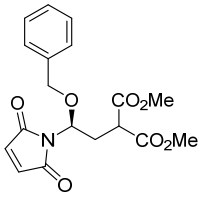
^{1}H NMR (600 MHz, $CDCl_3$) δ 7.89 (s, 1H), 6.34 (s, 1H), 6.26 (dd, *J* = 9.0, 7.2 Hz, 1H), 5.68 (d, *J* = 4.8 Hz, 1H), 5.57 (d, *J* = 9.6 Hz, 1H), 5.02 (t, *J* = 5.4 Hz, 1H), 4.91 (dd, *J* = 6.0, 1.2 Hz, 1H), 4.30 (dd, *J* = 3.6, 1.8 Hz, 1H), 3.83 (s, 3H), 3.82 (t, *J* = 1.8 Hz, 1H), 3.72 - 3.96 (m, 1H), 3.63 (s, 3H), 2.90 (dd, *J* = 13.8, 8.4 Hz, 1H), 2.76 - 2.71 (m, 4H), 2.50 (dd, *J* = 13.8, 7.2 Hz, 1H), 1.64 (s, 3H), 1.33 (s, 3H).

^{13}C NMR (150 MHz, $CDCl_3$) δ 175.9, 168.9, 168.7, 157.5, 149.8, 133.7, 129.9, 113.9, 92.9, 86.2, 84.2, 81.4, 80.4, 68.1, 66.5, 63.5, 53.7, 53.5, 35.8, 28.4, 27.7, 25.6.

HRMS (ESI): exact mass calcd for $C_{24}H_{28}ClN_5NaO_{10}^+$ $(M+Na)^+$ requires m/z 604.1417, found m/z 604.1415 (Δ = -2 ppm).

IR (neat): 2960, 1739, 1704, 1599, 1509, 1369, 1258, 1178, 1074, 851, 800, 726, 672, 648, 632, 575 cm^{-1}.

Dimethyl (*S*)-2-(2-(benzyloxy)-2-(2,5-dioxo-2,5-dihydro-1*H*-pyrrol-1-yl)ethyl)malonate (3ba)



Colorless oli: 34.7 mg, 96% yield, 93% ee; R_f = 0.66 (Pet/EtOAc/DCM/MeOH, 2/1/1/0.2, v/v/v); $[\alpha]_D^{23}$ = -5.11 (c = 1.00, $CHCl_3$); reaction time: 24 h; reaction temperature: 0 °C.

HPLC CHIRALPAK AD-H, n-hexane/2-propanol = 70/30, flow rate 0.8 mL/min, λ = 210 nm, retention time: 11.718 min (minor), 13.377 min (major).

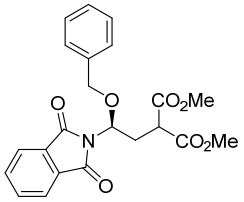
^{1}H NMR (600 MHz, $CDCl_3$) δ 7.31 - 7.28 (m, 2H), 7.25 - 7.22 (m, 3H), 6.57 (s, 2H), 5.34 (dd, *J* = 9.0, 4.8 Hz, 1H), 4.49 (d, *J* = 12.0 Hz, 1H), 4.43 (d, *J* = 12.0 Hz, 1H), 3.69 (s, 3H), 3.66 (s, 3H), 3.53 (dd, *J* = 9.0, 6.6 Hz, 1H), 3.02 - 2.98 (m, 1H), 2.45 - 2.30 (m, 1H).

^{13}C NMR (150 MHz, $CDCl_3$) δ 170.2, 169.1, 169.0, 136.9, 134.1, 128.5, 128.1, 128.0, 78.2, 71.6, 52.8, 48.3, 31.8.

HRMS (ESI): exact mass calcd for $C_{18}H_{19}NNaO_7^+$ $(M+Na)^+$ requires m/z 384.1054, found m/z 384.1053 (Δ = -1 ppm).

IR (neat): 2954, 1732, 1708, 1436, 1351, 1245, 1151, 1090, 913, 830, 738, 694, 645 cm^{-1}.

Dimethyl (*S*)-2-(2-(benzyloxy)-2-(1,3-dioxoisoindolin-2-yl)ethyl)malonate (3ca)



Colorless oli: 27.1 mg, 66% yield, 86% ee; R_f = 0.77 (Pet/EtOAc/DCM/MeOH, 1/1/1/0.1, v/v/v/v); **[α]$_D^{23}$** = -28.00 (c = 0.30, $CHCl_3$); reaction time: 10 days; reaction temperature: -40 °C.

HPLC CHIRALPAK IG, n-hexane/2-propanol = 60/40, flow rate 1.0 mL/min, λ = 210 nm, retention time: 24.337 min (minor), 34.810 min (major).

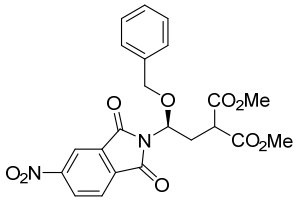
^{1}H NMR (400 MHz, $CDCl_3$) δ 7.77 - 7.71 (m, 2H), 7.67 - 7.63 (m, 2H), 7.21 - 7.18 (m, 2H), 7.16 - 7.12 (m, 2H), 7.08 - 7.04 (m, 1H), 5.48 (dd, *J* = 8.4, 4.8 Hz, 1H), 4.44 (s, 2H), 3.61 (s, 3H), 3.57 (s, 3H), 3.51 (dd, *J* = 8.8, 6.8 Hz , 1H), 3.08 - 3.01 (m, 1H), 2.52 - 2.45 (m, 1H).

^{13}C NMR (100 MHz, $CDCl_3$) δ 169.1, 169.0, 167.7, 136.6, 134.4, 131.6, 128.3, 128.1, 127.8, 123.6, 79.0, 71.5, 52.74, 52.70, 48.4, 31.9.

HRMS (ESI): exact mass calcd for $C_{22}H_{21}NNaO_7^+$ $(M+Na)^+$ requires m/z 434.1210, found m/z 434.1210 (Δ = 0 ppm).

IR (neat): 2956, 1777, 1732, 1713, 1436, 1324, 1257, 1156, 1087, 910, 719, 698, 645 cm^{-1}.

Dimethyl (*S*)-2-(2-(benzyloxy)-2-(5-nitro-1,3-dioxoisoindolin-2-yl)ethyl)malonate (3da)



White solid: 29.6 mg, 65% yield, 93% ee; m.p.: 96.2 - 97.7 °C; R_f = 0.77 (Pet/EtOAc/DCM/MeOH, 1/1/1/0.1, v/v/v/v); $[\alpha]_D^{24}$ = -4.07 (c = 0.80, $CHCl_3$); reaction time: 60h; reaction temperature: 0 °C.

HPLC CHIRALPAK AD-H, n-hexane/2-propanol = 60/40, flow rate 1.0 mL/min, λ = 254 nm, retention time: 22.633 min (major), 32.217 min (minor).

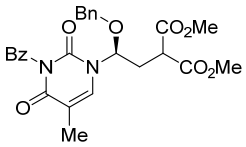
^{1}H NMR (600 MHz, $CDCl_3$) δ 8.58 - 8.56 (m, 2H), 7.97 (d, *J* = 7.8 Hz, 1H), 7.23 (d, *J* = 7.2 Hz, 2H), 7.16 (t, *J* = 7.8 Hz, 2H), 7.06 (t, *J* = 7.8 Hz, 1H), 5.58 (dd, *J* = 8.4, 4.8 Hz, 1H), 4.61 (d, *J* = 12.6 Hz, 1H), 4.48 (d, *J* = 12.6 Hz, 1H), 3.71 (s, 3H), 3.67 (s, 3H), 3.58 (dd, *J* = 8.4, 6.0 Hz, 1H), 3.12 – 3.07 (m, 1H), 2.54 - 2.50 (m, 1H).

^{13}C NMR (150 MHz, $CDCl_3$) δ 169.3, 169.1, 165.8, 165.6, 152.2, 136.9, 136.1, 133.2, 129.7, 128.7, 128.3, 128.2, 125.0, 119.2, 80.2, 72.5, 53.11, 53.08, 48.5, 32.1.

HRMS (ESI): exact mass calcd for $C_{22}H_{20}N_2NaO_9^+$ $(M+Na)^+$ requires m/z 479.1061, found m/z 479.1056 (Δ = -5 ppm).

IR (neat): 2959, 1782, 1748, 1728, 1706, 1510, 1434, 1346, 1247, 1193, 1063, 801, 722, 705 cm^{-1}.

Dimethyl (*S*)-2-(2-(3-benzoyl-5-methyl-2,4-dioxo-3,4-dihydropyrimidin-1(2H)-yl)-2-(benzyloxy) ethyl)malonate (3ea)



Colorless oil: 47.4 mg, 96% yield, 70% ee; R_f = 0.77 (Pet/EtOAc/MeOH, 2/1/0.1, v/v/v); $[\alpha]_D^{24}$ = 1.29 (c = 1.40, $CHCl_3$); reaction time: 24h; reaction temperature: 40 °C.

HPLC CHIRALPAK IA, n-hexane/2-propanol = 80/20, flow rate 0.8 mL/min, λ = 210 nm, retention time: 18.423 min (major), 21.150 min (minor),.

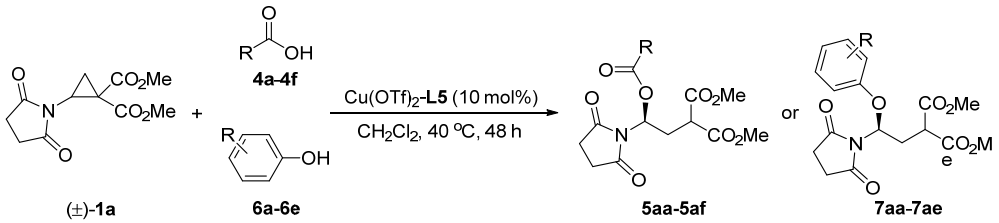
^{1}H NMR (600 MHz, $CDCl_3$) δ 7.91 (d, *J* = 7.2 Hz, 2H), 7.65 (t, *J* = 7.2 Hz, 1H), 7.51 (t, *J* = 7.8 Hz, 2H), 7.38 - 7.32 (m, 3H), 7.29 (d, *J* = 7.2 Hz, 2H), 7.22 (s, 1H), 5.89 (dd, *J* = 8.4, 4.8 Hz, 1H), 4.52 (t, *J* = 12.0 Hz, 2H), 3.68 (s, 3H), 3.66 (s, 3H), 3.52 (t, *J* = 7.2 Hz, 1H), 2.53 - 2.48 (m, 1H), 2.38 - 2.33 (m, 1H), 1.92 (s, 3H).

^{13}C NMR (150 MHz, $CDCl_3$) δ 169.0, 168.9, 168.6, 162.7, 149.8, 135.9, 135.2, 134.2, 131.7, 130.6, 129.3, 128.8, 128.7, 128.5, 111.9, 83.0, 72.3, 53.1, 53.0, 47.9, 34.1, 12.7.

HRMS (ESI): exact mass calcd for $C_{26}H_{26}N_2NaO_8^+$ $(M+Na)^+$ requires m/z 517.1581, found m/z 517.1581 (Δ = 0 ppm).

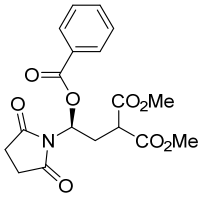
IR (neat): 2955, 1746, 1699, 1650, 1436, 1254, 1093, 1063, 978, 909, 762, 726, 699, 686 cm^{-1}.

Catalytic asymmetric ring-opening of aminocyclopropanes with acids and phenols



General method B - In a dry reaction tube, a mixture of $Cu(OTf)_2$ (3.6 mg, 0.01 mmol, 10 mol%), ligand **L5** (7.8 mg, 0.011 mmol, 11 mol%), and aminocyclopropane **1** (0.22 mmol) in DCM (3.0 mL) were stirred at room temperature for 30 minutes under the atmosphere of nitrogen. Then isoquinoline substrate **4** or **6** (0.1 mmol) in DCM (1.0 mL) was added to the mixture of catalyst via a syringe. Subsequently, the reaction was stirred at 40 °C for 48 h. After the reaction was complete (monitored by TLC), the reaction was filtered through a glass funnel within layer of silica gel (100-200 mesh) and purified by flash column chromatography (Pet/EtOAc/MeOH, v/v/v, 5:1:0.1-1:1:0.1; Pet/EtOAc/DCM/MeOH, v/v/v/v, 5:1:1:1:0.1-1:1:1:0.1) to give the product **5** or **7**.

Dimethyl (*S*)-2-(2-(benzoyloxy)-2-(2,5-dioxopyrrolidin-1-yl)ethyl)malonate (5aa)



Colorless oil: 29.3 mg, 77% yield, 92% ee; R_f = 0.71 (Pet/EtOAc/DCM/MeOH, 1/1/1/0.1, v/v/v/v). **[α]$_D^{25}$** = +16.57 (c = 0.36, $CHCl_3$); reaction time: 48 h; reaction temperature: 40 °C.

HPLC CHIRALPAK IA, n-hexane/2-propanol = 60/40, flow rate 1.0 mL/min, λ = 254 nm, retention time: 10.108 min (major), 11.785 min (minor).

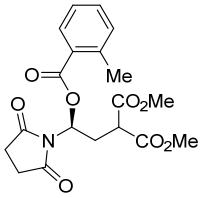
^{1}H NMR (600 MHz, $CDCl_3$) δ 8.03 (d, *J* = 7.2 Hz, 2H), 7.58 (t, *J* = 7.8 Hz, 1H), 7.44 (t, *J* = 7.8 Hz, 2H), 6.71 (t, *J* = 7.2 Hz, 1H), 3.73 (s, 3H), 3.70 (s, 3H), 3.52 (t, *J* = 7.2 Hz, 1H), 3.08 - 3.03 (m, 1H), 2.80 - 2.76 (m, 1H), 2.73 - 2.69 (m, 4H).

^{13}C NMR (150 MHz, $CDCl_3$) δ 175.5, 168.7, 164.8, 133.9, 130.2, 128.8, 128.7, 73.5, 53.09, 53.05, 48.21, 30.2, 28.1.

HRMS (ESI): exact mass calcd for $C_{18}H_{19}NNaO_8^+$ $(M+Na)^+$ requires m/z 400.1003, found m/z 400.1001 (Δ = -2 ppm).

IR (neat): 2921, 1727, 1703, 1435, 1373, 1258, 1157, 1088, 800, 710, 686, 663 cm^{-1}.

Dimethyl (*S*)-2-(2-(2,5-dioxopyrrolidin-1-yl)-2-((2-methylbenzoyl)oxy)ethyl)malonate (5ab)



Colorless oil: 30.5 mg, 78% yield, 96% ee; R_f = 0.71 (Pet/EtOAc/DCM/MeOH, 1/1/1/0.1, v/v/v/v). **$[\alpha]_D^{25}$** = -6.67 (c = 1.15, $CHCl_3$); reaction time: 48 h; reaction temperature: 40 °C.

HPLC CHIRALPAK IA, n-hexane/2-propanol = 60/40, flow rate 1.0 mL/min, λ = 254 nm, retention time: 7.922 min (major), 9.662 min (minor).

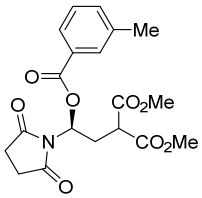
^{1}H NMR (600 MHz, $CDCl_3$) δ 7.96 (d, *J* = 7.8 Hz, 2H), 7.42 (td, *J* = 7.8, 1.2 Hz, 2H), 7.24 (t, *J* = 7.8 Hz, 2H), 6.68 (dd, *J* = 7.8, 6.6 Hz, 1H), 3.74 (s, 3H), 3.69 (s, 3H), 3.51 (dd, *J* = 7.8, 6.6 Hz, 1H), 3.04 - 3.00 (m, 1H), 2.79 - 2.76 (m, 1H), 2.74 - 2.69 (m, 4H), 2.59 (s, 3H).

^{13}C NMR (150 MHz, $CDCl_3$) δ 175.6, 168.7, 165.4, 141.4, 133.0, 132.0, 131.5, 127.9, 126.0, 73.3, 53.1, 53.0, 48.1, 30.2, 28.1, 22.0.

HRMS (ESI): exact mass calcd for $C_{19}H_{21}NNaO_8^+$ $(M+Na)^+$ requires m/z 414.1159, found m/z 414.1157 (Δ = -2 ppm).

IR (neat): 2923, 1727, 1710, 1436, 1371, 1241, 1163, 1050, 800, 738, 670, 663 cm^{-1}.

Dimethyl (S)-2-(2-(2,5-dioxopyrrolidin-1-yl)-2-((3-methylbenzoyl)oxy)ethyl)malonate (5ac)



Colorless oil: 23.9 mg, 61% yield, 94% ee; R_f = 0.71 (Pet/EtOAc/DCM/MeOH, 1/1/1/0.1, v/v/v/v). **[α]D^{25}** = +5.67 (c = 1.15, $CHCl_3$); reaction time: 48 h; reaction temperature: 40 °C.

HPLC CHIRALPAK IA, n-hexane/2-propanol = 60/40, flow rate 1.0 mL/min, λ = 254 nm, retention time: 8.655 min (major), 10.910 min (minor).

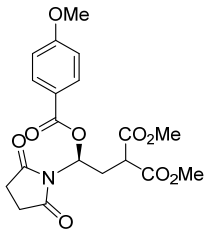
^{1}H NMR (400 MHz, $CDCl_3$) δ 7.81 (d, *J* = 4.4 Hz, 2H), 7.37 (d, *J* = 7.6 Hz, 1H), 7.31 (t, *J* = 8.0 Hz, 1H), 6.69 (t, *J* = 7.2 Hz, 1H), 3.73 (s, 3H), 3.70 (s, 3H), 3.51 (t, *J* = 7.2 Hz, 1H), 3.08 - 3.01 (m, 1H), 2.80 - 2.74 (m, 1H), 2.70 (s, 4H), 2.38 (s, 3H).

^{13}C NMR (100 MHz, $CDCl_3$) δ 175.5, 168.7, 165.0, 138.5, 134.6, 130.6, 128.7, 128.5, 127.3, 73.4, 53.04, 53.01, 48.1, 30.1, 28.1, 21.3.

HRMS (ESI): exact mass calcd for $C_{19}H_{21}NNaO_8^+$ $(M+Na)^+$ requires m/z 414.1159, found m/z 414.1155 (Δ = -4 ppm).

IR (neat): 2956, 1727, 1711, 1435, 1372, 1270, 1168, 1074, 817, 729, 673, 663 cm^{-1}.

Dimethyl (*S*)-2-(2-(2,5-dioxopyrrolidin-1-yl)-2-((4-methoxybenzoyl)oxy)ethyl)malonate (5ad)



Colorless oil: 36.6 mg, 90% yield, 93% ee; R_f = 0.71 (Pet/EtOAc/DCM/MeOH, 1/1/1/0.1, v/v/v/v). **[α]$_D^{23}$** = +4.71 (c = 0.75, $CHCl_3$); reaction time: 48 h; reaction temperature: 40 °C.

HPLC CHIRALPAK IA, n-hexane/2-propanol = 60/40, flow rate 1.0 mL/min, λ = 254 nm, retention time: 14.303 min (major), 17.492 min (minor).

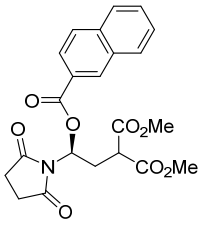
^{1}H NMR (600 MHz, $CDCl_3$) δ 7.98 (d, *J* = 8.4 Hz, 2H), 6.91 (d, *J* = 9.0 Hz, 2H), 6.69 (dd, *J* = 7.8, 6.6 Hz , 1H), 3.85 (s, 3H), 3.73 (s, 3H), 3.70 (s, 3H), 3.52 (dd, *J* = 7.8, 6.6 Hz , 1H), 3.07 - 3.02 (m, 1H), 2.77 - 2.73 (m, 1H), 2.72 - 2.66 (m, 4H).

^{13}C NMR (150 MHz, $CDCl_3$) δ 175.5, 168.73, 168.69, 164.5, 164.1, 132.3, 121.1, 113.9, 73.3, 55.6, 53.1, 53.0, 48.1, 30.2, 28.1.

HRMS (ESI): exact mass calcd for $C_{19}H_{21}NNaO_9^+$ $(M+Na)^+$ requires m/z 430.1109, found m/z 430.1109 (Δ = 0 ppm).

IR (neat): 2923, 1785, 1724, 1605, 1512, 1436, 1372, 1250, 1165, 1081, 849, 769, 734, 695, 671, 664 cm^{-1}.

Dimethyl (*S*)-2-(2-((2-naphthoyl)oxy)-2-(2,5-dioxopyrrolidin-1-yl)ethyl)malonate (5ae)



Colorless oil: 27.8 mg, 65% yield, 98% ee; R_f = 0.71 (Pet/EtOAc/DCM/MeOH, 1/1/1/0.1, v/v/v/v). **[α]$_D^{25}$** = +16.00 (c = 1.00, $CHCl_3$); reaction time: 48 h; reaction temperature: 40 °C.

HPLC CHIRALPAK IA, n-hexane/2-propanol = 60/40, flow rate 1.0 mL/min, λ = 254 nm, retention time: 13.892 min (major), 19.480 min (minor).

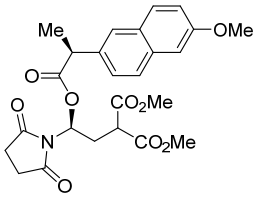
^{1}H NMR (400 MHz, $CDCl_3$) δ 8.61 (s, 1H), 8.02 (dd, *J* = 8.8, 2.0 Hz, 1H), 7.97 (d, *J* = 7.6 Hz, 1H), 7.87 (d, *J* = 8.4 Hz, 1H), 7.63 - 7.53 (m, 2H), 6.79 (dd, *J* = 8.0, 6.4 Hz, 1H), 3.75 (s, 3H), 3.71 (s, 3H), 3.57 (dd, *J* = 8.0, 6.8 Hz , 1H), 3.16 - 3.09 (m, 1H), 2.87 - 2.80 (m, 1H), 2.73 (s, 4H).

^{13}C NMR (150 MHz, $CDCl_3$) δ 175.4, 168.6, 164.9, 135.9, 132.4, 131.9, 129.5, 128.7, 128.4, 127.8, 126.9, 125.9, 125.2, 73.5, 52.99, 52.96, 48.0, 30.1, 28.0.

HRMS (ESI): exact mass calcd for $C_{22}H_{21}NNaO_8^+$ $(M+Na)^+$ requires m/z 450.1159, found m/z 450.1163 (Δ = +4 ppm).

IR (neat): 2955, 1785, 1726, 1710, 1435, 1373, 1277, 1168, 1079, 778, 763, 733, 663 cm^{-1}.

bDimethyl 2-((*S*)-2-(2,5-dioxopyrrolidin-1-yl)-2-(((*S*)-2-(6-methoxynaphthalen-2-yl) propanoyl)oxy)ethyl)malonate (5af)



Colorless oil: 33.2 mg, 73% yield, >20:1 dr; R_f = 0.75 (Pet/EtOAc/DCM/MeOH, 1/1/1/0.1, v/v/v/v). **[α]D^{25}** = -7.50 (c = 0.40, $CHCl_3$); reaction time: 48 h; reaction temperature: 40 °C.

HPLC CHIRALPAK AD-H, n-hexane/2-propanol = 60/40, flow rate 1.0 mL/min, λ = 254 nm, retention time: 15.390 min (major), 19.868 min (minor).

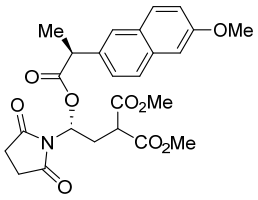
^{1}H NMR (600 MHz, $CDCl_3$) δ 7.69 (d, *J* = 4.2 Hz, 1H), 7.67 (d, *J* = 3.6 Hz, 1H), 7.59 (d, *J* = 1.8 Hz, 1H), 7.34 (dd, *J* = 9.0, 2.4 Hz, 1H), 7.13 (d, *J* = 9.0, 2.4 Hz, 1H), 7.09 (d, *J* = 2.4 Hz, 1H), 6.45 (dd, *J* = 7.8, 6.6 Hz, 1H), 3.91 (s, 3H), 3.85 (dd, *J* = 14.4, 7.2 Hz, 1H), 3.74 (s, 3H), 3.72 (s, 3H), 3.40 (dd, *J* = 8.4, 6.0 Hz, 1H), 2.90 - 2.85 (m, 1H), 2.67 - 2.62 (m, 1H), 2.41 - 2.35 (m, 2H), 2.32 - 2.26 (m, 2H), 1.57 (d, *J* = 7.2, 3H).

^{13}C NMR (150 MHz, $CDCl_3$) δ 175.2, 173.0, 168.61, 168.58, 157.9, 134.8, 133.8, 129.3, 128.9, 127.3, 126.4, 126.2, 119.3, 105.6, 73.2, 55.4, 53.1, 53.0, 47.9, 45.1, 29.7, 27.7, 18.0.

HRMS (ESI): exact mass calcd for $C_{25}H_{27}NNaO_9^+$ $(M+Na)^+$ requires m/z 508.1578, found m/z 508.1574 (Δ = -4 ppm).

IR (neat): 2923, 1785, 1731, 1719, 1605, 1436, 1371, 1260, 1159, 1028, 815, 734, 671, 662 cm^{-1}.

Dimethyl 2-((*R*)-2-(2,5-dioxopyrrolidin-1-yl)-2-(((*S*)-2-(6-methoxynaphthalen-2-yl) propanoyl)oxy)ethyl)malonate (5af')



Colorless oil: 30.9 mg, 68% yield, >20:1 dr; R_f = 0.75 (Pet/EtOAc/DCM/MeOH, 1/1/1/0.1, v/v/v/v). $[\alpha]_D^{25}$ = +4.52 (c = 0.90, $CHCl_3$); reaction time: 48 h; reaction temperature: 40 °C.

HPLC CHIRALPAK AD-H, n-hexane/2-propanol = 60/40, flow rate 1.0 mL/min, λ = 254 nm, retention time: 15.668 min (major), 20.635 min (minor).

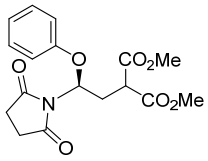
^{1}H NMR (600 MHz, $CDCl_3$) δ 7.70 (dd, *J* = 9.0, 5.4 Hz, 2H), 7.66 (d, *J* = 1.8 Hz, 1H), 7.37 (dd, *J* = 9.0, 2.4 Hz, 1H), 7.14 (dd, *J* = 9.0, 3.0 Hz, 1H), 7.11 (d, *J* = 3.0 Hz, 1H), 6.38 (dd, *J* = 8.4, 6.6 Hz, 1H), 3.91 (s, 3H), 3.86 (q, *J* = 7.2 Hz, 1H), 3.63 (s, 3H), 3.58 (s, 3H), 3.19 (dd, *J* = 9.0, 5.4 Hz, 1H), 2.79 - 2.74 (m, 1H), 2.66 - 2.59 (m, 4H), 2.56 - 2.51 (m, 1H), 1.54 (d, *J* = 7.2, 3H).

^{13}C NMR (150 MHz, $CDCl_3$) δ 175.4, 173.0, 168.52, 168.47, 157.8, 134.8, 133.9, 129.4, 129.0, 127.4, 126.3, 126.2, 119.1, 105.6, 73.3, 55.4, 52.9, 52.8, 47.4, 45.2, 29.7, 28.0, 18.2.

HRMS (ESI): exact mass calcd for $C_{25}H_{27}NNaO_9^+$ $(M+Na)^+$ requires m/z 508.1578, found m/z 508.1577 (Δ = -1 ppm).

IR (neat): 2922, 1785, 1733, 1714, 1605, 1436, 1372, 1259, 1154, 1028, 814, 734, 670, 663 cm^{-1}.

Dimethyl (*S*)-2-(2-(2,5-dioxopyrrolidin-1-yl)-2-phenoxyethyl)malonate (7aa)



Colorless oil: 29.7 mg, 85% yield, 94% ee; R_f = 0. 57 (Pet/EtOAc/MeOH, 1/1/0.1, v/v/v). **[α]$_D^{25}$** = -8.04 (c = 0.90, $CHCl_3$); reaction time: 48 h; reaction temperature: 40 °C.

HPLC CHIRALPAK OD-H, n-hexane/2-propanol = 70/30, flow rate 1.0 mL/min, λ = 254 nm, retention time: 13.230 min (major), 19.232 min (minor).

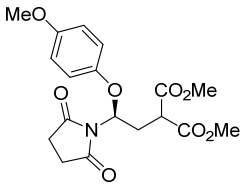
^{1}H NMR (400 MHz, $CDCl_3$) δ 7.29 - 7.23 (m, 2H), 7.03 - 7.00 (m, 1H), 6.97 - 6.94 (m, 2H), 6.13 (dd, *J* = 5.2, 8.4 Hz, 1H), 3.75 (s, 3H), 3.72 (s, 3H), 3.63 (dd, *J* = 8.8, 6.4 Hz, 1H), 3.17 - 3.10 (m, 1H), 2.66 - 2.59 (m, 5H).

^{13}C NMR (100 MHz, $CDCl_3$) δ 176.2, 168.97, 168.95, 155.7, 129.9, 123.0, 116.5, 77.7, 53.0, 48.1, 31.1, 28.1, 1.1.

HRMS (ESI): exact mass calcd for $C_{17}H_{19}NNaO_7^+$ $(M+Na)^+$ requires m/z 372.1054, found m/z 372.1050 (Δ = -4 ppm).

IR (neat): 2921, 1780, 1752, 1727, 1705, 1432, 1361, 1164, 1058, 753, 692, 664, 619 cm^{-1}.

Dimethyl (*S*)-2-(2-(2,5-dioxopyrrolidin-1-yl)-2-phenoxyethyl)malonate (7ab)



Colorless oil: 32.6 mg, 86% yield, 92% ee; R_f = 0. 57 (Pet/EtOAc/MeOH, 1/1/0.1, v/v/v). **$[\alpha]_D^{25}$** = -24.27 (c = 1.25, $CHCl_3$); reaction time: 48 h; reaction temperature: 40 ºC.

HPLC CHIRALPAK OD-H, n-hexane/2-propanol = 70/30, flow rate 1.0 mL/min, λ = 254 nm, retention time: 17.575 min (major), 24.372 min (minor).

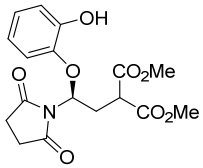
^{1}H NMR (400 MHz, $CDCl_3$) δ 6.88 (d, *J* = 9.0 Hz, 2H), 6.77 (d, *J* = 9.0 Hz, 2H), 5.98 (dd, *J* = 8.4, 5.4 Hz, 1H), 3.743 (s, 3H), 3.739 (s, 3H), 3.735 (s, 3H), 3.64 (dd, *J* = 9.0, 6.0 Hz, 1H), 3.14 - 3.09 (m, 1H), 2.66 - 2.57 (m, 5H).

^{13}C NMR (100 MHz, $CDCl_3$) δ 176.2, 169.01, 168.98, 155.6, 149.4, 118.4, 114.9, 78.9, 55.7, 53.0, 48.2, 31.0, 28.0.

HRMS (ESI): exact mass calcd for $C_{18}H_{21}NNaO_8^+$ $(M+Na)^+$ requires m/z 402.1159, found m/z 402.1155 (Δ = -4 ppm).

IR (neat): 2957, 1781, 1730, 1708, 1507, 1436, 1356, 1165, 1033, 829, 735, 671, 664 cm^{-1}.

Dimethyl (*S*)-2-(2-(2,5-dioxopyrrolidin-1-yl)-2-(2-hydroxyphenoxy)ethyl)malonate (7ac)



Colorless oil: 27.0 mg, 74% yield, 90% ee; R_f = 0. 57 (Pet/EtOAc/MeOH, 1/1/0.1, v/v/v). **[α]$_D^{25}$** = -7.69 (c = 0.65, $CHCl_3$); reaction time: 48 h; reaction temperature: 40 ºC.

HPLC CHIRALPAK OD-H, n-hexane/2-propanol = 80/20, flow rate 1.0 mL/min, λ = 254 nm, retention time: 18.610 min (major), 23.237 min (minor).

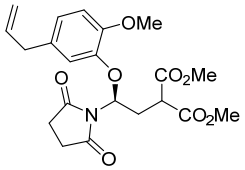
^{1}H NMR (400 MHz, $CDCl_3$) δ 6.96 - 6.87 (m, 2H), 6.79 - 6.75 (m, 1H), 6.14 - 6.10 (m, 2H), 3.76 (s, 3H), 3.74(s, 3H), 3.678 (dd, *J* = 8.0, 6.4 Hz, 1H), 3.17 - 3.11 (m, 1H), 2.64 - 2.56 (m, 5H).

^{13}C NMR (100 MHz, $CDCl_3$) δ 176.6, 169.04, 169.00, 147.9, 142.0, 124.7, 120.5, 116.5, 116.4, 79.3, 53.09, 53.06, 48.1, 31.0, 28.0.

HRMS (ESI): exact mass calcd for $C_{17}H_{19}NNaO_8^+$ $(M+Na)^+$ requires m/z 388.1003, found m/z 388.1000 (Δ = -3 ppm).

IR (neat): 2957, 1780, 1704, 1499, 1436, 1349, 1262, 1166, 1108, 1041, 818, 751, 666, 634 cm^{-1}.

Dimethyl (*S*)-2-(2-(5-allyl-2-methoxyphenoxy)-2-(2,5-dioxopyrrolidin-1-yl)ethyl)malonate (7ad)



Colorless oil: 31.4 mg, 75% yield, 92% ee; R_f = 0. 57 (Pet/EtOAc/MeOH, 1/1/0.1, v/v/v). **[α]D^{25}** = -7.69 (c = 0.65, $CHCl_3$); reaction time: 48 h; reaction temperature: 40 ºC.

HPLC CHIRALPAK OD-H, n-hexane/2-propanol = 70/30, flow rate 1.0 mL/min, λ = 254 nm, retention time: 12.052 min (major), 16.298 min (minor).

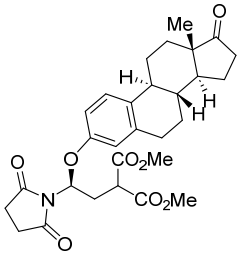
^{1}H NMR (400 MHz, $CDCl_3$) δ 6.78 (d, *J* = 8.0 Hz, 1H), 6.67 (d, *J* = 2.0 Hz, 1H), 6.61 (dd, *J* = 8.0, 1.6 Hz, 1H), 5.94 - 5.86 (m, 2H), 5.06 (t, *J* = 1.6 Hz, 1H), 5.03 - 5.01 (m, 1H), 3.84 (dd, *J* = 9.6, 5.2 Hz, 1H), 3.79 (s, 3H), 3.77 (s, 3H), 3.73 (s, 3H), 3.29 (d, *J* = 6.4 Hz, 2H), 3.25 - 3.18 (m, 1H), 2.66 - 2.51 (m, 5H).

^{13}C NMR (100 MHz, $CDCl_3$) δ 176.3, 169.2, 169.1, 151.7, 143.1, 137.4, 137.3, 121.2, 121.0, 116.1, 113.4, 80.5, 56.0, 52.9, 52.8, 48.3, 40.0, 31.1, 28.0.

HRMS (ESI): exact mass calcd for $C_{21}H_{25}NNaO_8^+$ requires m/z 442.1472, found m/z 442.1470 (Δ = -2 ppm).

IR (neat): 2955, 1783, 1748, 1709, 1506, 1435, 1354, 1264, 1169, 1034, 911, 820, 728, 663, 648 cm^{-1}.

Dimethyl 2-((*S*)-2-(2,5-dioxopyrrolidin-1-yl)-2-(((8*R*,9*S*,13*S*,14*S*)-13-methyl-17-oxo-7,8,9,11,12,13,14,15,16,17-decahydro-6*H*-cyclopenta[a]phenanthren-3-yl)oxy)ethyl) malonate (7ae)



Colorless oil: 39.9mg, 76% yield, >20:1 dr; R_f = 0.75(Pet/EtOAc/DCM/MeOH, 1/1/1/0.1, v/v/v/v). **[α]$_D^{25}$** = +16.24 (c = 1.10, $CHCl_3$); reaction time: 48 h; reaction temperature: 40 ºC.

HPLC CHIRALPAK AD-H, n-hexane/2-propanol = 60/40, flow rate 1.0 mL/min, λ = 210 nm, retention time: 14.543 min (major), 26.708 min (minor).

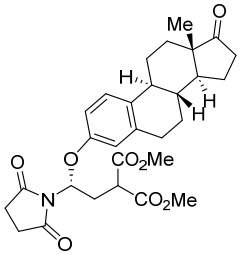
^{1}H NMR (400 MHz, $CDCl_3$) δ 7.16 (d, *J* = 8.4 Hz, 1H), 6.74 (dd, *J* = 8.4, 2.8 Hz, 1H), 6.70 (d, *J* = 2.8 Hz, 1H), 6.09 (dd, *J* = 8.0, 5.2 Hz, 1H), 3.75 (s, 3H), 3.73 (s, 3H), 3.61 (dd, *J* = 8.4, 6.0 Hz, 1H), 3.14 - 3.07 (m, 1H), 2.85 (dd, *J* = 8.8, 4.0 Hz, 1H), 2.63 (s, 4H), 2.53 - 2.46 (m, 1H), 2.38 - 2.33 (m, 1H), 2.24 - 2.18 (m, 1H), 2.15 - 1.93 (m, 4H), 1.66 - 1.35 (m, 7H), 0.89 (s, 3H).

^{13}C NMR (100 MHz, $CDCl_3$) δ 176.2, 169.0, 168.9, 153.6, 138.3, 134.4, 126.7, 116.7, 113.4, 53.0, 50.5, 48.07, 48.05, 44.1, 38.3, 36.0, 31.7, 31.1, 29.6, 28.1, 26.5, 25.9, 21.7, 14.0.

HRMS (ESI): exact mass calcd for $C_{29}H_{35}NNaO_8^+$ $(M+Na)^+$ requires m/z 548.2255, found m/z 548.2258 (Δ = +3 ppm).

IR (neat): 2924, 1781, 1731, 1708, 1497, 1435, 1355, 1242, 1155, 1054, 819, 733, 701, 671, 663 cm^{-1}.

Dimethyl 2-((*R*)-2-(2,5-dioxopyrrolidin-1-yl)-2-(((8*R*,9*S*,13*S*,14*S*)-13-methyl-17-oxo-7,8,9,11,12,13,14,15,16,17-decahydro-6*H*-cyclopenta[a]phenanthren-3-yl)oxy)ethyl) malonate(7ae')



Colorless oil: 34.1mg, 65% yield, >20:1 dr; R_f = 0.75(Pet/EtOAc/DCM/MeOH, 1/1/1/0.1, v/v/v/v). **[α]$_D^{25}$** = +5.75 (c = 1.60, $CHCl_3$); reaction time: 48 h; reaction temperature: 40 °C.

HPLC CHIRALPAK AD-H, n-hexane/2-propanol = 60/40, flow rate 1.0 mL/min, λ = 210 nm, retention time: 14.545 min (minor), 26.065 min (major).

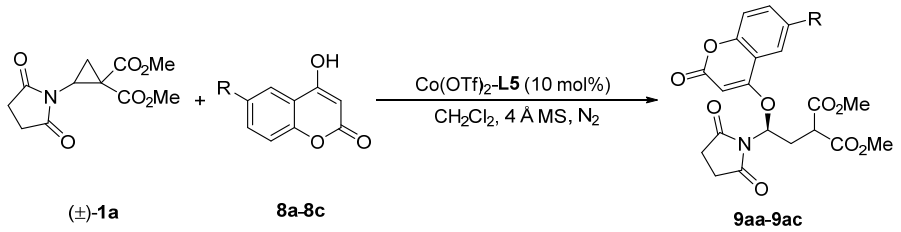
^{1}H NMR (400 MHz, $CDCl_3$) δ 7.15 (d, *J* = 8.4 Hz, 1H), 6.73 (dd, *J* = 8.8, 2.8 Hz, 1H), 6.69 (d, *J* = 2.8 Hz, 1H), 6.07 (dd, *J* = 8.4, 5.6 Hz, 1H), 3.74 (s, 3H), 3.72 (s, 3H), 3.60 (dd, *J* = 8.4, 6.0 Hz, 1H), 3.11 - 3.06 (m, 1H), 2.84 (dd, *J* = 9.2, 4.4 Hz, 1H), 2.63 (s, 4H), 2.57 (dd, *J* = 8.4, 5.6 Hz, 1H), 2.48 (dd, *J* = 18.8, 8.8 Hz, 1H), 2.36 - 2.33 (m, 1H), 2.23 - 2.17 (m, 1H), 2.48 (dd, *J* = 19.2, 9.2 Hz, 1H), 2.05 - 2.19 (m, 3H), 1.63 - 1.34 (m, 6H), 0.89 (s, 3H).

^{13}C NMR (100 MHz, $CDCl_3$) δ 176.2, 169.0, 168.9, 153.6, 138.3, 134.4, 126.7, 116.7, 113.4, 53.0, 50.5, 48.0, 44.1, 38.3, 35.9, 31.6, 31.0, 29.6, 28.1, 26.5, 25.9, 21.7, 13.9.

HRMS (ESI): exact mass calcd for $C_{29}H_{35}NNaO_8^+$ $(M+Na)^+$ requires m/z 548.2255, found m/z 548.2253 (Δ = -2 ppm).

IR (neat): 2923, 1781, 1731, 1708, 1497, 1435, 1355, 1242, 1155, 1054, 819, 733, 701, 671, 662 cm^{-1}.

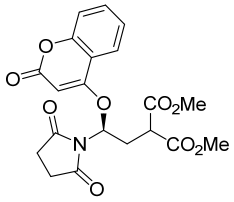
Catalytic asymmetric ring-opening of aminocyclopropanes with 4-hydroxycoumarins



(±)-**1a** **8a-8c** **9aa-9ac**

General method C - In a dry reaction tube, a mixture of $Co(OTf)_2$ (3.6 mg, 0.01 mmol, 10 mol%), ligand **L5** (7.8 mg, 0.011 mmol, 11 mol%), and aminocyclopropane **1a** (0.22 mmol) in DCM (3.0 mL) were stirred at room temperature for 30 minutes under the atmosphere of nitrogen. Then isoquinoline substrate **8** (0.1 mmol) in DCM (1.0 mL) was added to the mixture of catalyst via a syringe. Subsequently, the reaction was stirred at 40 °C or 60 °C or 80 °C for 8-24 h. After the reaction was complete (monitored by TLC), the reaction was filtered through a glass funnel within layer of silica gel (100-200 mesh) and purified by flash column chromatography (Pet/EtOAc/MeOH, v/v/v, 3:1:0.1-1:2:0.1) to give the product **9**.

Dimethyl (*S*)-2-(2-(2,5-dioxopyrrolidin-1-yl)-2-((2-oxo-2*H*-chromen-4-yl)oxy)ethyl) malonate (9aa)



Colorless oil: 39.8mg, 95% yield, 96% ee; R_f = 0.63 (Pet/EtOAc/MeOH, 1/2/0.1, v/v/v). **$[\alpha]_D^{25}$** = +2.25 (c = 0.60, $CHCl_3$); reaction time: 24 h; reaction temperature: 40 ºC.

HPLC CHIRALPAK IA, n-hexane/2-propanol = 60/40, flow rate 1.0 mL/min, λ = 254 nm, retention time: 11.072 min (major), 18.690 min (minor).

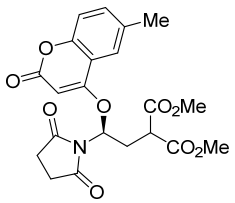
^{1}H NMR (400 MHz, $CDCl_3$) δ 7.81 - 7.77 (m, 1H), 7.52 - 7.48 (m, 1H), 7.25 - 7.21 (m, 2H), 6.20 (dd, *J* = 7.6, 6.0 Hz, 1H), 5.80 (s, 1H), 3.70 (s, 3H), 3.69 (s, 3H), 3.50 (t, *J* = 7.2 Hz, 1H), 3.20 - 3.13 (m, 1H), 2.81 - 2.74 (m, 1H), 2.72 (s, 4H).

^{13}C NMR (100 MHz, $CDCl_3$) δ 175.6, 168.52, 168.47, 162.5, 162.1, 153.5, 132.9, 124.3, 123.4, 116.8, 115.1, 92.5, 76.9, 53.23, 53.20, 47.8, 30.4, 28.1.

HRMS (ESI): exact mass calcd for $C_{20}H_{19}NNaO_9^+$ $(M+Na)^+$ requires m/z 440.0952, found m/z 440.0949 (Δ = -3 ppm).

IR (neat): 2922, 1782, 1708, 1623, 1435, 1350, 1238, 1156, 1102, 1031, 918, 817, 766, 728, 671, 664 cm^{-1}.

Dimethyl (*S*)-2-(2-(2,5-dioxopyrrolidin-1-yl)-2-((6-methyl-2-oxo-2*H*-chromen-4-yl)oxy) ethyl)malonate (9ab)



Colorless oil: 35.3 mg, 82% yield, 96% ee; R_f = 0.63 (Pet/EtOAc/MeOH, 1/2/0.1, v/v/v). **$[\alpha]_D^{24}$** = +3.60 (c = 0.45, $CHCl_3$); reaction time: 12 h; reaction temperature: 60 °C.

HPLC CHIRALPAK IA, n-hexane/2-propanol = 60/40, flow rate 1.0 mL/min, λ = 254 nm, retention time: 10.597 min (major), 16.545 min (minor).

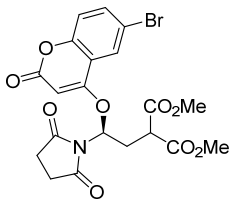
^{1}H NMR (600 MHz, $CDCl_3$) δ 7.59 (s, 1H), 7.34 (d, *J* = 8.4 Hz, 1H), 7.17 (d, *J* = 8.4 Hz, 1H), 6.22 (t, *J* = 6.6 Hz , 1H), 5.81 (s, 1H), 3.746 (s, 3H), 3.739 (s, 3H), 3.53 (t, *J* = 7.2, 1H), 3.22 - 3.17 (m, 1H), 2.86 - 2.80 (m, 1H), 2.75 (t, *J* = 13.2, 4H) 2.41 (s, 3H).

^{13}C NMR (150 MHz, $CDCl_3$) δ 175.6, 168.5, 162.5, 162.4, 151.7, 134.1, 134.0, 123.0, 116.6, 114.7, 92.4, 55.3, 53.2, 47.8,30.5, 28.1, 21.0.

HRMS (ESI): exact mass calcd for $C_{21}H_{21}NNaO_9^+$ $(M+Na)^+$ requires m/z 454.1109, found m/z 454.1106 (Δ = -3 ppm).

IR (neat): 2962, 1782, 1713, 1628, 1434, 1350, 1258, 1156, 1015, 795, 732, 703, 672, 663 cm^{-1}.

Dimethyl (*S*)-2-(2-((6-bromo-2-oxo-2*H*-chromen-4-yl)oxy)-2-(2,5-dioxopyrrolidin-1-yl) ethyl)malonate (9ac)



Colorless oil: 37.6 mg, 76% yield, 97% ee; R_f = 0.75 (Pet/EtOAc/MeOH, 1/2/0.1, v/v/v). **[α]$_D^{25}$** = +7.80 (c = 1.00, $CHCl_3$); reaction time: 8 h; reaction temperature: 80 °C.

HPLC CHIRALPAK IA, n-hexane/2-propanol = 60/40, flow rate 1.0 mL/min, λ = 254 nm, retention time: 13.178 min (major), 19.595 min (minor).

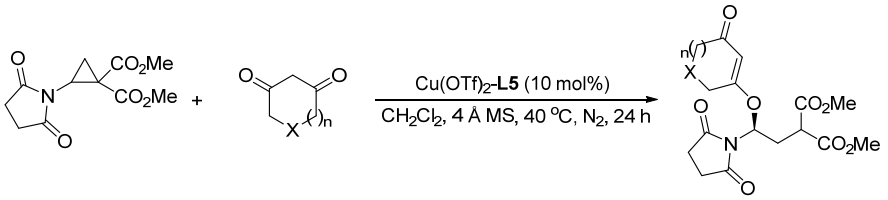
^{1}H NMR (600 MHz, $CDCl_3$) δ 7.86 (d, *J* = 2.4 Hz, 1H), 7.61 (dd, *J* = 9.0, 2.4 Hz, 1H), 7.14 (d, *J* = 9.0 Hz , 1H), 6.21 (t, *J* = 7.2 Hz, 1H), 5.85 (s, 1H), 3.76 (s, 3H), 3.74 (s, 3H), 3.50 (t, *J* = 7.2, 1H), 3.21 - 3.16 (m, 1H), 2.87 - 2.82 (m, 1H), 2.79 - 2.76 (m, 4H).

^{13}C NMR (150 MHz, $CDCl_3$) δ 175.6, 168.4, 161.4, 161.3, 152.4, 135.8, 125.9, 118.6, 117.2, 116.6, 93.2, 53.3, 47.8, 30.3, 28.2.

HRMS (ESI): exact mass calcd for $C_{20}H_{18}BrNNaO_9^+$ $(M+Na)^+$ requires m/z 518.0057, found m/z 518.0055 (Δ = -2 ppm).

IR (neat): 2962, 1782, 1718, 1622, 1427, 1346, 1258, 1162, 1012, 792, 702, 672, 662 cm^{-1}.

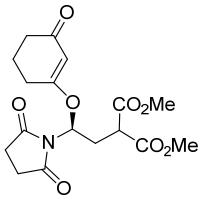
Catalytic asymmetric ring-opening of aminocyclopropanes with 1,3-cyclodiones



(±)-**1a** **10a-10c** **11aa-11ac**

General method D - In a dry reaction tube, a mixture of $Cu(OTf)_2$ (3.6 mg, 0.01 mmol, 10 mol%), ligand **L5** (7.8 mg, 0.011 mmol, 11 mol%), and aminocyclopropane **1a** (0.22 mmol) in DCM (3.0 mL) were stirred at room temperature for 30 minutes under the atmosphere of nitrogen. Then isoquinoline substrate **10** (0.1 mmol) in DCM (1.0 mL) was added to the mixture of catalyst via a syringe. Subsequently, the reaction was stirred at 40 °C for 24 h. After the reaction was complete (monitored by TLC), the reaction was filtered through a glass funnel within layer of silica gel (100-200 mesh) and purified by flash column chromatography (Pet/EtOAc/DCM/MeOH, v/v/v/v, 5:1:1:0.1-1:1:1:0.1) to give the product **11**.

Dimethyl (*S*)-2-(2-(2,5-dioxopyrrolidin-1-yl)-2-((3-oxocyclohex-1-en-1-yl)oxy)ethyl) malonate (11aa)



Colorless oil: 29.3 mg, 80% yield, 97% ee; R_f = 0.29 (Pet/EtOAc/DCM/MeOH, 1/1/1/0.1, v/v/v/v). **[α]D^{25}** = -4.20 (c = 0.60, $CHCl_3$); reaction time: 24 h; reaction temperature: 40 °C.

HPLC CHIRALPAK IA, n-hexane/2-propanol = 60/40, flow rate 1.0 mL/min, λ = 254 nm, retention time: 8.938 min (major), 11.858 min (minor).

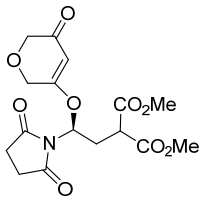
^{1}H NMR (600 MHz, $CDCl_3$) δ 5.89 (t, *J* = 6.6 Hz, 1H), 5.36 (s,1H), 3.73 (s, 3H), 3.71 (s, 3H), 3.43 (t, *J* = 7.8 Hz, 1H), 2.94 - 2.89 (m, 1H), 2.69 (s, 4H), 2.64 - 2.59 (m, 1H), 2.39 - 2.32 (m, 2H), 2.29 - 2.26 (m, 2H), 1.95 - 1.90 (m, 2H).

^{13}C NMR (150 MHz, $CDCl_3$) δ 199.3, 175.6, 174.1, 168.51, 168.47, 104.5, 76.4, 53.1, 53.0, 47.7, 36.7, 30.3, 29.7, 28.3, 28.0, 20.9.

HRMS (ESI): exact mass calcd for $C_{17}H_{21}NNaO_8^+$ $(M+Na)^+$ requires m/z 390.1159, found m/z 390.1162 (Δ = +3 ppm).

IR (neat): 2955, 1781, 1708, 1651, 1609, 1433, 1375, 1166, 1040, 915, 818, 728, 670, 663 cm^{-1}.

Dimethyl (*S*)-2-(2-(2,5-dioxopyrrolidin-1-yl)-2-((5-oxo-5,6-dihydro-2H-pyran-3-yl)oxy)ethyl)malonate (11ab)



Colorless oil: 30.3 mg, 82% yield, 96% ee; R_f = 0.43 (Pet/EtOAc/DCM/MeOH, 1/1/1/0.1, v/v/v/v). **$[\alpha]_D^{23}$** = -18.84 (c = 0.52, $CHCl_3$); reaction time: 24 h; reaction temperature: 40 °C.

HPLC CHIRALPAK IA, n-hexane/2-propanol = 60/40, flow rate 1.0 mL/min, λ = 254 nm, retention time: 12.855 min (major), 16.557 min (minor).

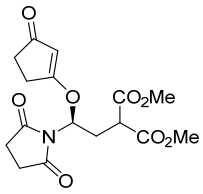
^{1}H NMR (400 MHz, $CDCl_3$) δ 5.98 (t, *J* = 6.8 Hz, 1H), 5.58 (s,1H), 4.24 (dd, *J* = 25.2, 16.0 Hz, 2H), 4.05 (s,2H), 3.76 (s, 3H), 3.75 (s, 3H), 3.43 (t, *J* = 7.2 Hz, 1H), 3.00 - 2.93 (m, 1H), 2.74 (s, 4H), 2.70 - 2.67 (m, 1H).

^{13}C NMR (100 MHz, $CDCl_3$) δ 194.6, 175.4, 171.5, 168.5, 168.4, 102.0, 71.5, 65.2, 53.23, 53.20, 47.7, 30.1, 28.1.

HRMS (ESI): exact mass calcd for $C_{16}H_{19}NNaO_9^+$ $(M+Na)^+$ requires m/z 392.0952, found m/z 392.0952 (Δ = 0 ppm).

IR (neat): 2922, 1783, 1710, 1669, 1616, 1436, 1359, 1165, 1047, 916, 818, 729, 671, 663 cm^{-1}.

Dimethyl (*S*)-2-(2-(2,5-dioxopyrrolidin-1-yl)-2-((3-oxocyclopent-1-en-1-yl)oxy)ethyl) malonate (11ac)



White solid: 25.1 mg, 71% yield, 93% ee; m.p.: 113.8 - 114.5 °C; R_f = 0.29 (Pet/EtOAc/DCM/MeOH, 1/1/1/0.1, v/v/v/v). **$[\alpha]_D^{25}$** = -26.33 (c = 1.10, $CHCl_3$); reaction time: 24 h; reaction temperature: 40 °C.

HPLC CHIRALPAK IA, n-hexane/2-propanol = 60/40, flow rate 1.0 mL/min, λ = 254 nm, retention time: 9.870 min (major), 13.223 min (minor).

^{1}H NMR (600 MHz, $CDCl_3$) δ 5.91 (dd, *J* = 7.2, 6.6 Hz, 1H), 5.40 (s,1H), 3.75 (s, 3H), 3.74 (s, 3H), 3.47 (dd, *J* = 7.8, 6.6 Hz, 1H), 3.04 - 2.99 (m, 1H), 2.73 (s, 4H), 2.71 - 2.67 (m, 1H), 2.65 - 2.54 (m, 2H), 2.47 - 2.37 (m, 2H).

^{13}C NMR (150 MHz, $CDCl_3$) δ 205.7, 186.5, 175.6, 168.5, 106.9, 79.4, 53.18, 53.15, 47.7, 34.3, 30.2, 28.3, 28.1.

HRMS (ESI): exact mass calcd for $C_{16}H_{19}NNaO_8^+$ $(M+Na)^+$ requires m/z 376.1003, found m/z 376.0999 (Δ = -4 ppm).

IR (neat): 2920, 1783, 1731, 1703, 1594, 1431, 1340, 1249, 1166, 1041, 913, 813, 664, 639 cm^{-1}.

X-ray data of 3ak

Figure S1. X-Ray crystal structure of **3ak** (Recrystallization solvent: DCM/EE). (CCDC: 2307260)

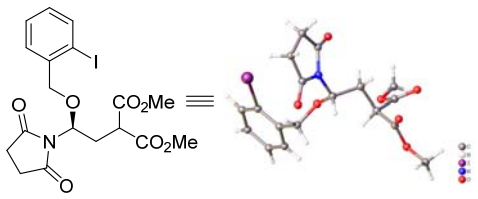
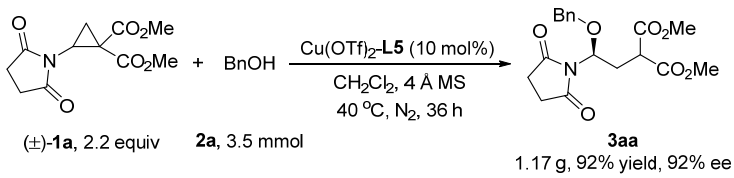


Table S4. Crystal data and structure refinement for (*S*)-3ak

Identification code	(*S*)-**3ak**
Empirical formula	$C_{18}H_{20}INO_7$
Formula weight	489.25
Temperature/K	150.00(10)
Crystal system	monoclinic
Space group	P21
a/Å	11.68310(10)
b/Å	6.78090(10)
c/Å	12.62400(10)
α/°	90
β/°	104.7010(10)
γ/°	90
Volume/Å3	967.358(19)
Z	2
ρcalcg/cm3	1.680
μ/mm-1	13.363
F(000)	488.0
Crystal size/mm3	0.25 × 0.2 × 0.18
Radiation	CuKα (λ = 1.54178)
2Θ range for data collection/°	7.24 to 143.678
Index ranges	-12 ≤ h ≤ 14, -8 ≤ k ≤ 8, -15 ≤ l ≤ 15
Reflections collected	25397
Independent reflections	3749 [Rint = 0.0605, Rsigma = 0.0299]
Data/restraints/parameters	3749/1/246
Goodness-of-fit on F2	1.046
Final R indexes [I>=2σ (I)]	R1 = 0.0286, wR2 = 0.0758
Final R indexes [all data]	R1 = 0.0288, wR2 = 0.0761
Largest diff. peak/hole / e Å-3	0.95/-0.86
Flack parameter	-0.018(6)

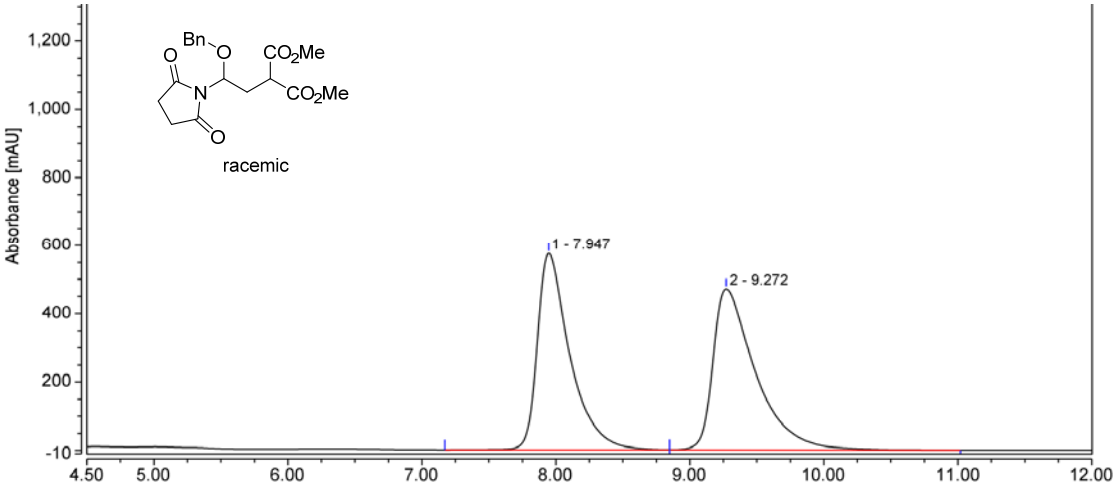
Gram-scale synthesis of 3aa



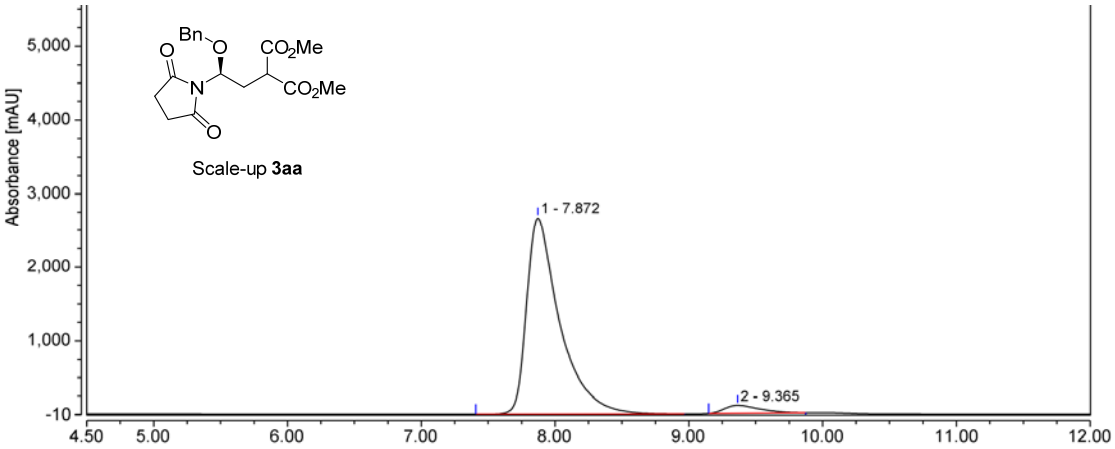
(±)-**1a**, 2.2 equiv **2a**, 3.5 mmol **3aa**
1.17 g, 92% yield, 92% ee

In a dry reaction tube, a mixture of $Cu(OTf)_2$ (126.5 mg, 0.35 mmol, 10 mol%), ligand **L5** (271.4 mg, 0.39 mmol, 11 mol%), 4 Å MS (350 mg), and aminocyclopropane **1a** (1.964 g, 7.7 mmol) in DCM (35 mL) were stirred at room temperature for 2 h under the atmosphere of nitrogen. Then, phenylmethanol **2a** (378.2 mg, 3.5 mmol) in DCM (35 mL) was added to the mixture of catalyst via a syringe. Subsequently, the reaction was stirred at 40 °C for 36 h. After the reaction was complete (monitored by TLC), the reaction was filtered through a glass funnel within layer of silica gel (100-200 mesh) and purified by flash column chromatography (Pet/EtOAc/MeOH, v/v/v, 10:1:0.1-5:1:0.1) to give the product **3aa** as a colorless oil (1.17 g, 92% yield, 92% ee).

Figure S2. HPLC spectra of **9aa** on a gram-scale

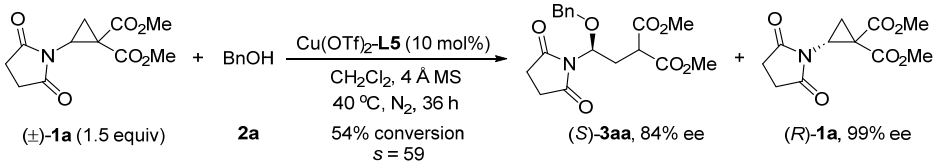


Peak	Retention Time min	Area mAU*min	Height mAU	Area %	Height %
1	7.947	162.318	574.379	48.36	55.00
2	9.272	173.345	469.941	51.64	45.00
Total:		**335.663**	**1044.320**	**100.00**	**100.00**



Peak	Retention Time min	Area mAU*min	Height mAU	Area %	Height %
1	7.872	766.931	2673.830	95.88	96.11
2	9.365	32.923	108.142	4.12	3.89
Total:		**799.854**	**2781.972**	**100.00**	**100.00**

Kinetic resolution of 1a

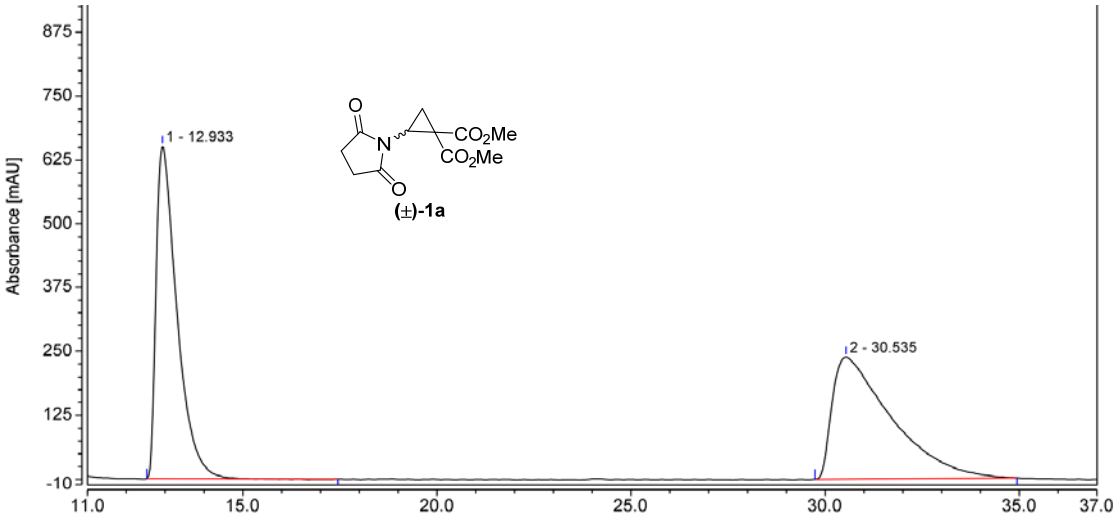


In a dry reaction tube, a mixture of $Cu(OTf)_2$ (3.6 mg, 0.01 mmol, 10 mol%), ligand **L5** (7.8 mg, 0.011 mmol, 11 mol%), 4 Å MS (10 mg), and aminocyclopropane **1a** (0.15 mmol) in DCM (3.0 mL) were stirred at room temperature for 30 minutes under the atmosphere of nitrogen. Then benzyl alcohol **2a** (0.1 mmol) in DCM (1.0 mL) was added to the mixture of catalyst via a syringe. Subsequently, the reaction was stirred at 40 °C for 36 h. Then, the reaction was filtered through a glass funnel within layer of silica gel (100-200 mesh) and purified by flash column chromatography (Pet/EtOAc/MeOH, v/v/v, 10:1:0.1-5:1:0.1) to give the product **3aa** with 84% ee and the *R*-**1a** with 99% ee, s = 59.2.

$C = ee^1/(ee^3 + ee^1)$, $s = \ln[(1 - C)(1 - ee^1)]/\ln[(1 - C)(1 + ee^1)]$, where ee^1 = ee of the recovered substrate and ee^3 = ee of the product.

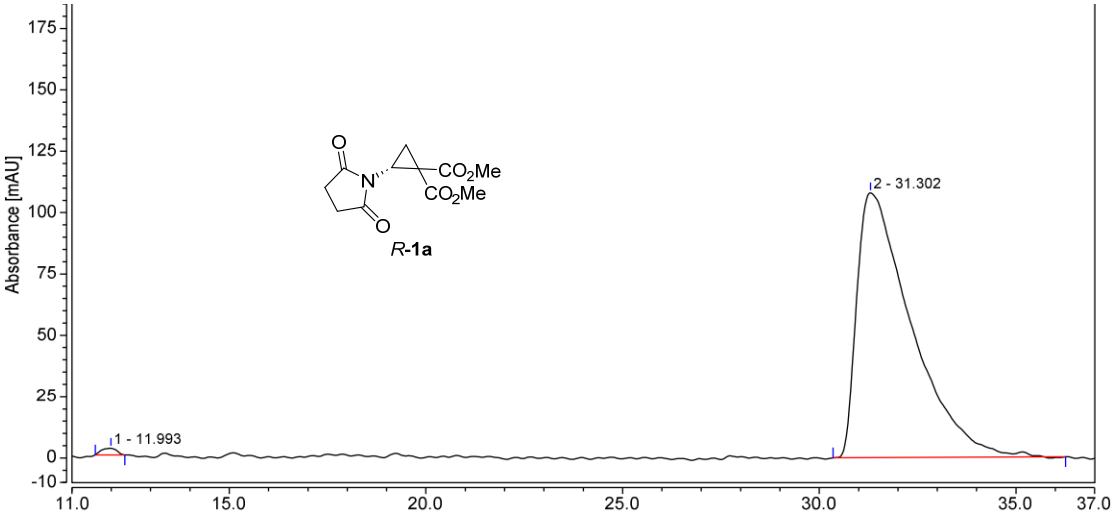
The absolute configuration of product *R*-**1a** was determined by comparison the HPLC spectra with the prepared reference sample.[1-2]

HPLC Spectrum of (±)-**1a**



Peak	Retention Time min	Area mAU*min	Height mAU	Area %	Height %
1	12.933	403.438	651.588	49.04	73.23
2	30.535	419.221	238.220	50.96	26.77
Total:		**822.659**	**889.809**	**100.00**	**100.00**

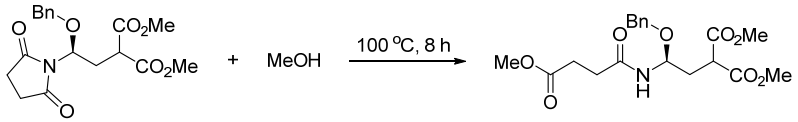
HPLC Spectrum of (*R*)-**1a**



Peak	Retention Time min	Area mAU*min	Height mAU	Area %	Height %
1	11.993	1.219	2.694	0.70	2.44
2	31.302	172.997	107.911	99.30	97.56
Total:		**174.216**	**110.605**	**100.00**	**100.00**

Figure S3 HLPC of *R*-**1a**

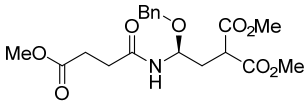
Ring-opening of 3aa



3aa, 94% ee **12aa**, 99% yield, 93% ee

In a dry reaction tube, **3aa** (0.1 mmol) in MeOH (0.5 mL) was stirred at 100 °C for 8 h. After the reaction was complete (monitored by TLC), the reaction was filtered through a glass funnel within layer of silica gel (100-200 mesh) and purified by flash column chromatography (DCM/MeOH, v/v, 100:1-20:1) to give the product **12aa**.

Dimethyl (*S*)-2-(2-(benzyloxy)-2-(4-methoxy-4-oxobutanamido)ethyl)malonate (12aa)



Colorless oil: 39.1 mg, 99% yield, 93% ee; R_f = 0.50 (DCM/MeOH, 20/1, v/v). $[\alpha]_D^{25}$ = +2.33 (c = 1.30, $CHCl_3$); reaction time: 8 h; reaction temperature: 100 °C.

HPLC CHIRALPAK IG, n-hexane/2-propanol = 70/30, flow rate 1.0 mL/min, λ = 210 nm, retention time: 14.377 min (minor), 17.748 min (major).

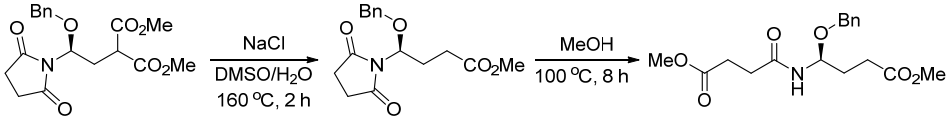
^{1}H NMR (400 MHz, $CDCl_3$) δ 7.34 - 7.23 (m, 5H), 6.27 (d, *J* = 9.6 Hz, 1H), 5.43 - 5.37 (m, 1H), 4.57 (d, *J* = 11.6 Hz, 1H), 6.27 (d, *J* = 11.6 Hz, 1H), 3.68 (s, 3H), 3.67 (s, 3H), 3.64 (s, 3H), 3.56 (t, *J* = 7.2 Hz, 1H), 2.68 - 2.64 (m, 2H), 2.68 - 2.64 (m, 2H), 2.46 (t, *J* = 6.4 Hz, 2H), 2.34 - 2.22 (m, 2H).

^{13}C NMR (100 MHz, $CDCl_3$) δ 173.4, 171.8, 169.7, 169.5, 137.9, 128.4, 128.1, 127.8, 70.5, 52.83, 52.76, 52.0, 48.2, 34.4, 31.1, 29.1.

HRMS (ESI): exact mass calcd for $C_{19}H_{25}NNaO_8^+$ $(M+Na)^+$ requires m/z 418.1472, found m/z 418.1467 (Δ = -5 ppm).

IR (neat): 3311, 2954, 2355, 1732, 1662, 1528, 1436, 1349, 1160, 1058, 916, 733, 699 cm^{-1}.

Decarboxylation and ring-opening of 3aa

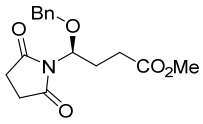


3aa, 94% ee **13aa**, 62% yield, 92% ee **14aa**, 98% yield, 92% ee

To the solution of **3aa** (0.3 mmol, 1.0 equiv) in DMSO (1mL) was added NaCl (36.5 mg, 0.63 mmol, 2.1 equiv) and H_2O (10 μL). The reaction was stirred at 160 °C for 2 h. The organic layer was extracted with EtOAc for 3 times, and the collected organic layer was dried over Na_2SO_4. After removing the solvent under reduced pressure, the reaction was filtered through a glass funnel within layer of silica gel (100-200 mesh) and purified by flash column chromatography (Pet/EtOAc/MeOH, v/v/v, 10:1:0.1-3:1:0.1) to give the product **13aa**.

Then, in a dry reaction tube, 1**3aa** (0.1 mmol) in MeOH (0.5 mL) was stirred at 100 °C for 8 h. After the reaction was complete (monitored by TLC), the reaction was filtered through a glass funnel within layer of silica gel (100-200 mesh) and purified by flash column chromatography (DCM/MeOH, v/v, 100:1-20:1) to give the product **14aa**.

Methyl (*S*)-4-(benzyloxy)-4-(2,5-dioxopyrrolidin-1-yl)butanoate (13aa)



Colorless oil: 47.3 mg, 62% yield, 92% ee; R_f = 0.50 (Pet/EtOAc/ MeOH, 3/1/0.1, v/v/v). **$[\alpha]_D^{25}$** = -2.45 (c = 1.26, $CHCl_3$); reaction time: 2 h; reaction temperature: 160 °C.

HPLC CHIRALPAK IG, n-hexane/2-propanol = 70/30, flow rate 1.0 mL/min, λ = 210 nm, retention time: 9.885 min (minor), 13.583 min (major).

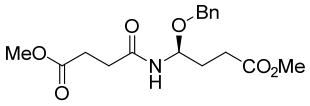
^{1}H NMR (600 MHz, $CDCl_3$) δ 7.34 - 7.26 (m, 5H), 5.35 (t, *J* = 7.2 Hz, 1H), 4.65 (d, *J* = 12.6 Hz, 1H), 4.45 (d, *J* = 12.6 Hz, 1H), 3.63 (s, 3H), 2.71 - 2.63 (m, 1H), 2.42 (dd, *J* = 16.8, 7.8 Hz, 1H), 2.38 (s, 4H), 2.35 - 2.30 (m, 1H), 2.19 - 2.14 (m, 1H).

^{13}C NMR (150 MHz, $CDCl_3$) δ 176.8, 172.9, 137.3, 128.4, 128.1, 128.0, 81.7, 72.4, 51.8, 30.0, 27.9, 27.4.

HRMS (ESI): exact mass calcd for $C_{16}H_{19}NNaO_5^+$ $(M+Na)^+$ requires m/z 328.1155, found m/z 328.1153 (Δ = -2 ppm).

IR (neat): 2950, 1778, 1732, 1701, 1436, 1350, 1163, 1088, 819, 739, 699, 663, 633 cm^{-1}.

Methyl (*S*)-4-(benzyloxy)-4-(4-methoxy-4-oxobutanamido)butanoate (14aa)



Colorless oil: 33.0 mg, 98% yield, 92% ee; R_f = 0.50 (DCM/MeOH, 20/1, v/v). **$[\alpha]_D^{25}$** = +3.36 (c = 1.26, $CHCl_3$); reaction time: 8 h; reaction temperature: 100 °C.

HPLC CHIRALPAK IG, n-hexane/2-propanol = 70/30, flow rate 1.0 mL/min, λ = 210 nm, retention time: 16.375 min (major), 19.238 min (minor).

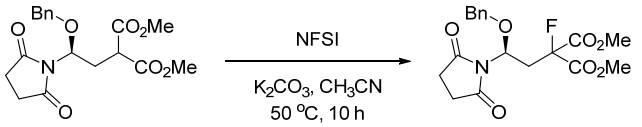
^{1}H NMR (400 MHz, $CDCl_3$) δ 7.35 - 7.27 (m, 5H), 6.19 (d, *J* = 9.6 Hz, 1H), 5.38 - 5.32 (m, 1H), 4.60 (d, *J* = 12.0 Hz, 1H), 4.50 (d, *J* = 11.6 Hz, 1H), 3.68 (s, 3H), 3.64 (s, 3H), 2.68 (t, *J* = 6.8 Hz, 1H), 2.51 - 2.45 (m, 3H), 2.40 - 2.32 (m, 1H), 2.04 - 1.93 (m, 2H).

^{13}C NMR (100 MHz, $CDCl_3$) δ 173.9, 173.4, 171.9, 138.2, 128.7, 128.5,128.0, 127.8, 127.1, 78.7, 70.4, 52.0, 51.9, 31.2, 30.5, 29.6, 29.2.

HRMS (ESI): exact mass calcd for $C_{17}H_{23}NNaO_6^+$ $(M+Na)^+$ requires m/z 360.1418, found m/z 360.1420 (Δ = +2 ppm).

IR (neat): 3305, 2953, 1734, 1658, 1535, 1436, 1361, 1165, 1071,1022, 919, 732, 698 cm^{-1}.

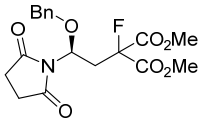
The transformations of the product 3aa



3aa, 94% ee **15aa**, 86% yield, 92% ee

To a solution of 3**aa** (36.3 mg, 0.1 mmol, 1.0 equiv) in MeCN (1.0 mL) was added K_2CO_3 (15.2 mg, 0.11 mmol, 1.1 equiv), NFSI (35 mg, 0.11mmol, 1.1 equiv) was then added. After stirring at 50 °C 10 h, the crude compound was purified by column chromatography on silica gel (Pet/EtOAc/DCM/MeOH, 3/1/1/0.1, v/v/v/v), affording the desired compound 15**aa**.

Dimethyl (*S*)-2-(2-(benzyloxy)-2-(2,5-dioxopyrrolidin-1-yl)ethyl)-2-fluoromalonate (15aa)



Colorless oil: 32.8 mg, 86% yield, 92% ee; R_f = 0.50 (Pet/EtOAc/DCM/MeOH, 3/1/1/0.1, v/v/v/v). **[α]$_D^{24}$** = 11.2 (c = 0.25, $CHCl_3$); reaction time: 10 h; reaction temperature: 50 °C.

HPLC CHIRALPAK IG, n-hexane/2-propanol = 60/40, flow rate 1.0 mL/min, λ = 210 nm, retention time: 14.198 min (minor), 17.495 min (major).

^{1}H NMR (400 MHz, $CDCl_3$) δ 7.32 - 7.24 (m, 5H), 5.58 (dd, *J* = 8.8, 4.0 Hz, 1H), 4.64 (d, *J* = 12.4 Hz, 1H), 4.38 (d, *J* = 12.4 Hz, 1H), 3.81 (s, 3H), 3.69 (s, 3H), 3.57 - 3.43 (m, 1H), 2.64 - 2.57 (m, 1H), 2.36 (s, 4H).

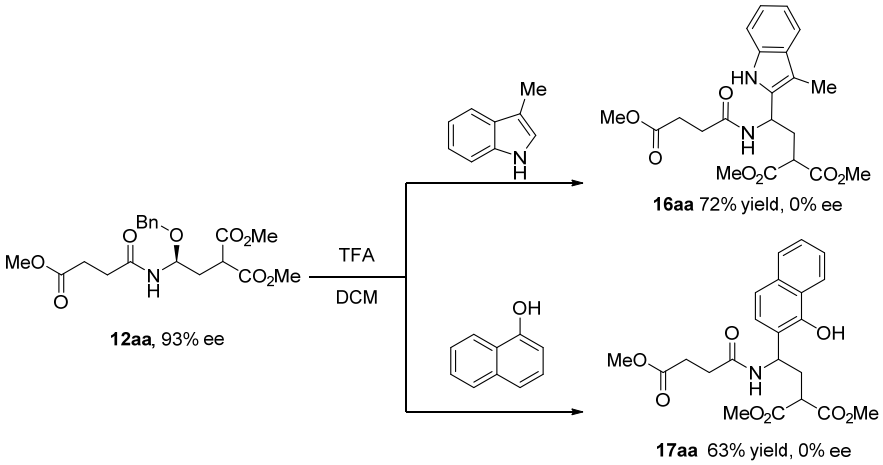
^{13}C NMR (100 MHz, $CDCl_3$) δ 176.4, 166.1 (d, $J_{C\text{-}F}$ = 23.0 Hz), 165.9 (d, $J_{C\text{-}F}$ = 21.0 Hz), 137.1, 128.4, 128.1, 127.9, 93.4, 91.4, 72.7, 53.8 (d, $J_{C\text{-}F}$ = 3.0 Hz), 53.4, (d, $J_{C\text{-}F}$ = 2.0 Hz), 37.2 (d, $J_{C\text{-}F}$ = 20.0 Hz), 28.0.

^{9}F NMR (376 MHz, CDCl3): -167.6.

HRMS (ESI): exact mass calcd for $C_{18}H_{20}FNNaO_7^+$ $(M+Na)^+$ requires m/z 404.1116, found m/z 404.1112 (Δ = -4 ppm).

IR (neat): 2957, 1753, 1706, 1436, 1352, 1303, 1255, 1178, 1103, 912, 812, 729, 699 cm^{-1}.

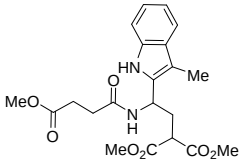
The transformations of the product 12aa



To a solution of **12aa** (39.5 mg, 0.1 mmol, 1.0 equiv) in DCM (1.0 mL) was added 3-methyl-1H-indole (14.4 mg, 0.11 mmol, 1.1 equiv), TFA (23.0μL, 0.3 mmol, 3 equiv) was then added. The reaction mixture was stirred at room temperature for 2 hour, the crude compound was purified by column chromatography on silica gel (Pet/EtOAc/DCM/MeOH, 2/1/1/0.1, v/v/v/v), affording the desired compound **16aa.**

To a solution of **12aa** (39.5 mg, 0.1 mmol, 1.0 equiv) in DCM (1.0 mL) was added naphthalen-1-ol (15.8 mg, 0.11 mmol, 1.1 equiv), TFA (23.0μL, 0.3 mmol, 3 equiv) was then added. The reaction mixture was stirred at room temperature for 5 hour, the crude compound was purified by column chromatography on silica gel (Pet/EtOAc/DCM/MeOH, 3/1/1/0.1, v/v/v/v), affording the desired compound **17aa.**

Dimethyl 2-(2-(4-methoxy-4-oxobutanamido)-2-(3-methyl-1*H*-indol-2-yl)ethyl)malonate (16aa)



Colorless oil: 30.1 mg, 72% yield, R_f = 0.50 (Pet/EtOAc/DCM/MeOH, 3/1/1/0.1, v/v/v/v); reaction time: 2 h; reaction temperature: 25 °C.

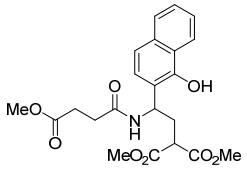
^{1}H NMR (600 MHz, $CDCl_3$) δ 9.00 (s, 1H), 7.49 (d, *J* = 7.8 Hz, 1H), 7.25 (d, *J* = 9.0 Hz, 1H), 7.15 - 7.12 (m, 1H), 7.08 - 7.06 (m, 1H), 6.76 (d, *J* = 7.8 Hz, 1H), 5.18 (q, *J* = 7.8 Hz, 1H), 3.73 (s, 3H), 3.64 (s, 3H), 3.59 (s, 3H), 3.39 (t, *J* = 7.2 Hz, 1H), 2.66 - 2.57 (m, 4H), 2.44 (t, *J* = 6.6 Hz, 1H), 2.27 (s, 3H).

^{13}C NMR (150 MHz, $CDCl_3$) δ 173.9, 171.9, 169.9, 169.7, 135.7, 132.7, 131.9, 128.9, 122.1, 119.2, 118.8, 111.1, 108.5, 53.0, 52.9, 52.0, 49.0, 45.7, 33.4, 31.1, 29.4, 8.7.

HRMS (ESI): exact mass calcd for $C_{21}H_{26}N_2NaO_7^+$ $(M+Na)^+$ requires m/z 441.1632, found m/z 441.1632 (Δ = 0 ppm).

IR (neat): 3361, 2954, 1730, 1644, 1534, 1436, 1334, 1236, 1160, 1007, 907, 726, 647 cm^{-1}.

Dimethyl 2-(2-(1-hydroxynaphthalen-2-yl)-2-(4-methoxy-4-oxobutanamido)ethyl)malonate (17aa)



Colorless oil: 27.2 mg, 63% yield, R_f = 0.50 (Pet/EtOAc/DCM/MeOH, 3/1/1/0.1, v/v/v/v); reaction time: 5 h; reaction temperature: 25 ºC.

^{1}H NMR (600 MHz, $CDCl_3$) δ 9.51 (s, 1H), 8.35 - 8.33 (m, 1H), 7.74 - 7.72 (m, 1H), 7.47 - 7.44 (m, 2H), 7.38 (d, *J* = 8.4 Hz, 1H), 7.25 (d, *J* = 1.8 Hz, 1H), 6.63 (d, *J* = 7.8 Hz, 1H), 5.28 - 5.25 (m, 1H), 3.77 (s, 3H), 3.71 (s, 3H), 3.59 (s, 3H), 3.48 (dd, *J* = 8.4, 6.0 Hz, 1H), 2.81 - 2.75 (m, 1H), 2.69 - 2.64 (m, 1H), 2.57 - 2.54 (m, 1H), 2.52 - 2.46 (m, 1H).

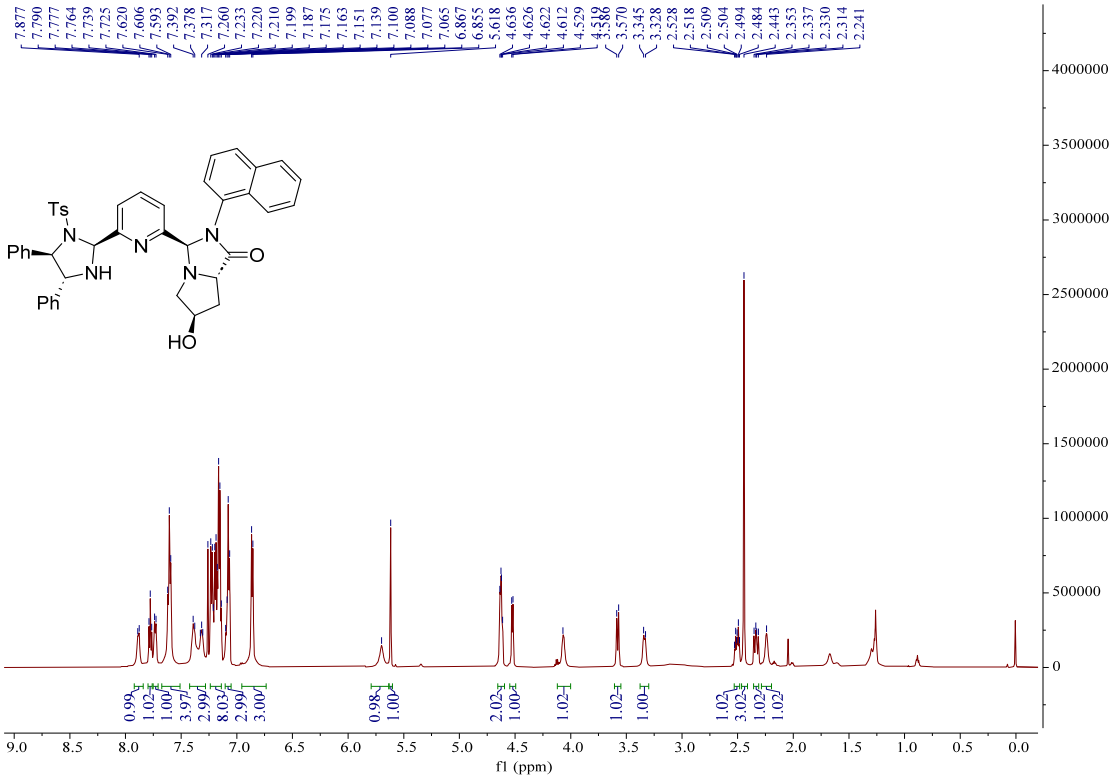
^{13}C NMR (150 MHz, $CDCl_3$) δ 173.8, 173.2, 170.1, 169.5, 154.4, 134.3, 127.3, 126.8, 126.7, 125.6, 123.5, 122.7, 120.5, 120.7, 53.2, 53.1, 52.0, 49.6, 46.8, 31.9, 30.8, 29.2.

HRMS (ESI): exact mass calcd for $C_{22}H_{25}NNaO_8^+$ $(M+Na)^+$ requires m/z 454.1472, found m/z 454.1468 (Δ = -4 ppm).

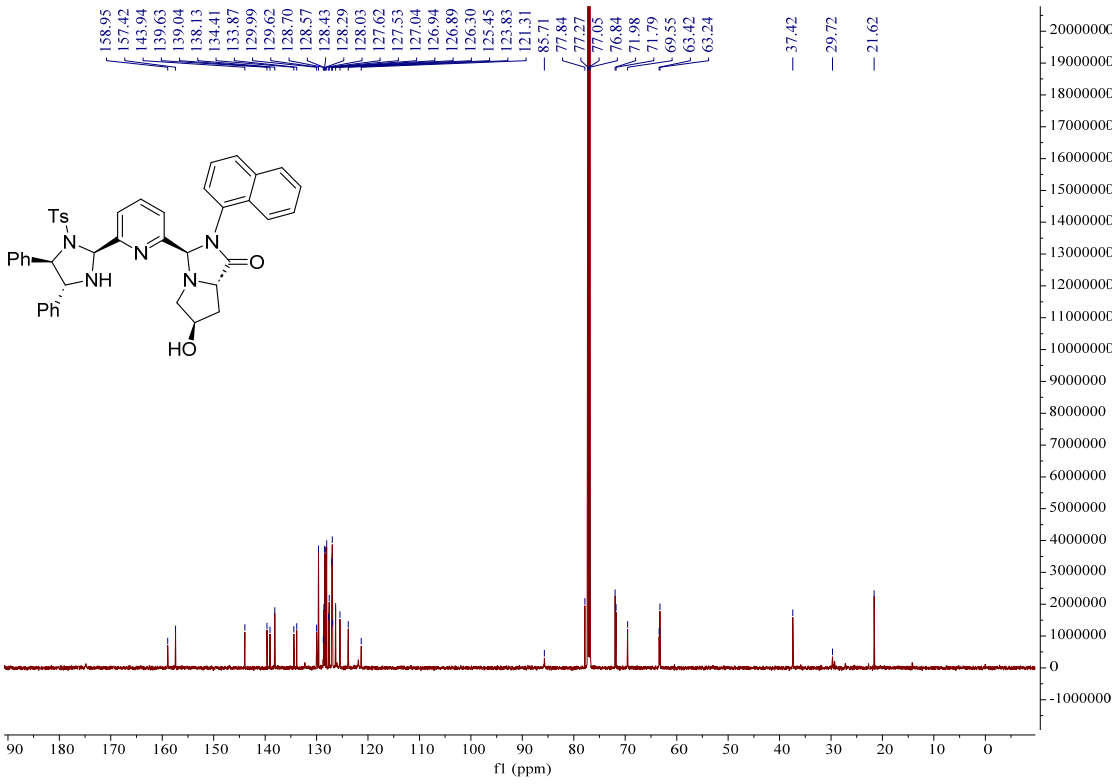
IR (neat): 3355, 2954, 1730, 1638, 1574, 1534, 1436, 1363, 1233, 1162, 908, 811, 727, 647 cm^{-1}.

NMR Spectra

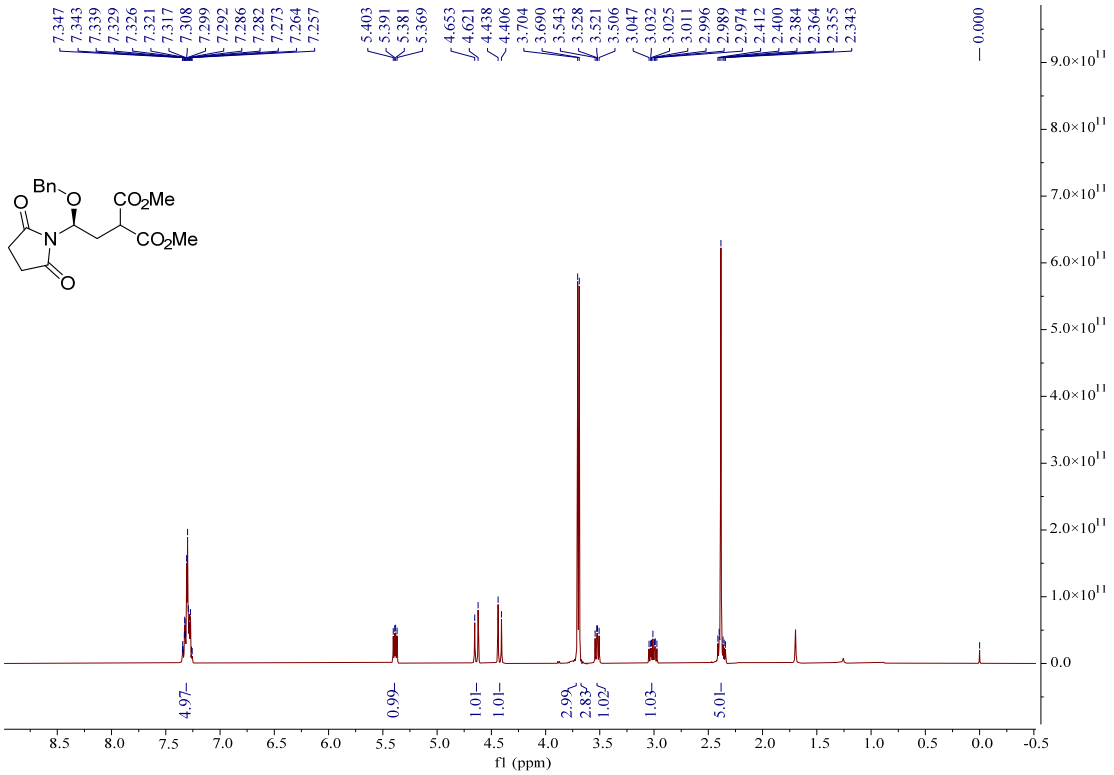
^{1}H NMR Spectrum of **L6** (600 MHz, $CDCl_3$)



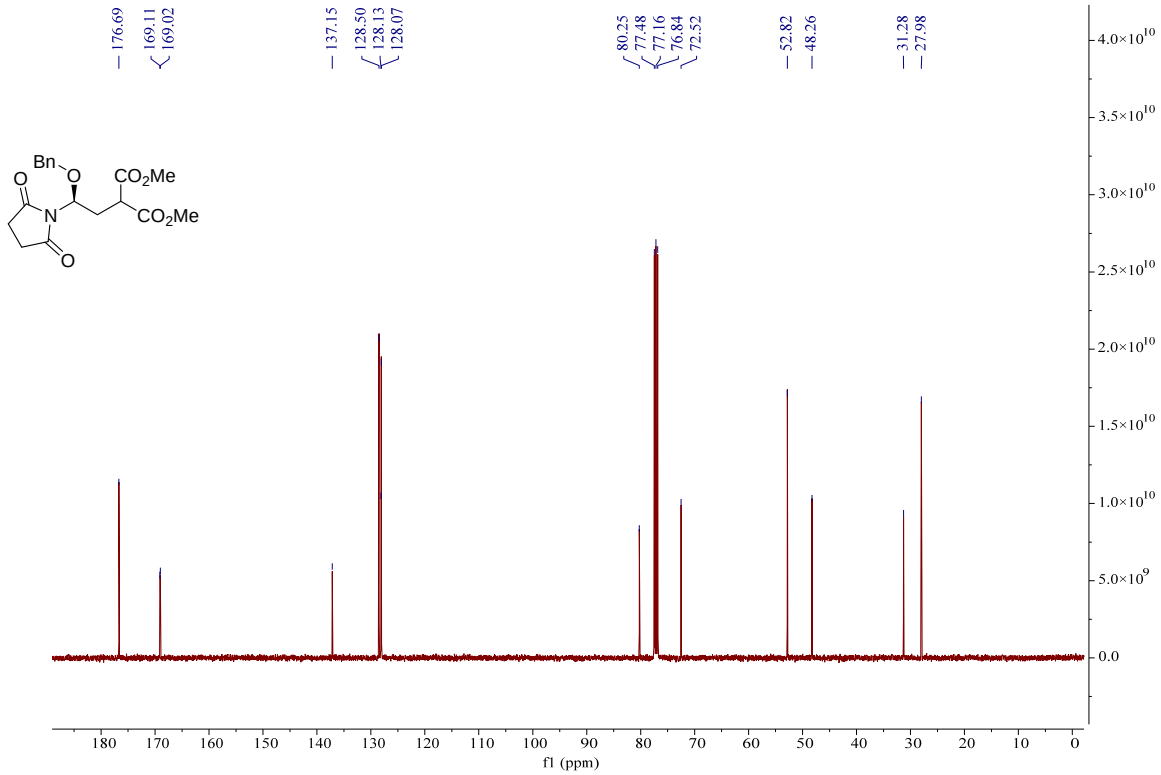
^{13}C NMR Spectrum of **L6** (150 MHz, $CDCl_3$)



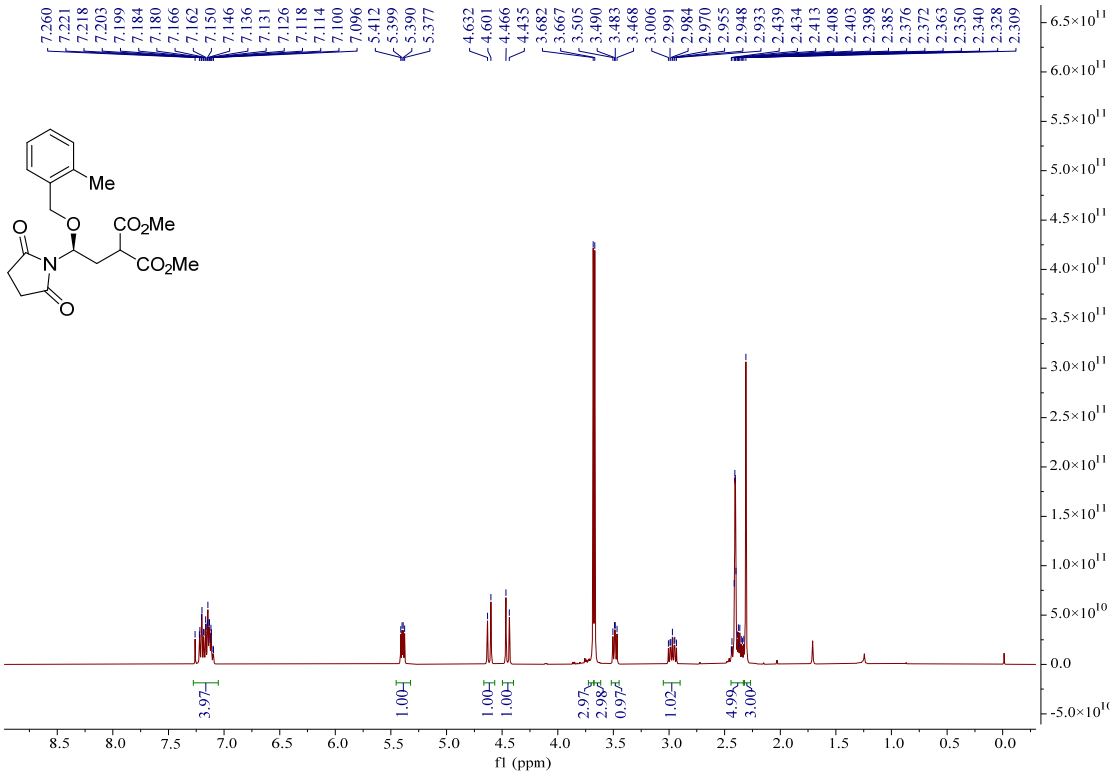
^{1}H NMR Spectrum of **3aa** (400 MHz, $CDCl_3$)



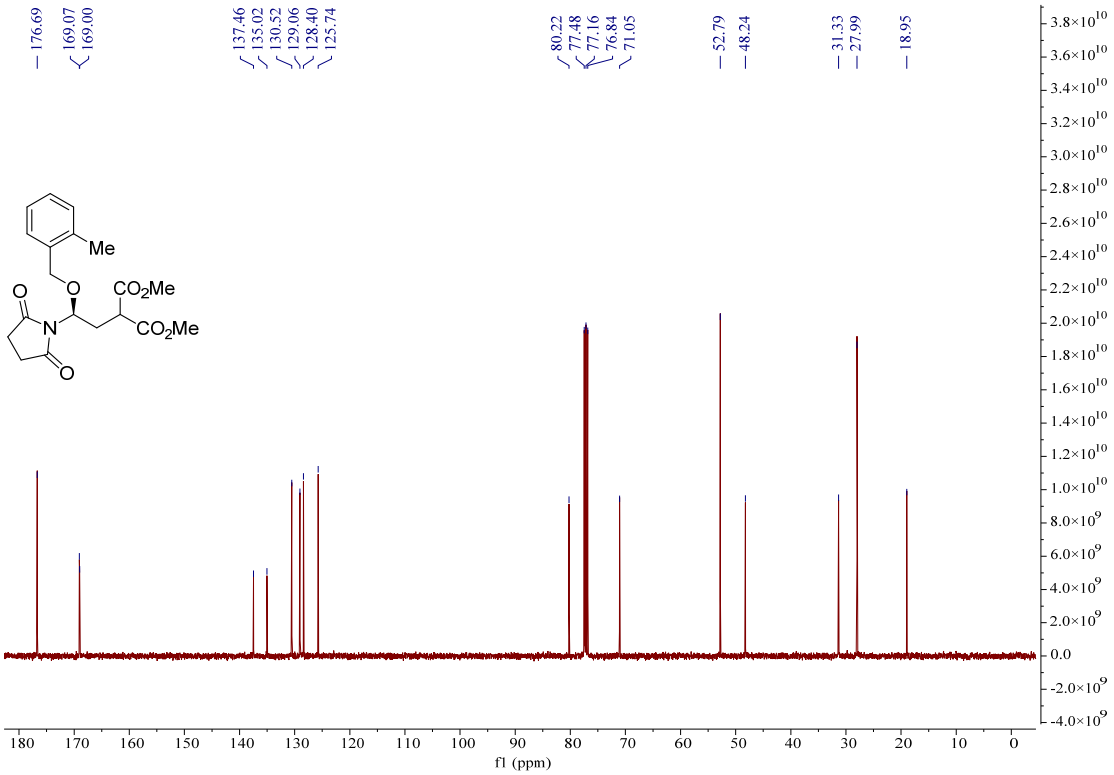
^{13}C NMR Spectrum of **3aa** (100 MHz, $CDCl_3$)



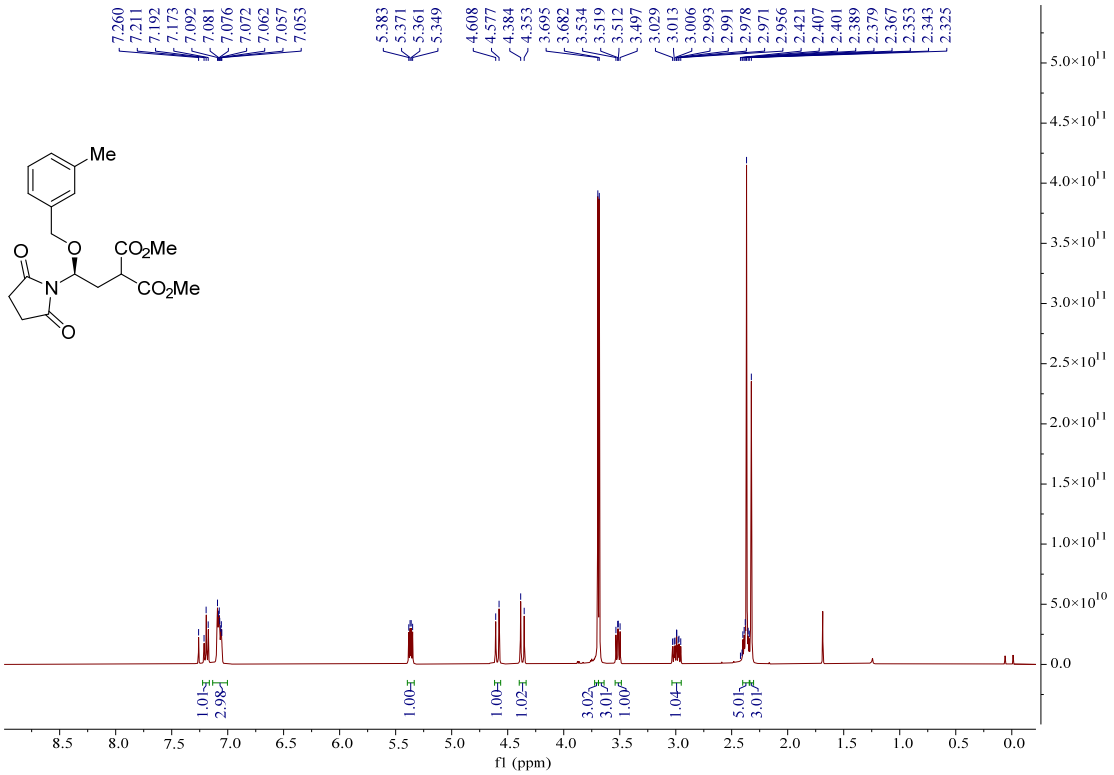
^{1}H NMR Spectrum of **3ab** (400 MHz, $CDCl_3$)



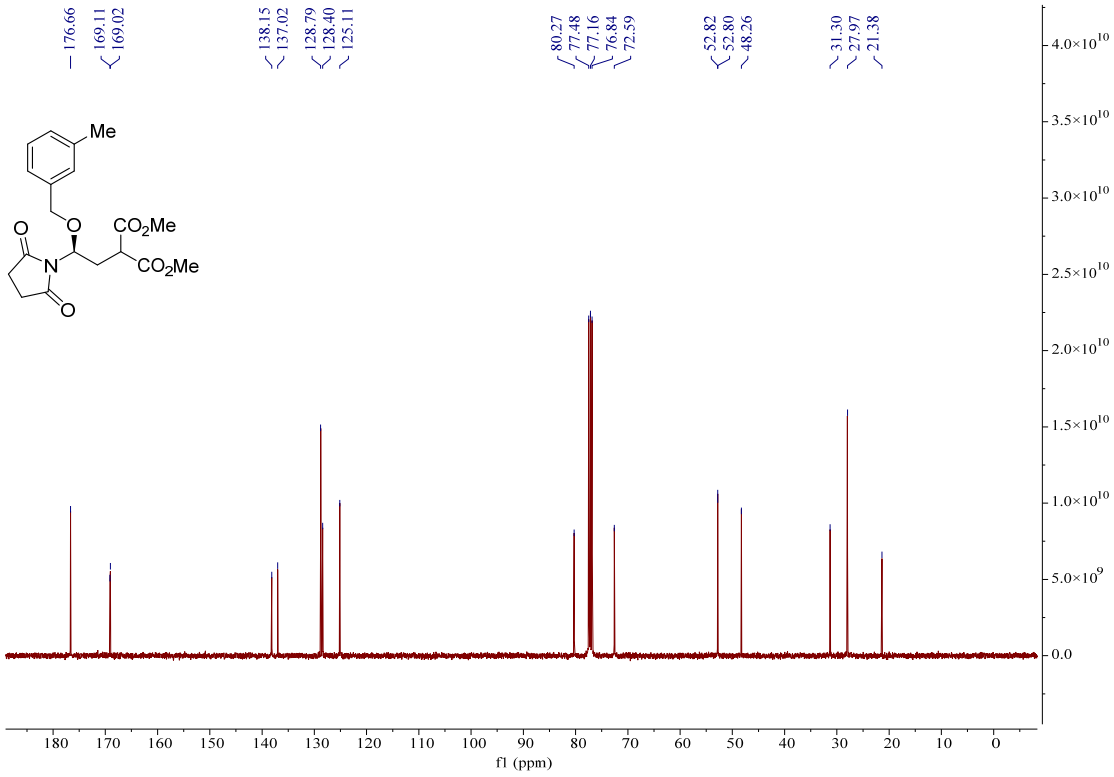
^{13}C NMR Spectrum of **3ab** (100 MHz, $CDCl_3$)



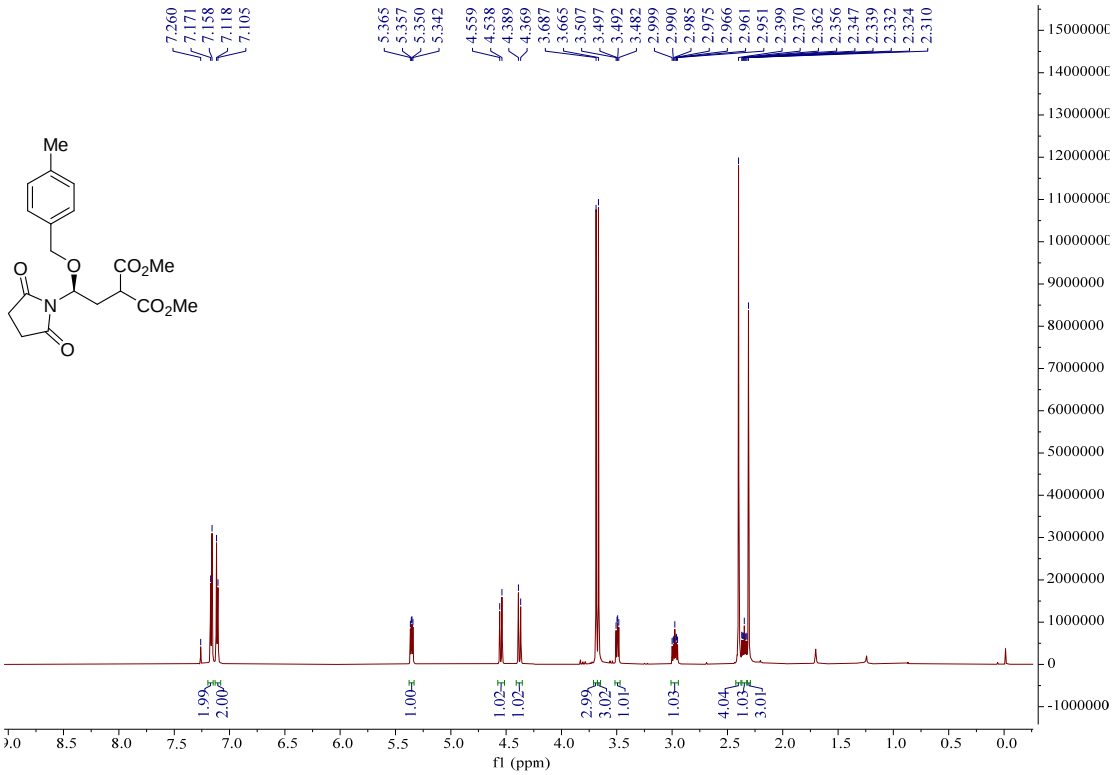
^{1}H NMR Spectrum of **3ac**(400 MHz, $CDCl_3$)



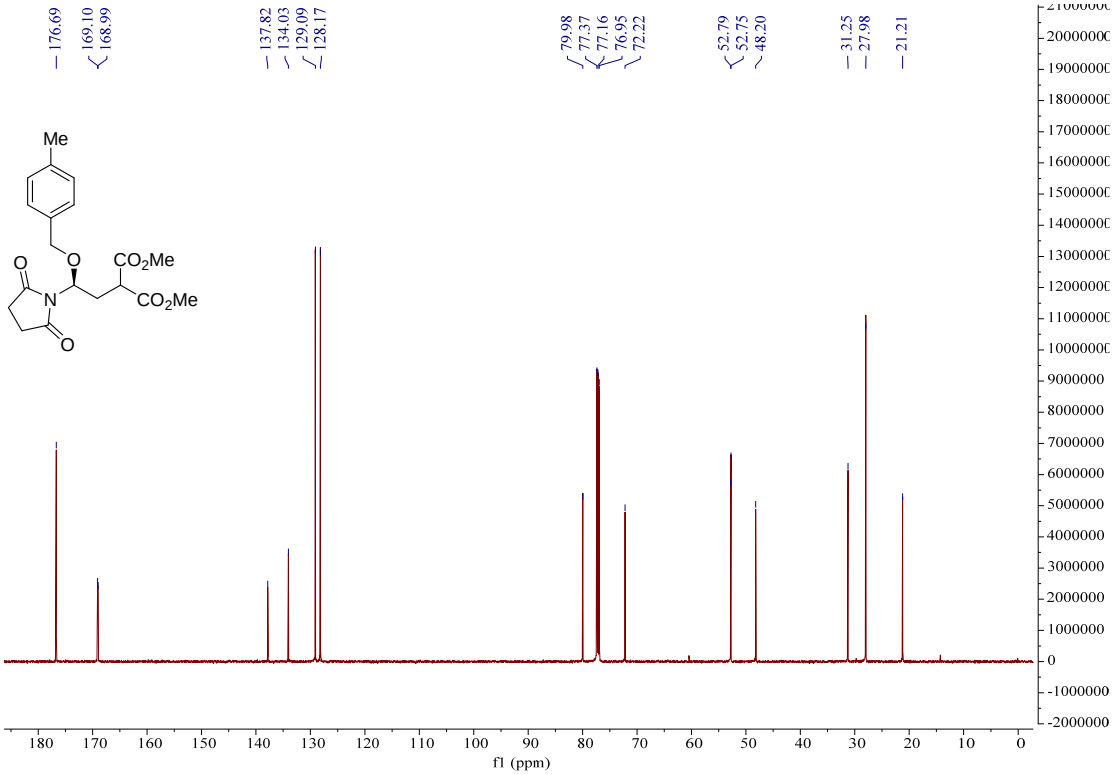
^{13}C NMR Spectrum of **3ac** (100 MHz, $CDCl_3$)



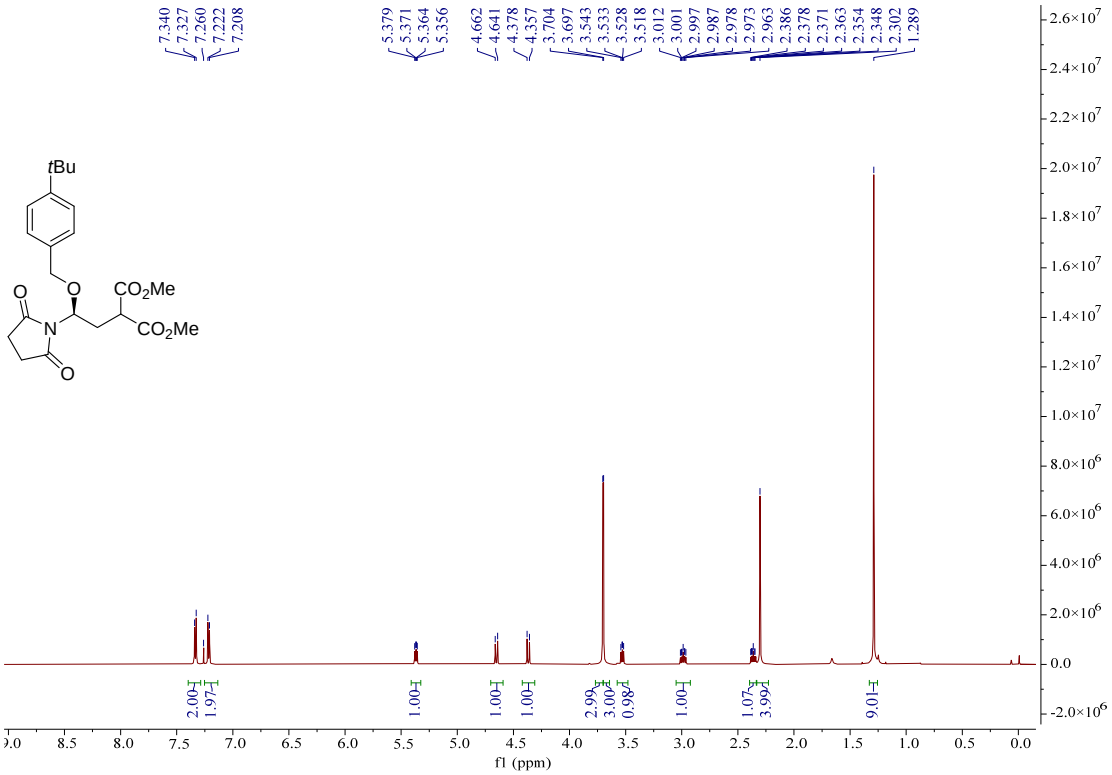
^{1}H NMR Spectrum of **3ad** (600 MHz, $CDCl_3$)



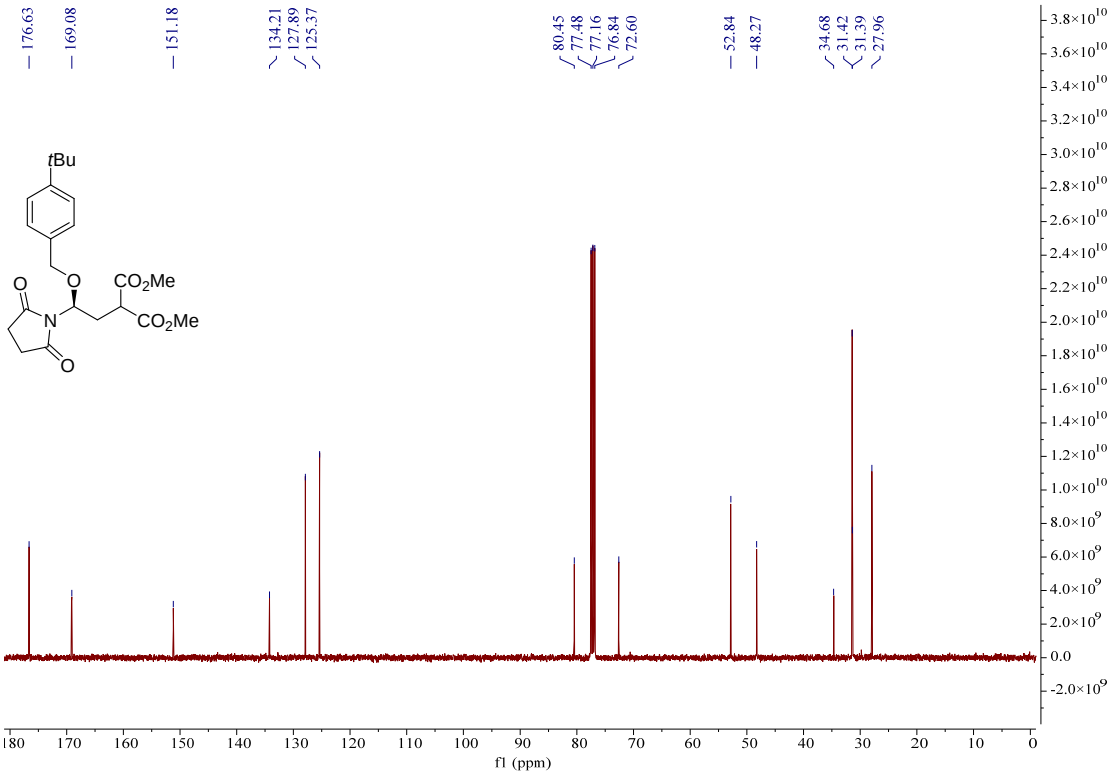
^{13}C NMR Spectrum of **3ad** (150 MHz, $CDCl_3$)



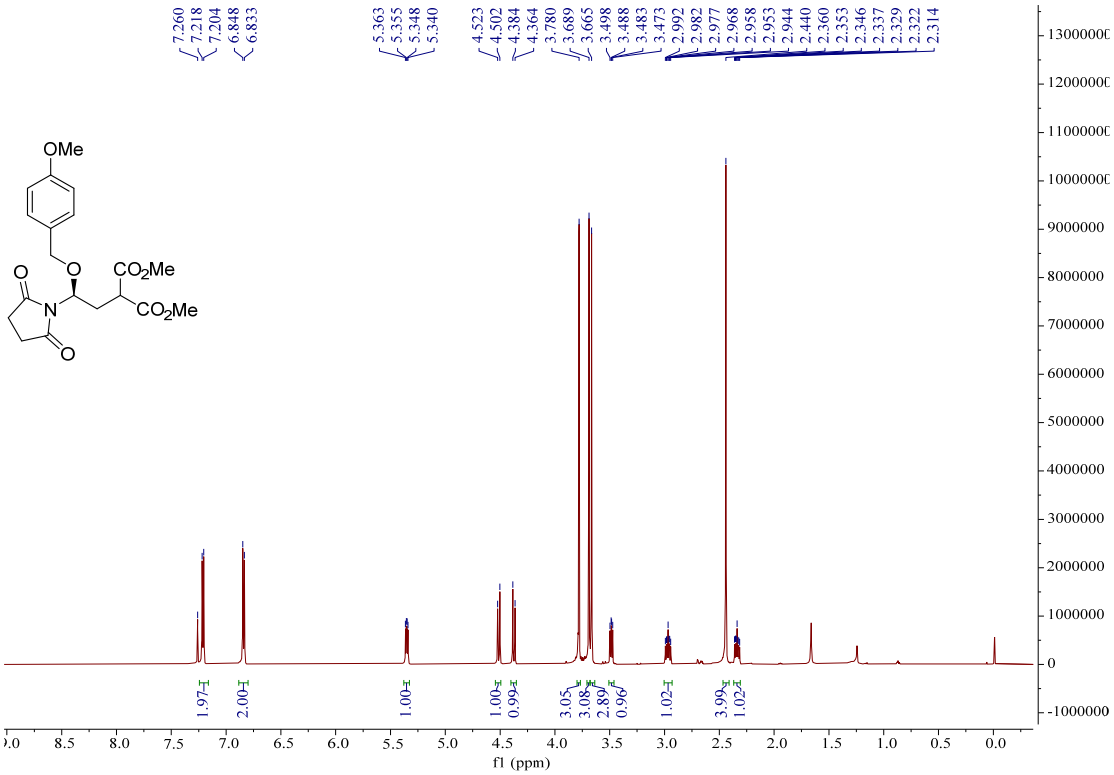
^{1}H NMR Spectrum of **3ae** (600 MHz, $CDCl_3$)



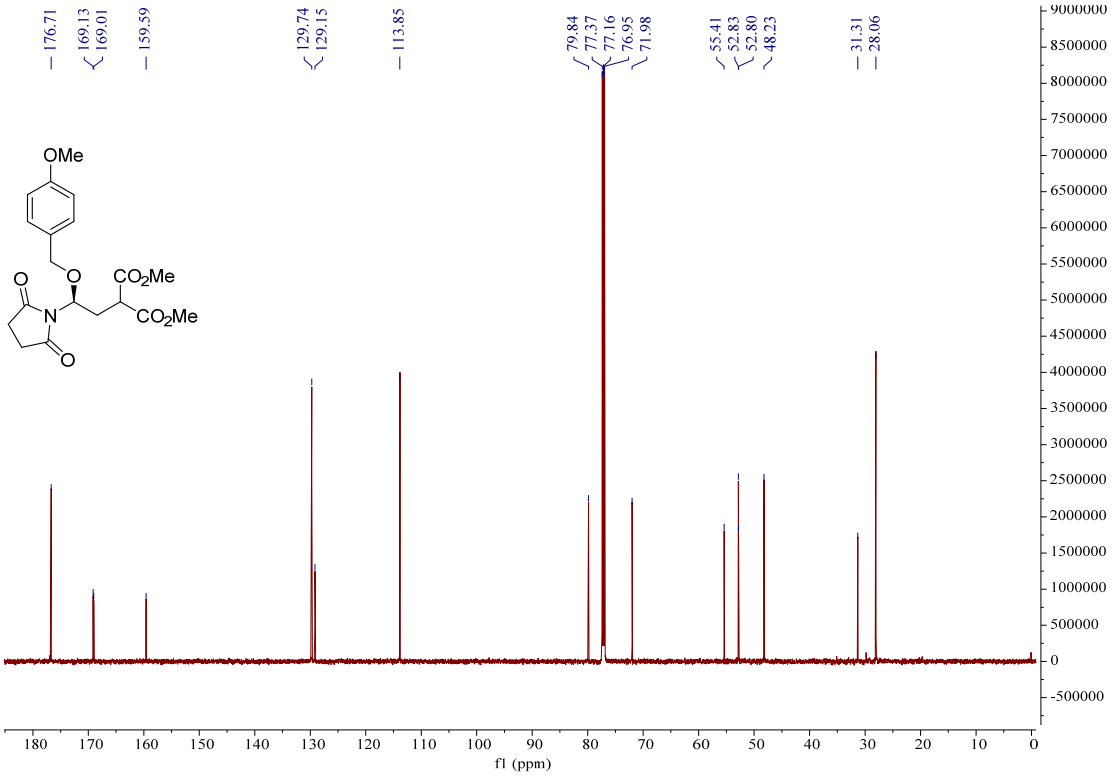
^{13}C NMR Spectrum of **3ae** (150 MHz, $CDCl_3$)



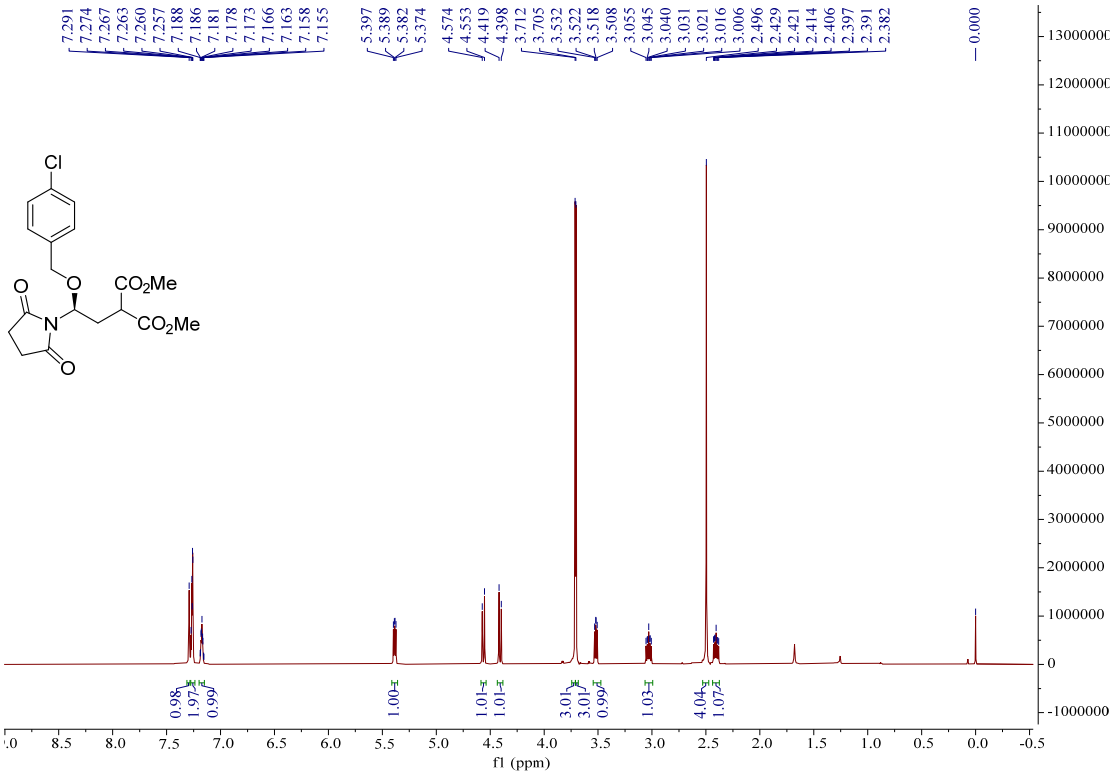
^{1}H NMR Spectrum of **3af** (600 MHz, $CDCl_3$)



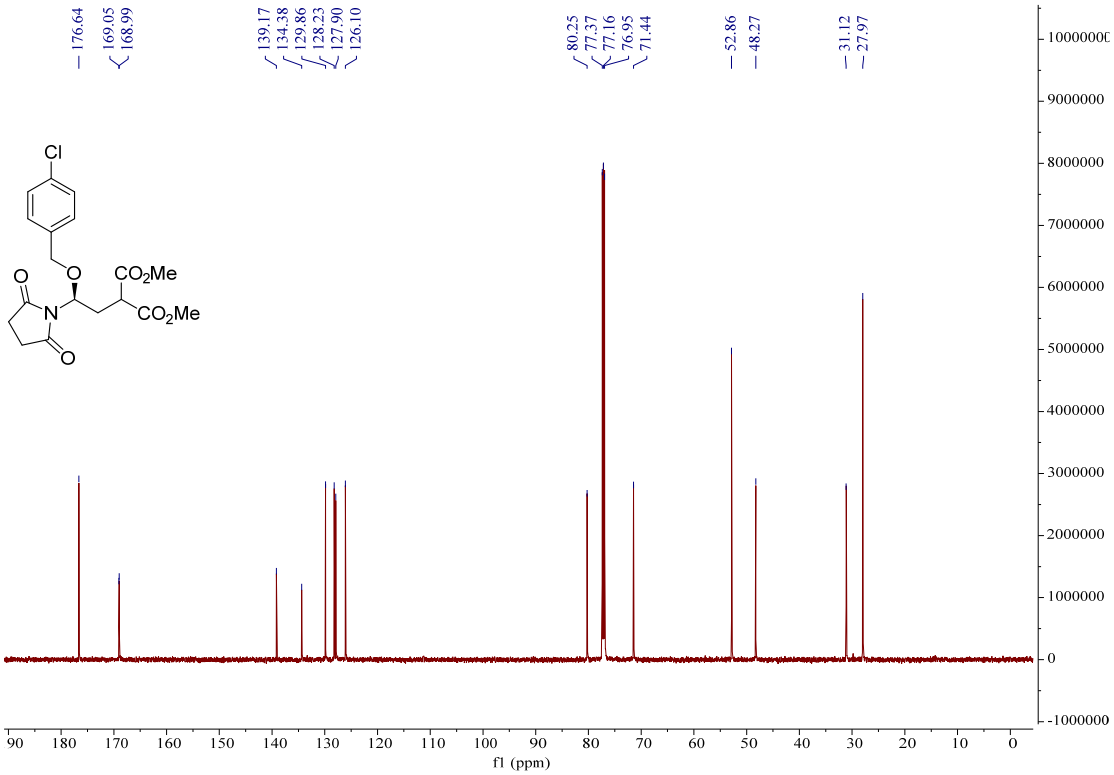
^{13}C NMR Spectrum of **3af** (150 MHz, $CDCl_3$)



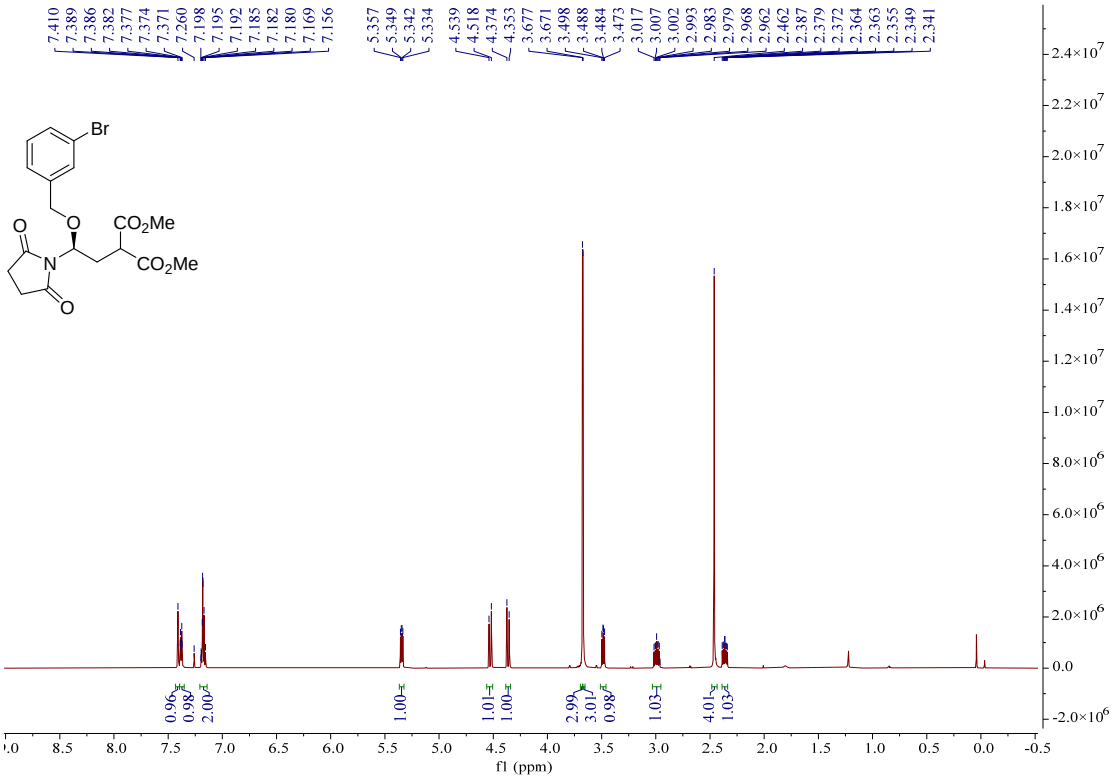
^{1}H NMR Spectrum of **3ag** (600 MHz, $CDCl_3$)



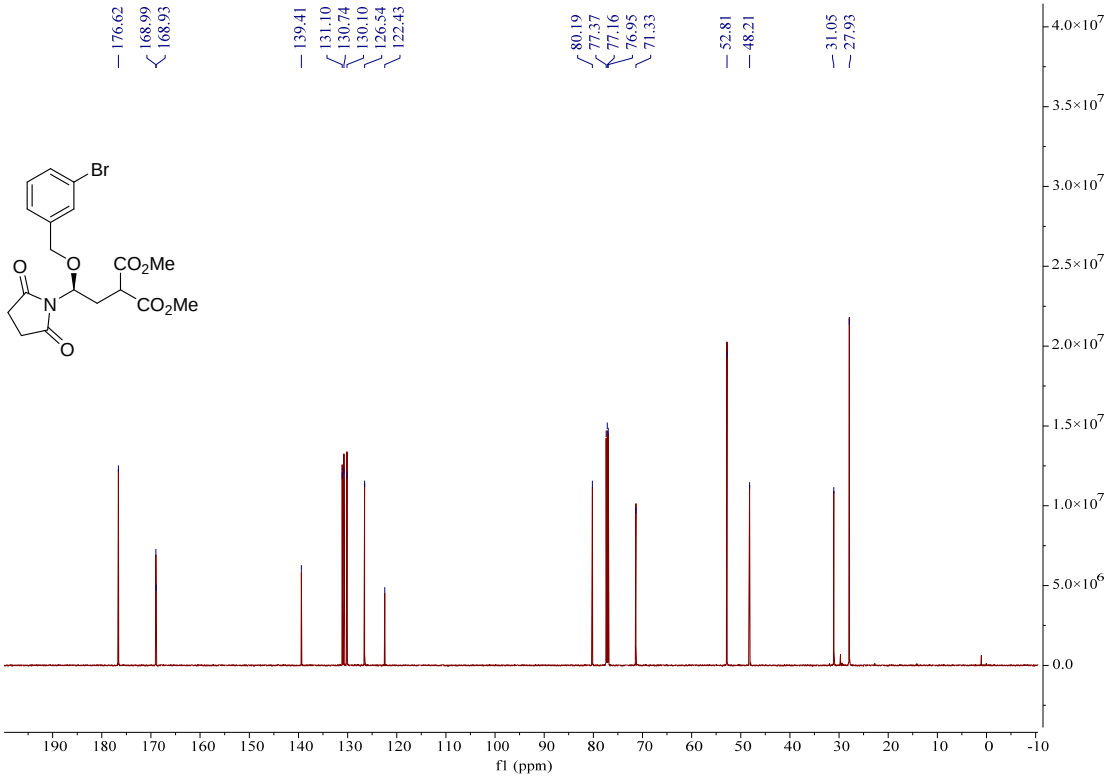
^{13}C NMR Spectrum of **3ag** (150 MHz, $CDCl_3$)



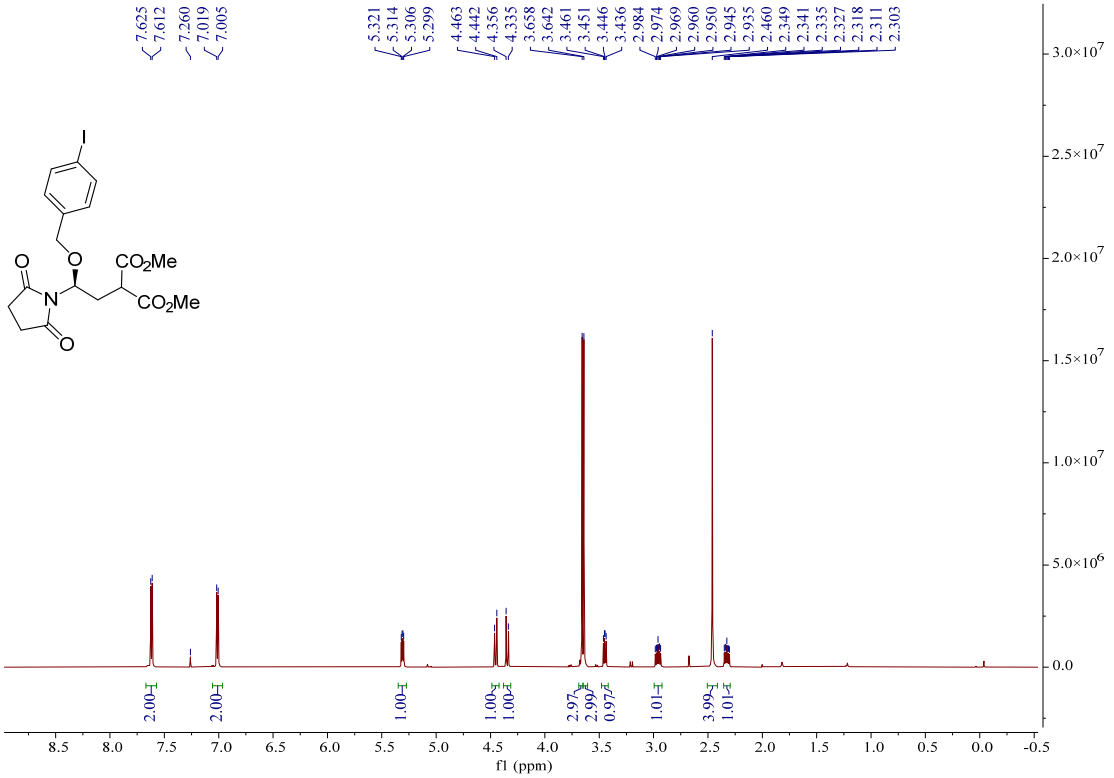
^{1}H NMR Spectrum of **3ah** (600 MHz, $CDCl_3$)



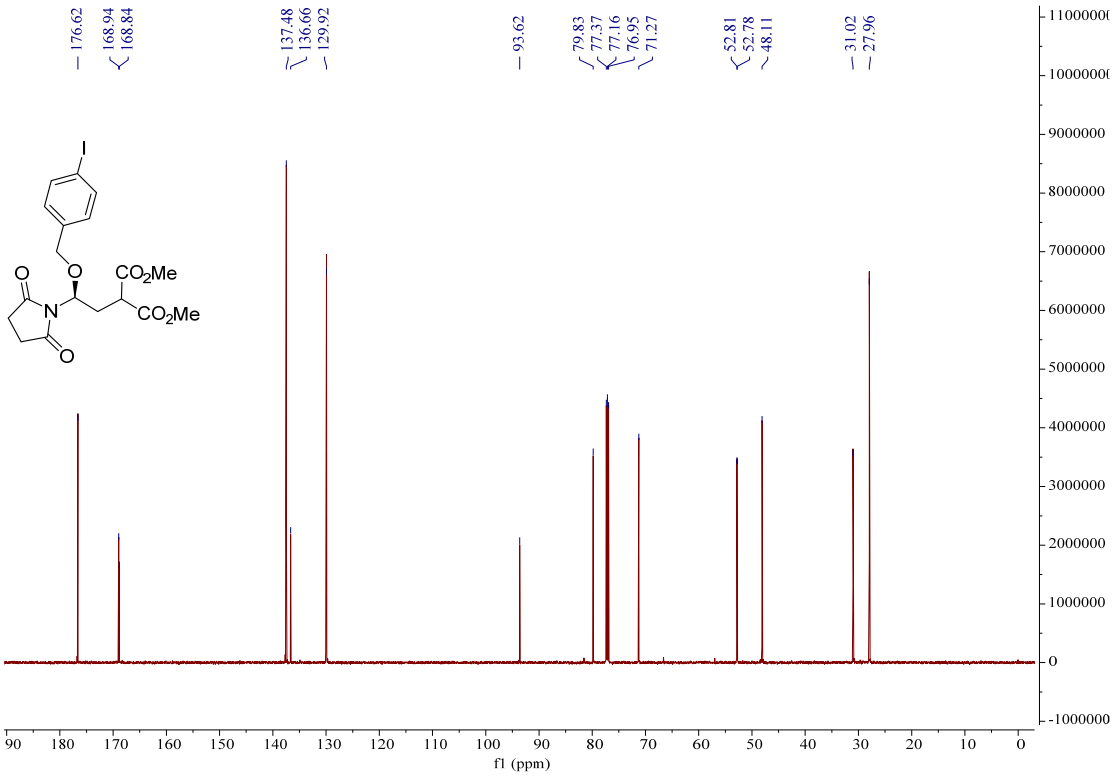
^{13}C NMR Spectrum of **3ah** (150 MHz, $CDCl_3$)



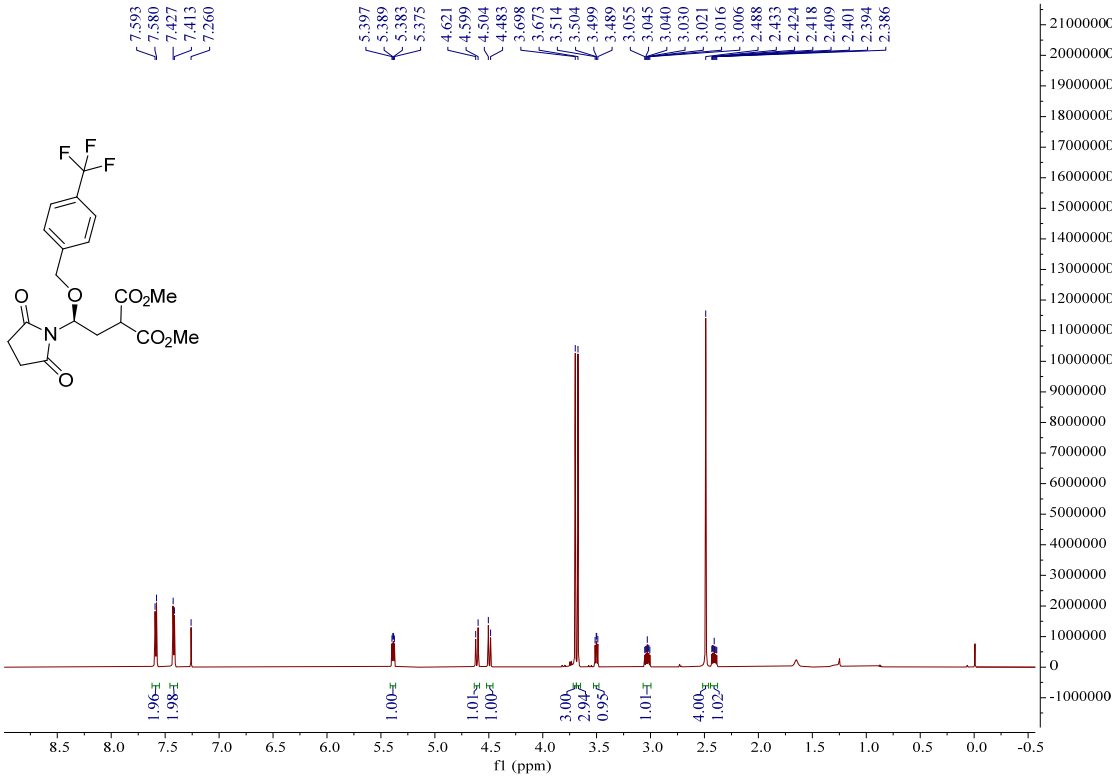
^{1}H NMR Spectrum of **3ai** (600 MHz, $CDCl_3$)



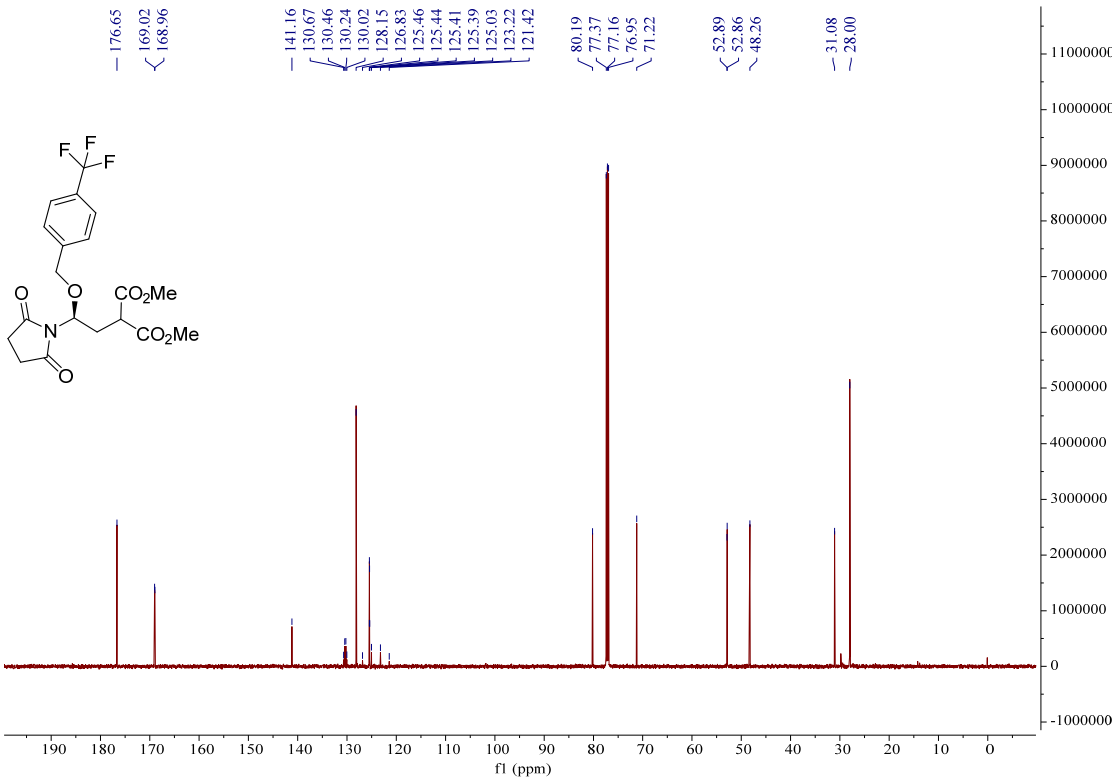
^{13}C NMR Spectrum of **3ai** (150 MHz, $CDCl_3$)



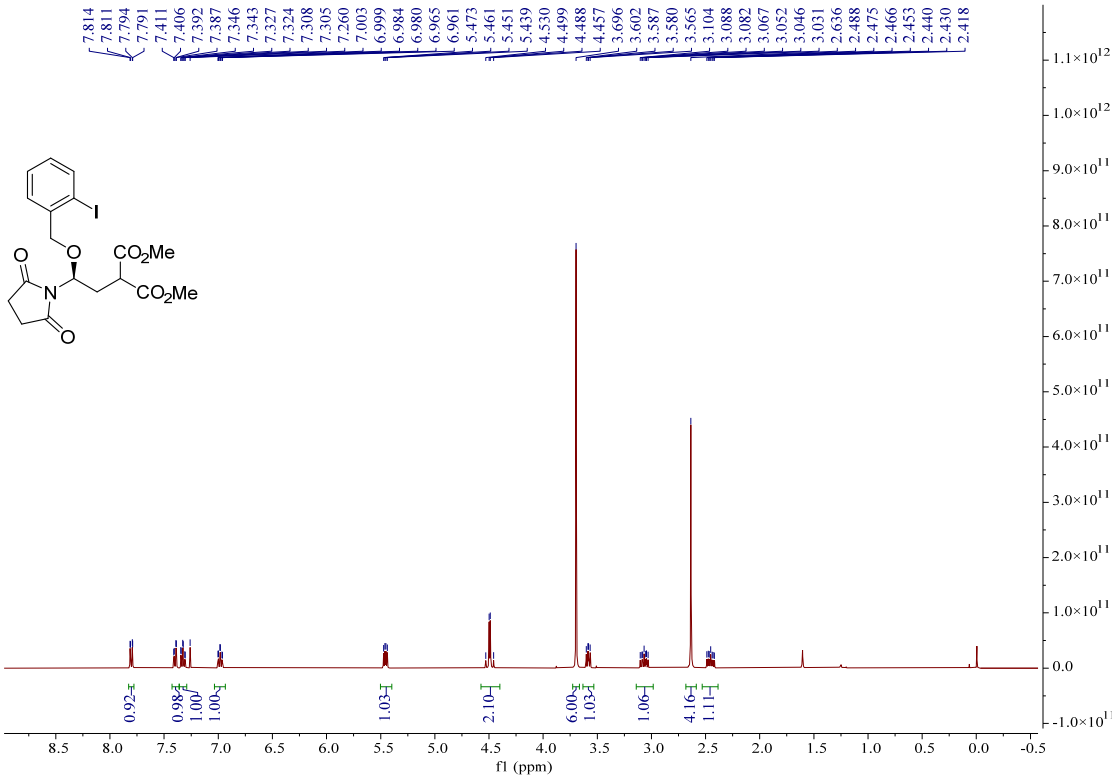
^{1}H NMR Spectrum of **3aj** (600 MHz, $CDCl_3$)



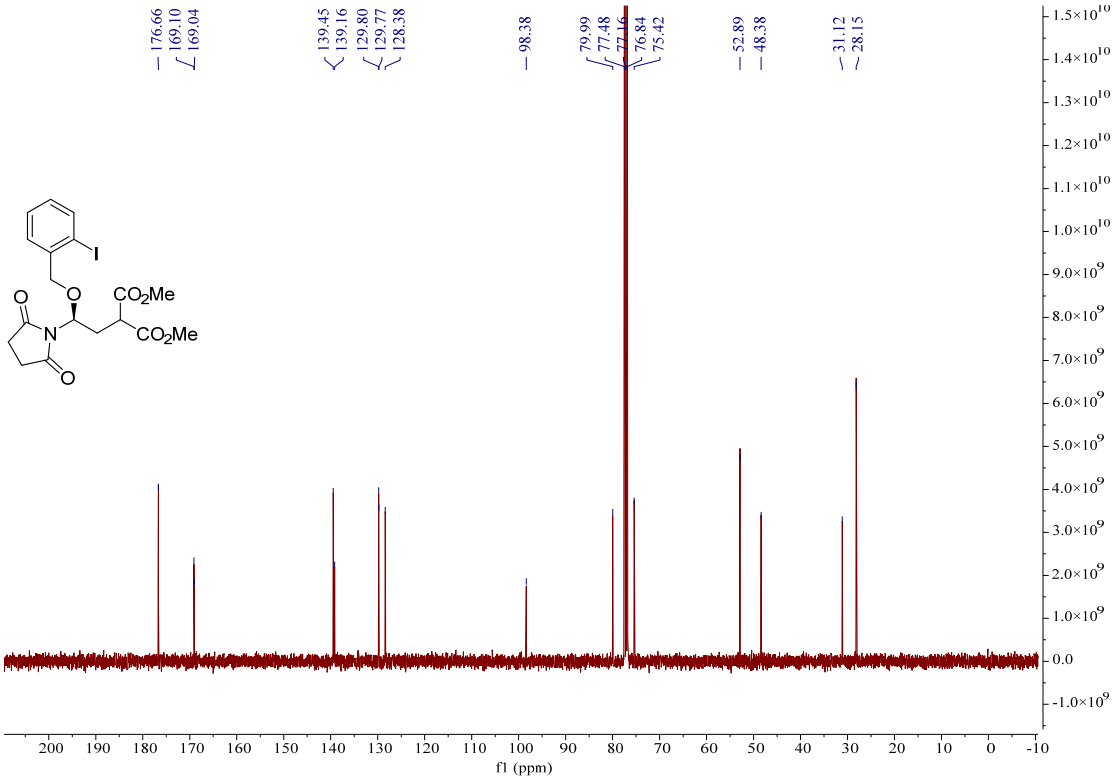
^{13}C NMR Spectrum of **3aj** (150 MHz, $CDCl_3$)



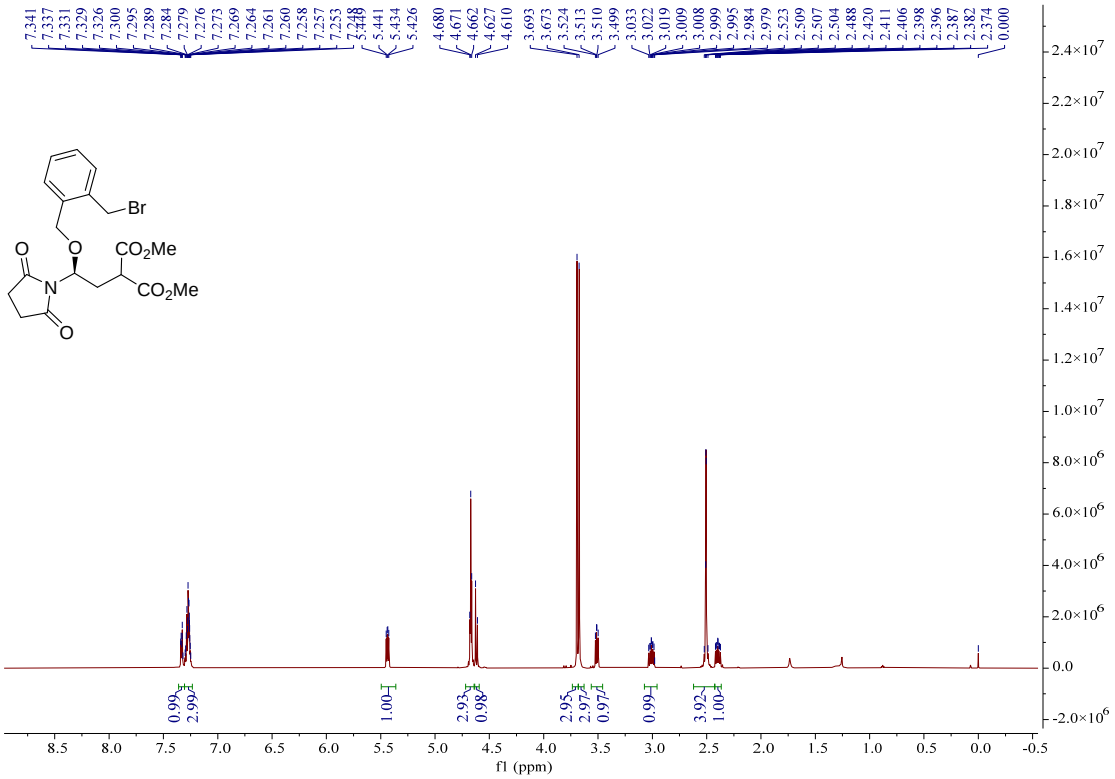
^{1}H NMR Spectrum of **3ak** (400 MHz, $CDCl_3$)



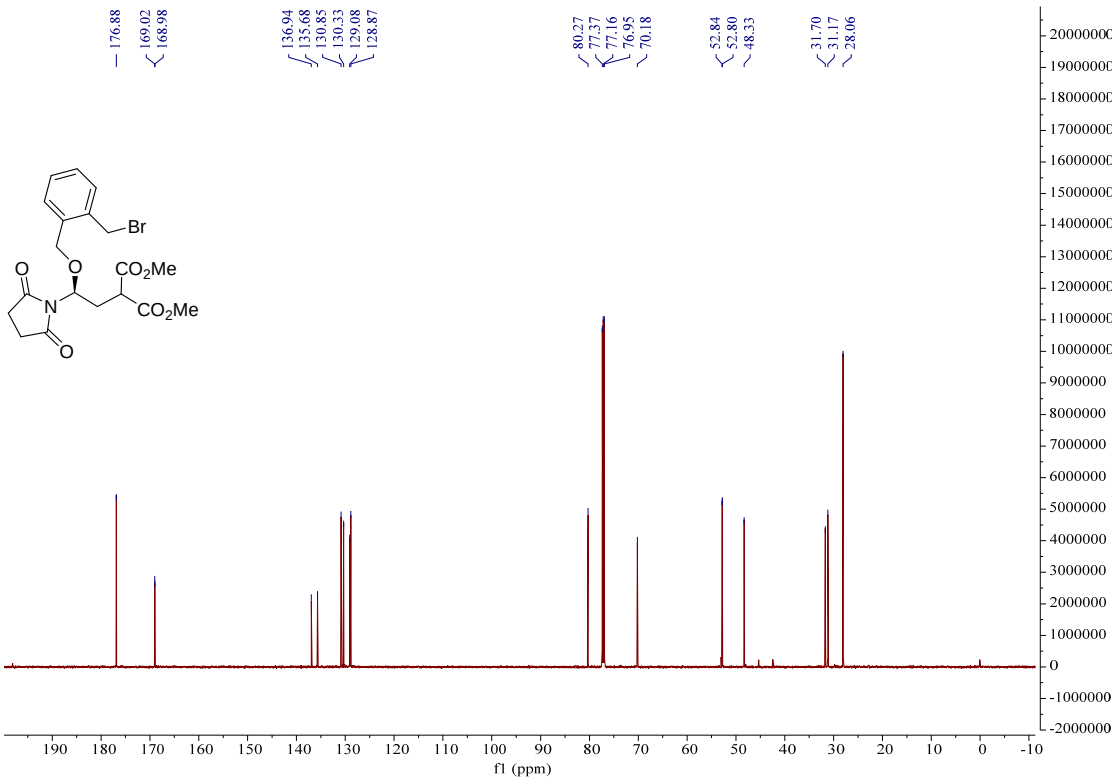
^{13}C NMR Spectrum of **3ak** (100 MHz, $CDCl_3$)



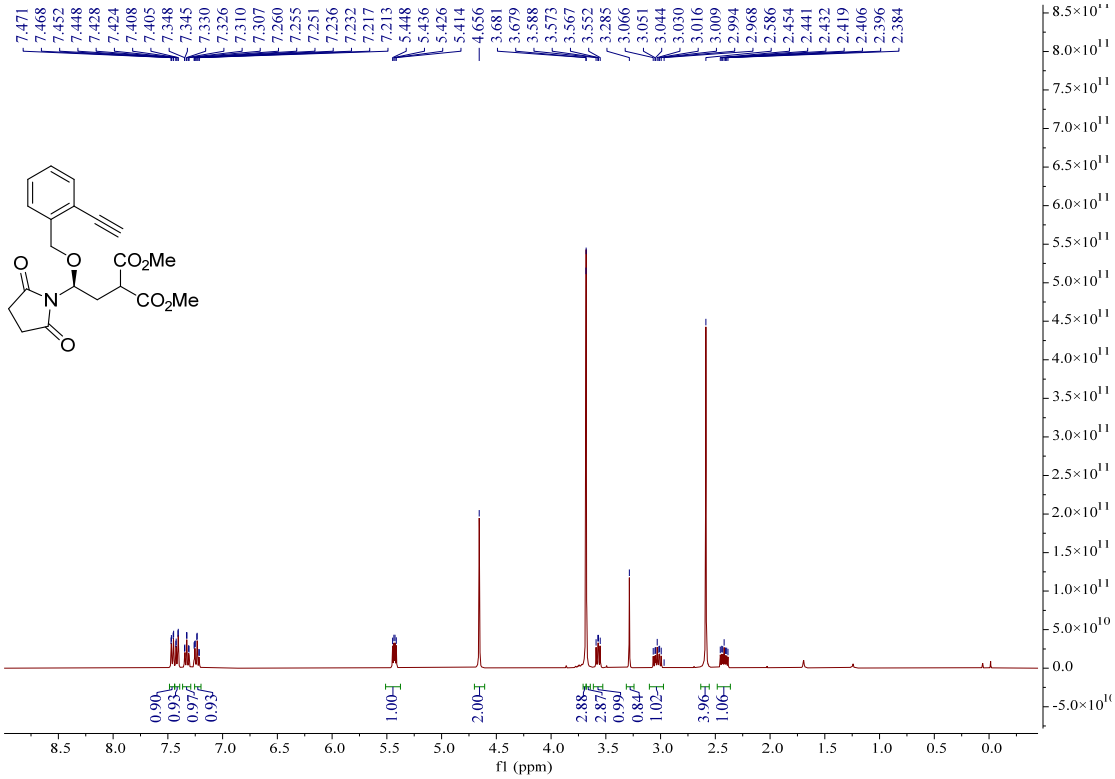
^{1}H NMR Spectrum of **3al** (600 MHz, $CDCl_3$)



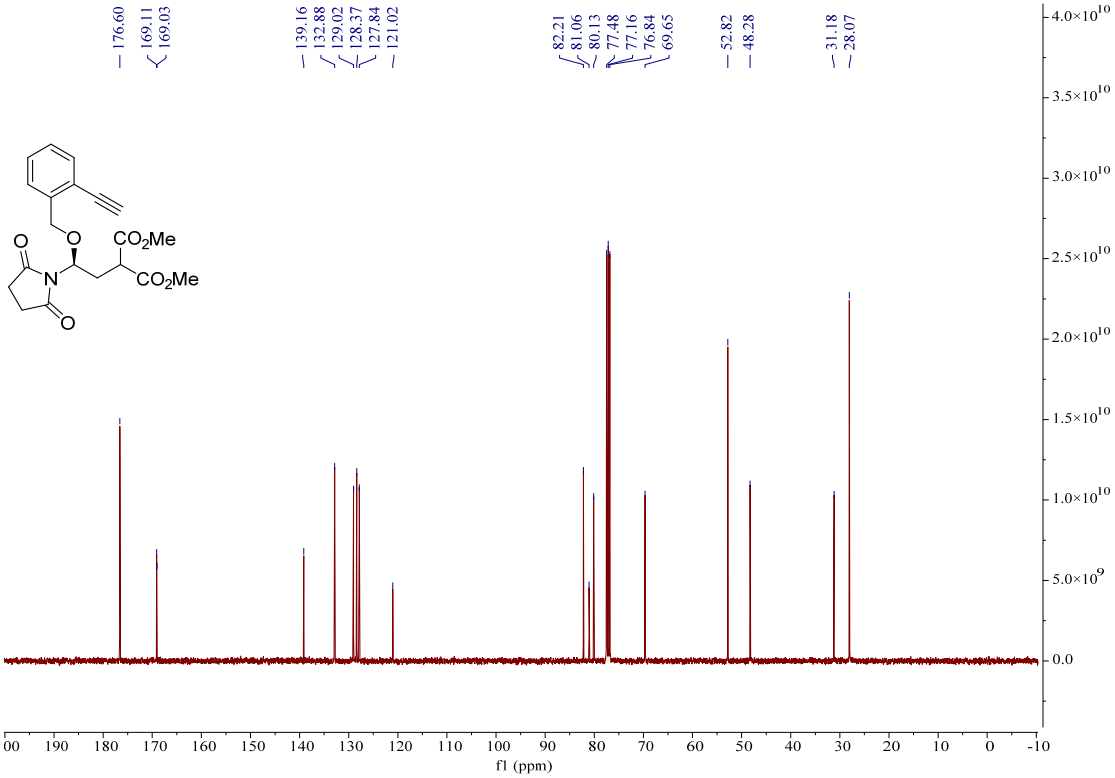
^{13}C NMR Spectrum of **3al** (150 MHz, $CDCl_3$)



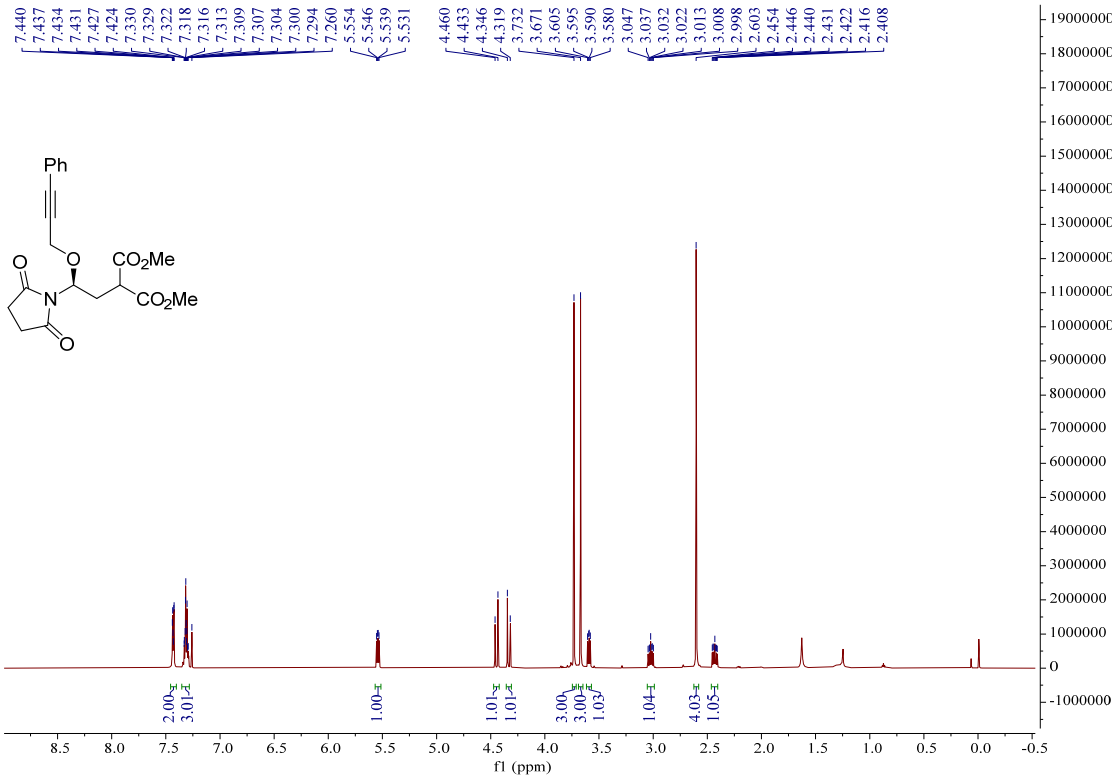
^{1}H NMR Spectrum of **3am** (400 MHz, $CDCl_3$)



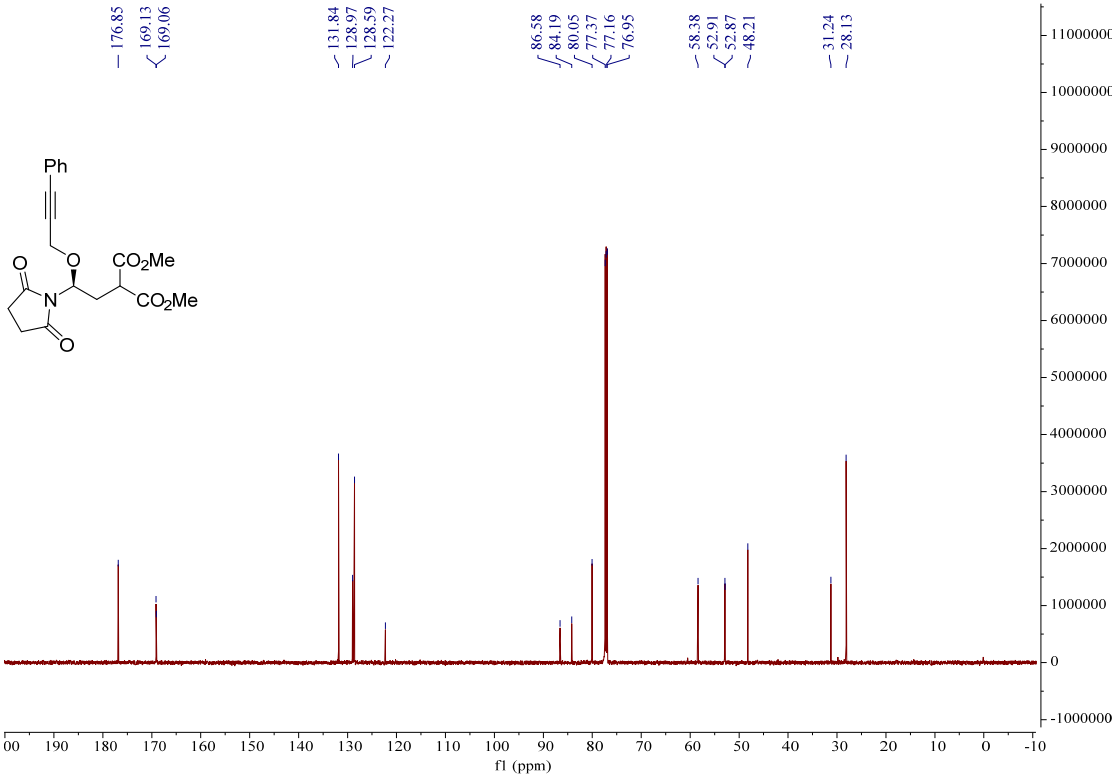
^{13}C NMR Spectrum of **3am** (100 MHz, $CDCl_3$)



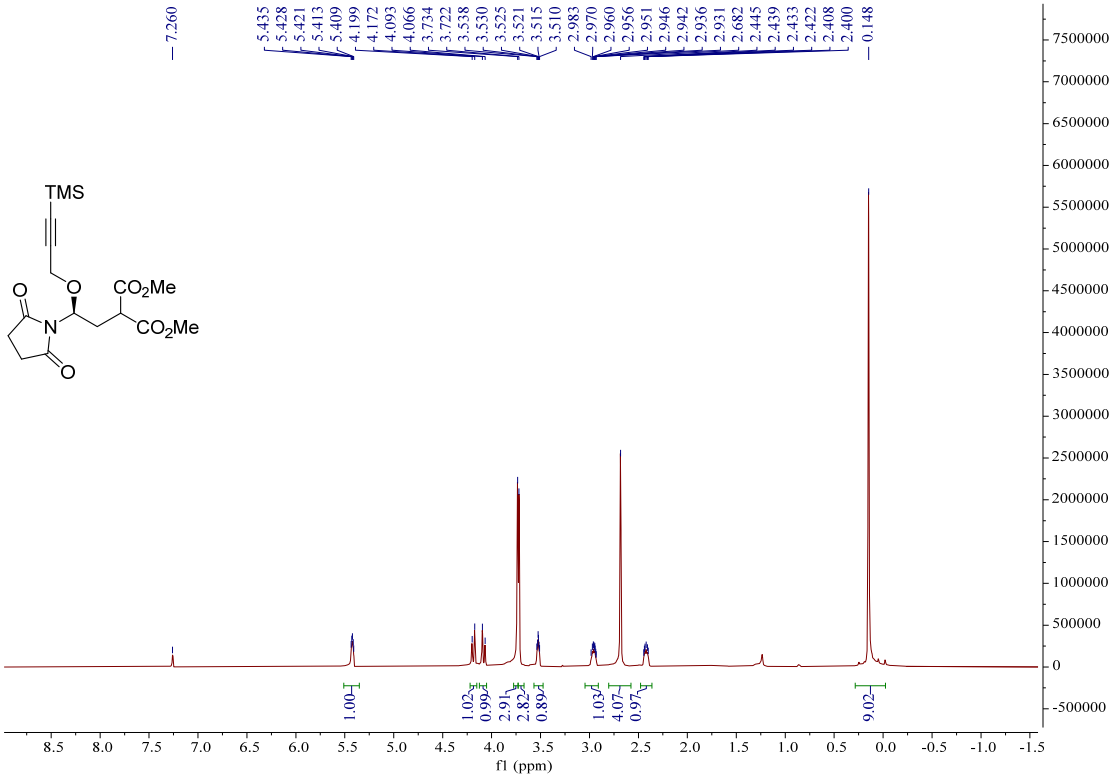
^{1}H NMR Spectrum of **3an** (600 MHz, $CDCl_3$)



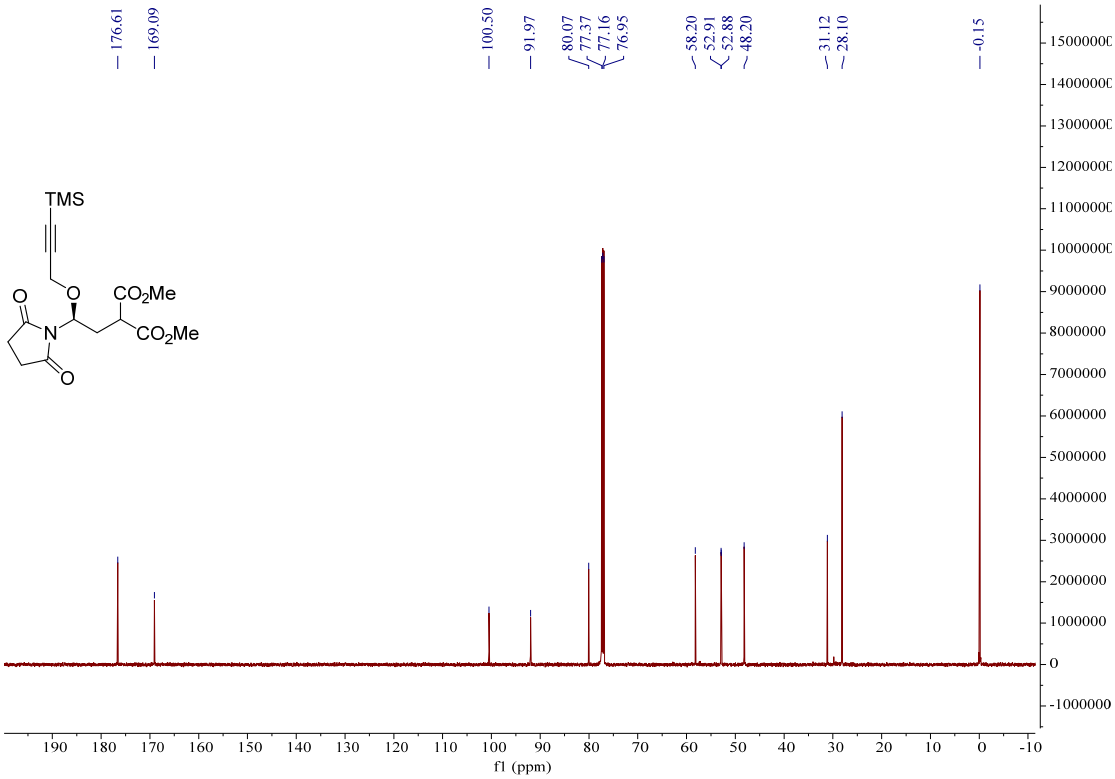
^{13}C NMR Spectrum of **3an** (150 MHz, $CDCl_3$)



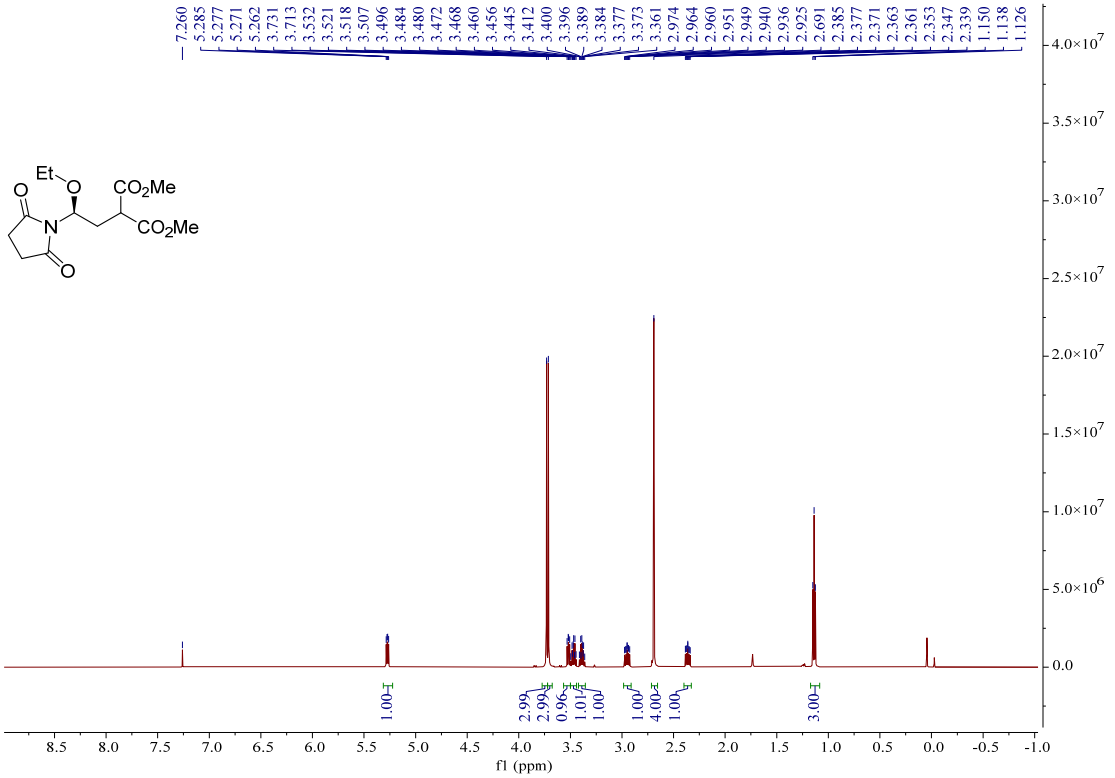
^{1}H NMR Spectrum of **3ao** (600 MHz, $CDCl_3$)



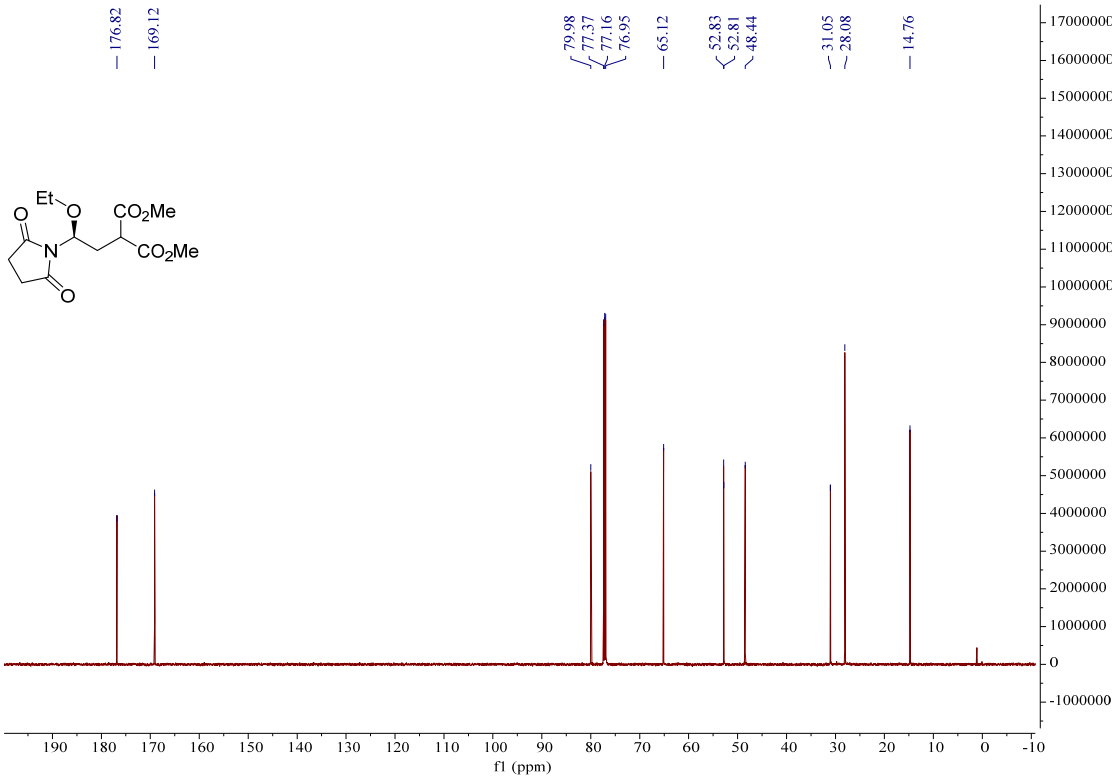
^{13}C NMR Spectrum of **3ao** (150 MHz, $CDCl_3$



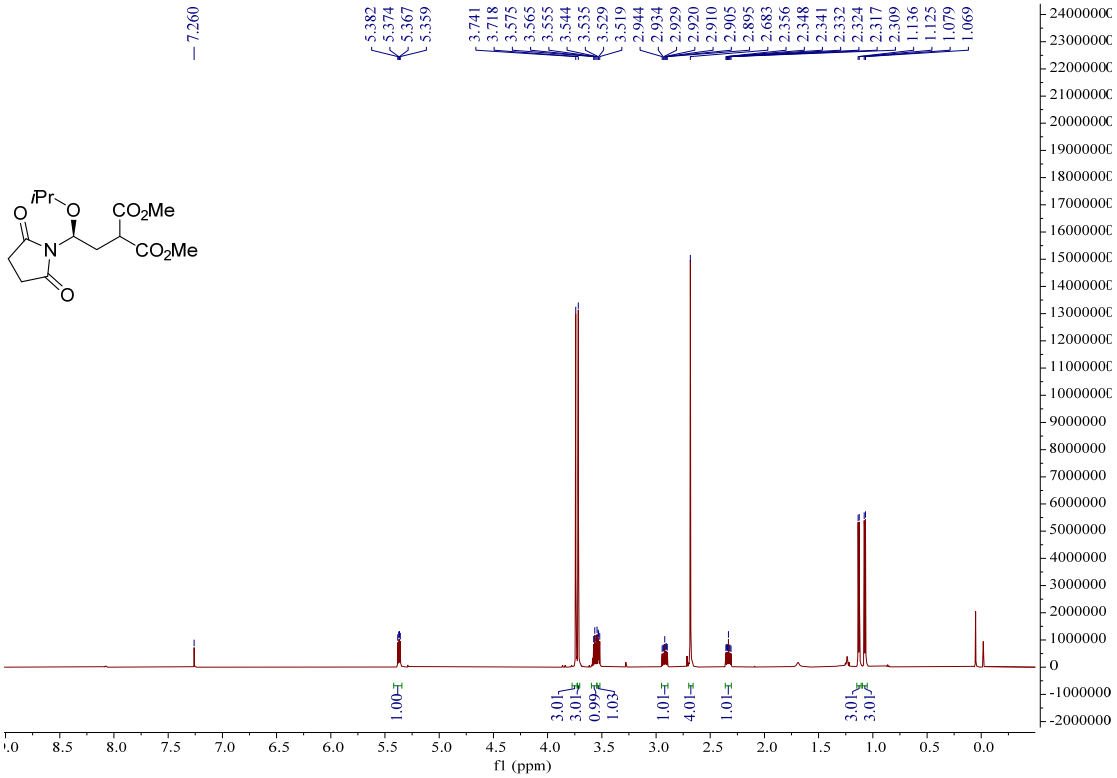
^{1}H NMR Spectrum of **3ap** (600 MHz, $CDCl_3$)



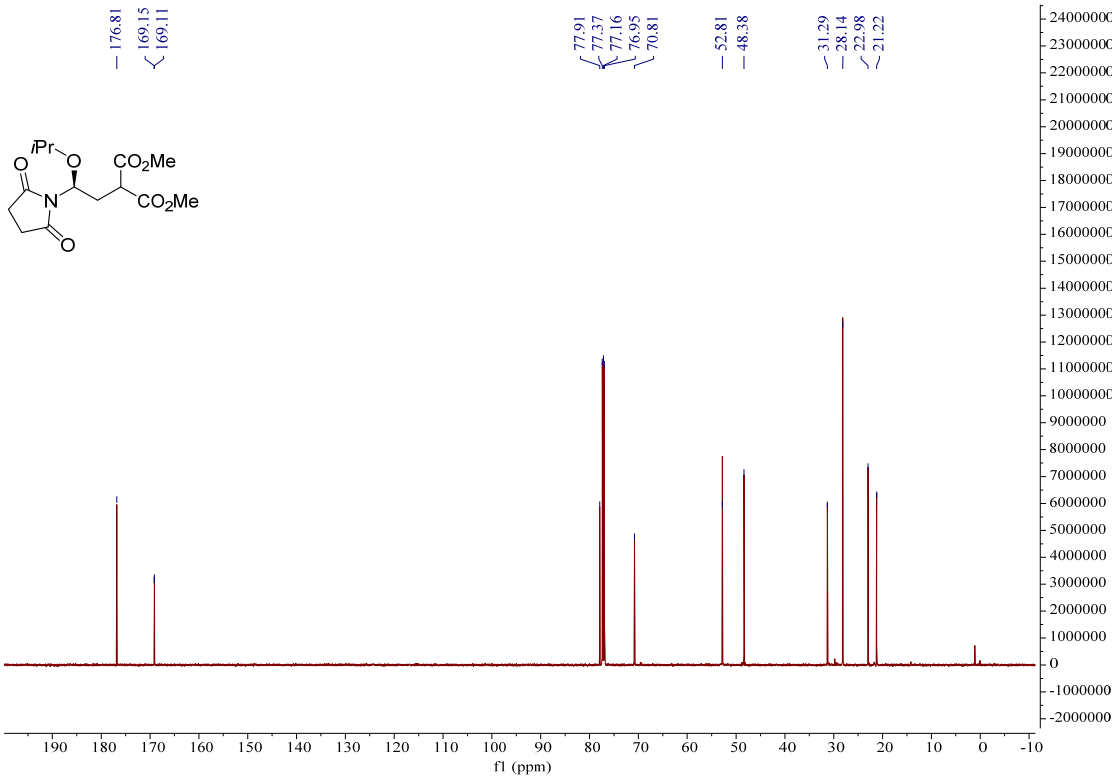
^{13}C NMR Spectrum of **3ap** (150 MHz, $CDCl_3$)



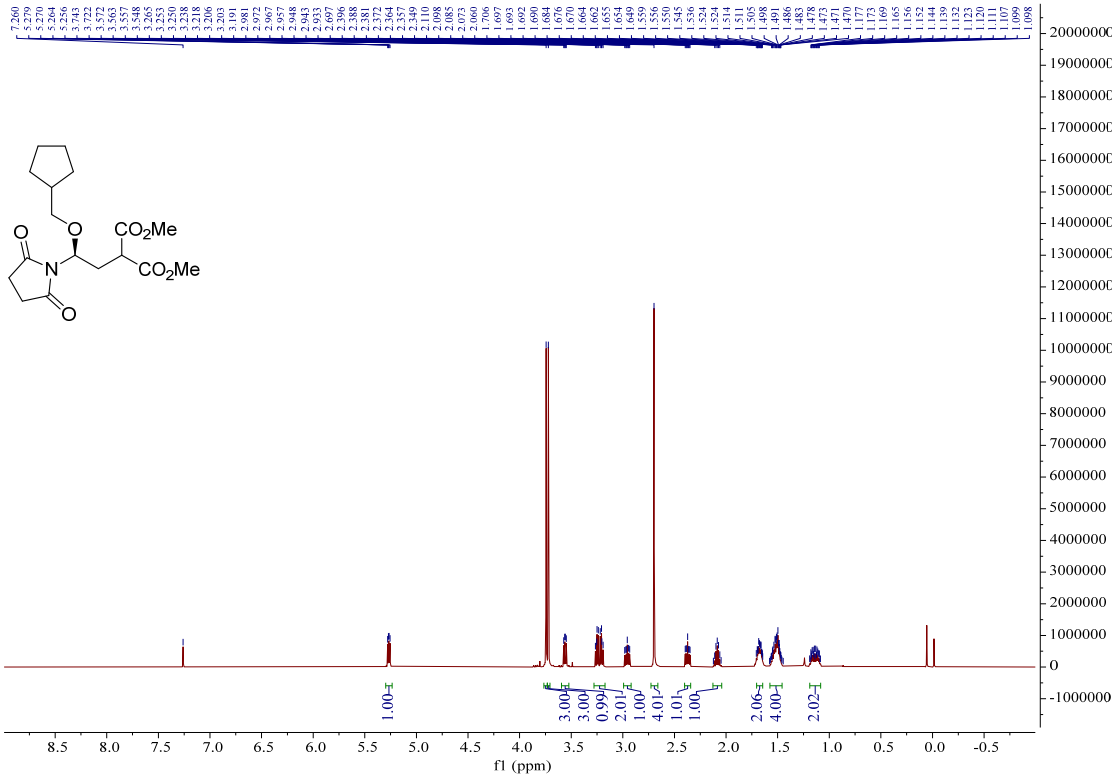
^{1}H NMR Spectrum of **3aq** (600 MHz, $CDCl_3$)



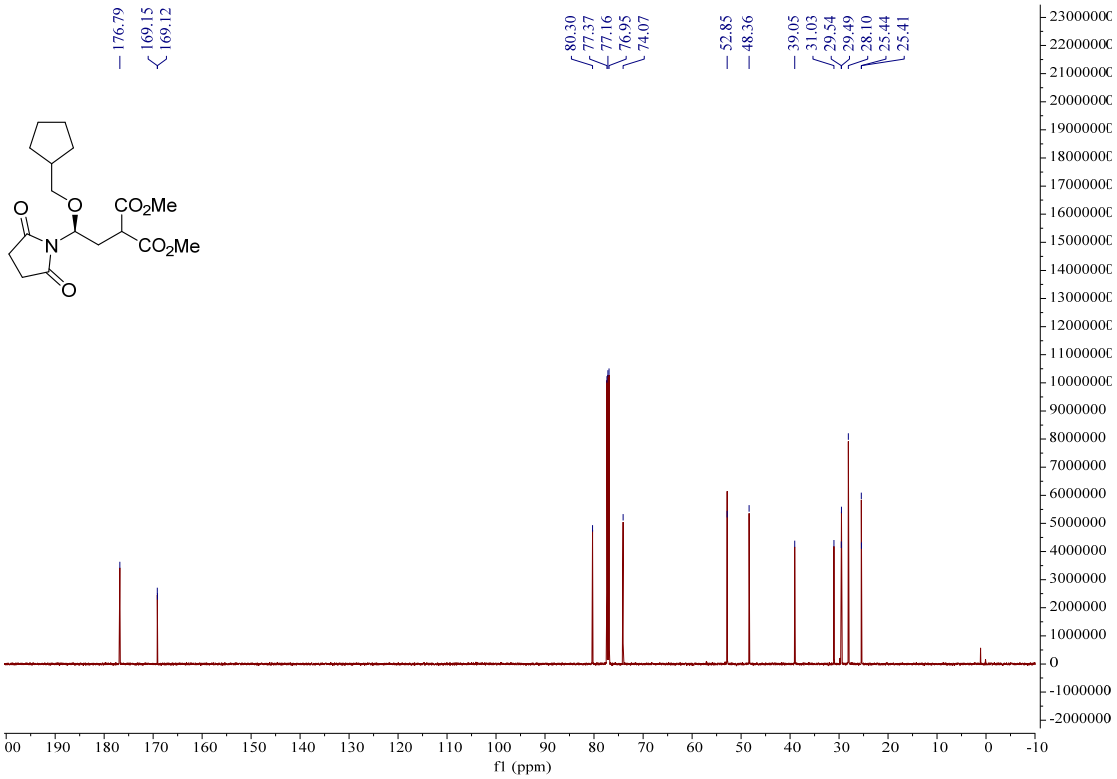
^{13}C NMR Spectrum of **3aq** (150 MHz, $CDCl_3$)



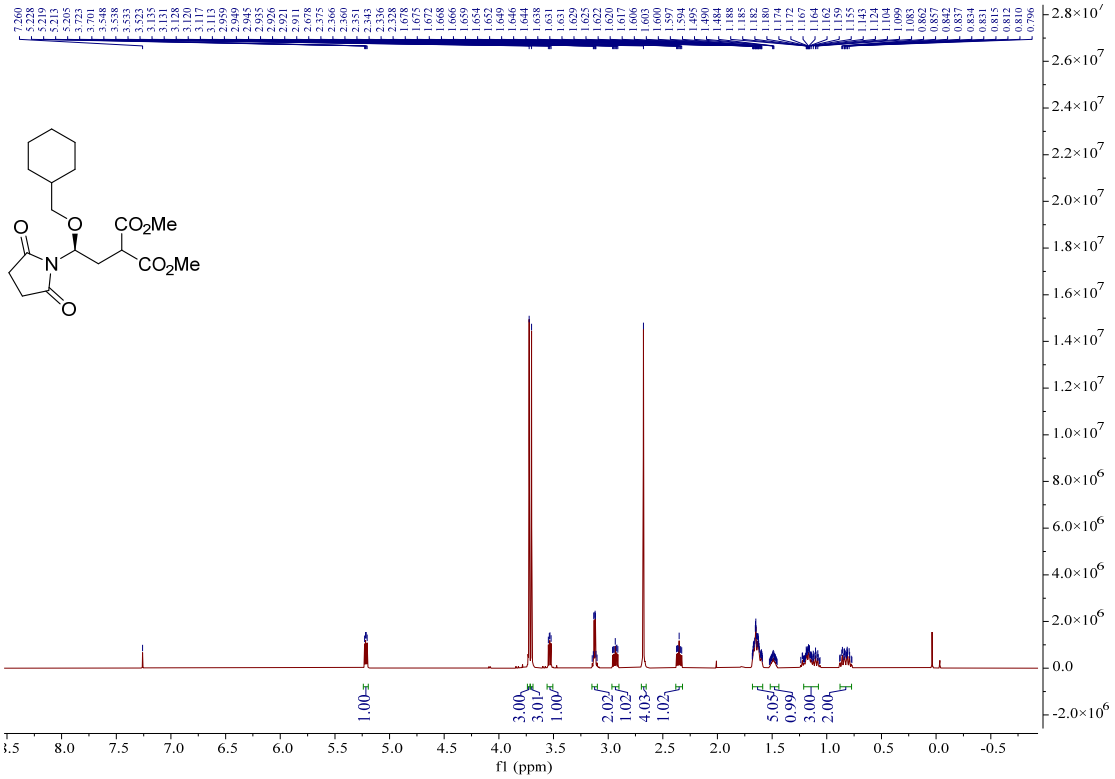
^{1}H NMR Spectrum of **3ar** (600 MHz, $CDCl_3$)



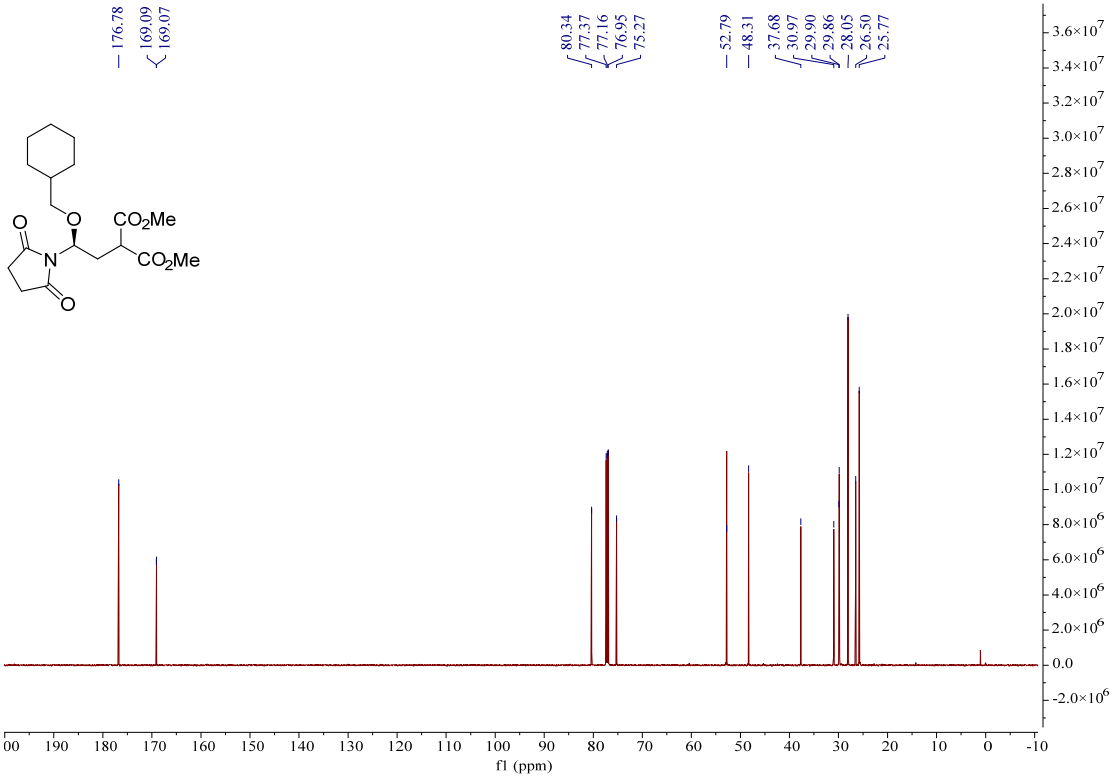
^{13}C NMR Spectrum of **3ar** (150 MHz, $CDCl_3$)



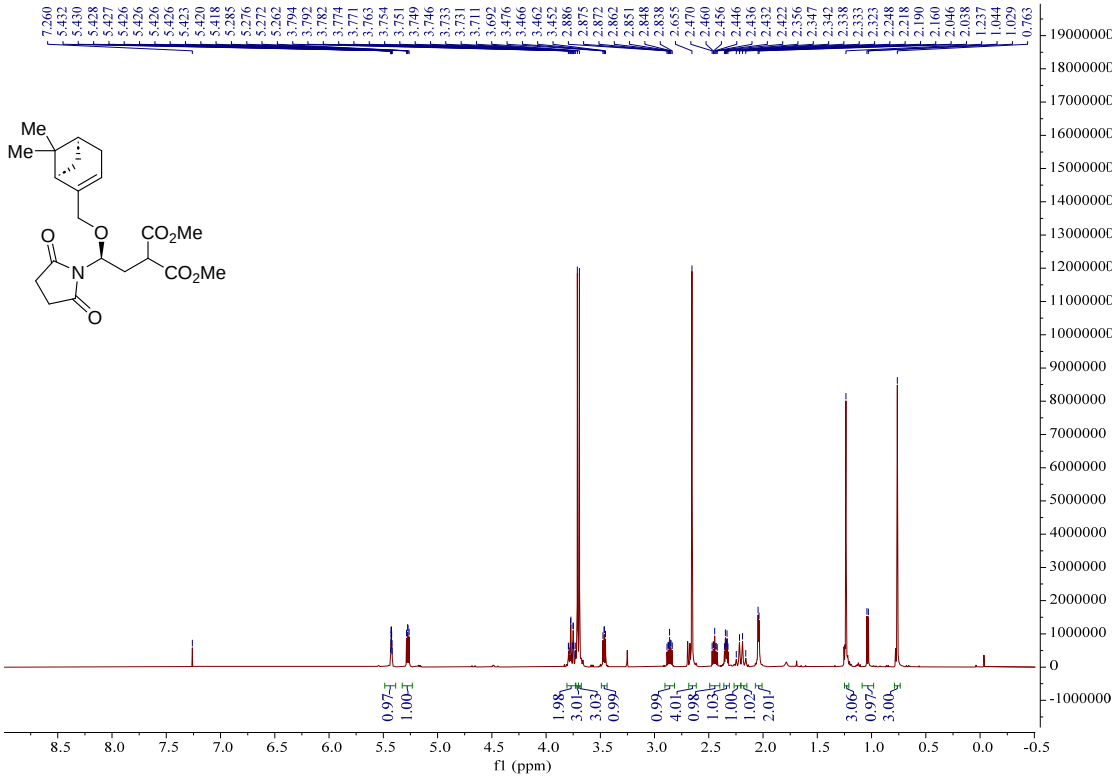
^{1}H NMR Spectrum of **3as** (600 MHz, $CDCl_3$)



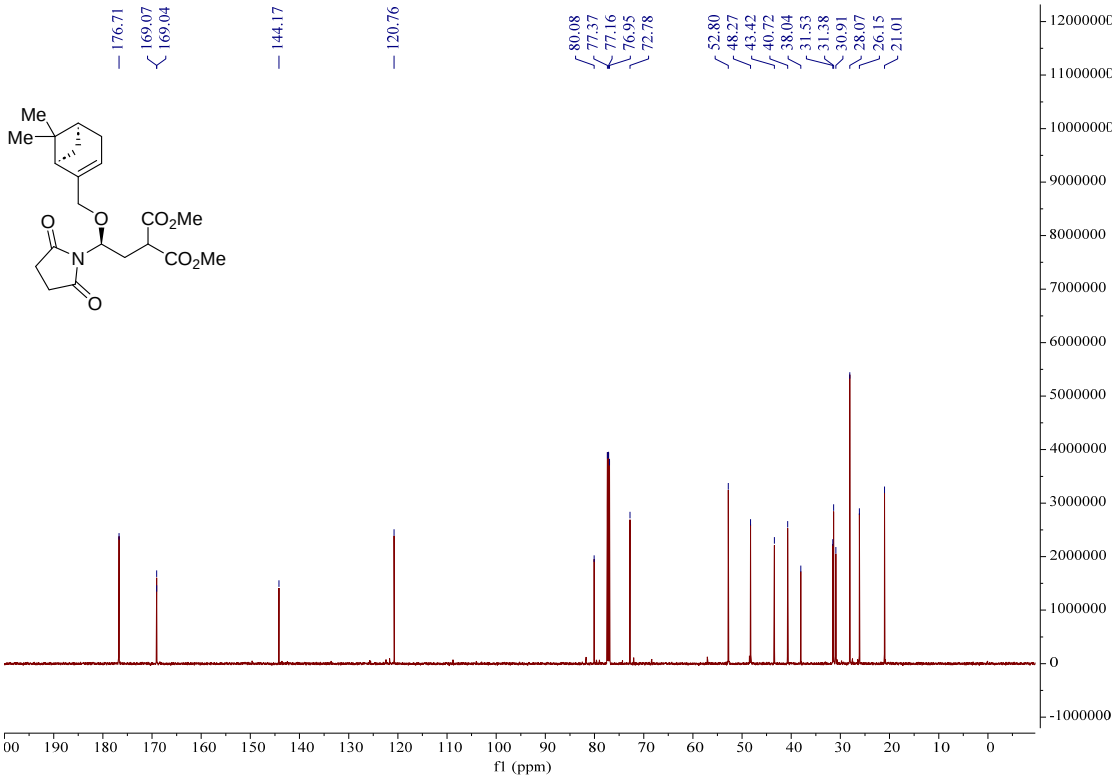
^{13}C NMR Spectrum of **3as** (150 MHz, $CDCl_3$)



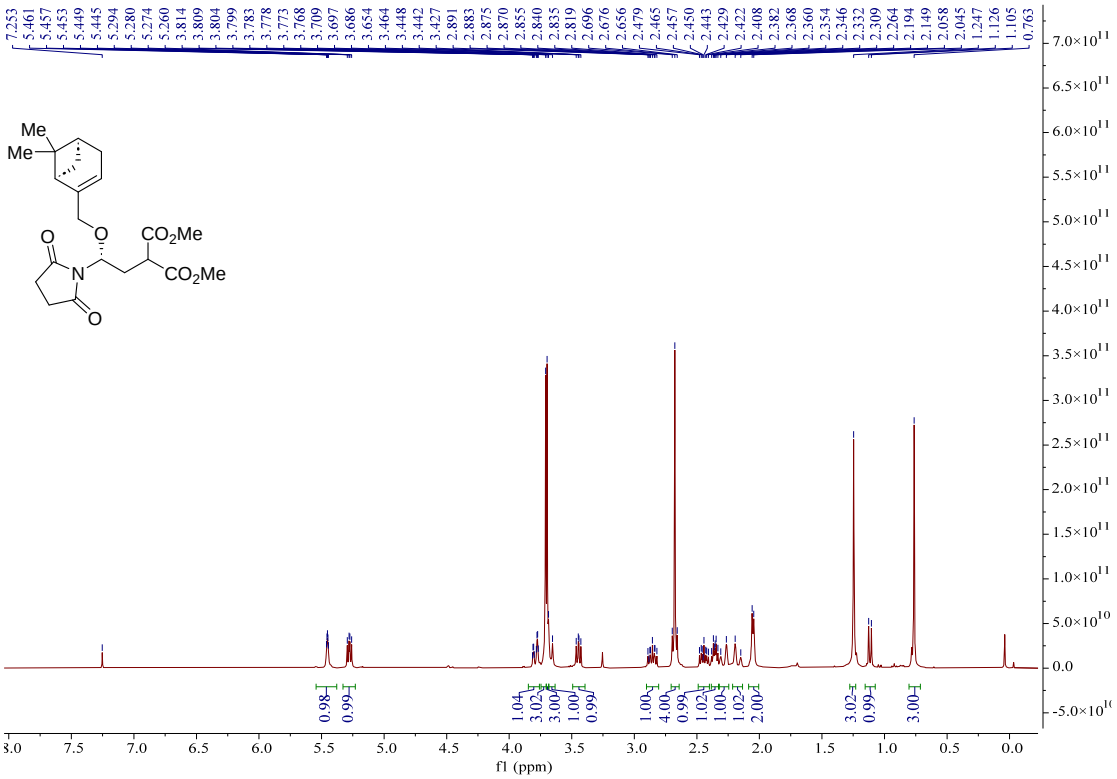
^{1}H NMR Spectrum of **3at** (600 MHz, $CDCl_3$)



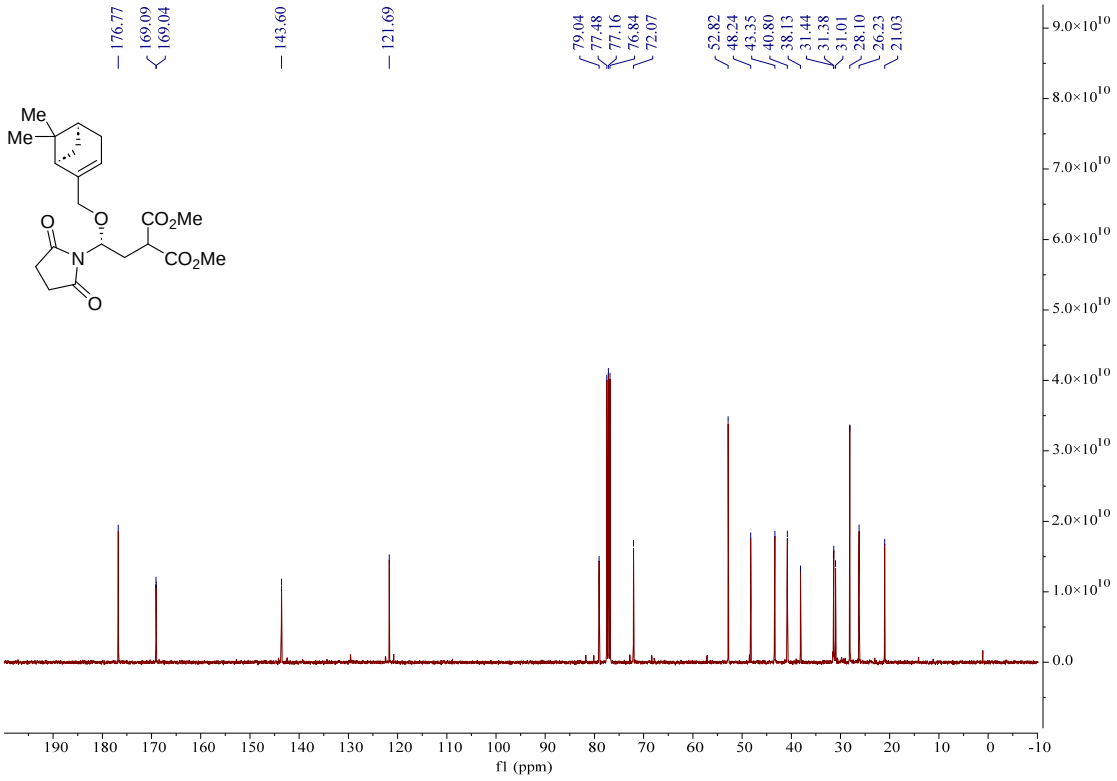
^{13}C NMR Spectrum of **3at** (150 MHz, $CDCl_3$)



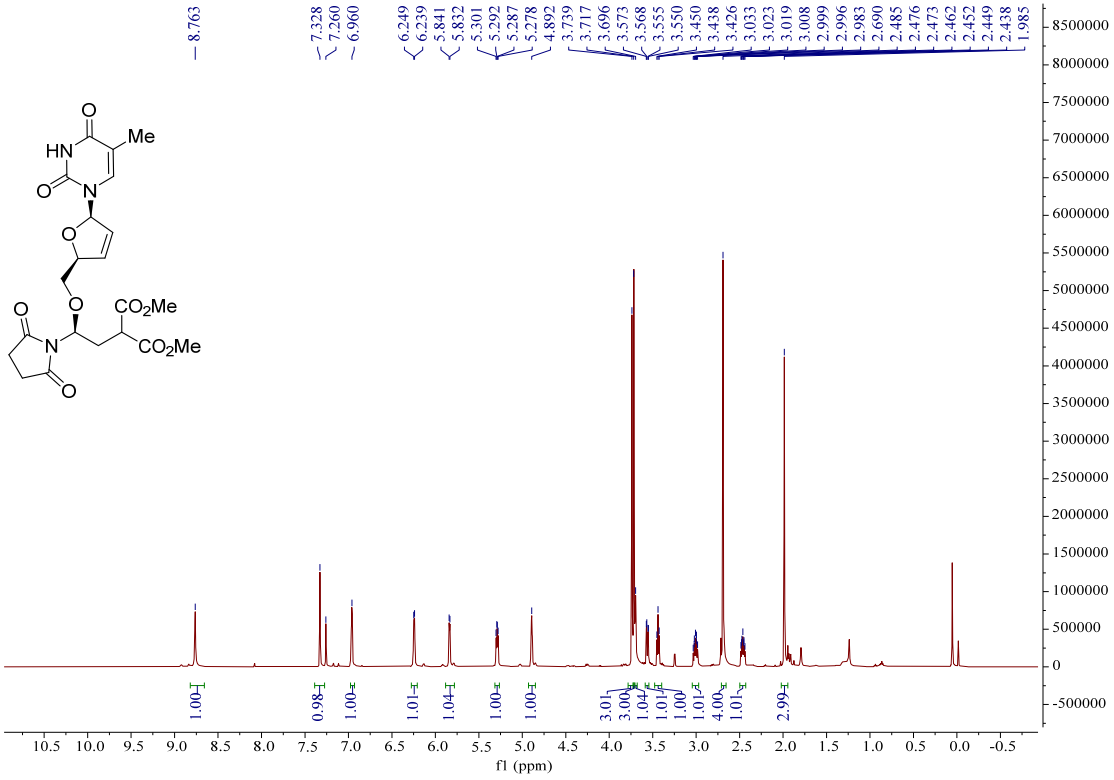
^{1}H NMR Spectrum of **3at'** (400 MHz, $CDCl_3$)



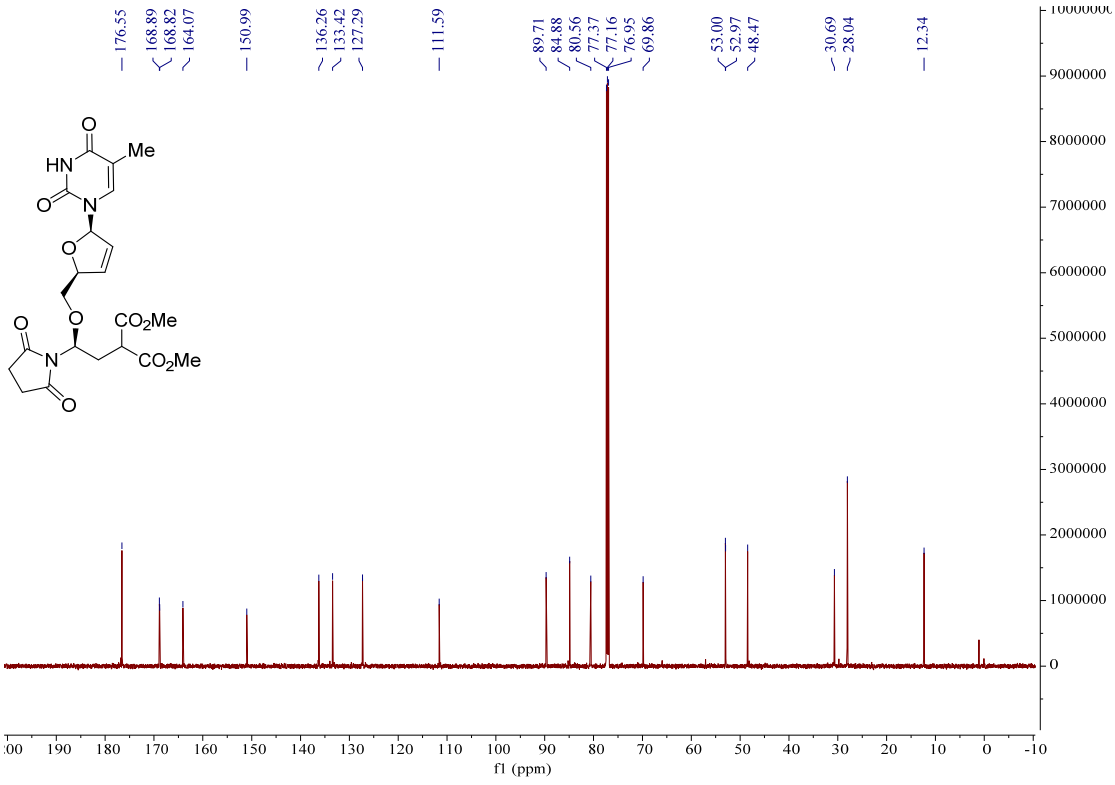
^{13}C NMR Spectrum of **3at'** (100 MHz, $CDCl_3$)



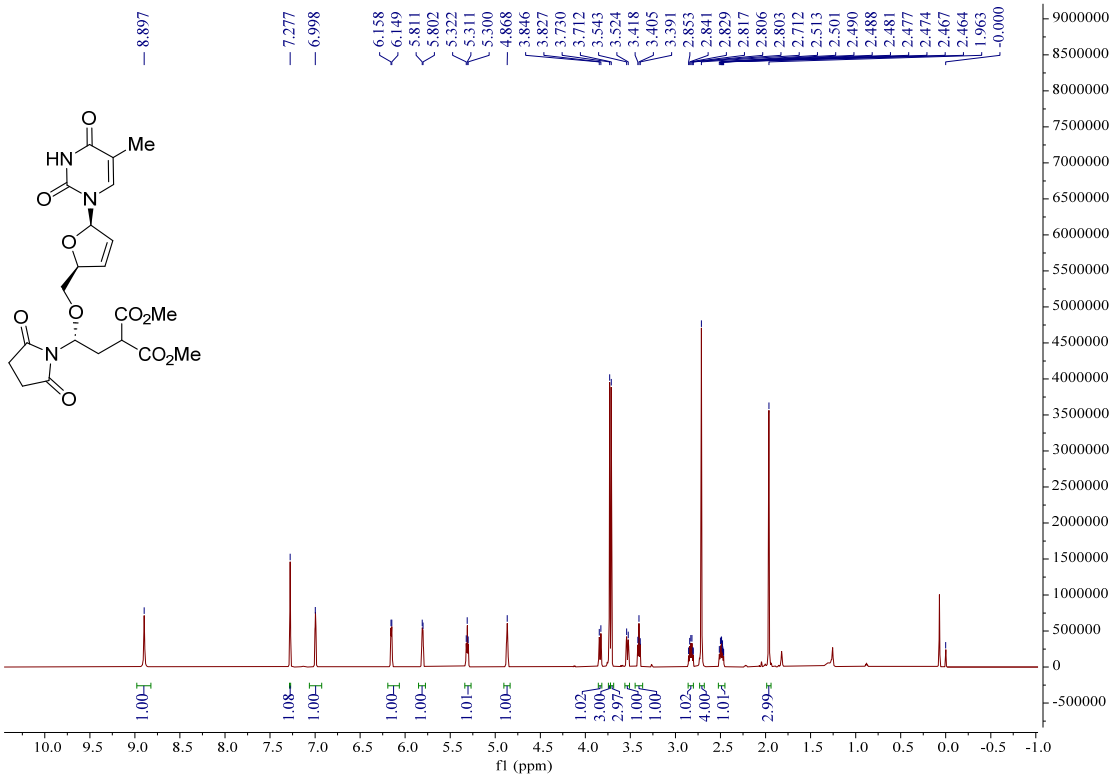
^{1}H NMR Spectrum of **3au** (600 MHz, $CDCl_3$)



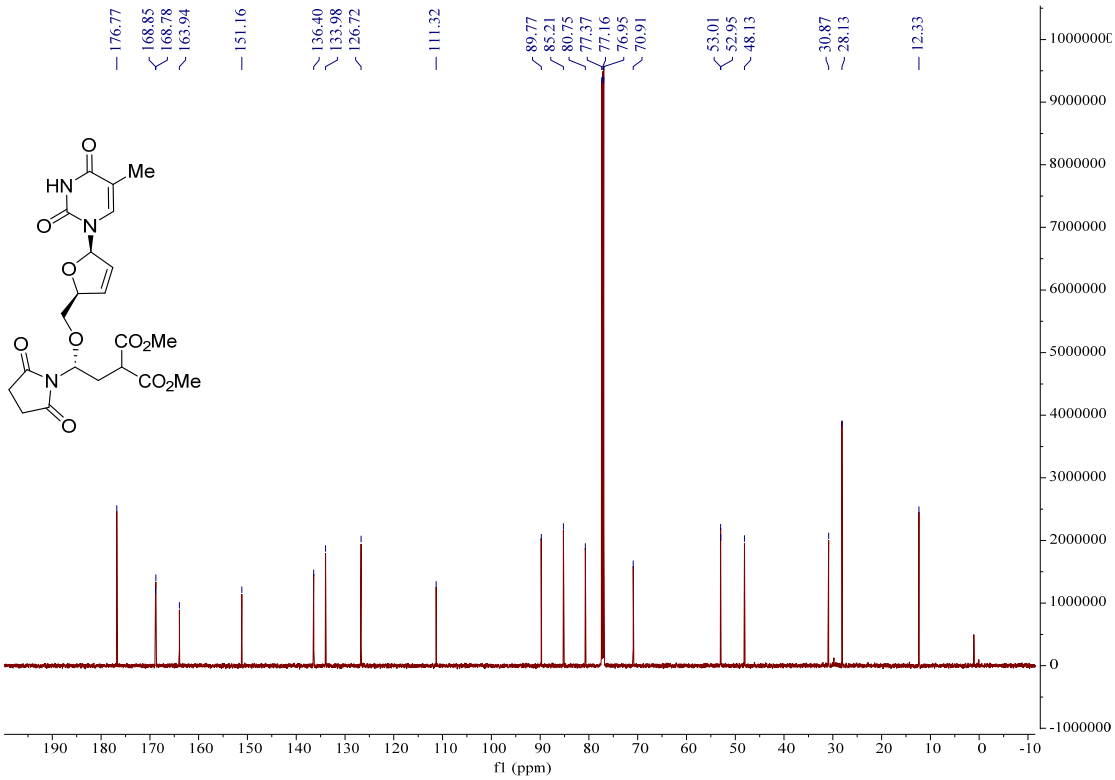
^{13}C NMR Spectrum of **3au** (150 MHz, $CDCl_3$)



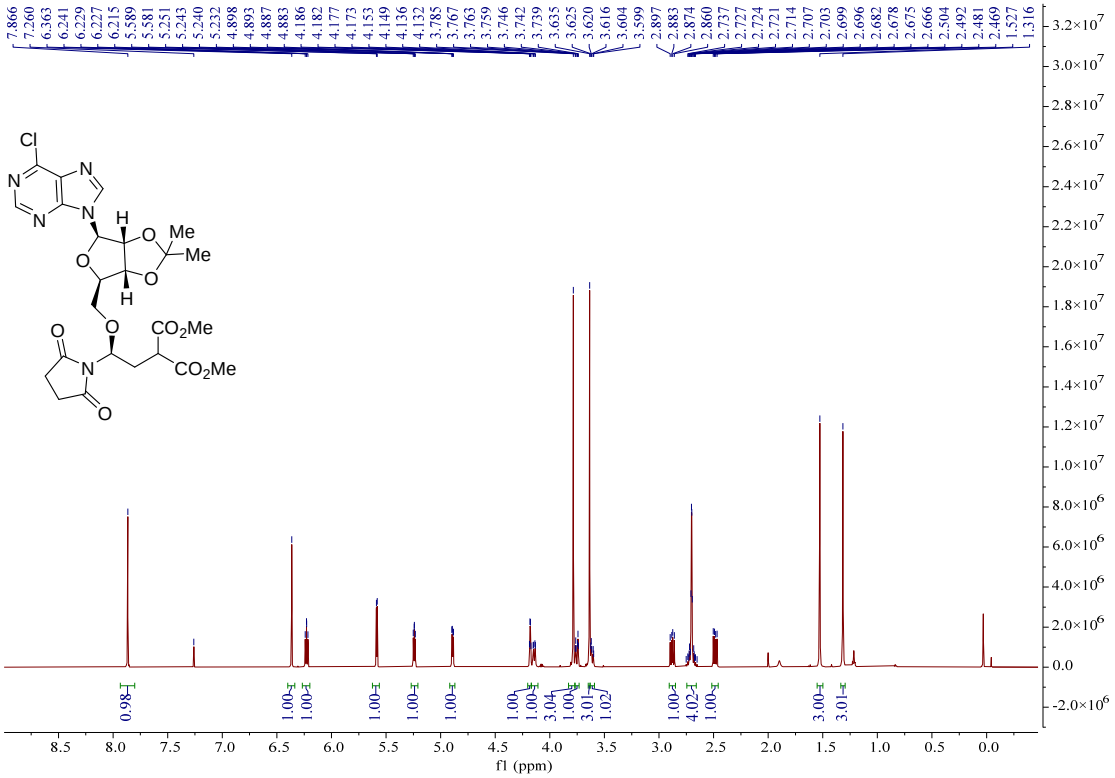
^{1}H NMR Spectrum of **3au'** (600 MHz, $CDCl_3$)



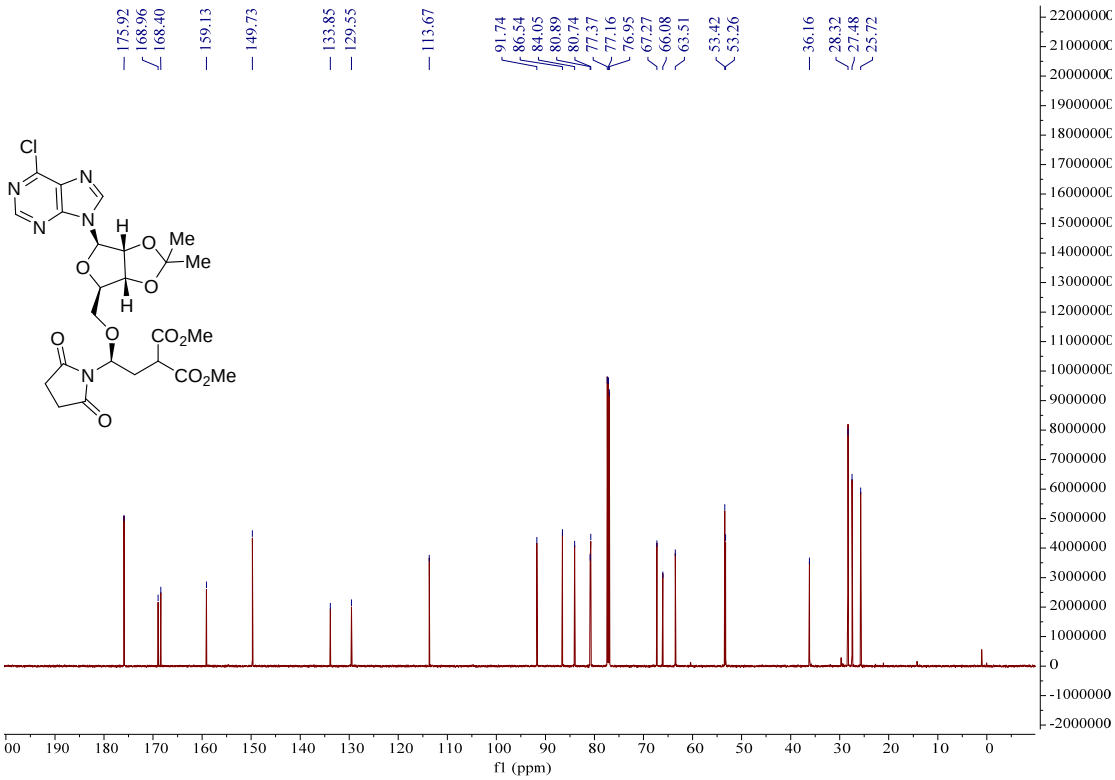
^{13}C NMR Spectrum of **3au'** (150 MHz, $CDCl_3$)



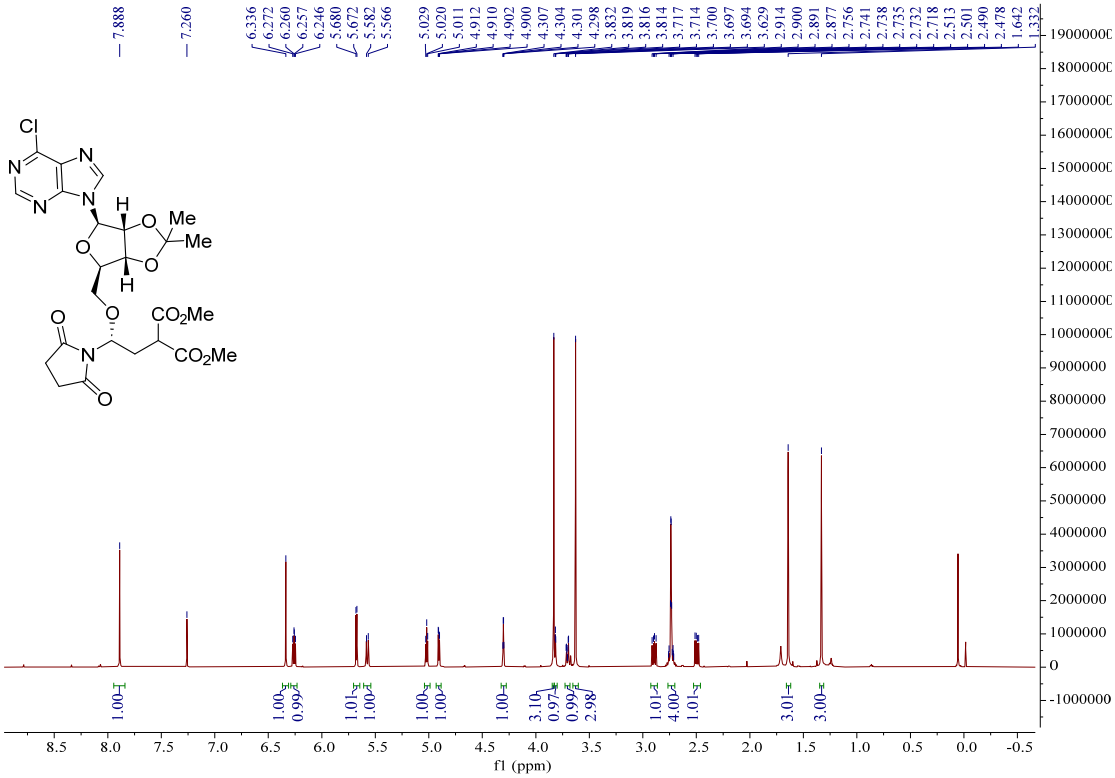
^{1}H NMR Spectrum of **3av** (600 MHz, $CDCl_3$)



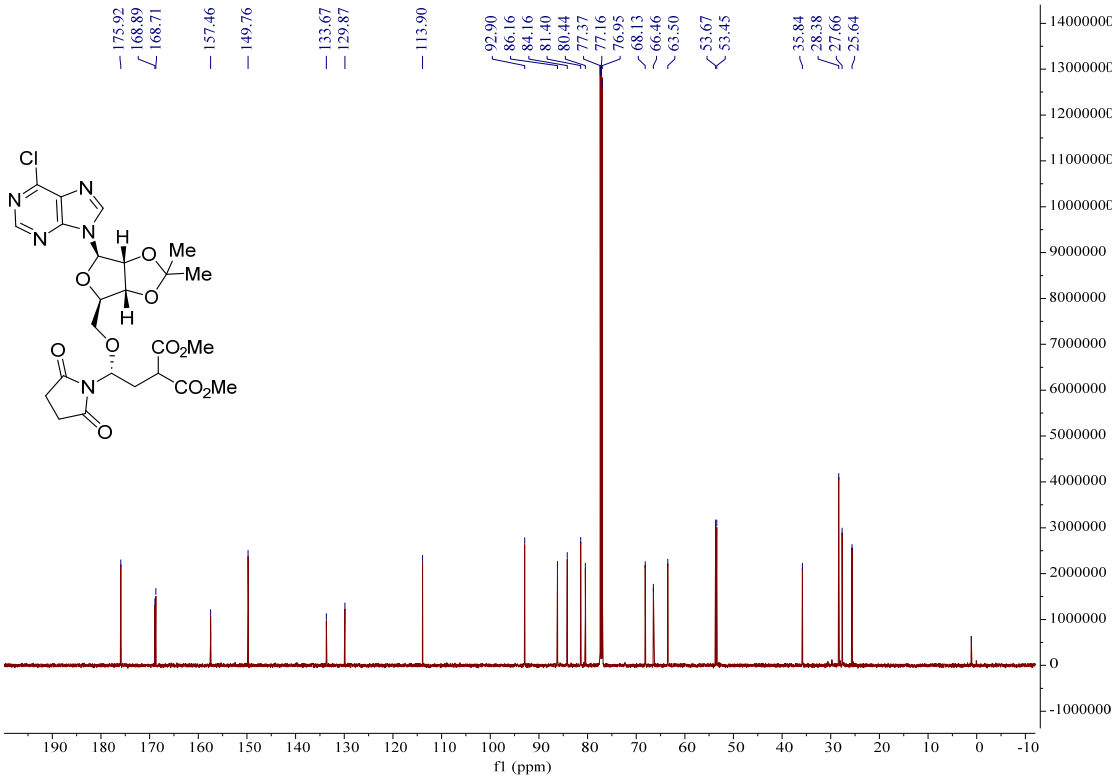
^{13}C NMR Spectrum of **3av** (150 MHz, $CDCl_3$)



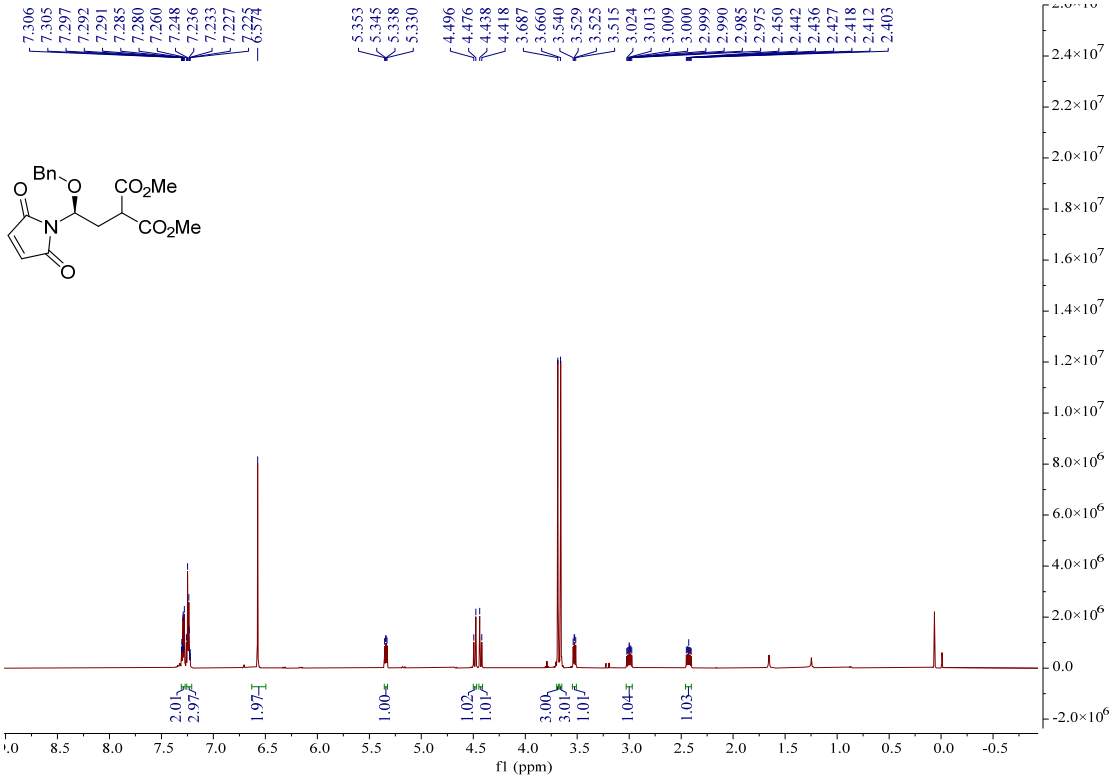
^{1}H NMR Spectrum of **3av'** (600 MHz, $CDCl_3$)



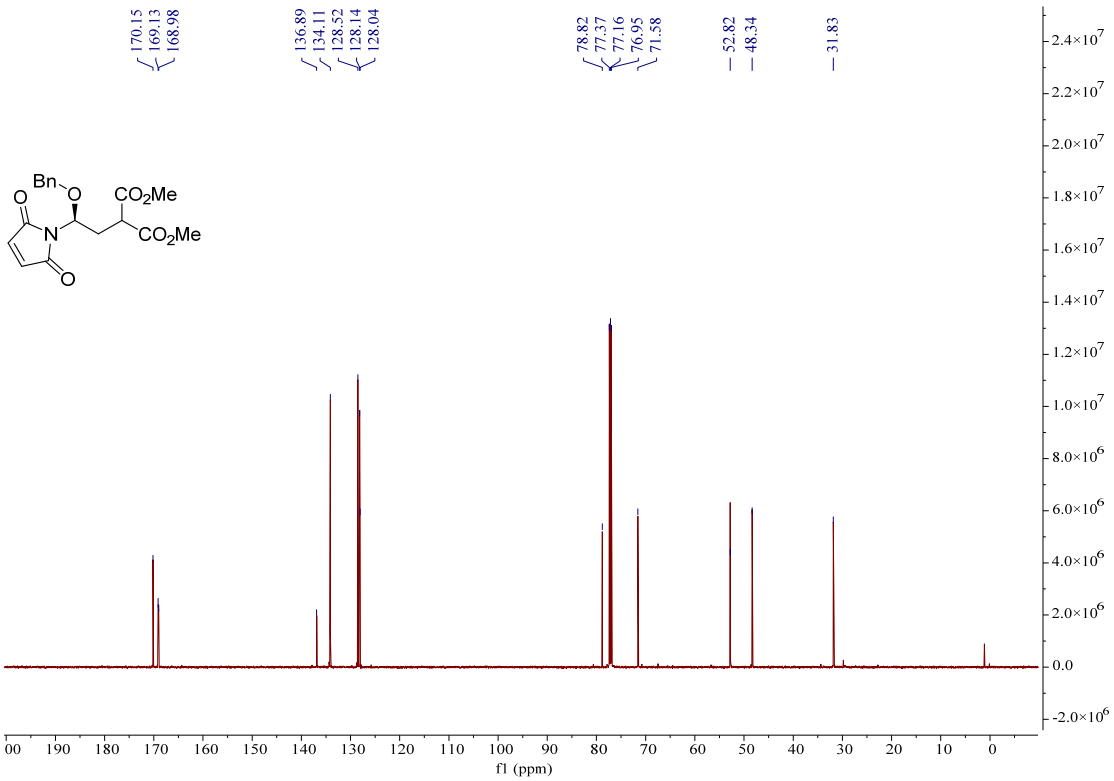
^{13}C NMR Spectrum of **3av'** (150 MHz, $CDCl_3$)



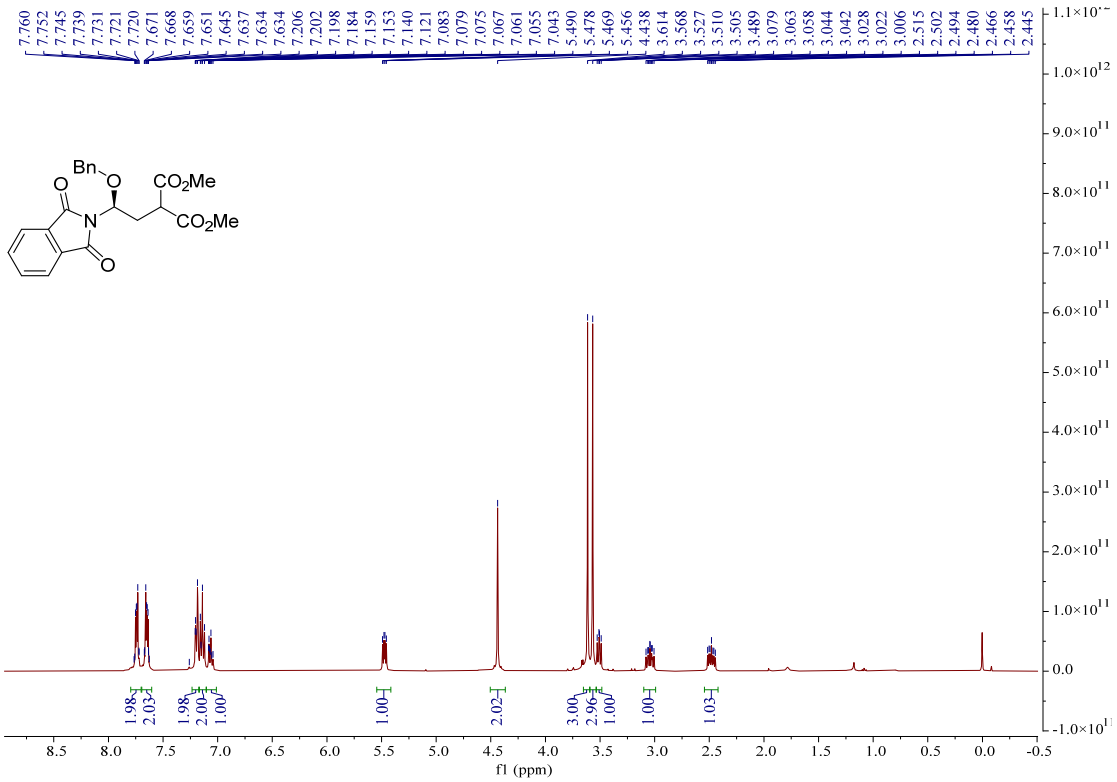
^{1}H NMR Spectrum of **3ba** (600 MHz, $CDCl_3$)



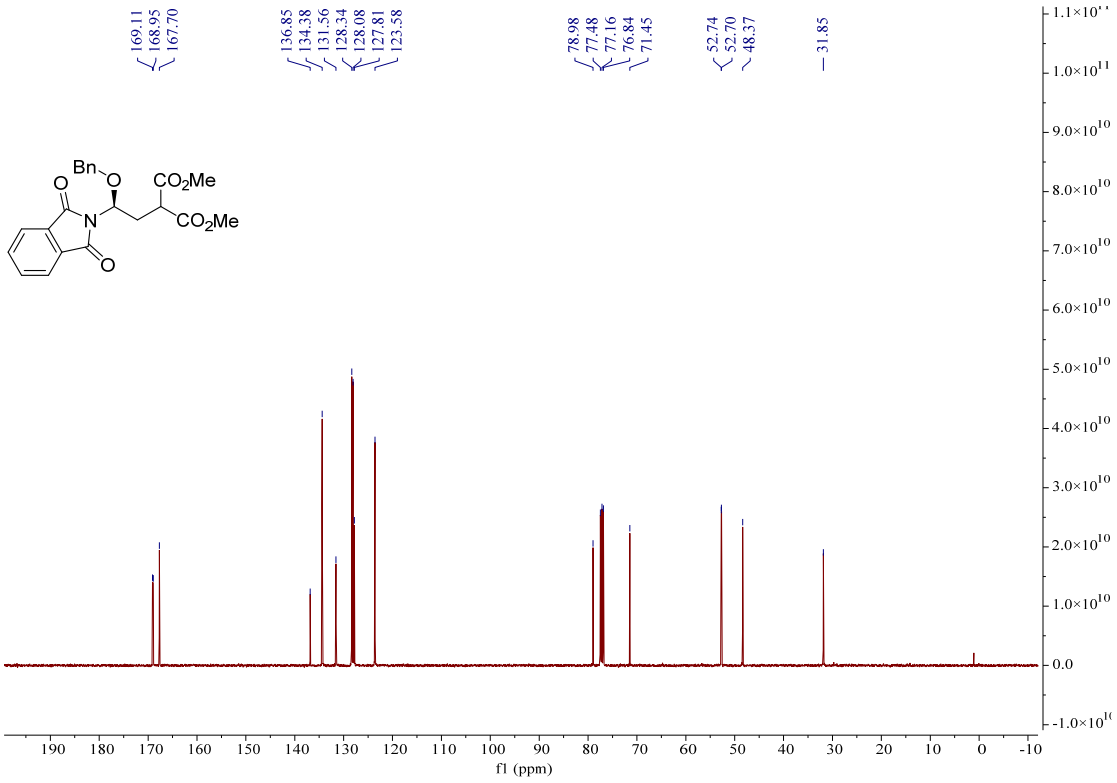
^{13}C NMR Spectrum of **3aw** (150 MHz, $CDCl_3$)



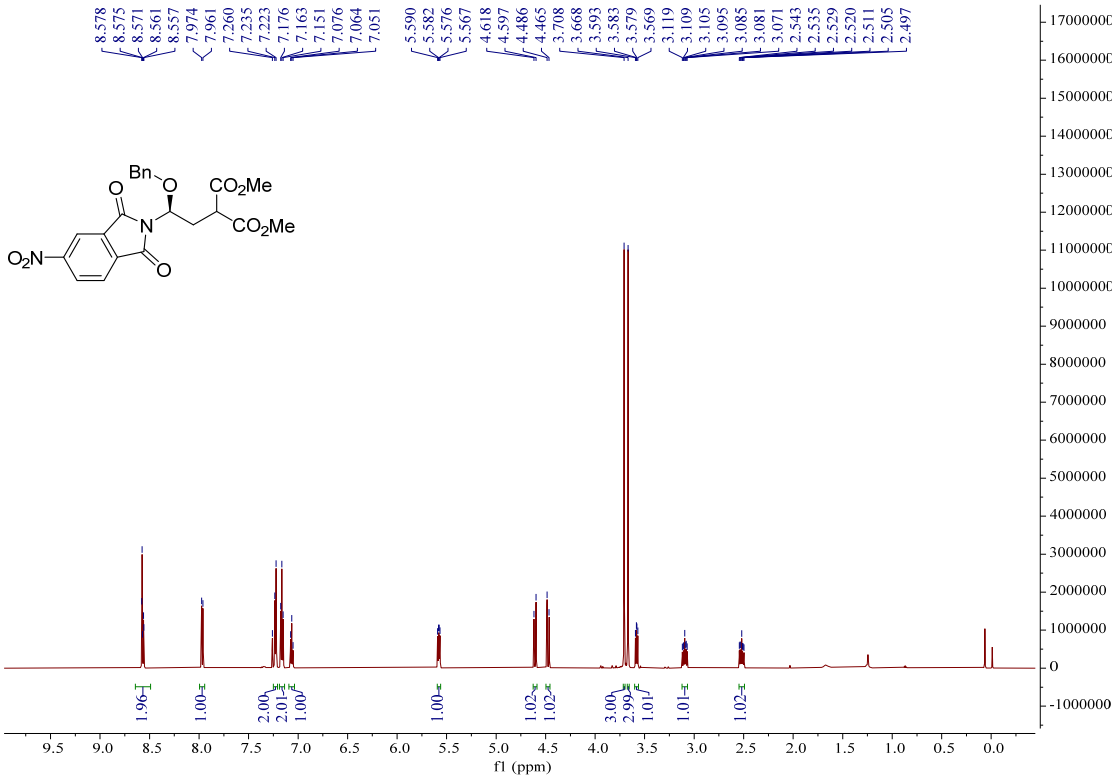
^{1}H NMR Spectrum of **3ca** (400 MHz, $CDCl_3$)



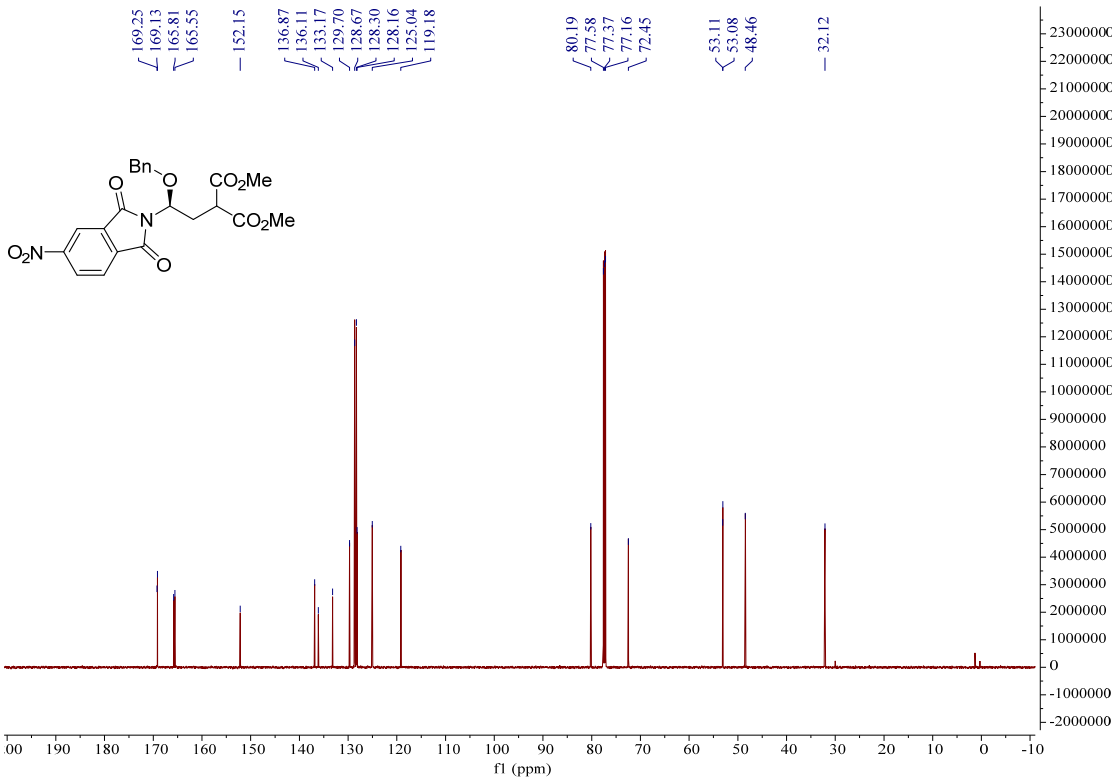
^{13}C NMR Spectrum of **3ca** (100 MHz, $CDCl_3$)



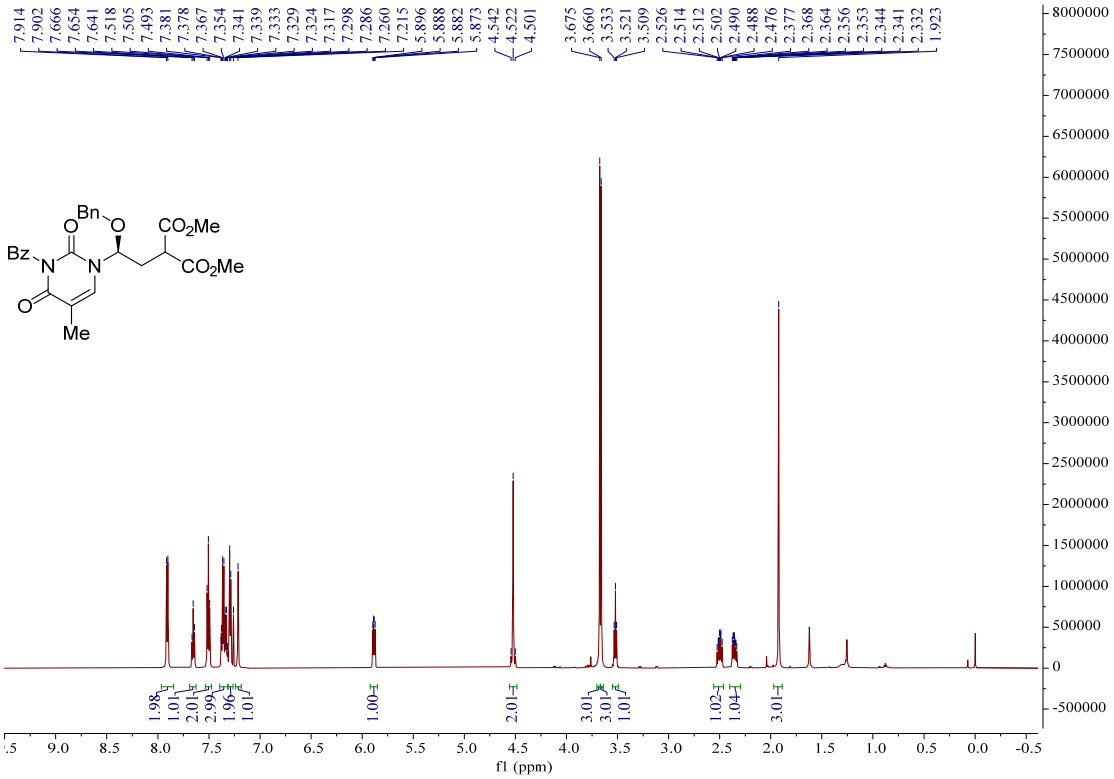
^{1}H NMR Spectrum of **3da** (600 MHz, $CDCl_3$)



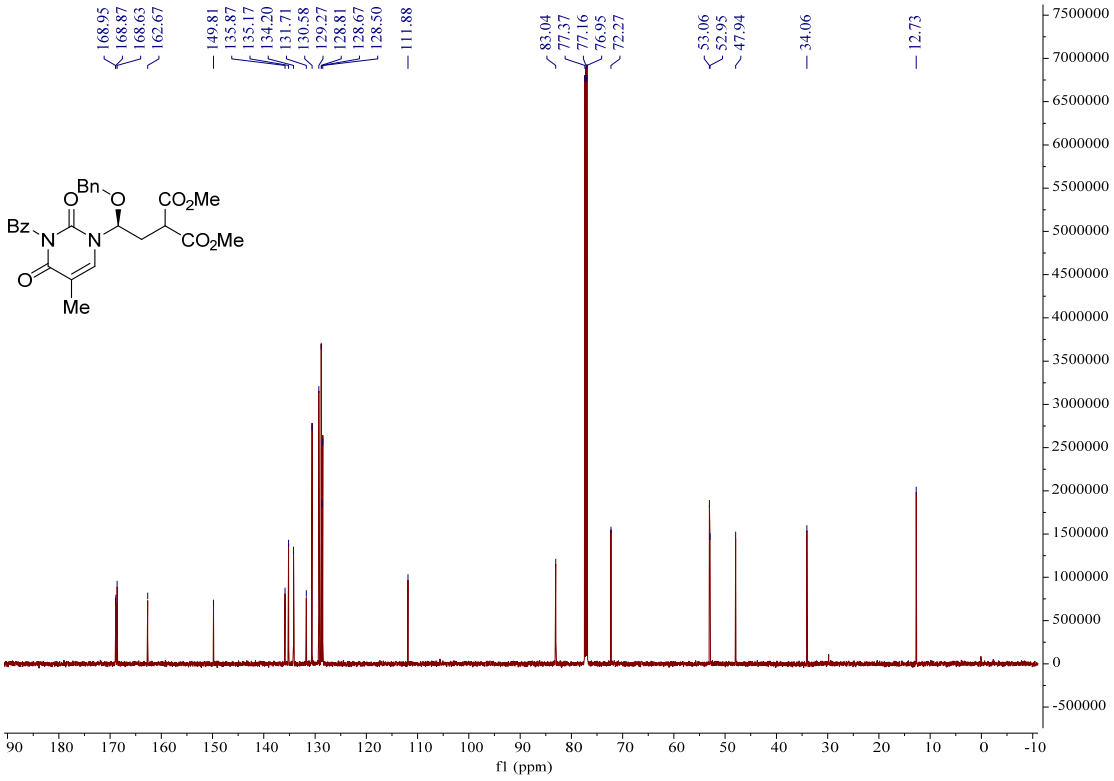
^{13}C NMR Spectrum of **3da** (150 MHz, $CDCl_3$)



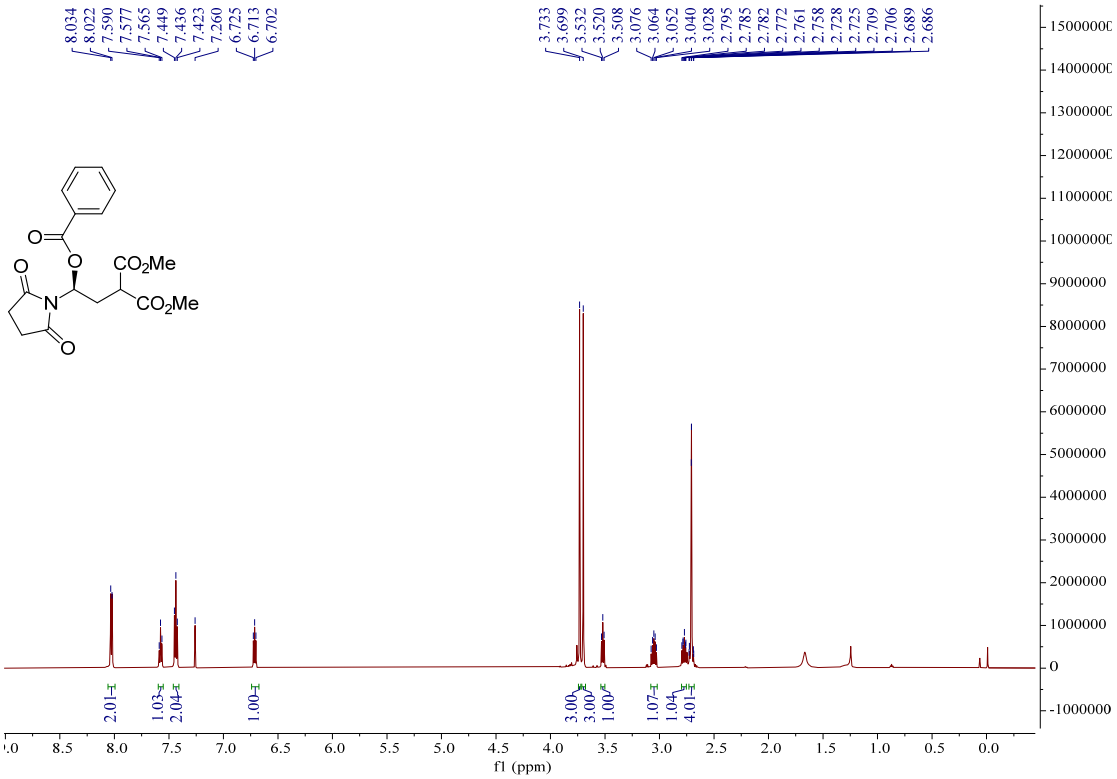
^{1}H NMR Spectrum of **3ea** (600 MHz, $CDCl_3$)



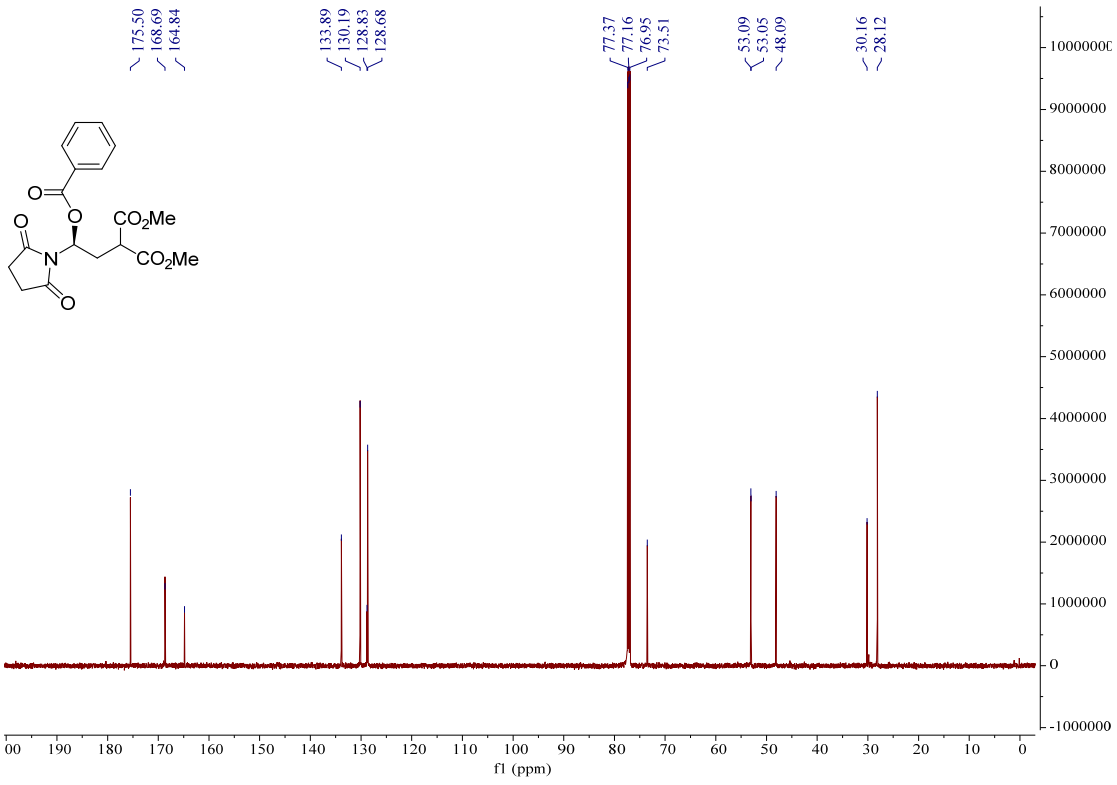
^{13}C NMR Spectrum of **3ea** (150 MHz, $CDCl_3$)



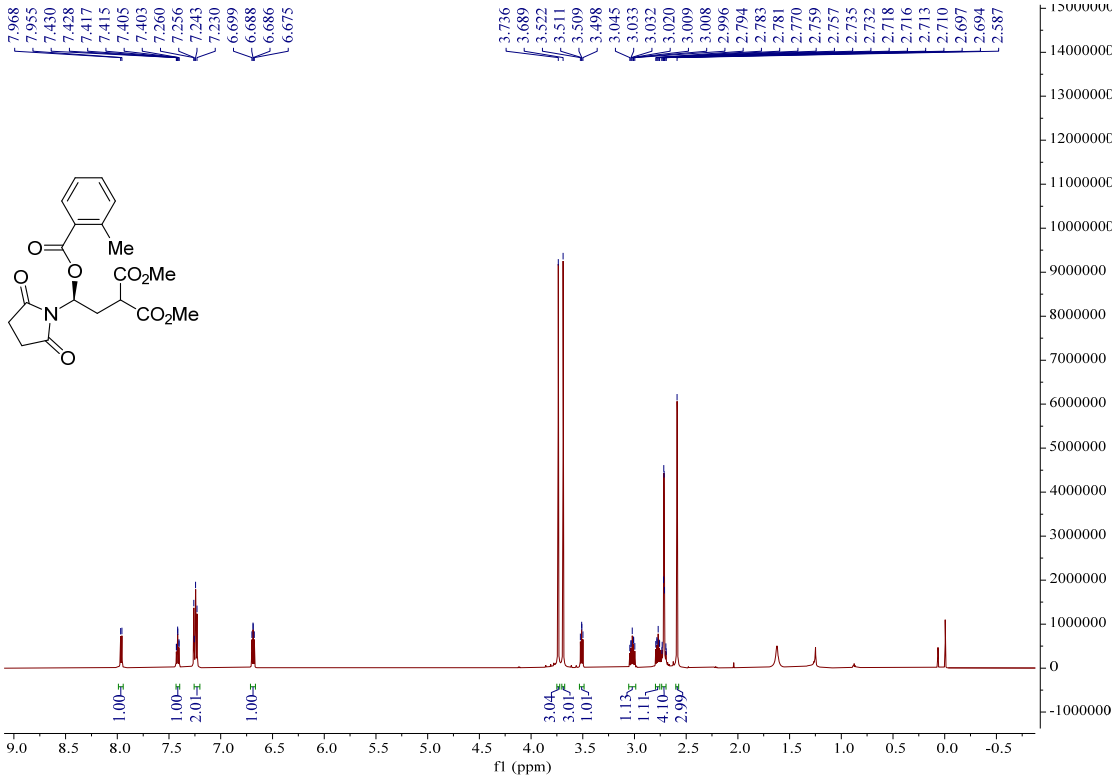
^{1}H NMR Spectrum of **5aa** (600 MHz, $CDCl_3$)



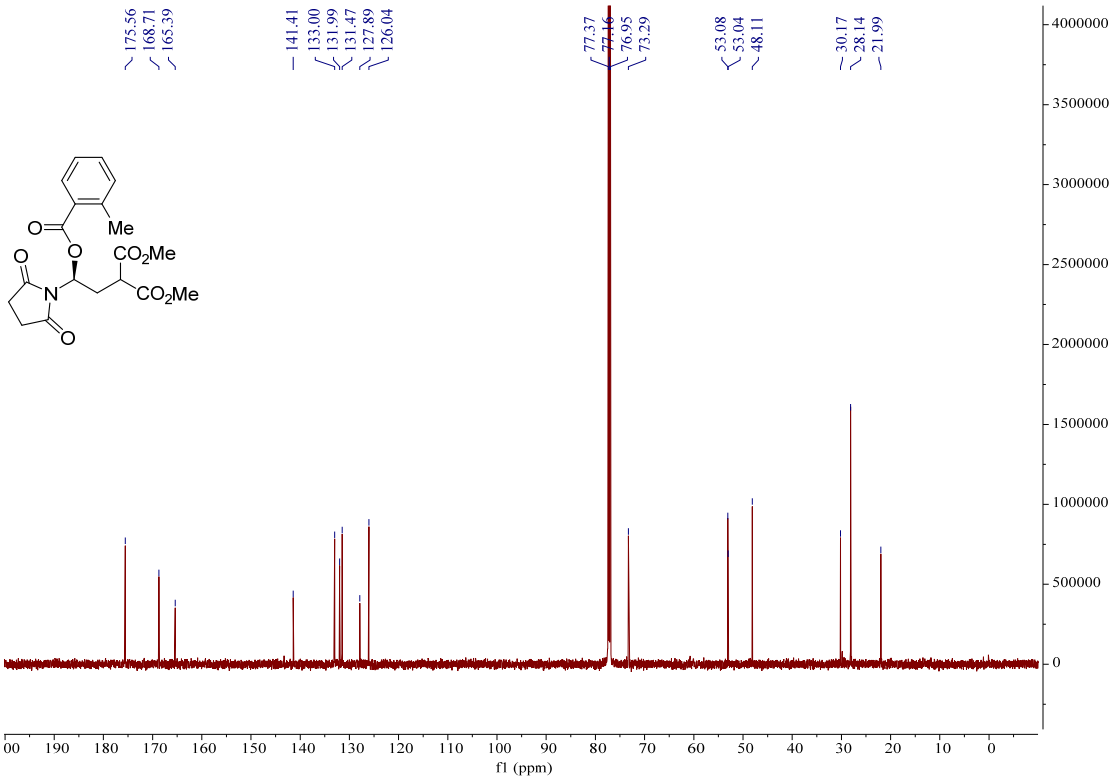
^{13}C NMR Spectrum of **5aa** (150 MHz, $CDCl_3$)



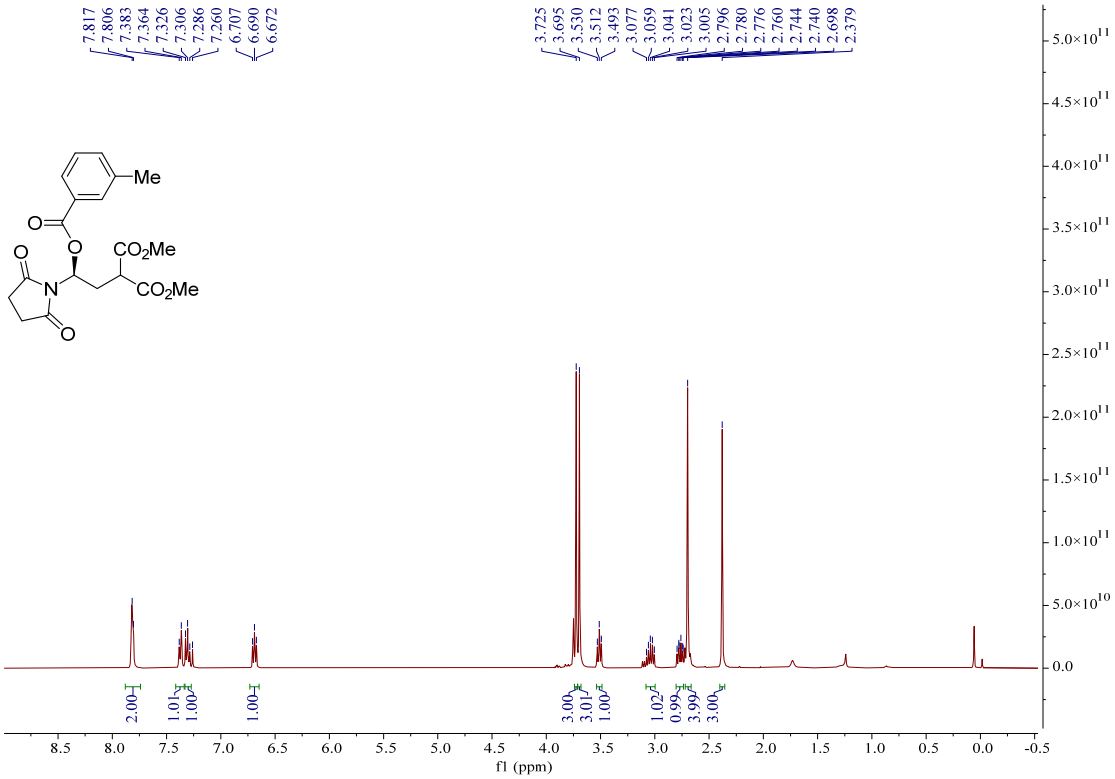
^{1}H NMR Spectrum of **5ab** (600 MHz, $CDCl_3$)



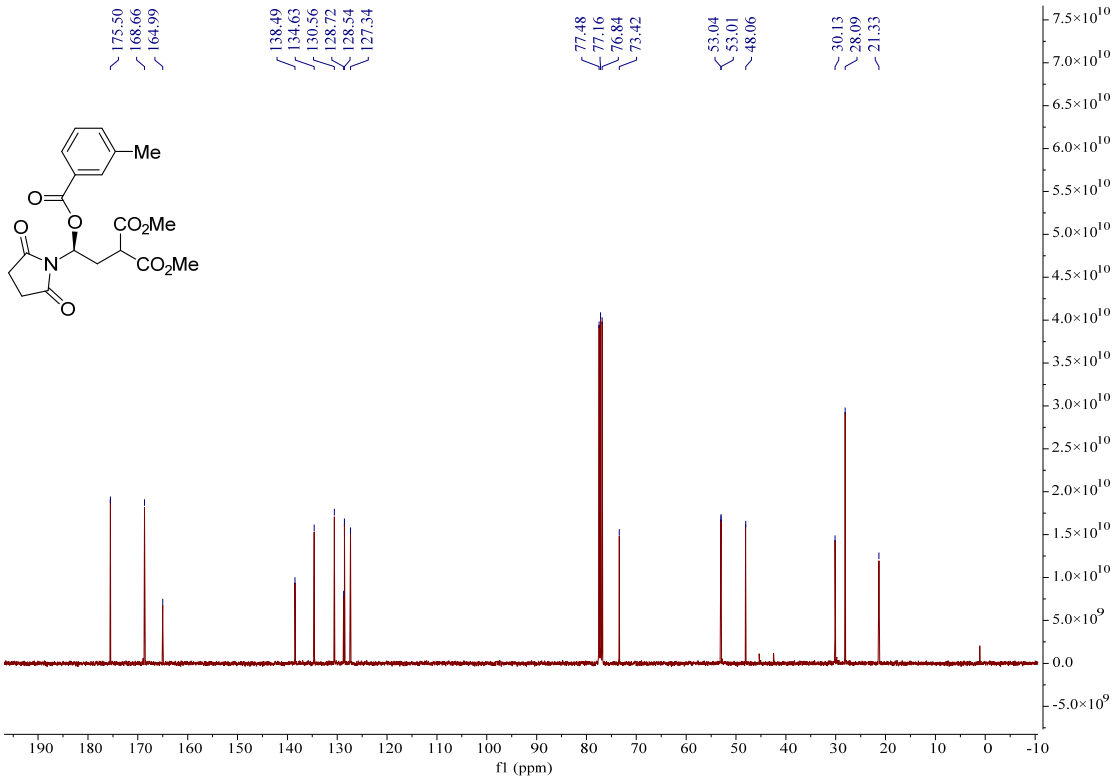
^{13}C NMR Spectrum of **5ab** (150 MHz, $CDCl_3$)



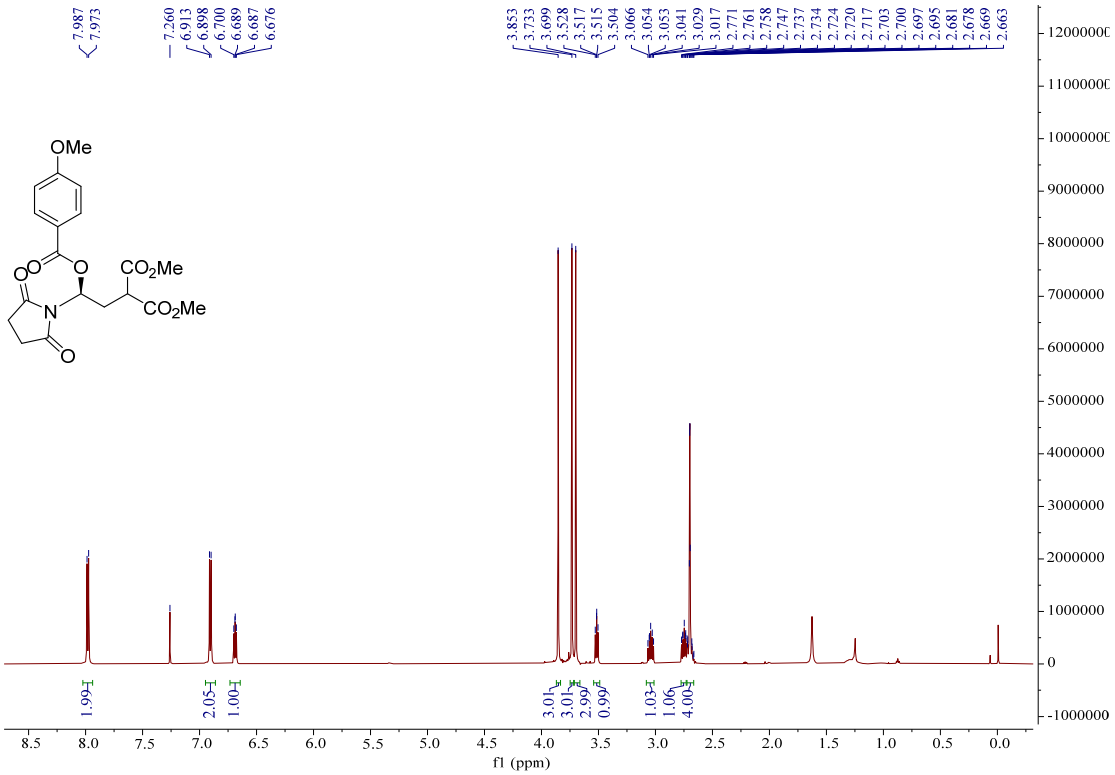
^{1}H NMR Spectrum of **5ac** (400 MHz, $CDCl_3$)



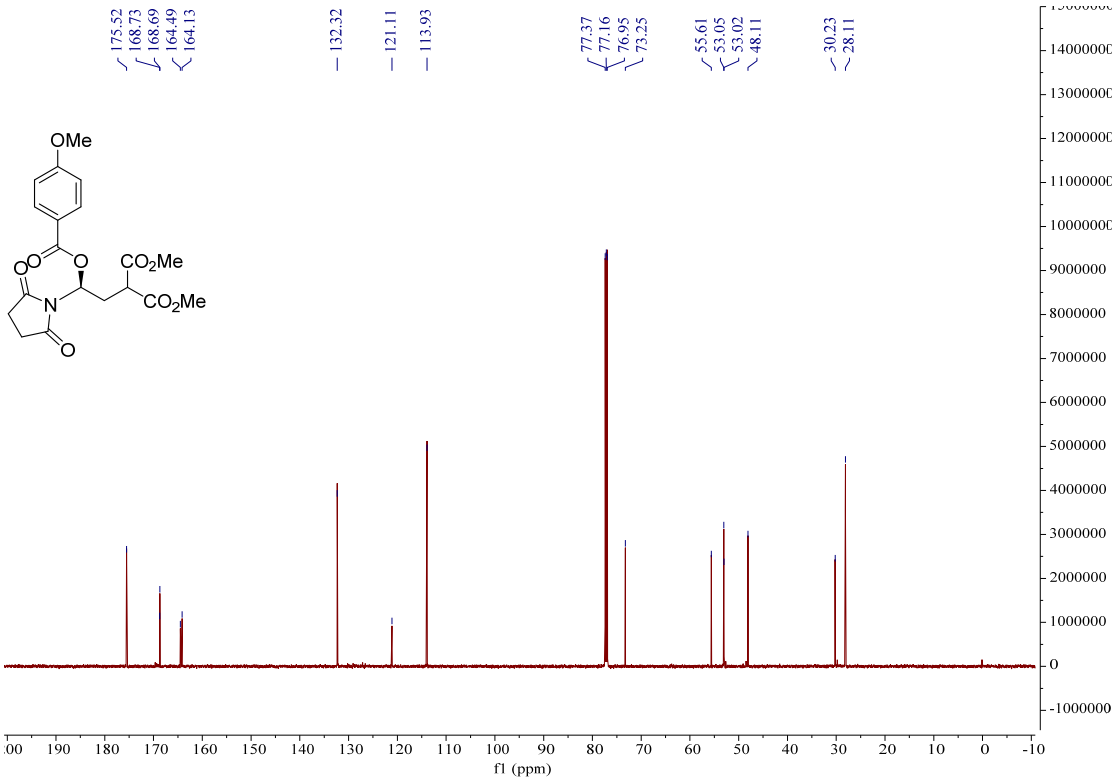
^{13}C NMR Spectrum of **5ac** (100 MHz, $CDCl_3$)



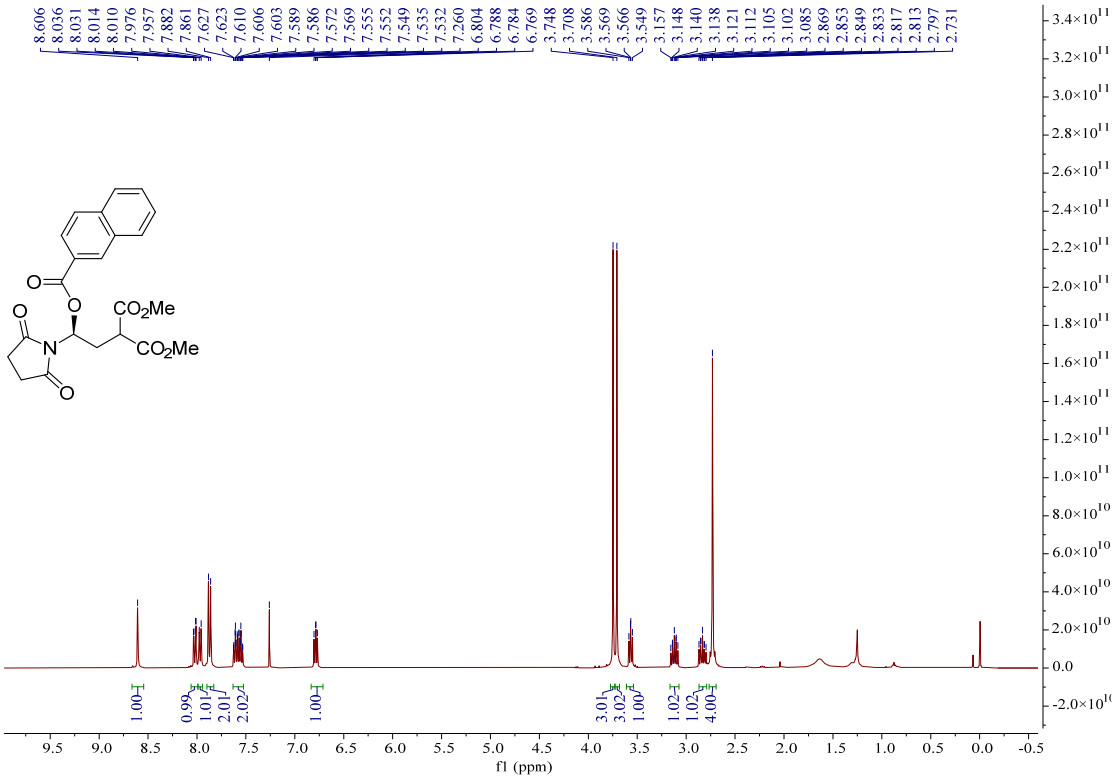
^{1}H NMR Spectrum of **5ad** (600 MHz, $CDCl_3$)



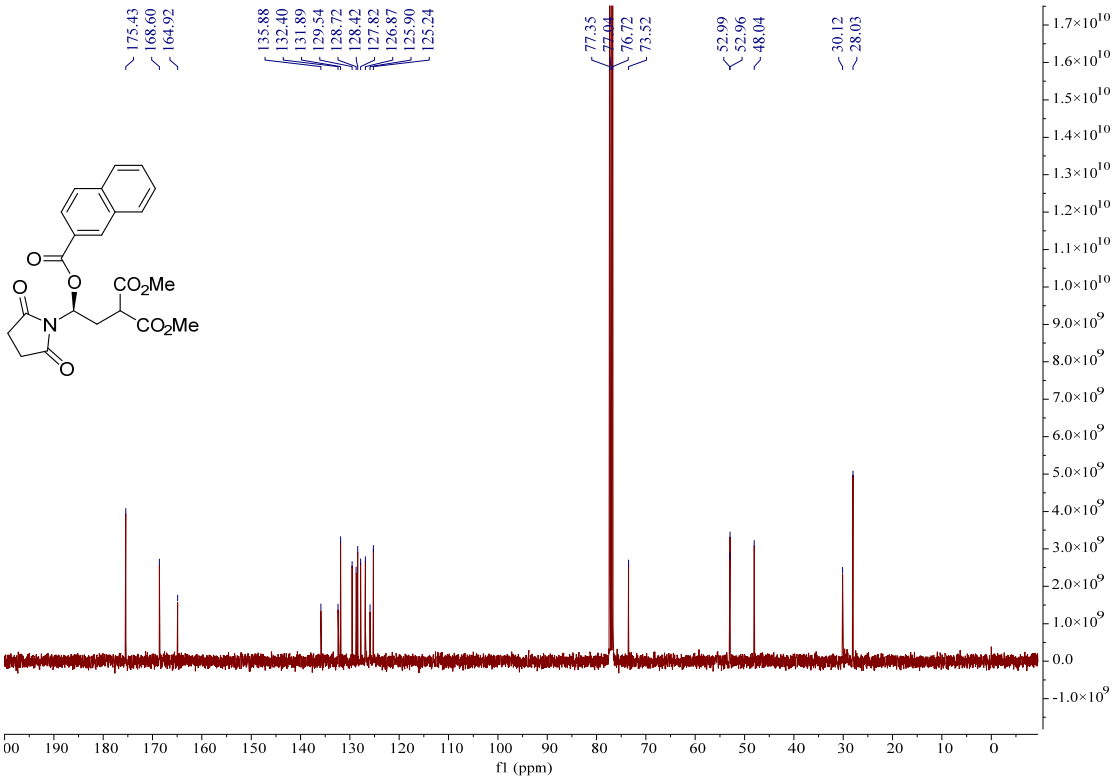
^{13}C NMR Spectrum of **5ad** (150 MHz, $CDCl_3$)



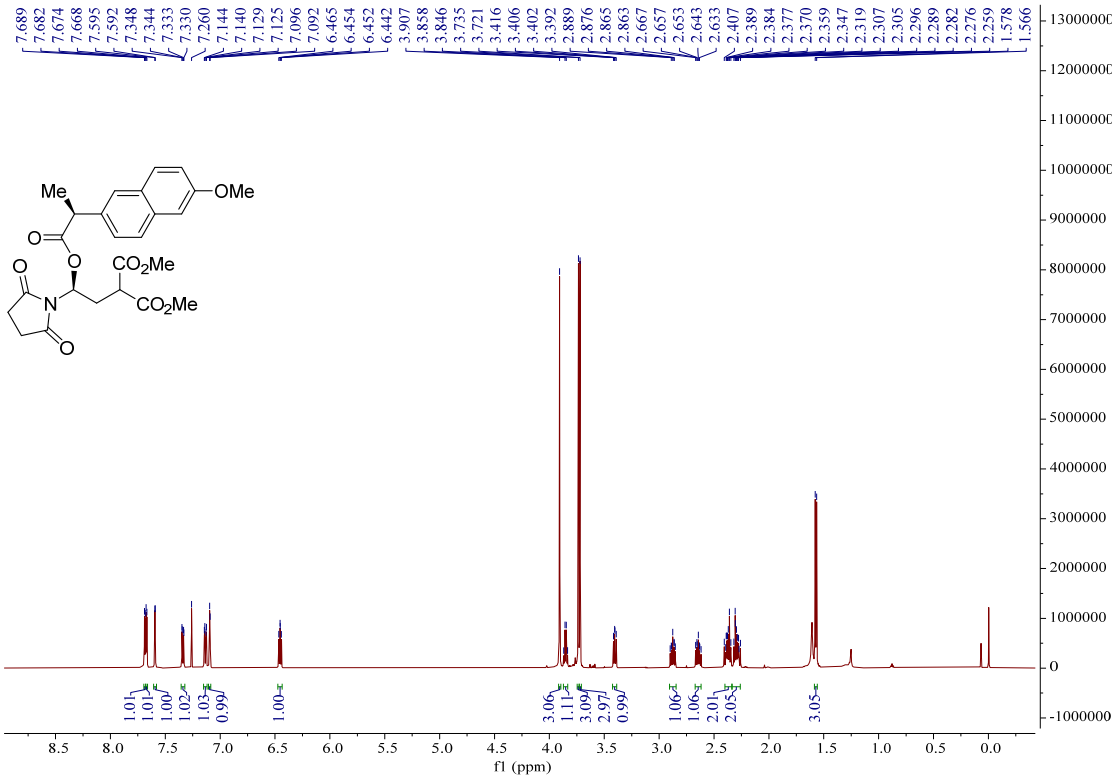
^{1}H NMR Spectrum of **5ae** (400 MHz, $CDCl_3$)



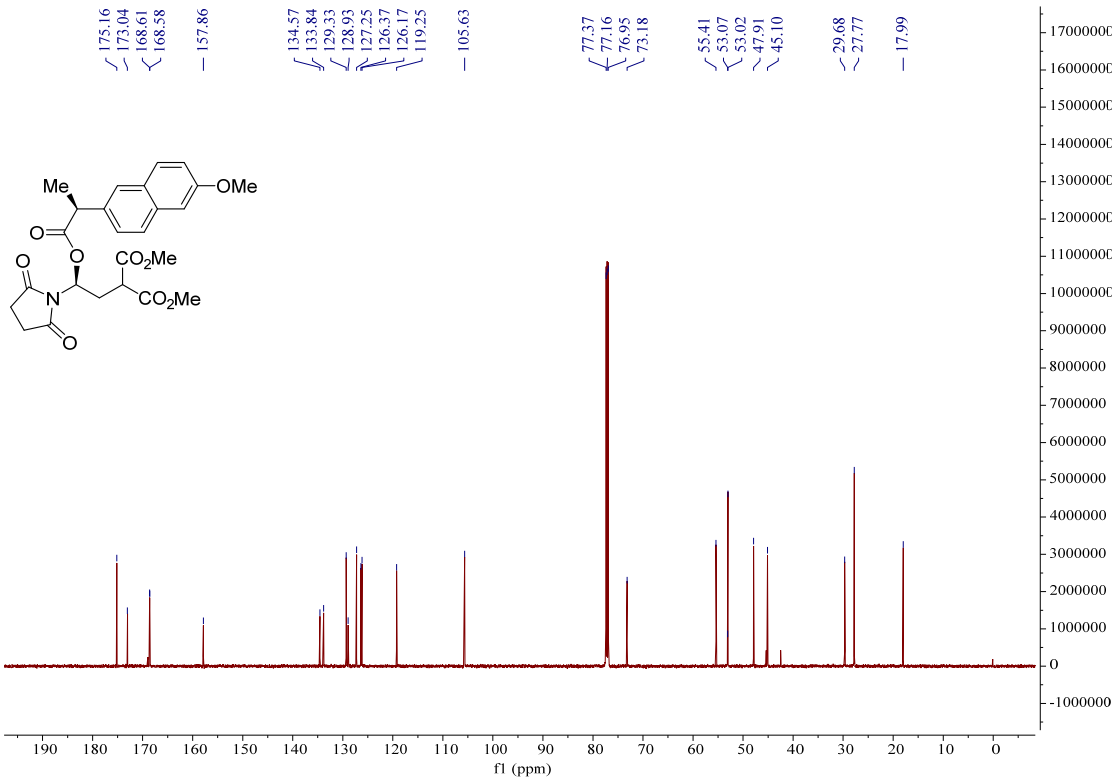
^{13}C NMR Spectrum of **5ae** (100 MHz, $CDCl_3$)



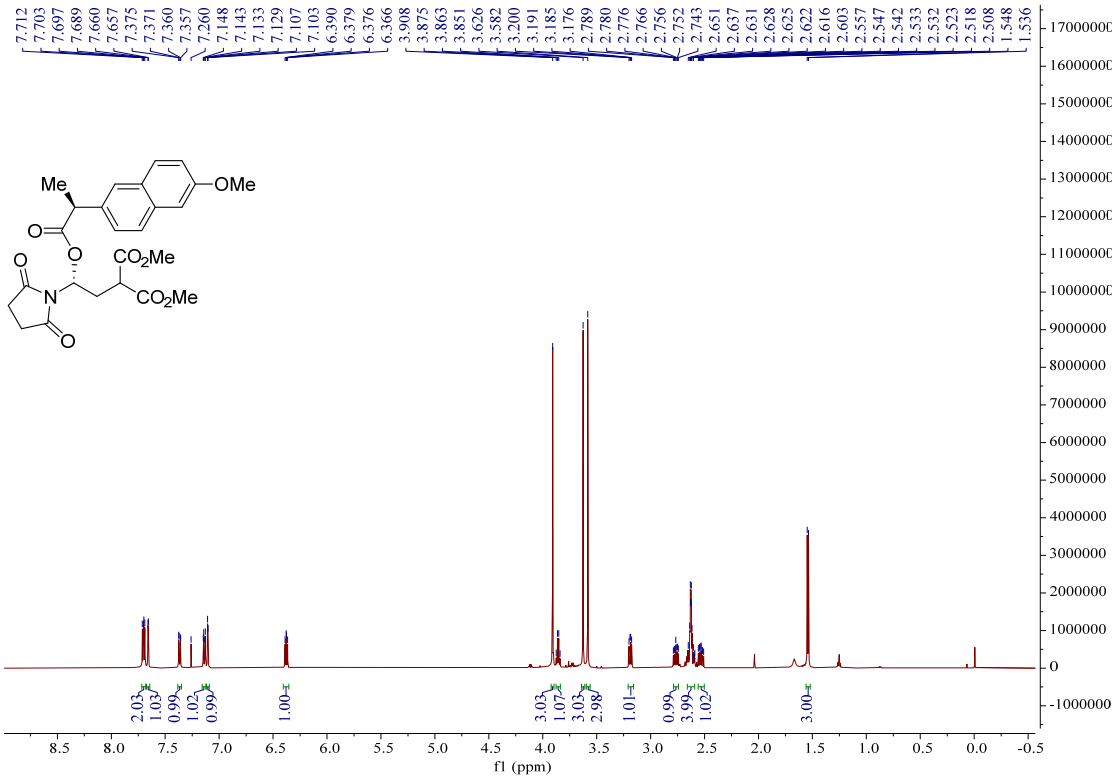
^{1}H NMR Spectrum of **5af** (600 MHz, $CDCl_3$)



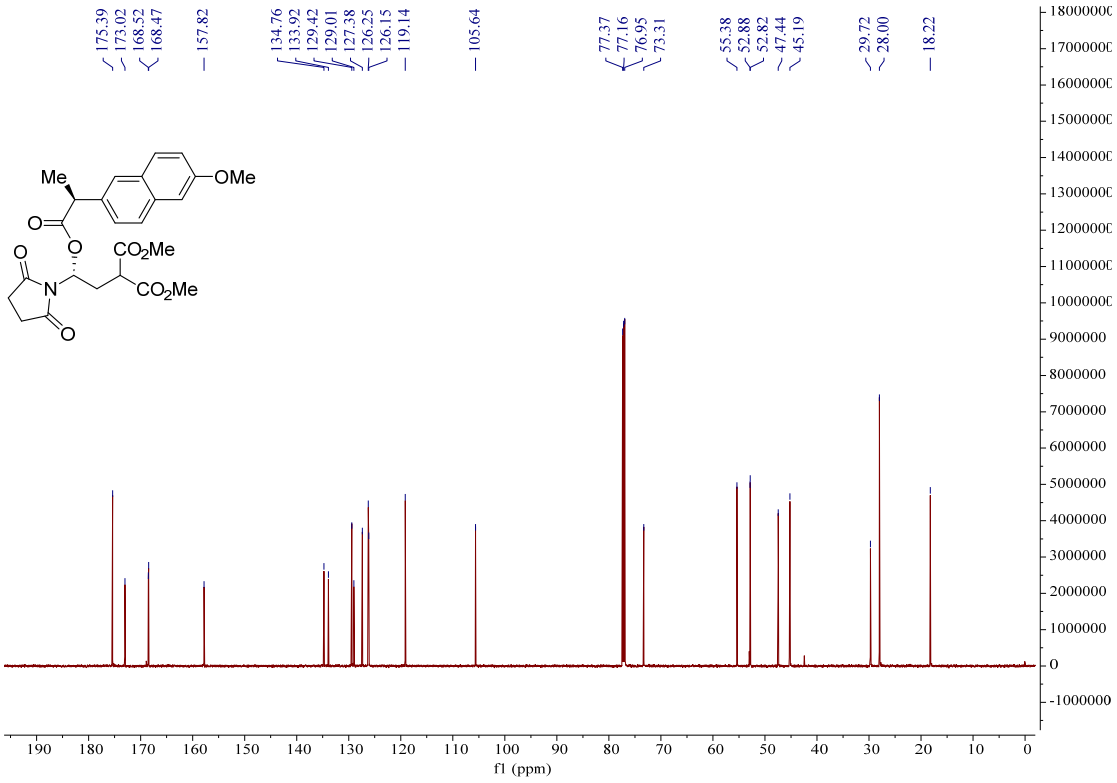
^{13}C NMR Spectrum of **5af** (150 MHz, $CDCl_3$)



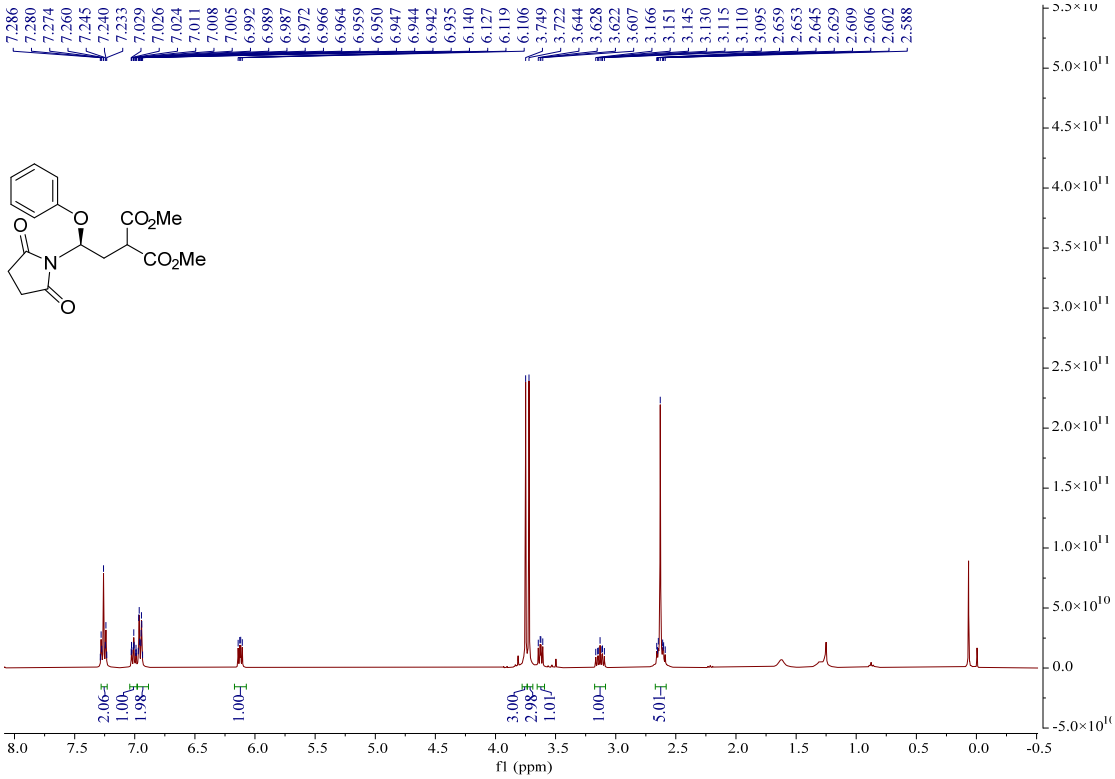
^{1}H NMR Spectrum of **5af'** (600 MHz, $CDCl_3$)



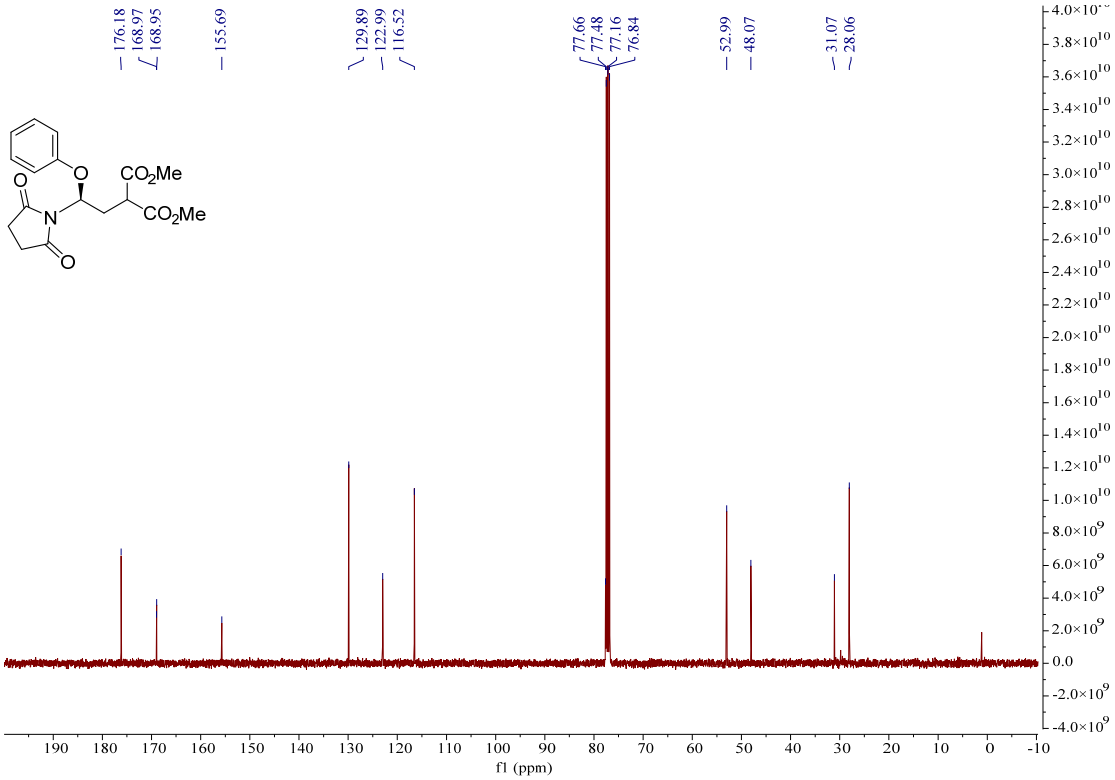
^{13}C NMR Spectrum of **5af'** (150 MHz, $CDCl_3$)



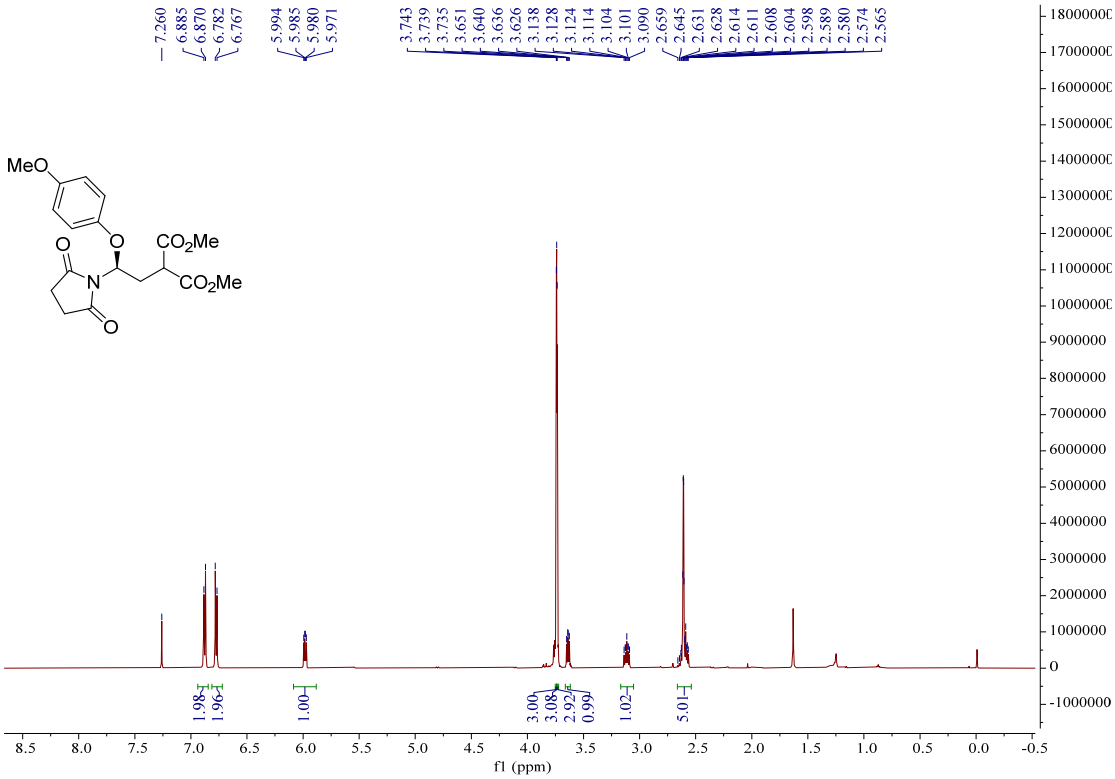
^{1}H NMR Spectrum of **7aa** (400 MHz, $CDCl_3$)



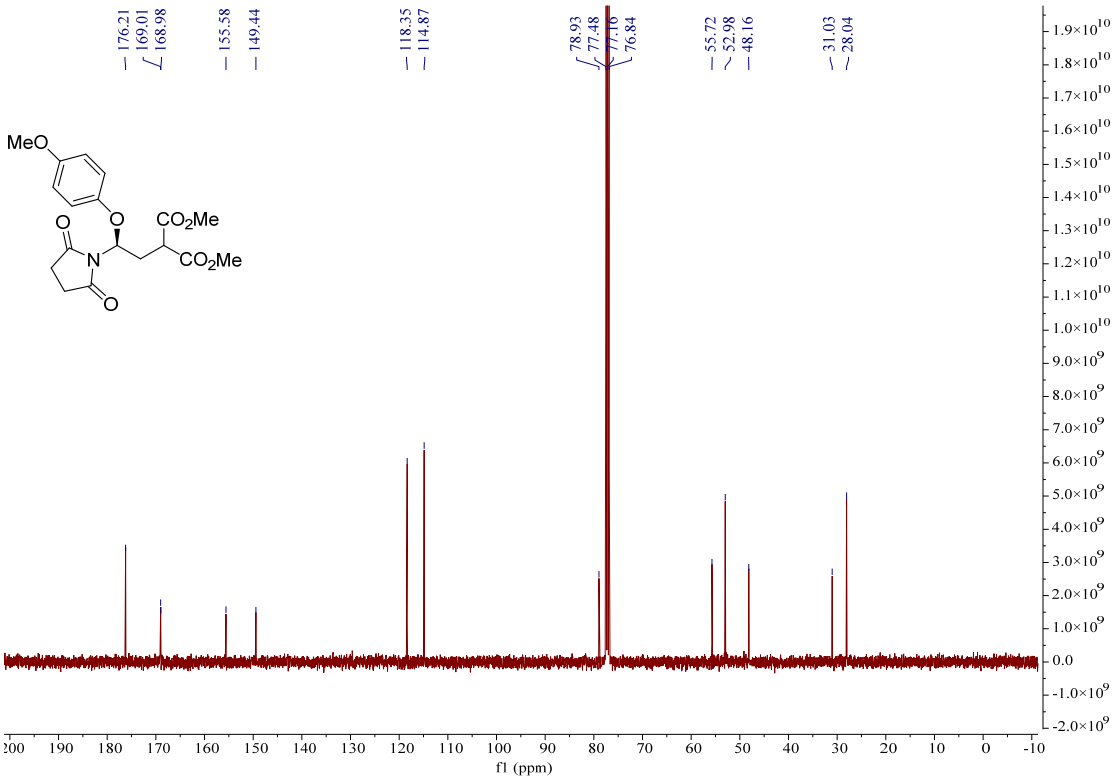
^{13}C NMR Spectrum of **7aa** (100 MHz, $CDCl_3$)



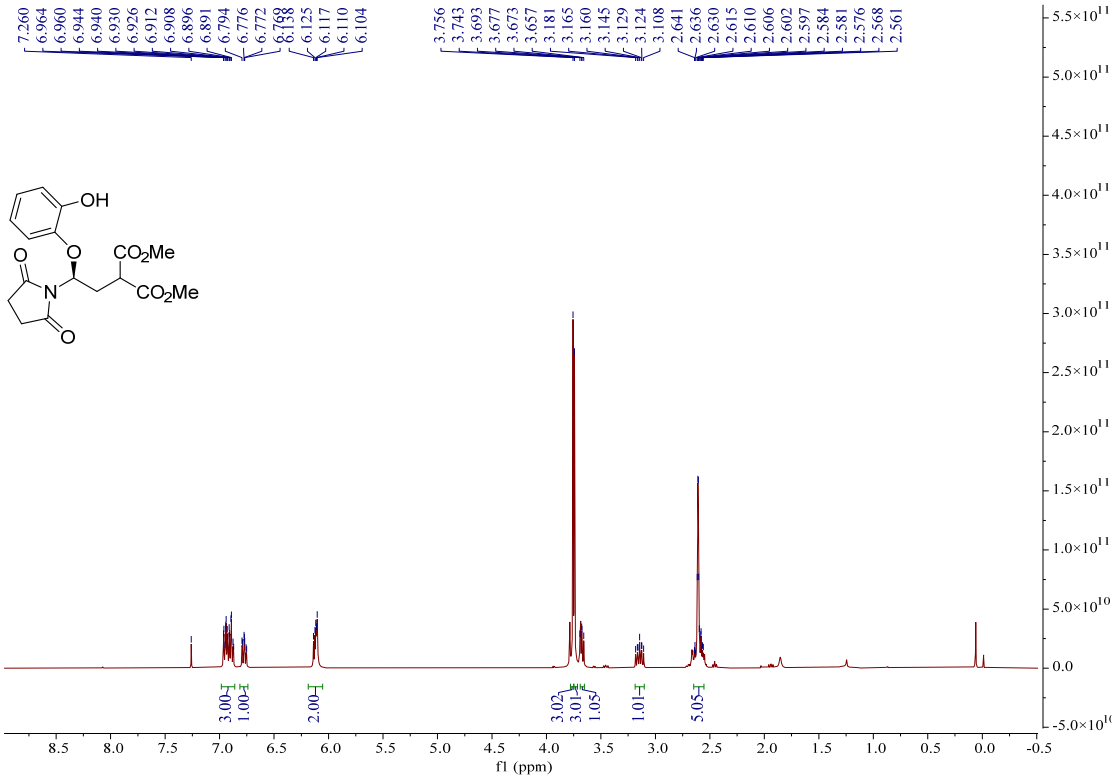
^{1}H NMR Spectrum of **7ab** (600 MHz, $CDCl_3$)



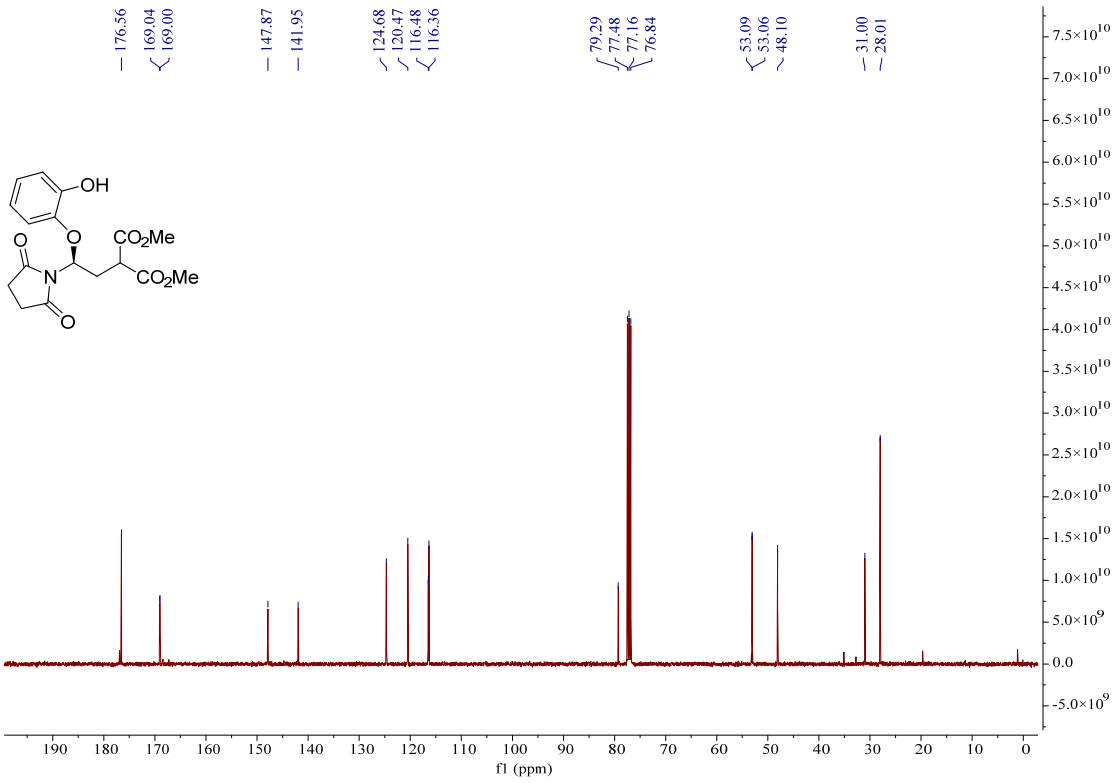
^{13}C NMR Spectrum of **7ab** (150 MHz, $CDCl_3$)



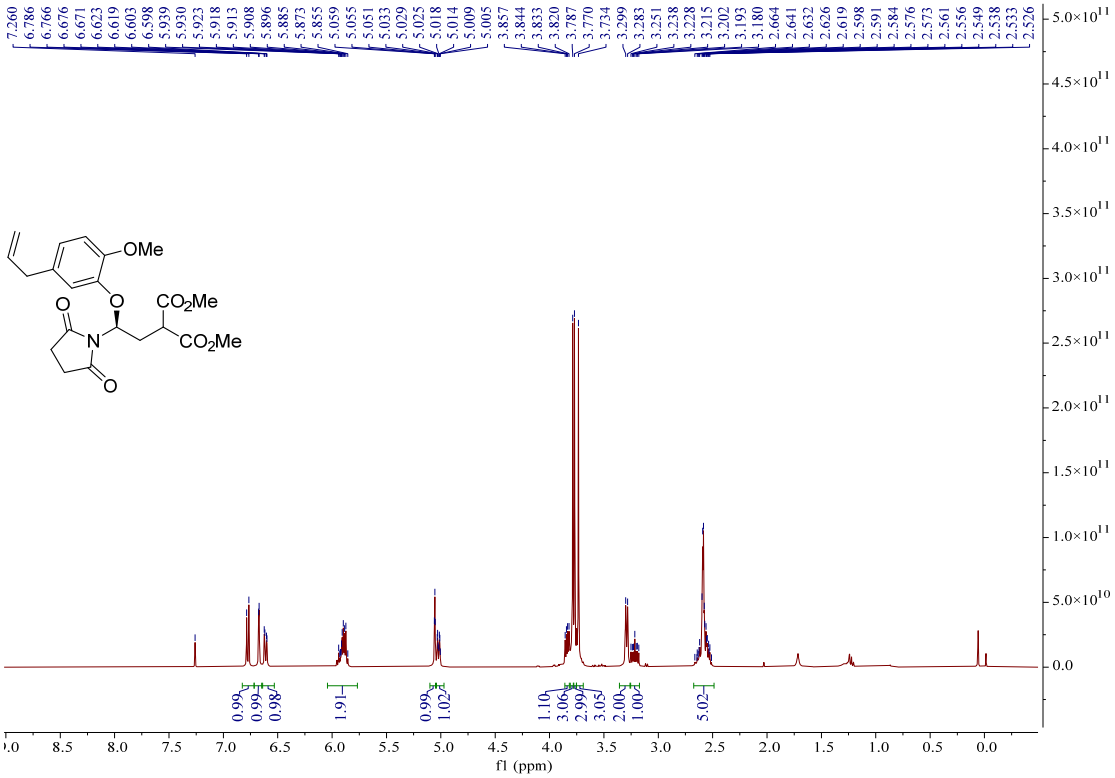
^{1}H NMR Spectrum of **7ac** (400 MHz, $CDCl_3$)



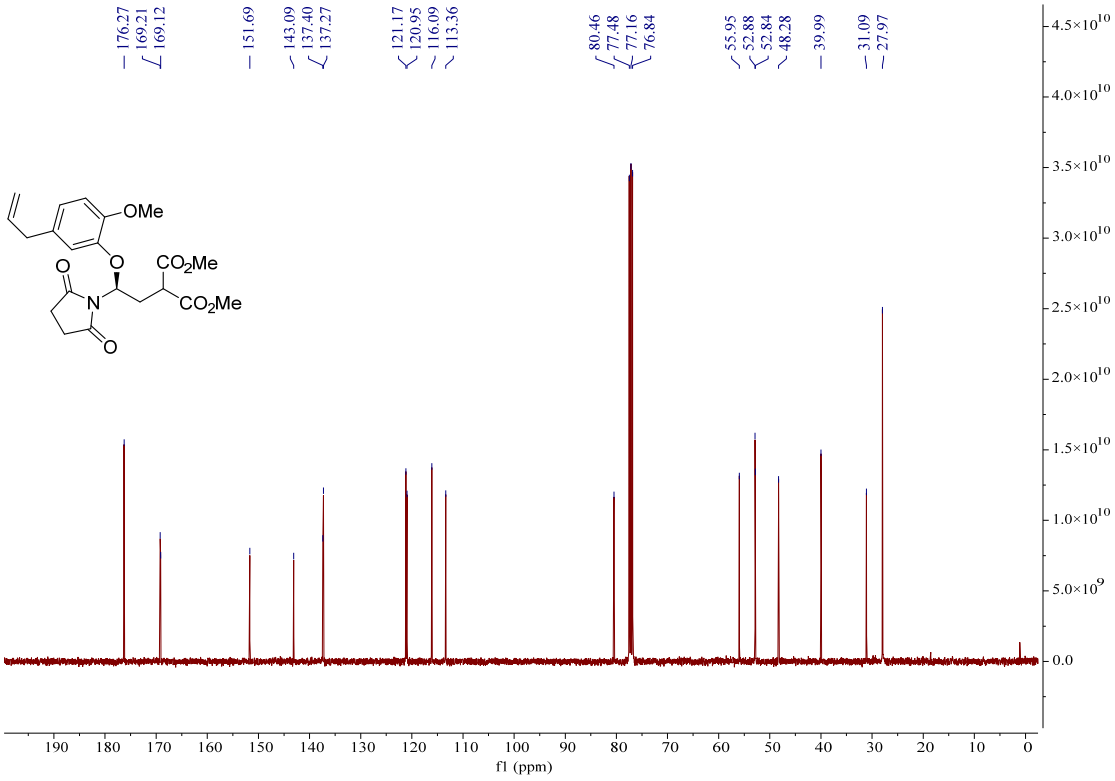
^{13}C NMR Spectrum of **7ac** (100 MHz, $CDCl_3$)



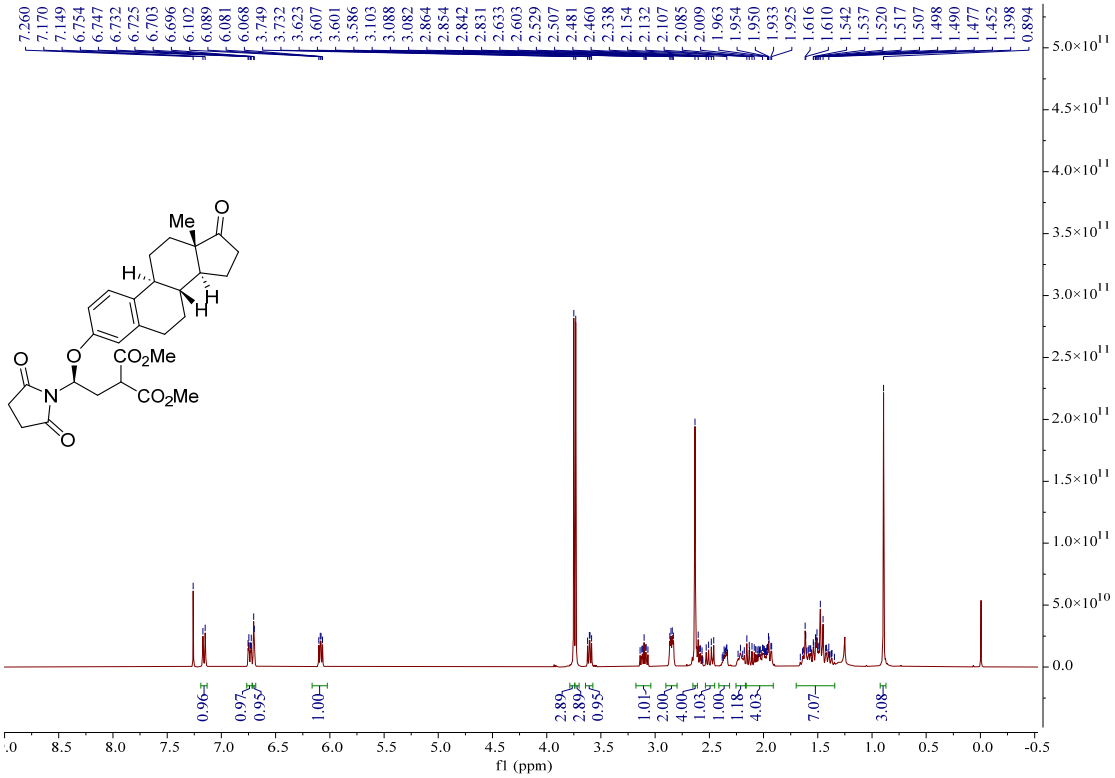
^{1}H NMR Spectrum of **7ad** (400 MHz, $CDCl_3$)



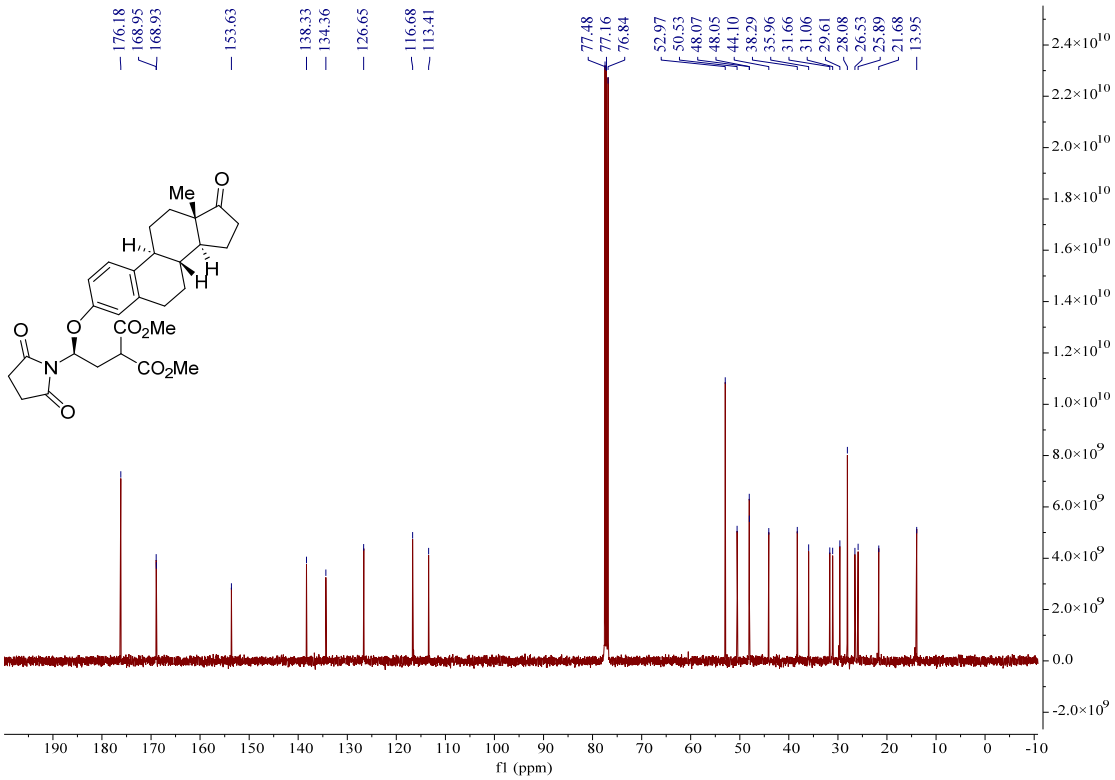
^{13}C NMR Spectrum of **7ad** (100 MHz, $CDCl_3$)



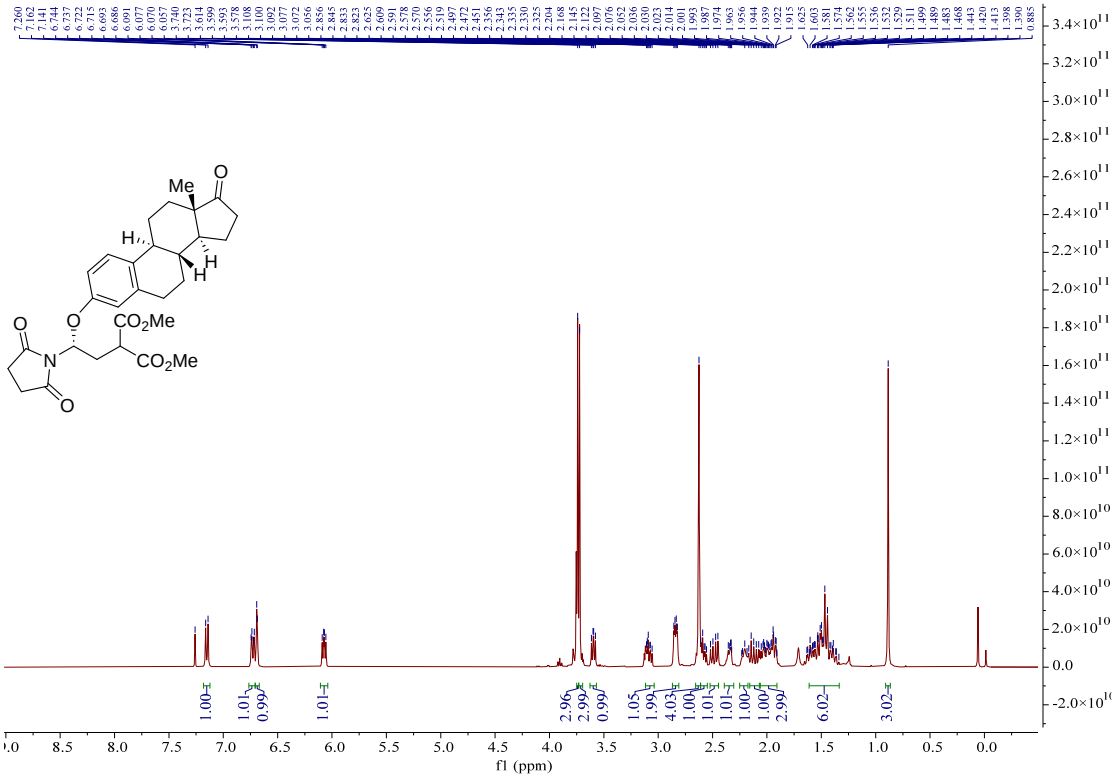
^{1}H NMR Spectrum of **7ae** (400 MHz, $CDCl_3$)



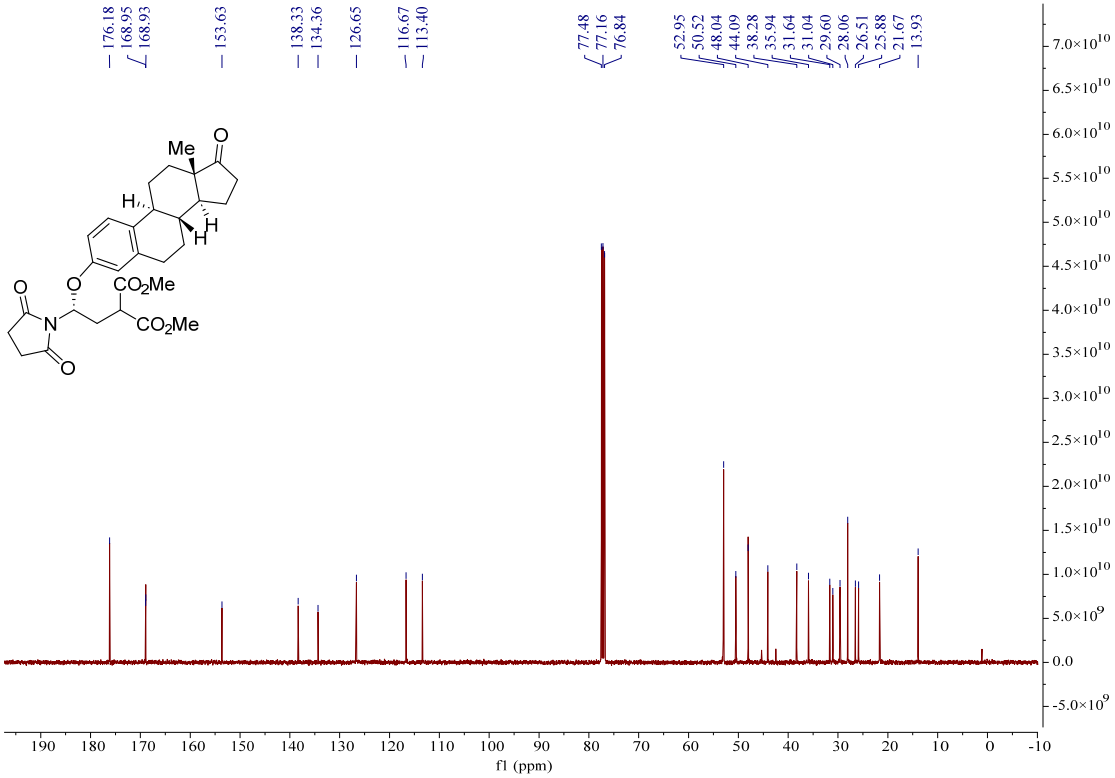
^{13}C NMR Spectrum of **7ae** (100 MHz, $CDCl_3$)



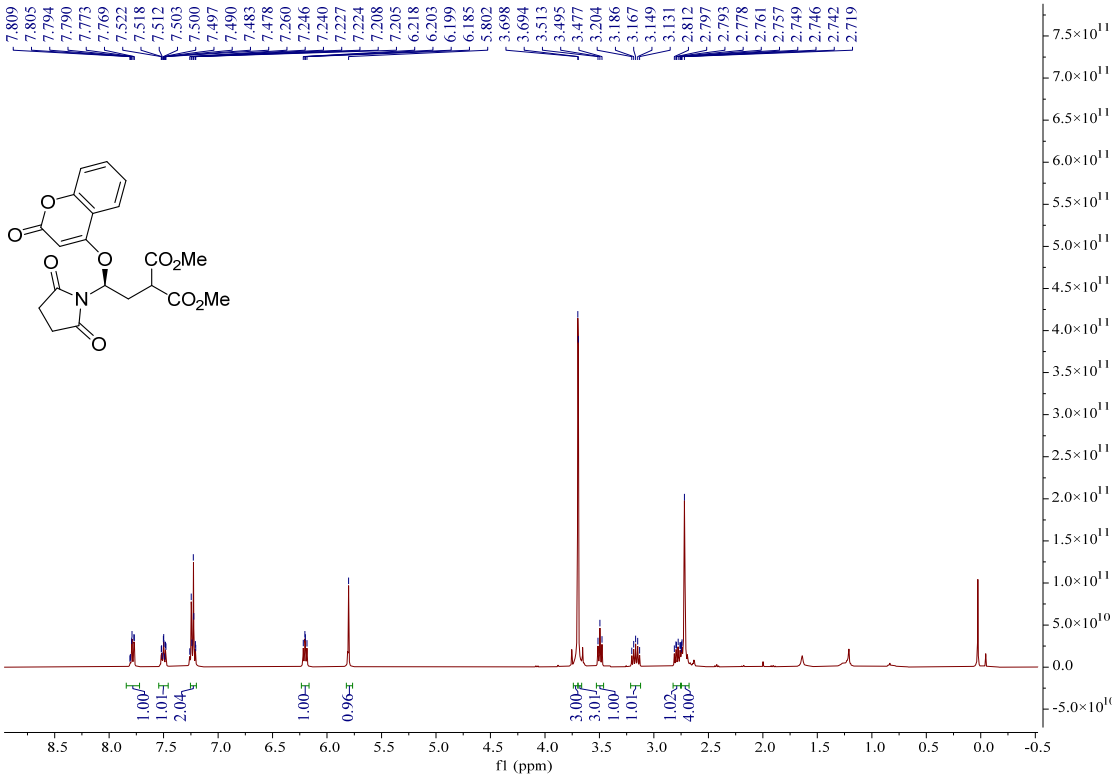
^{1}H NMR Spectrum of **7ae'** (400 MHz, $CDCl_3$)



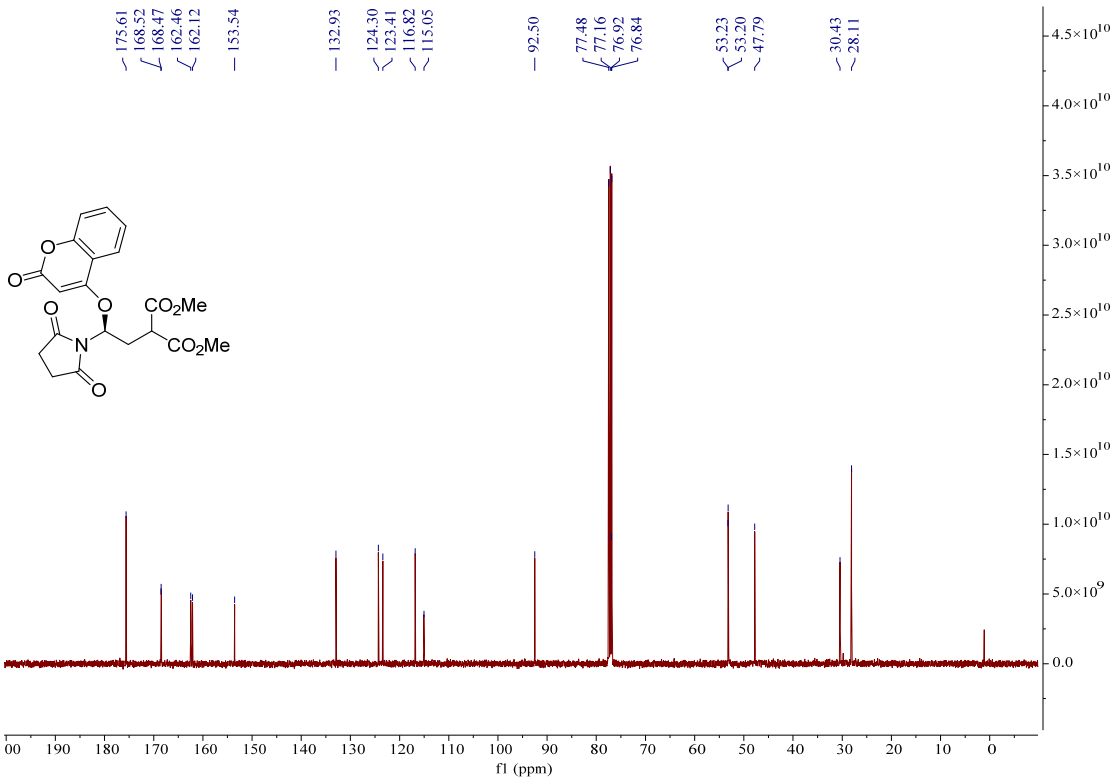
^{13}C NMR Spectrum of **7ae'** (100 MHz, $CDCl_3$)



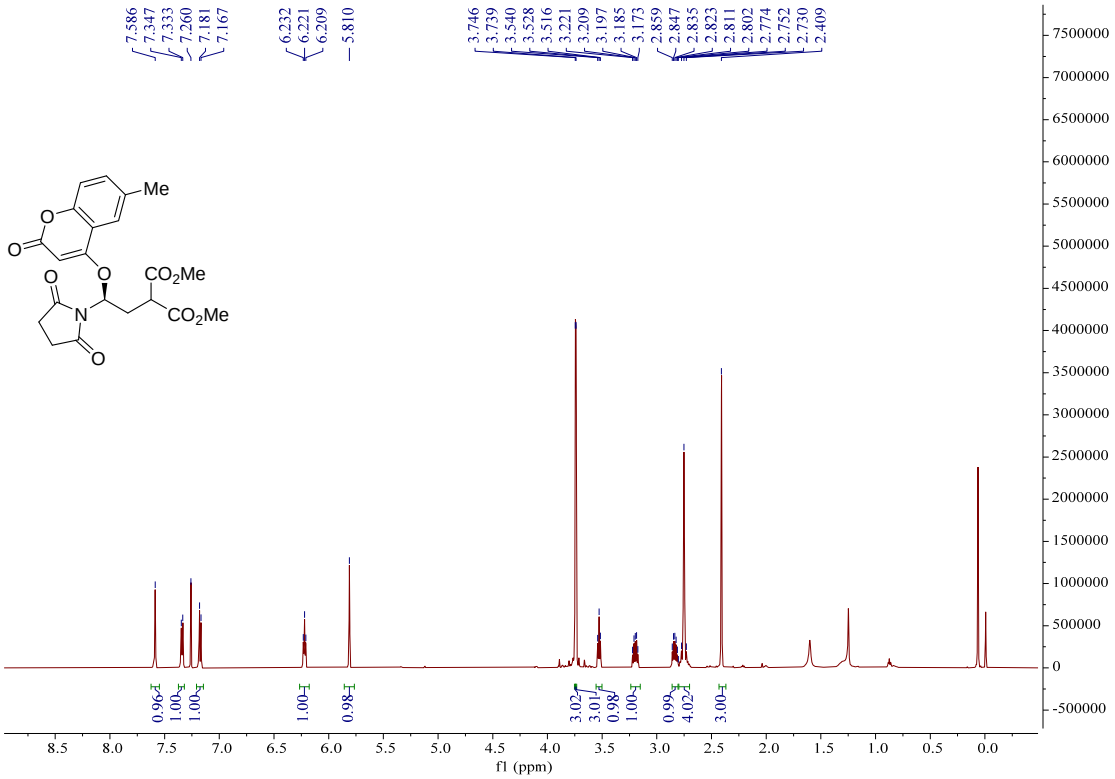
^{1}H NMR Spectrum of **9aa** (400 MHz, $CDCl_3$)



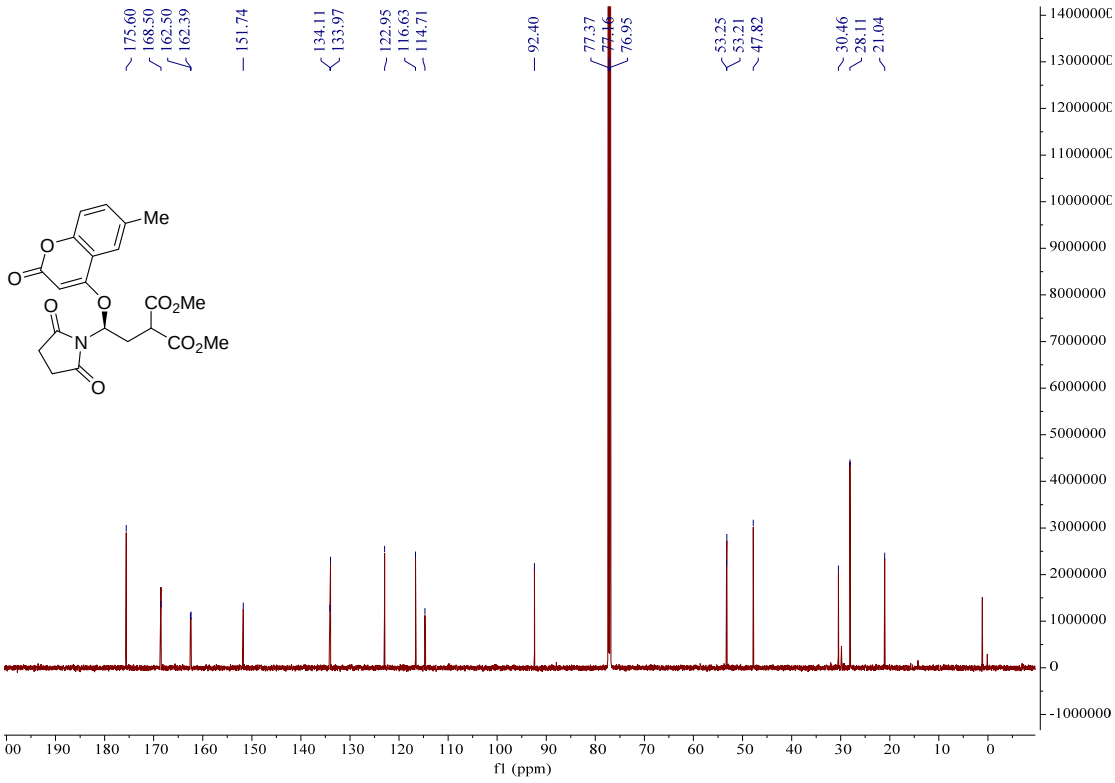
^{13}C NMR Spectrum of **9aa** (100 MHz, $CDCl_3$)



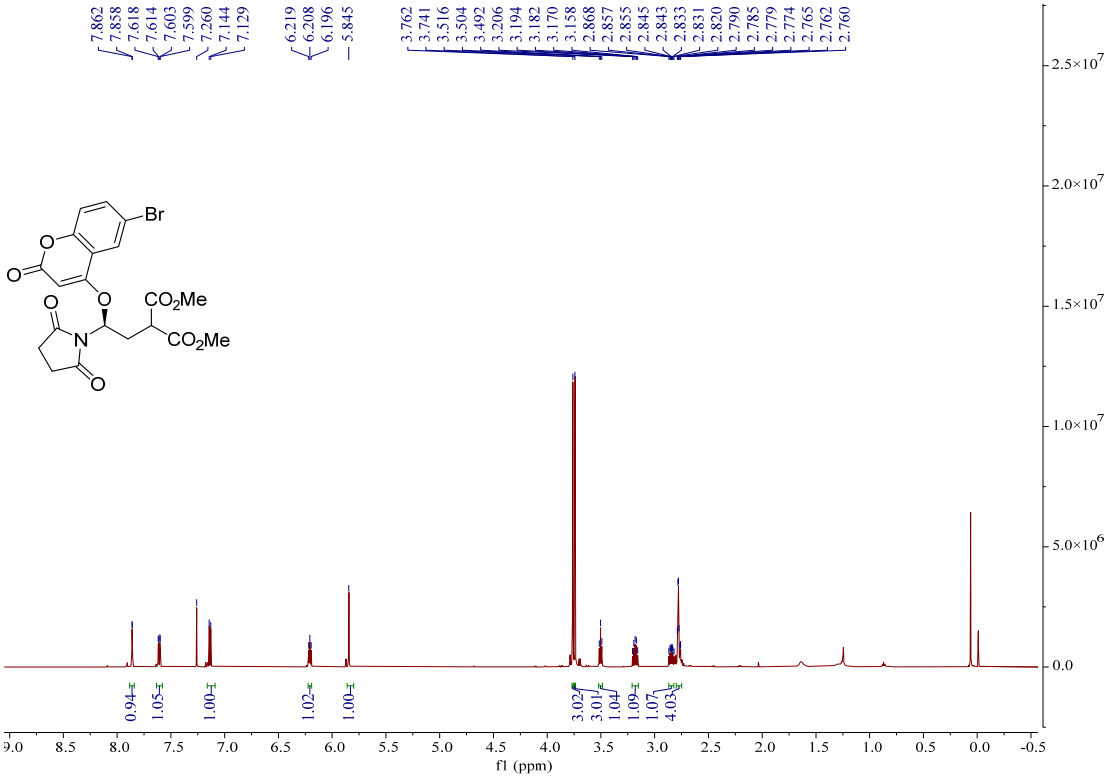
^{1}H NMR Spectrum of **9ab** (600 MHz, $CDCl_3$)



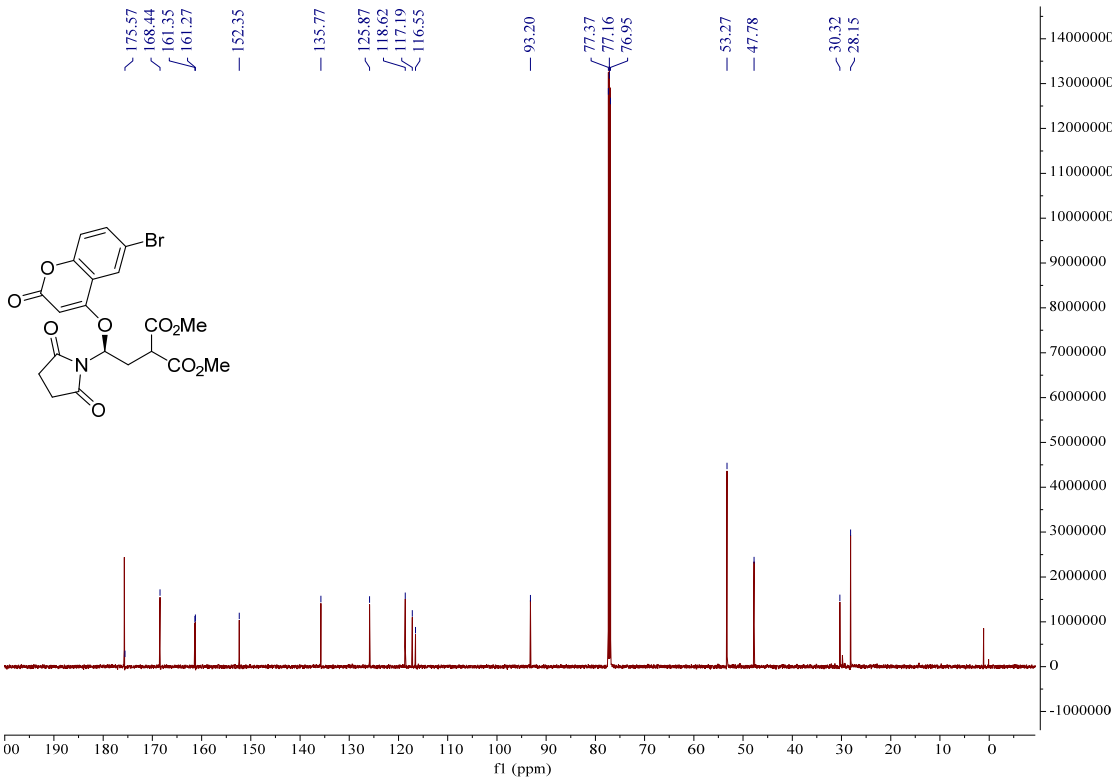
^{13}C NMR Spectrum of **9ab** (150 MHz, $CDCl_3$)



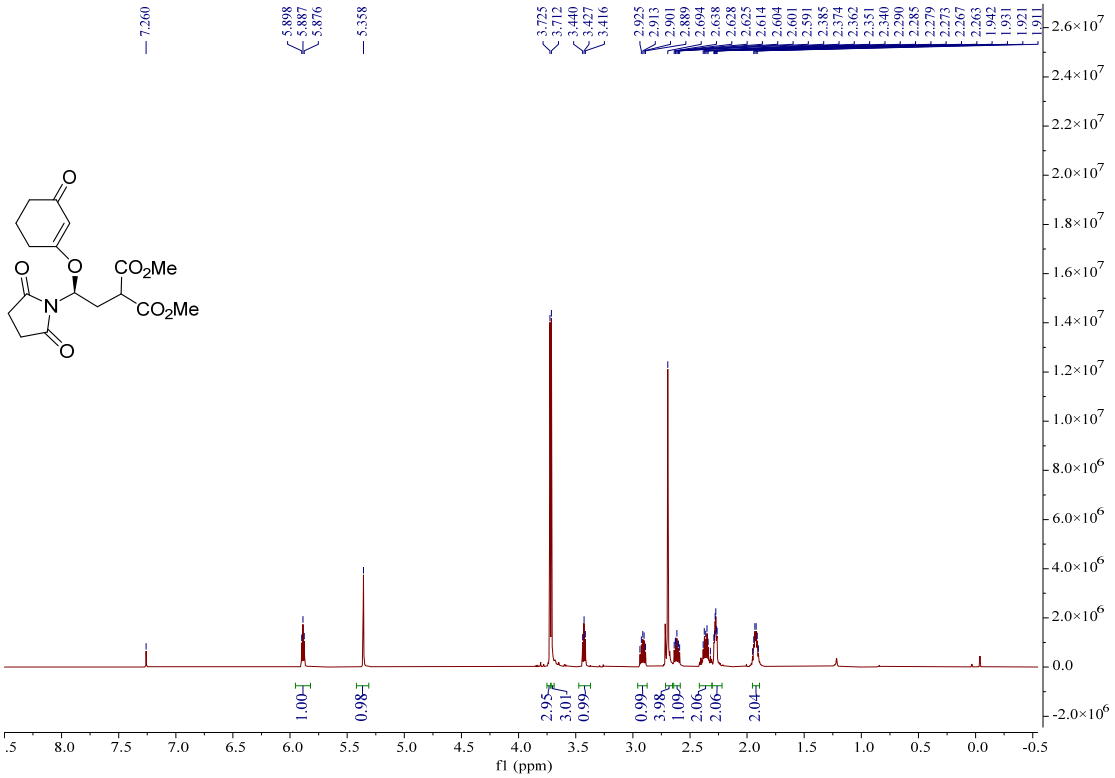
^{1}H NMR Spectrum of **9ac** (600 MHz, $CDCl_3$)



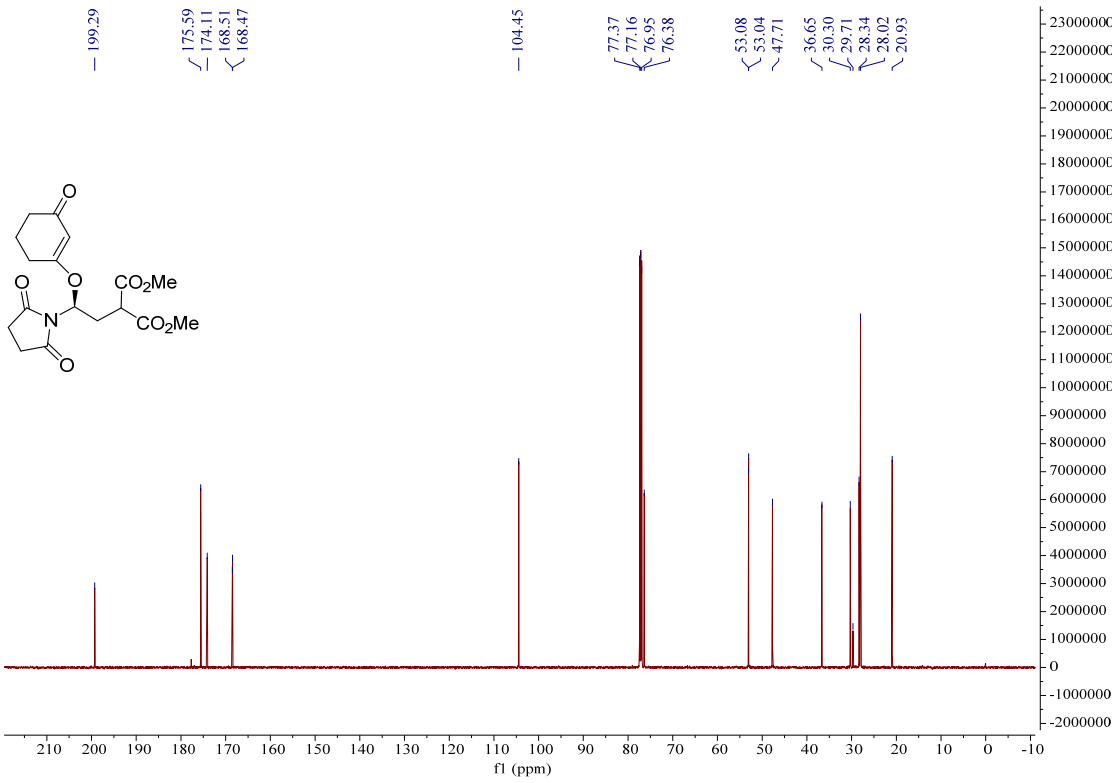
^{13}C NMR Spectrum of **9ac** (150 MHz, $CDCl_3$)



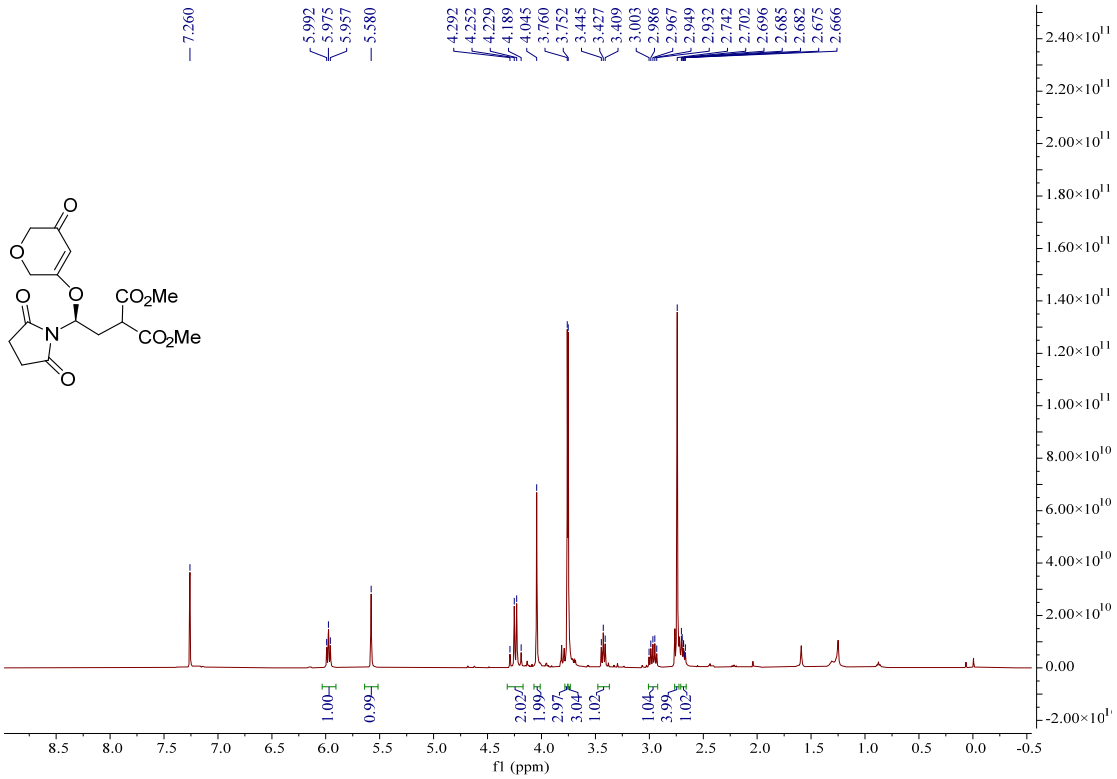
^{1}H NMR Spectrum of **11aa** (600 MHz, $CDCl_3$)



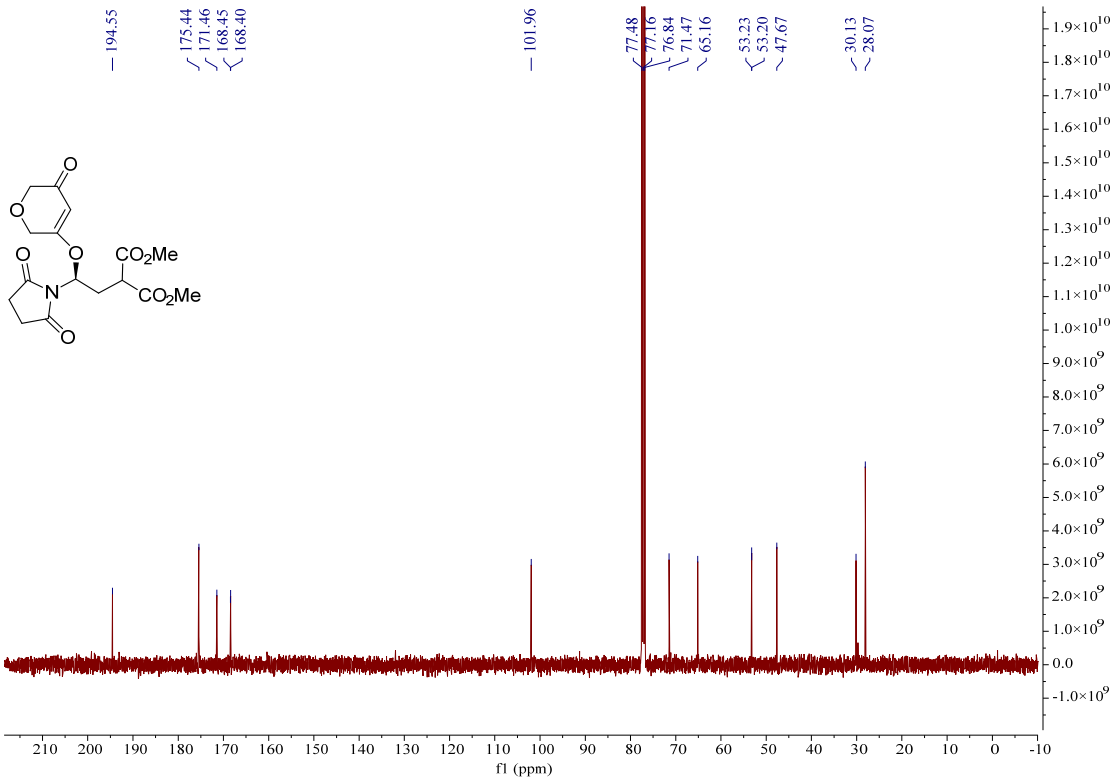
^{13}C NMR Spectrum of **11aa** (150 MHz, $CDCl_3$)



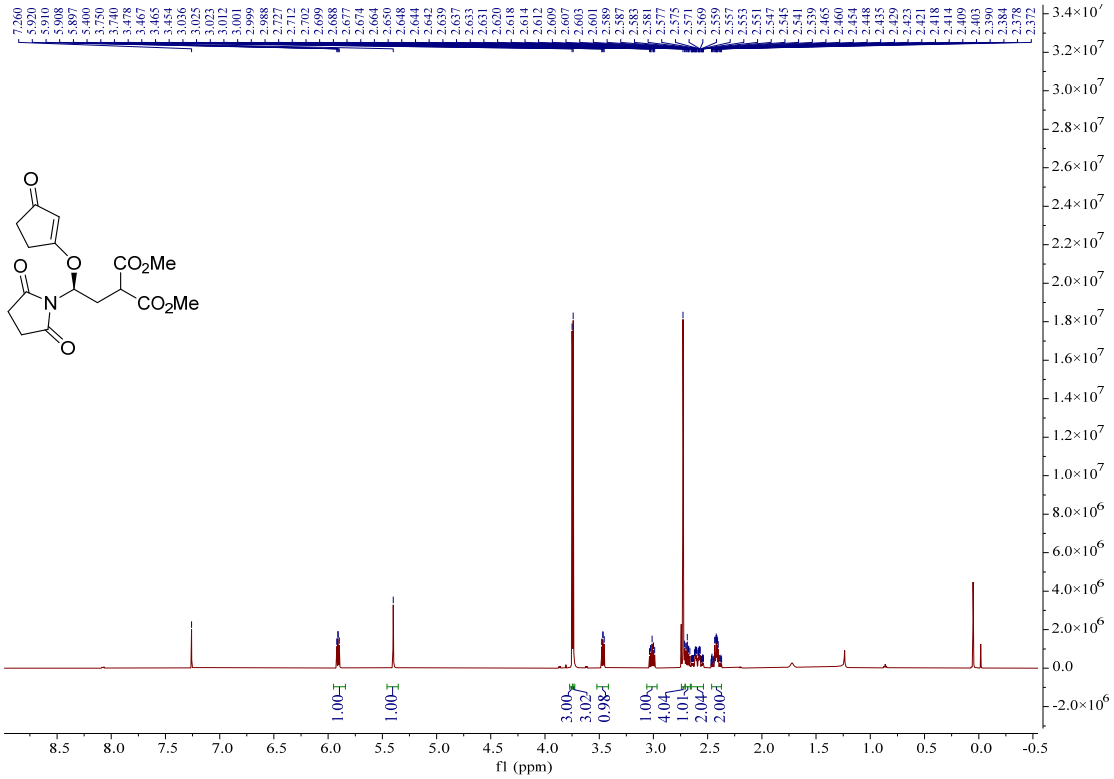
^{1}H NMR Spectrum of **11ab** (400 MHz, $CDCl_3$)



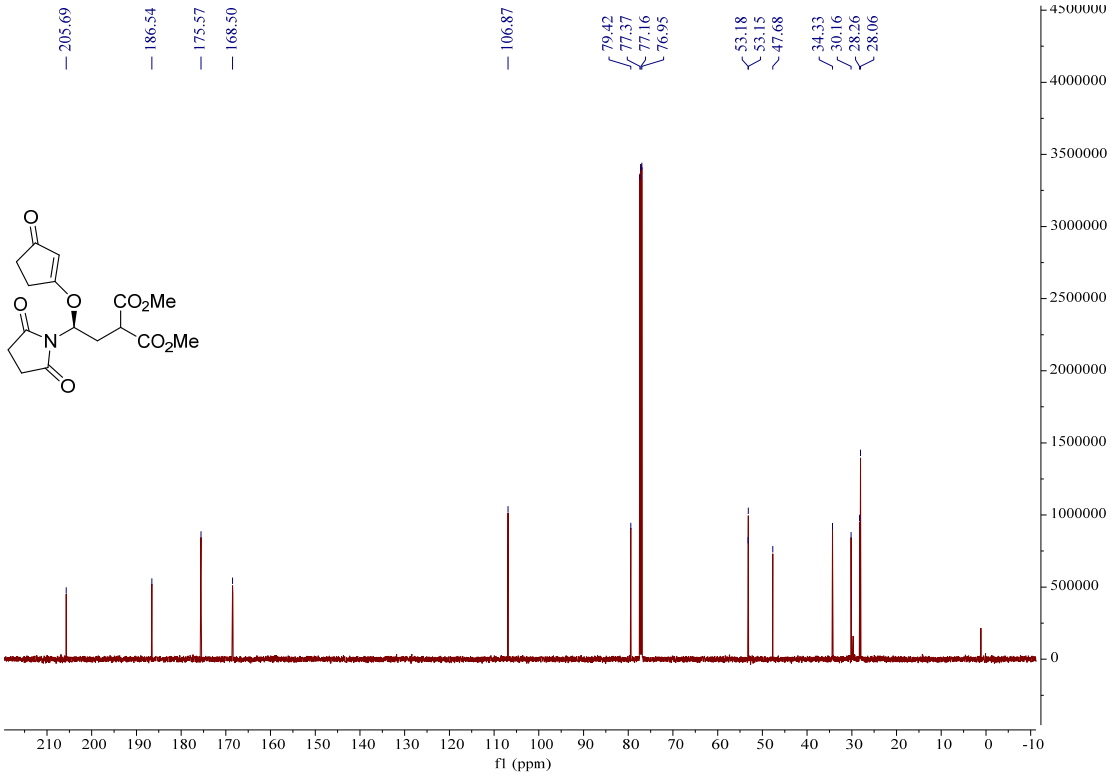
^{13}C NMR Spectrum of **11ab** (100 MHz, $CDCl_3$)



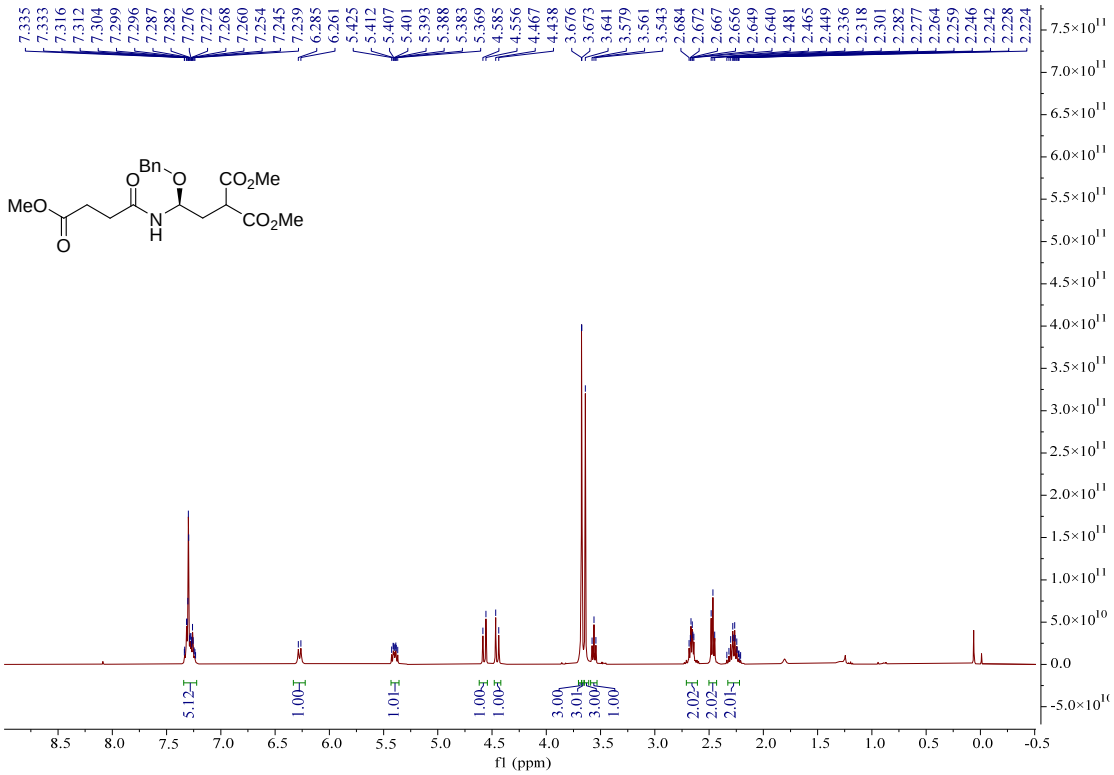
^{1}H NMR Spectrum of **11ac** (600 MHz, $CDCl_3$)



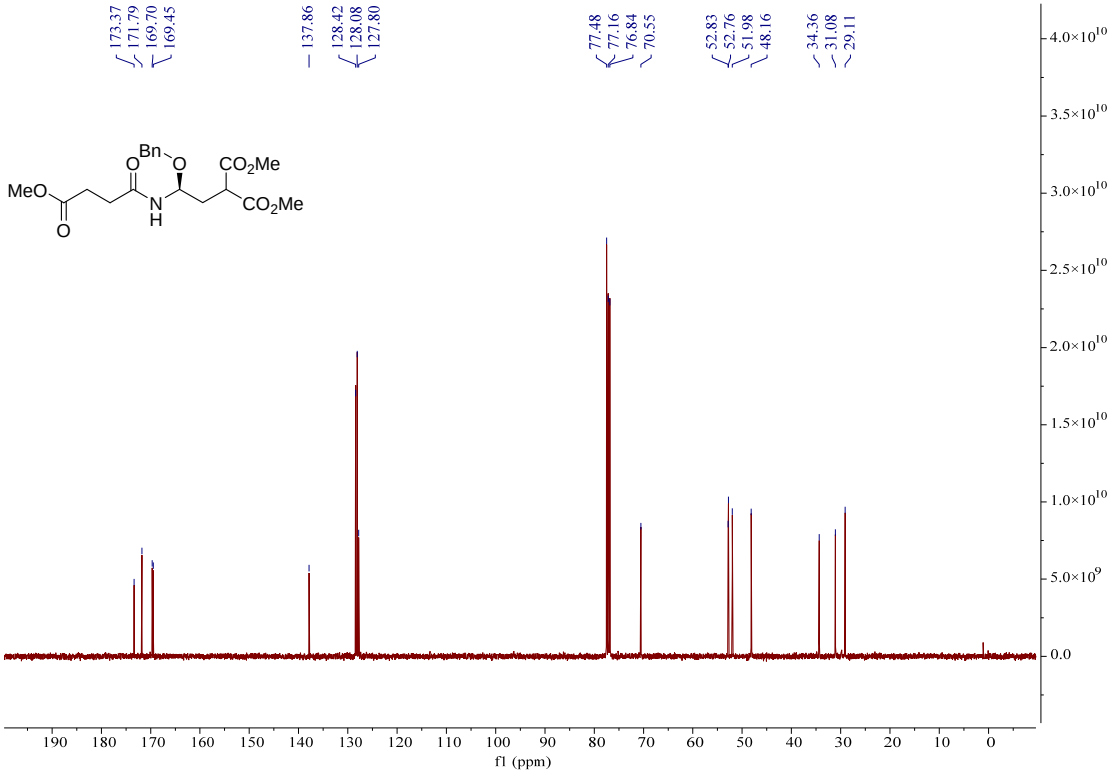
^{13}C NMR Spectrum of **11ac** (150 MHz, $CDCl_3$)



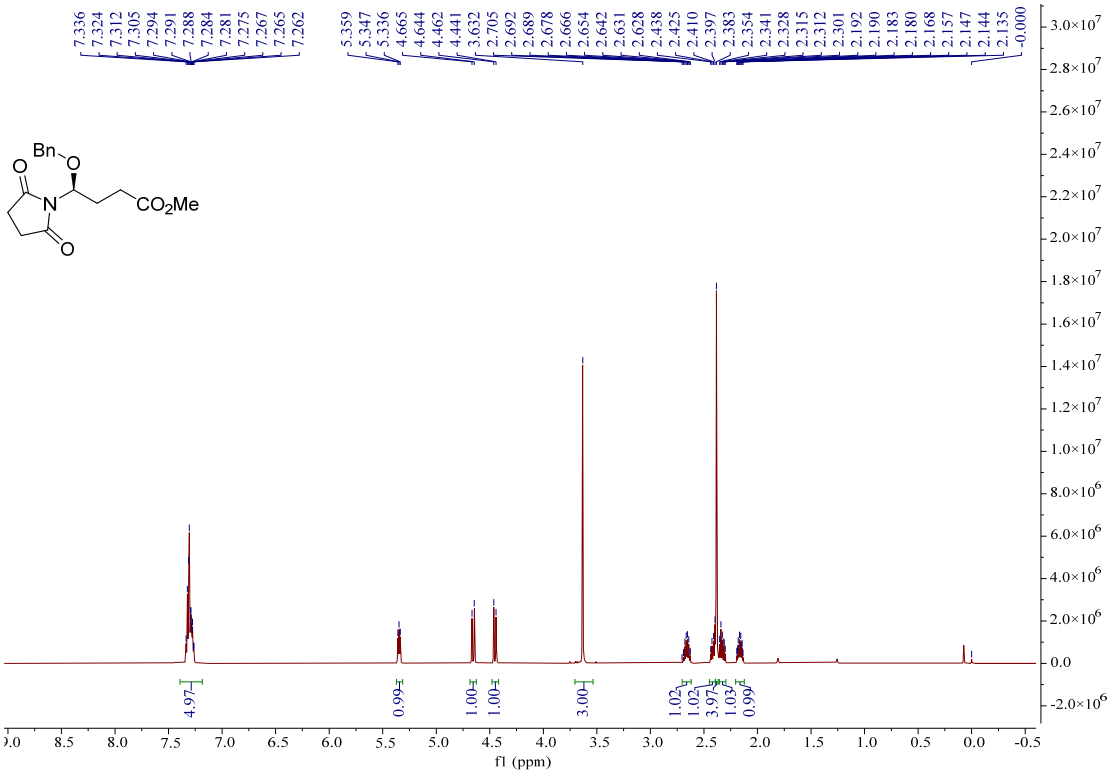
^{1}H NMR Spectrum of **12aa** (400 MHz, $CDCl_3$)



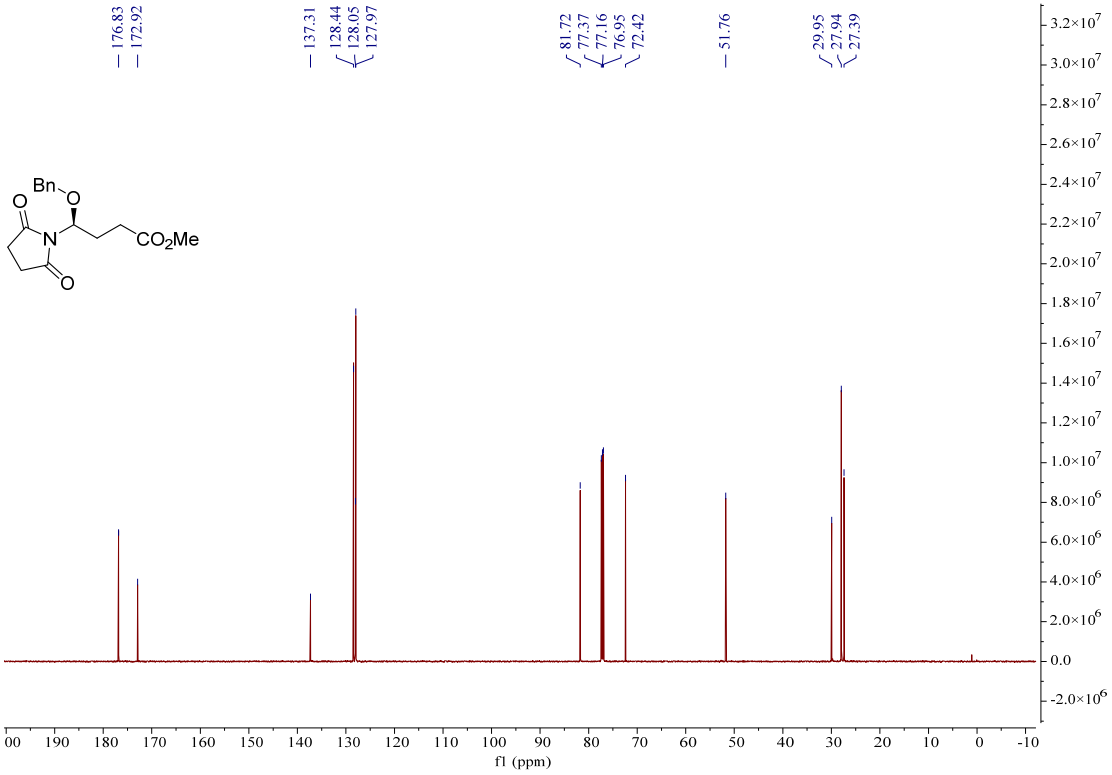
^{13}C NMR Spectrum of **12aa** (100 MHz, $CDCl_3$)



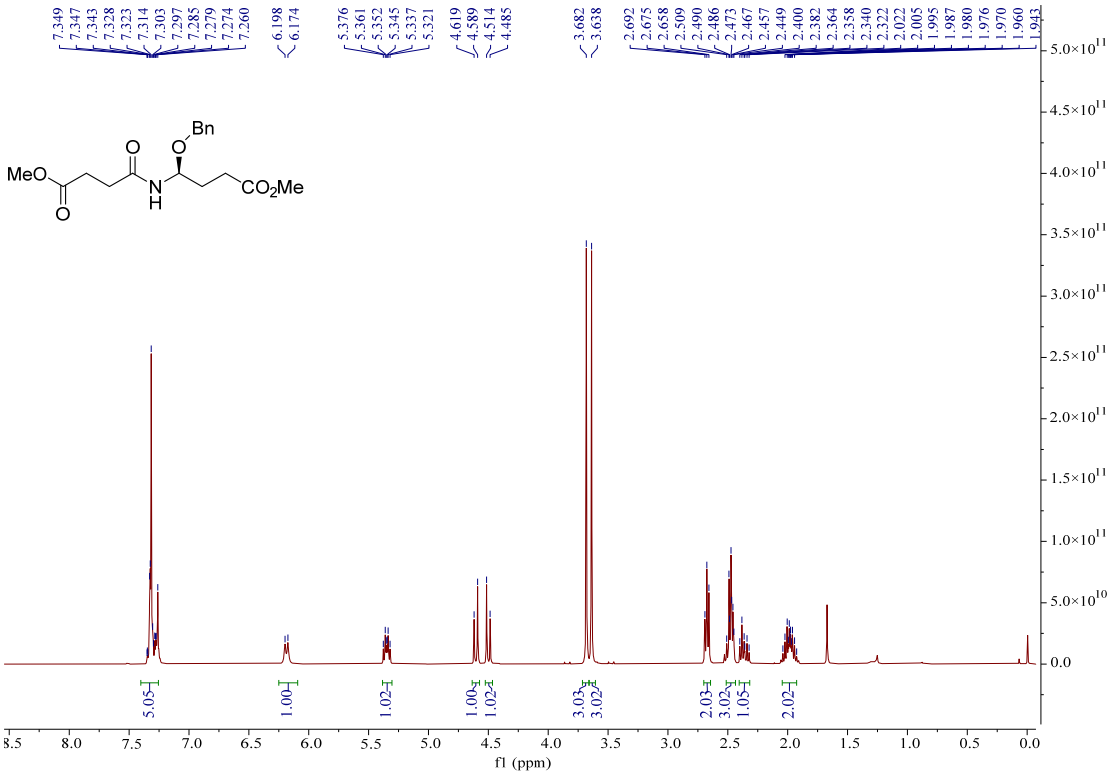
^{1}H NMR Spectrum of **13aa** (600 MHz, $CDCl_3$)



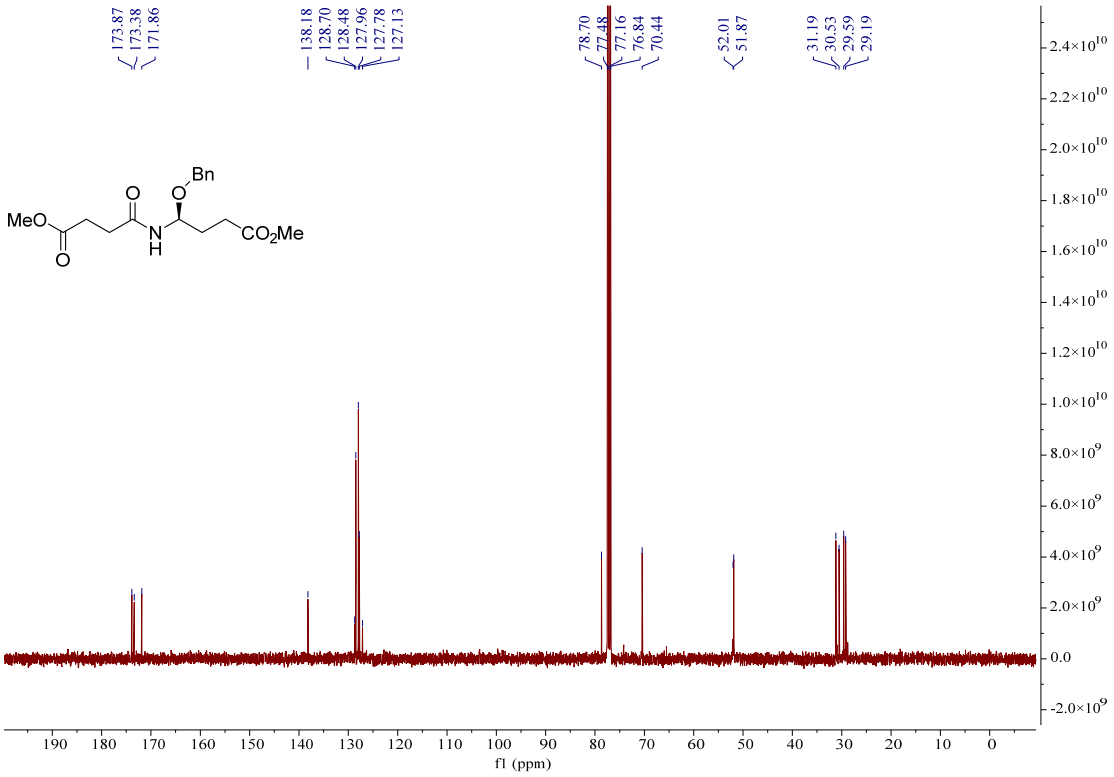
^{13}C NMR Spectrum of **13aa** (150 MHz, $CDCl_3$)



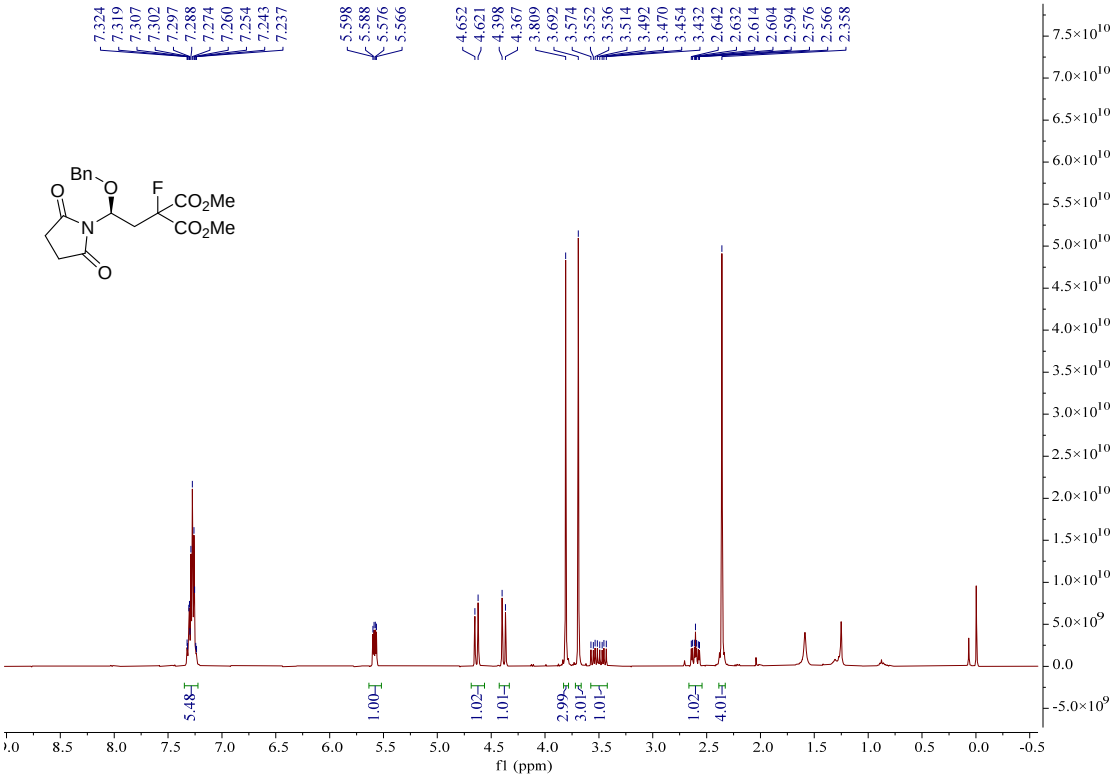
^{1}H NMR Spectrum of **14aa** (400 MHz, $CDCl_3$)



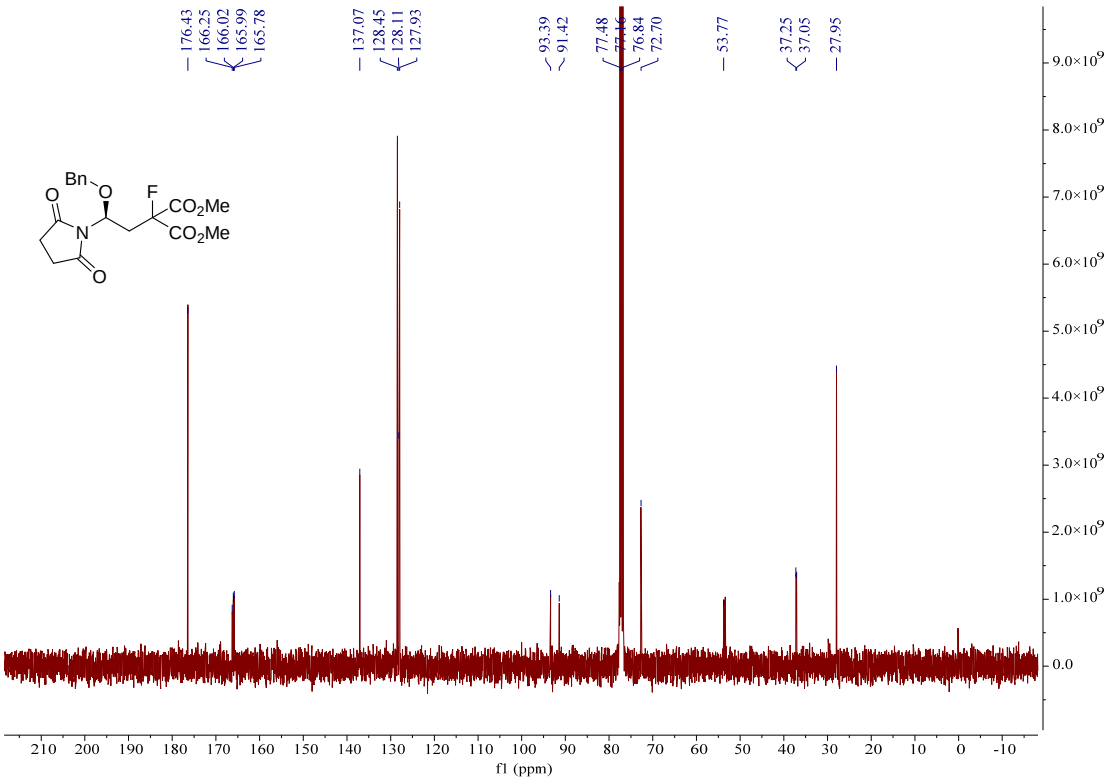
^{13}C NMR Spectrum of **14aa** (100 MHz, $CDCl_3$)



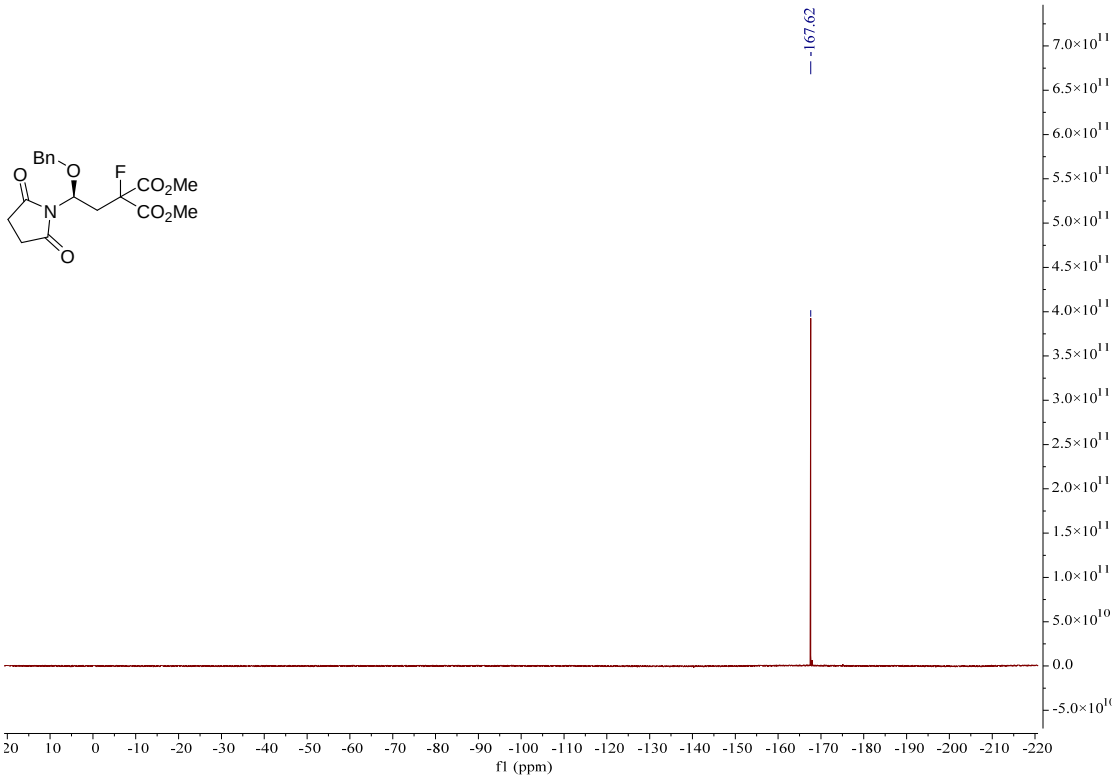
^{1}H NMR Spectrum of **15aa** (400 MHz, $CDCl_3$)



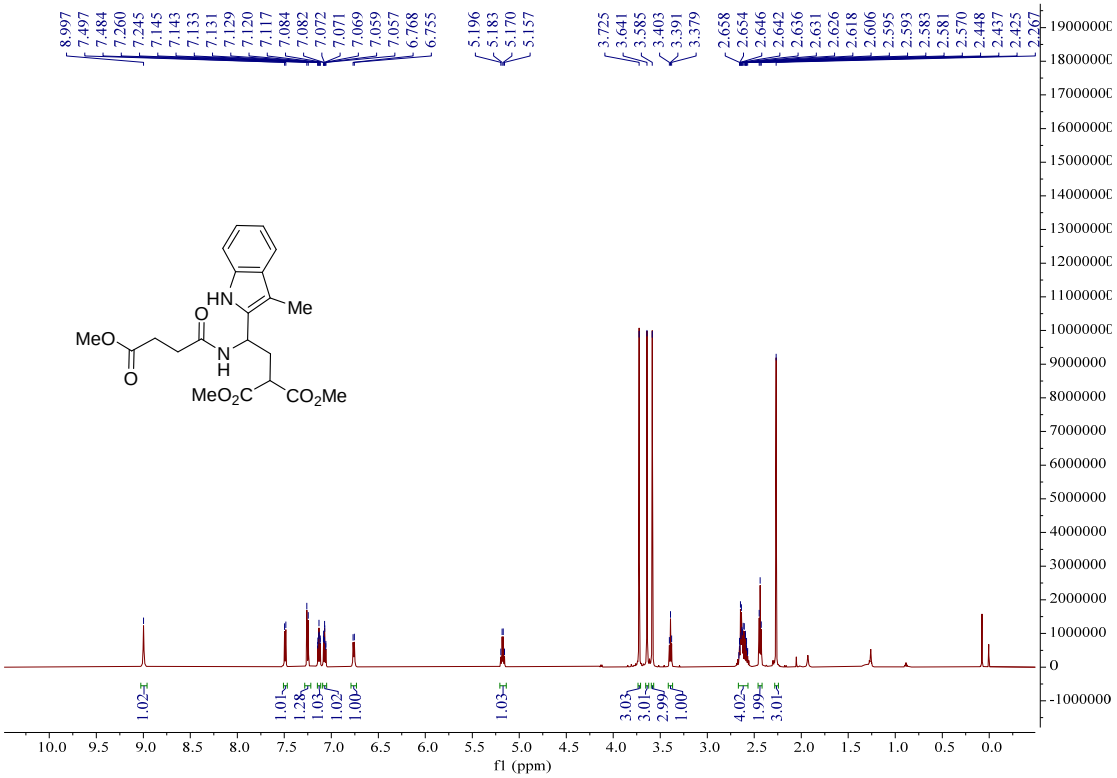
^{13}C NMR Spectrum of **15aa** (100 MHz, $CDCl_3$)



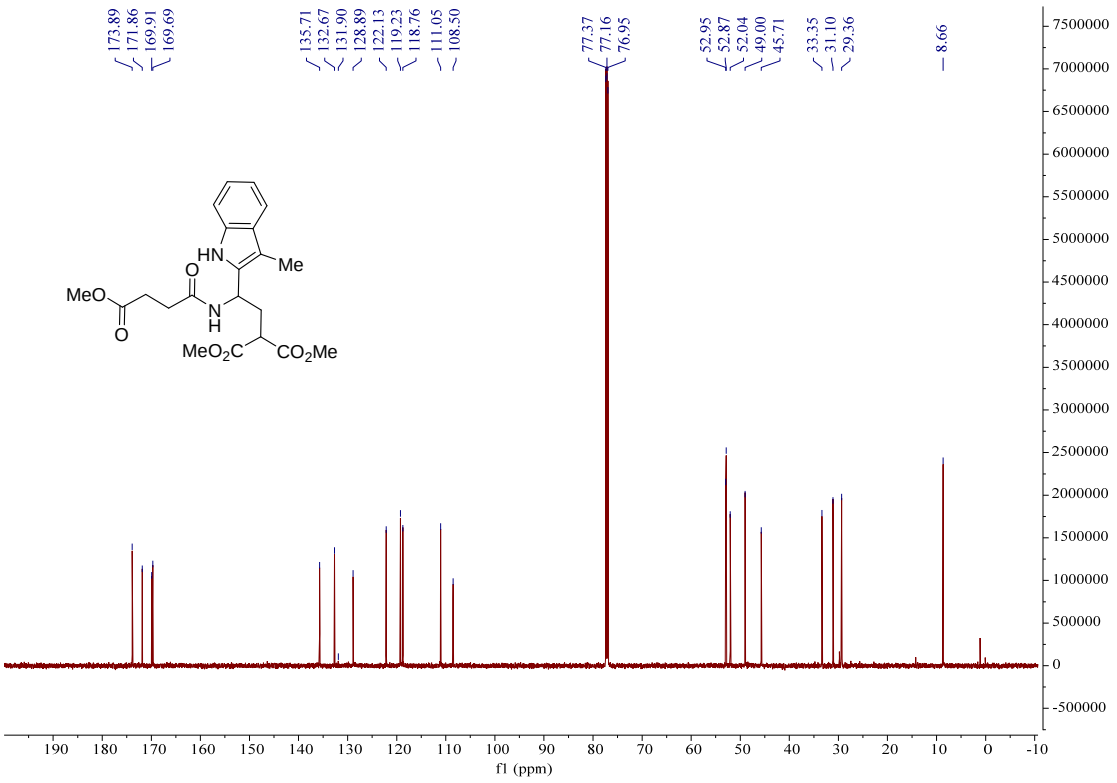
^{9}F NMR Spectrum of **15aa** (376 MHz, $CDCl_3$)



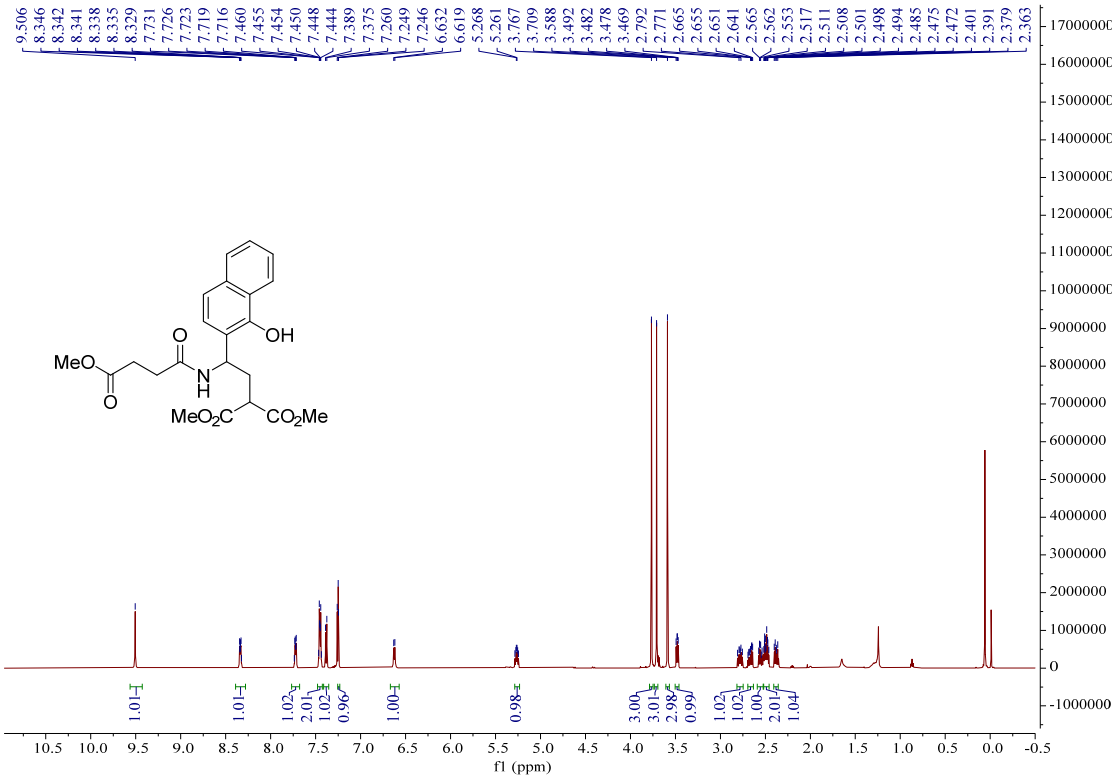
^{1}H NMR Spectrum of **16aa** (600 MHz, $CDCl_3$)



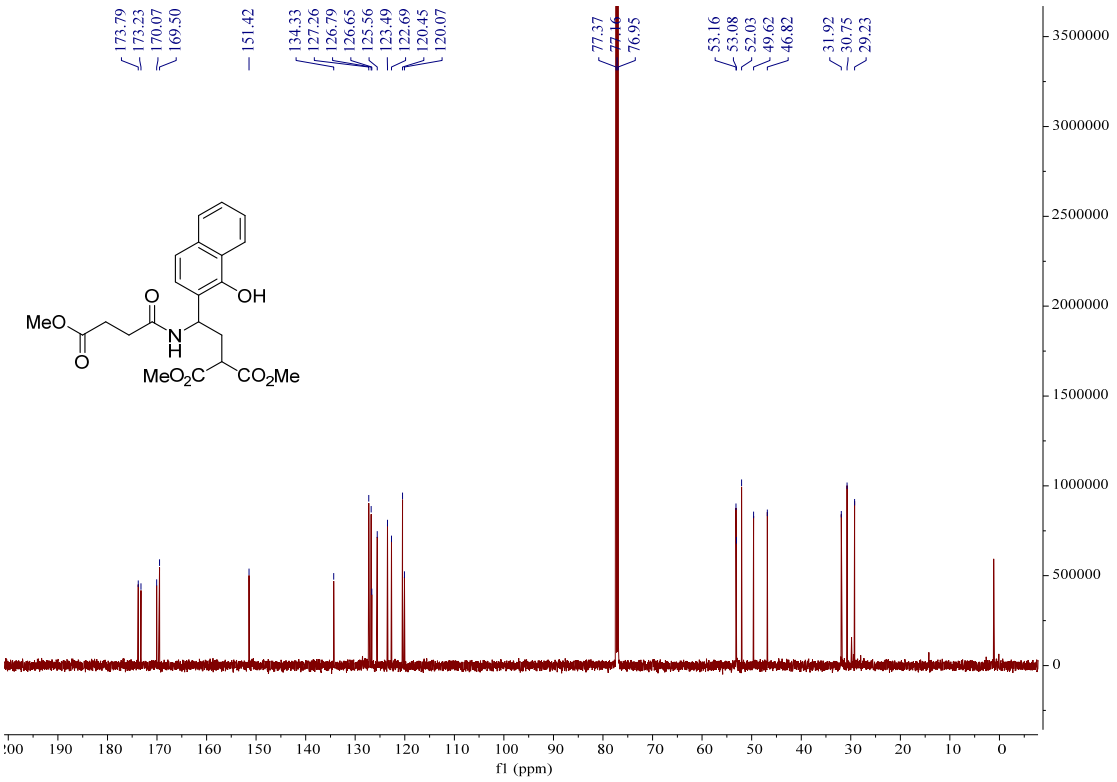
^{13}C NMR Spectrum of **16aa** (150 MHz, $CDCl_3$)



^{1}H NMR Spectrum of **17aa** (600 MHz, $CDCl_3$)

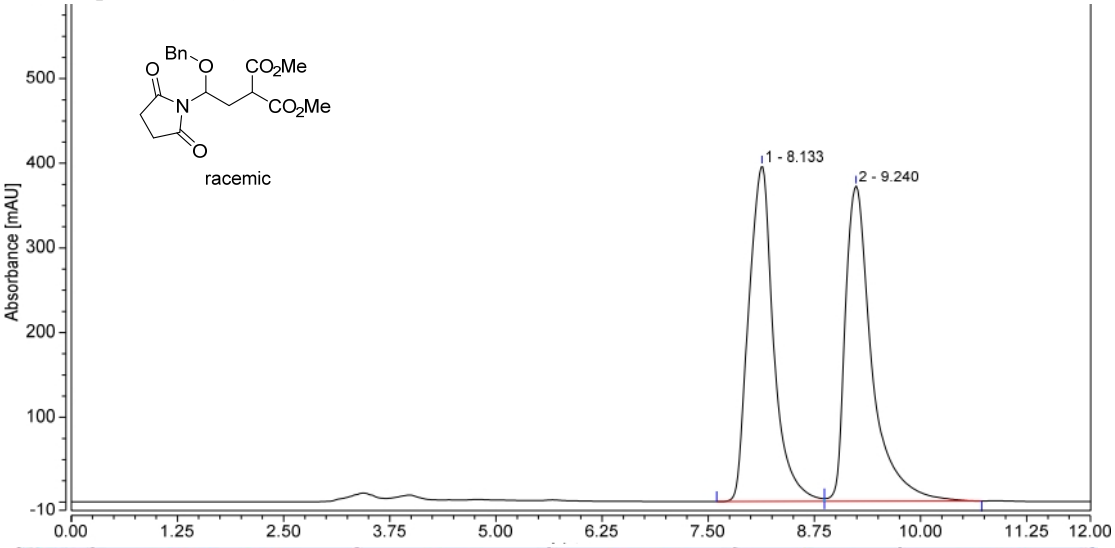


^{13}C NMR Spectrum of **17aa** (150 MHz, $CDCl_3$)



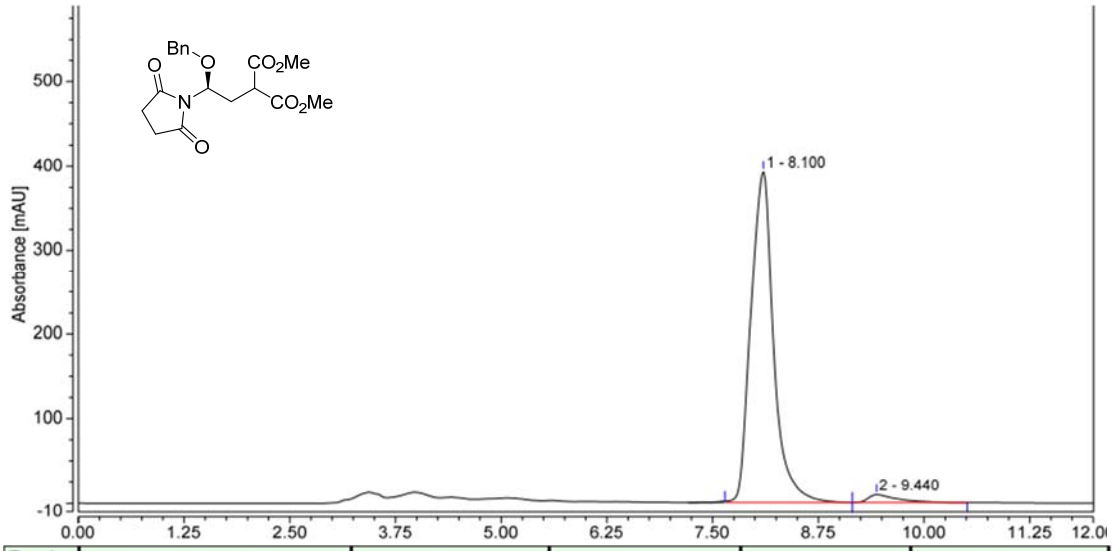
HPLC spectra

HPLC Spectrum of (±)-**3aa**



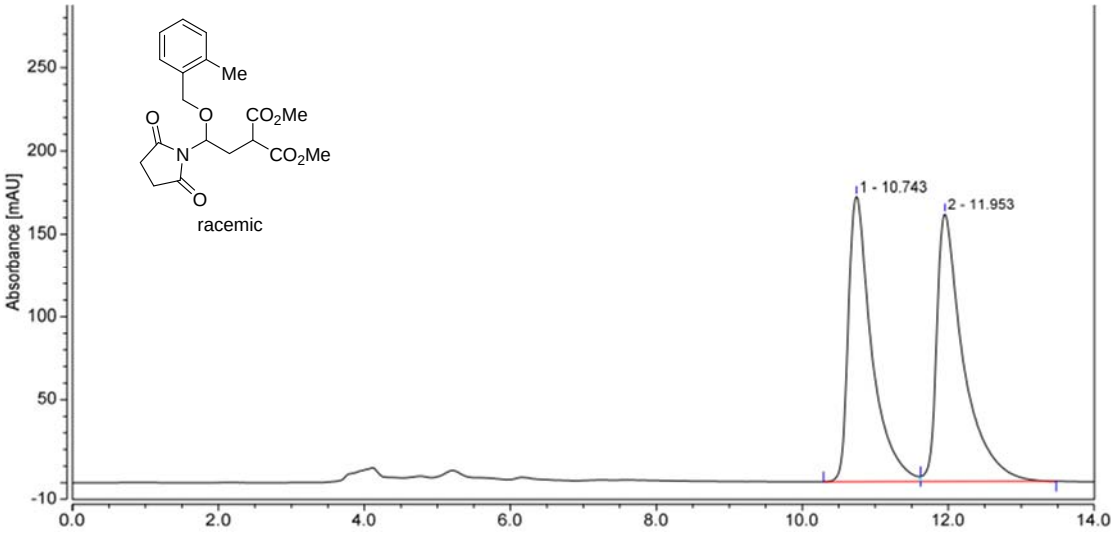
Peak	Retention Time min	Area mAU*min	Height mAU	Area %	Height %
1	8.133	134.556	396.434	49.94	51.56
2	9.240	134.871	372.469	50.06	48.44
Total:		**269.427**	**768.903**	**100.00**	**100.00**

HPLC Spectrum of (*S*)-**3aa**



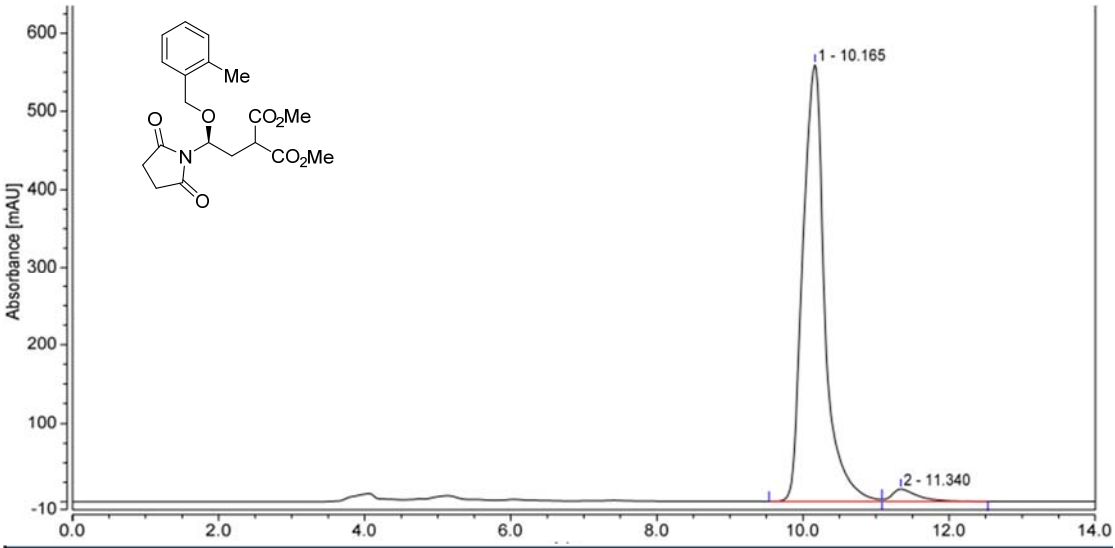
Peak	Retention Time min	Area mAU*min	Height mAU	Area %	Height %
1	8.100	122.320	393.353	96.91	97.65
2	9.440	3.900	9.469	3.09	2.35
Total:		**126.220**	**402.821**	**100.00**	**100.00**

HPLC Spectrum of (±)-**3ab**



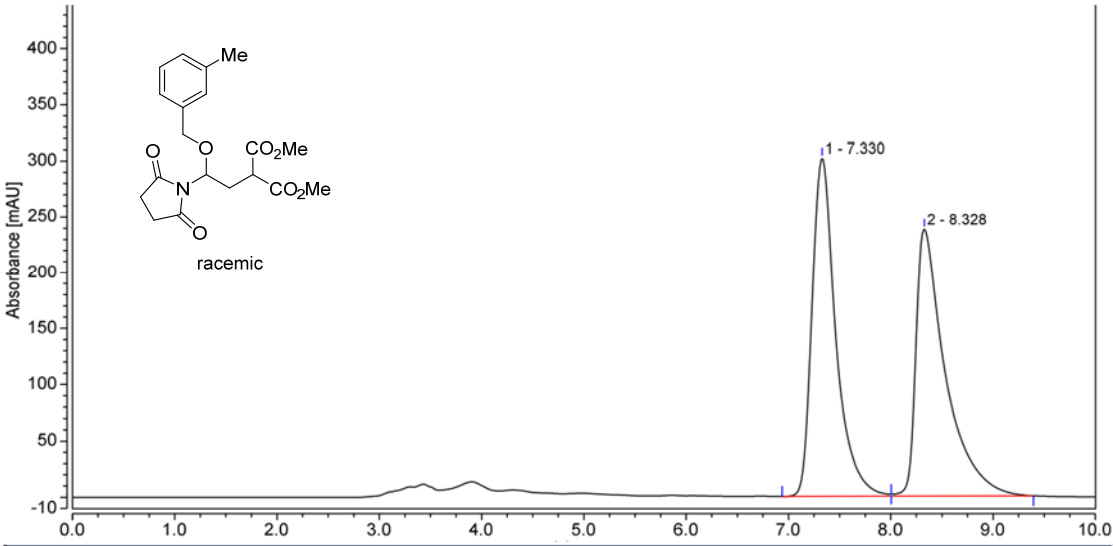
Peak	Retention Time min	Area mAU*min	Height mAU	Area %	Height %
1	10.743	63.899	172.308	48.38	51.61
2	11.953	68.184	161.584	51.62	48.39
Total:		**132.083**	**333.892**	**100.00**	**100.00**

HPLC Spectrum of (*S*)-**3ab**



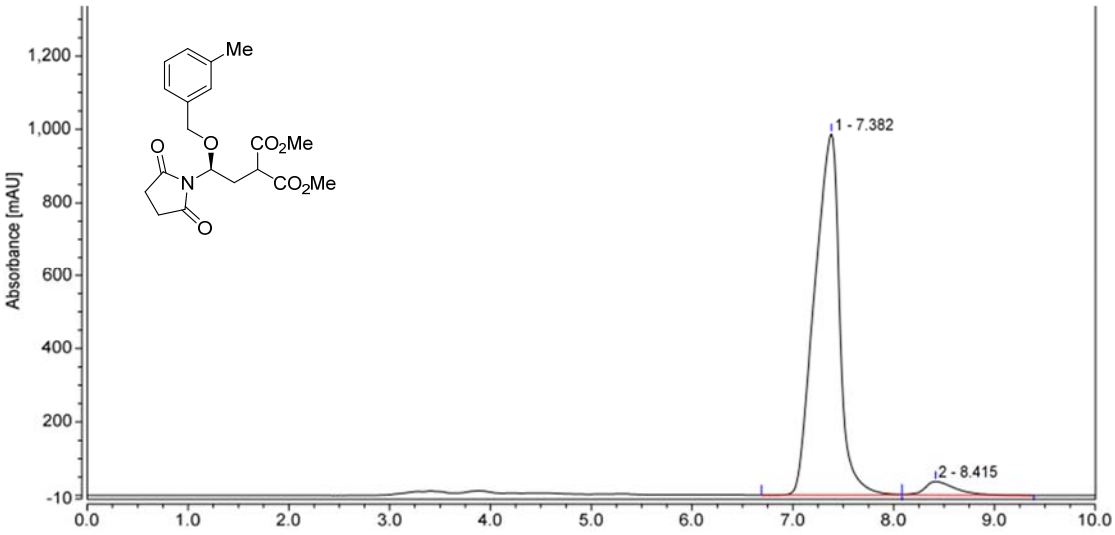
Peak	Retention Time min	Area mAU*min	Height mAU	Area %	Height %
1	10.165	193.828	559.553	96.80	97.26
2	11.340	6.399	15.789	3.20	2.74
Total:		**200.226**	**575.342**	**100.00**	**100.00**

HPLC Spectrum of (±)-**3ac**



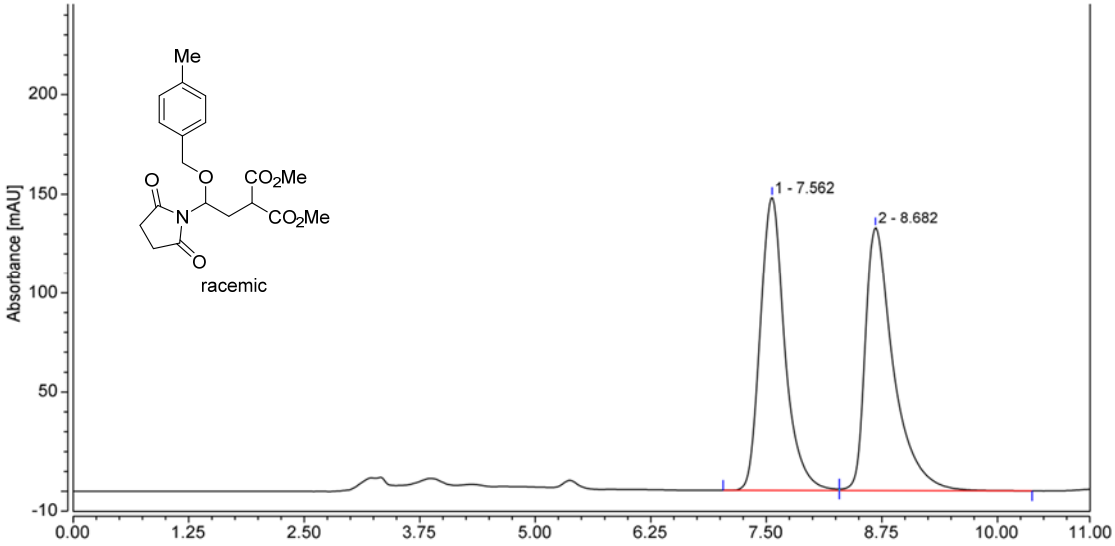
Peak	Retention Time min	Area mAU*min	Height mAU	Area %	Height %
1	7.330	80.819	301.812	50.46	55.89
2	8.328	79.361	238.186	49.54	44.11
Total:		**160.180**	**539.997**	**100.00**	**100.00**

HPLC Spectrum of (*S*)-**3ab**



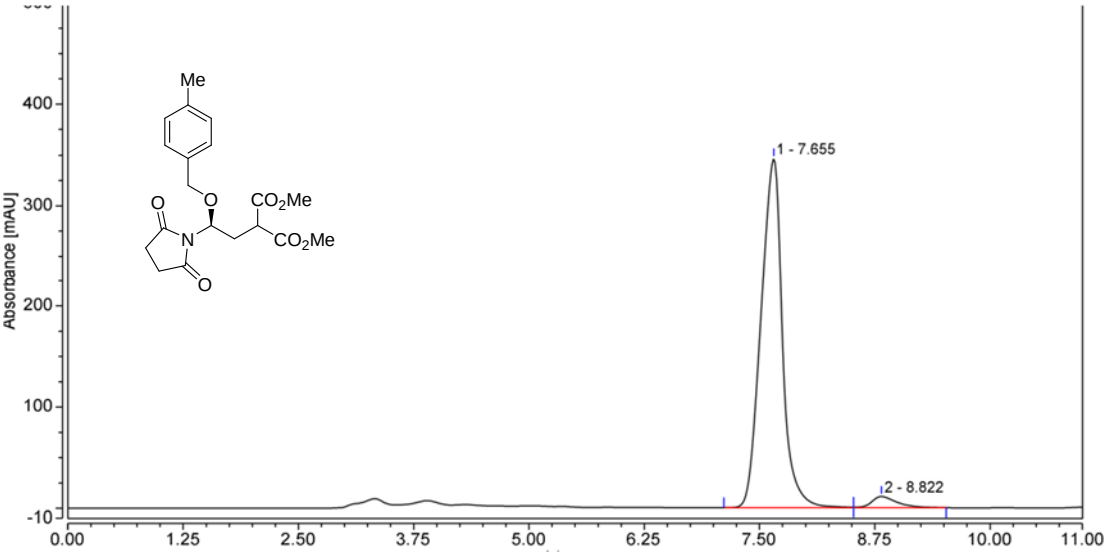
Peak	Retention Time min	Area mAU*min	Height mAU	Area %	Height %
1	7.382	284.006	986.482	95.52	96.36
2	8.415	13.335	37.244	4.48	3.64
Total:		**297.341**	**1023.726**	**100.00**	**100.00**

HPLC Spectrum of (±)-**3ad**



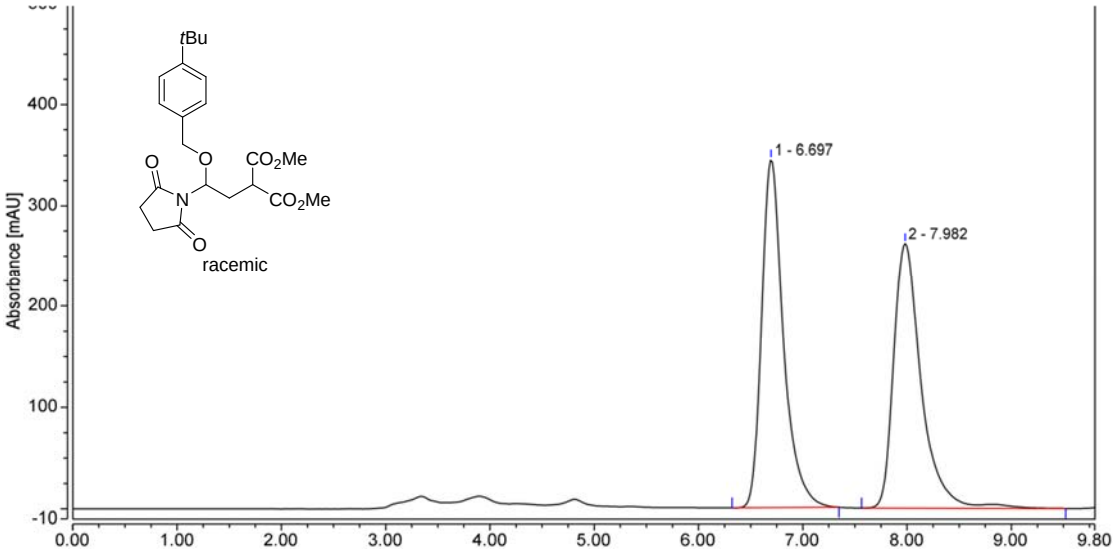
Peak	Retention Time min	Area mAU*min	Height mAU	Area %	Height %
1	7.562	45.656	148.089	49.43	52.71
2	8.682	46.718	132.879	50.57	47.29
Total:		**92.375**	**280.968**	**100.00**	**100.00**

HPLC Spectrum of (*S*)-**3ad**



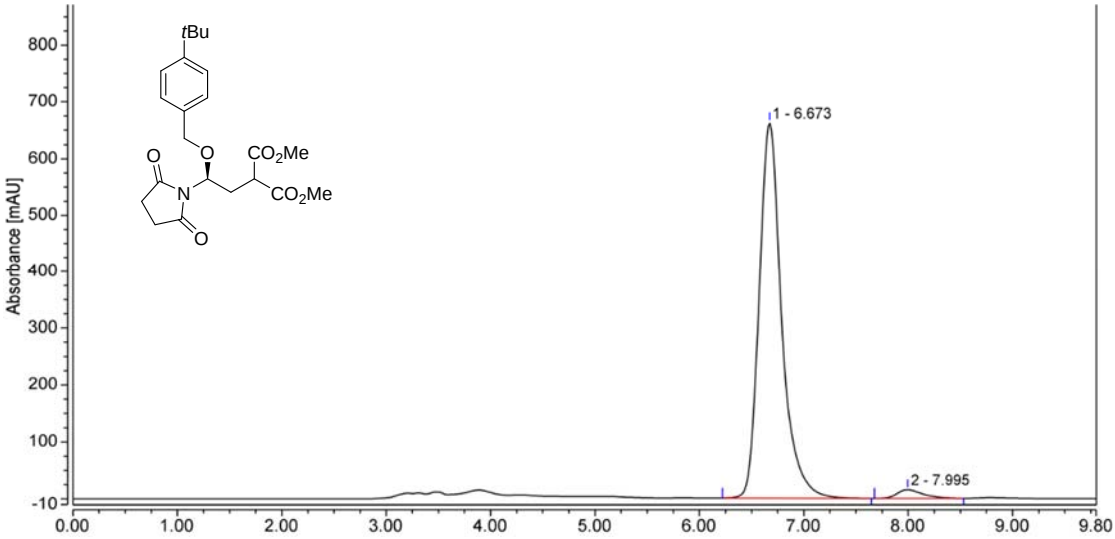
Peak	Retention Time min	Area mAU*min	Height mAU	Area %	Height %
1	7.655	93.168	346.041	96.32	96.87
2	8.822	3.555	11.164	3.68	3.13
Total:		**96.723**	**357.205**	**100.00**	**100.00**

HPLC Spectrum of (±)-**3ae**



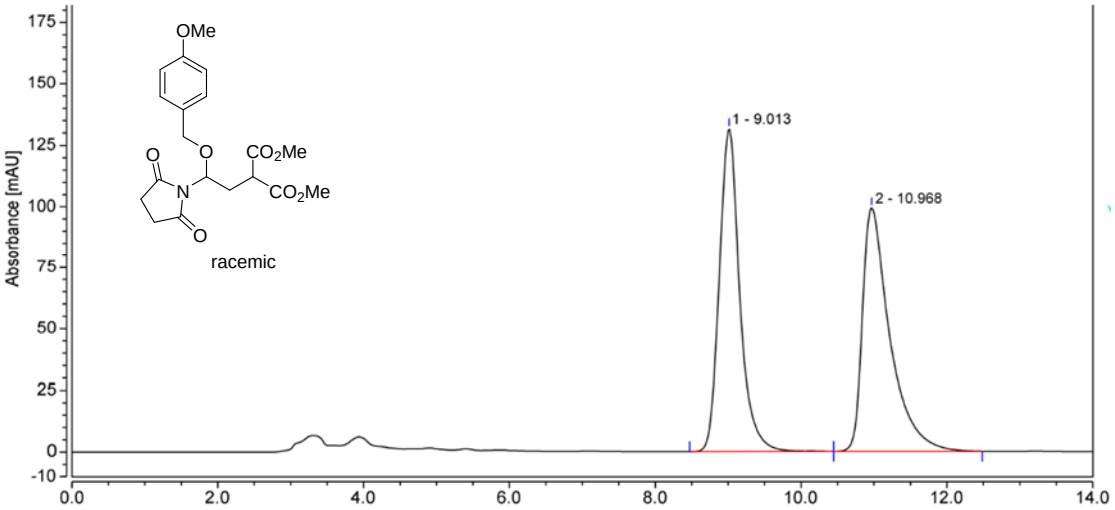
Peak	Retention Time min	Area mAU*min	Height mAU	Area %	Height %
1	6.697	83.364	344.699	50.99	56.83
2	7.982	80.119	261.817	49.01	43.17
Total:		**163.482**	**606.516**	**100.00**	**100.00**

HPLC Spectrum of (*S*)-**3ae**



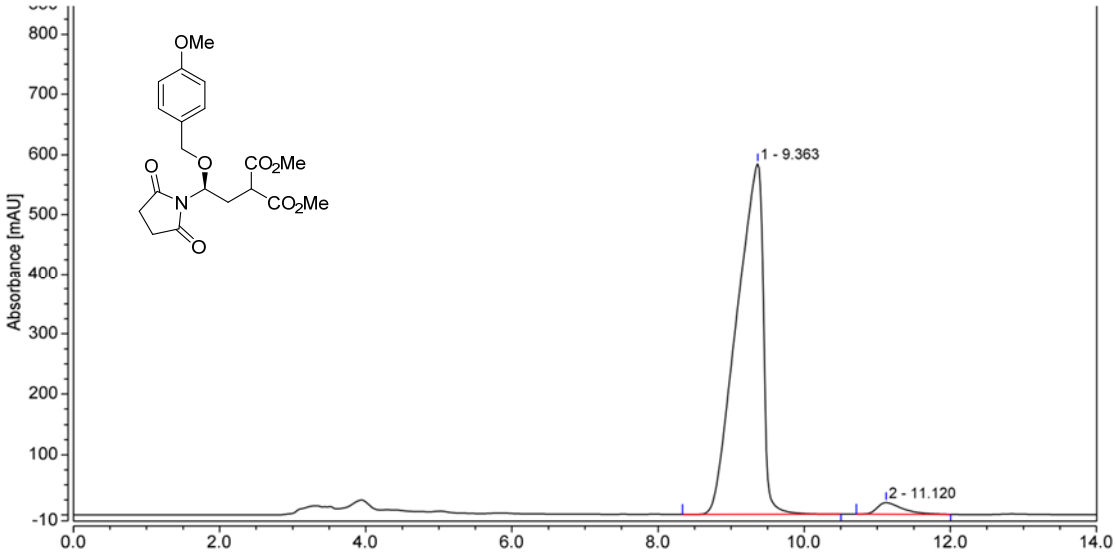
Peak	Retention Time min	Area mAU*min	Height mAU	Area %	Height %
1	6.673	164.490	661.434	97.45	97.76
2	7.995	4.300	15.189	2.55	2.24
Total:		**168.790**	**676.623**	**100.00**	**100.00**

HPLC Spectrum of (±)-**3af**



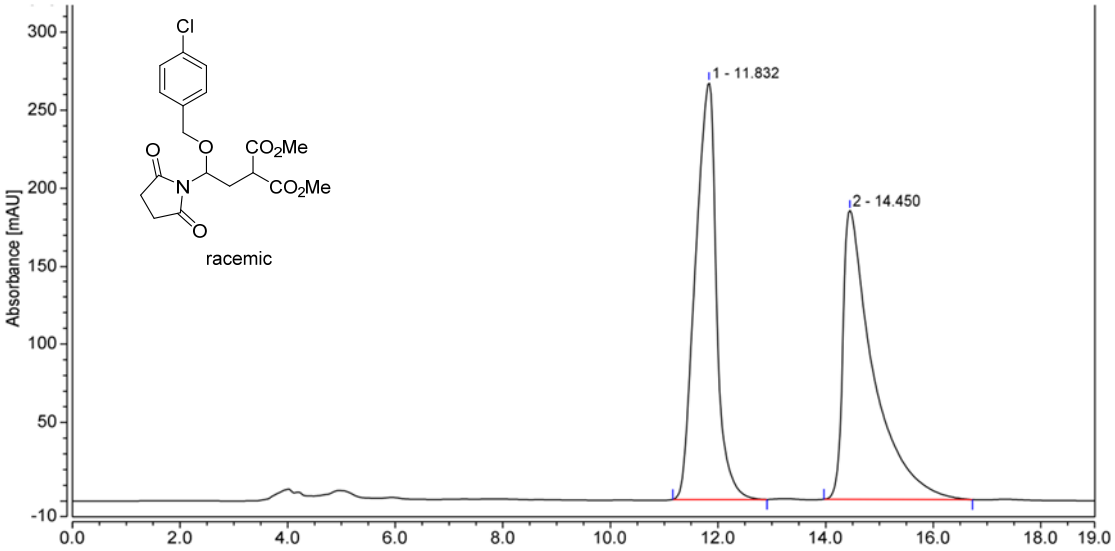
Peak	Retention Time min	Area mAU*min	Height mAU	Area %	Height %
1	9.013	42.737	131.489	49.78	56.96
2	10.968	43.123	99.354	50.22	43.04
Total:		**85.860**	**230.843**	**100.00**	**100.00**

HPLC Spectrum of (*S*)-**3af**



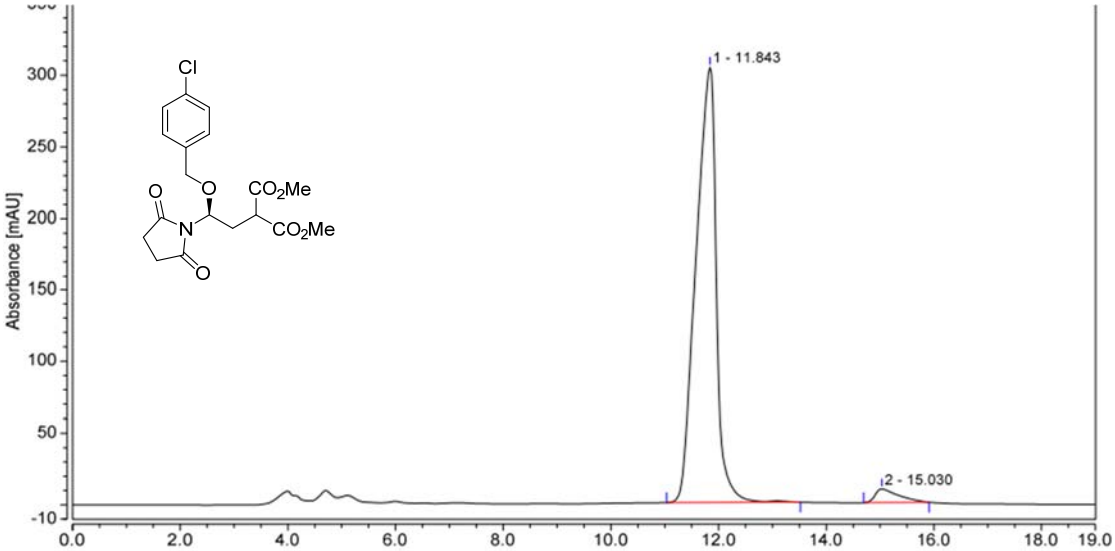
Peak	Retention Time min	Area mAU*min	Height mAU	Area %	Height %
1	9.363	243.548	584.193	96.90	96.80
2	11.120	7.797	19.308	3.10	3.20
Total:		**251.345**	**603.501**	**100.00**	**100.00**

HPLC Spectrum of (±)-**3ag**



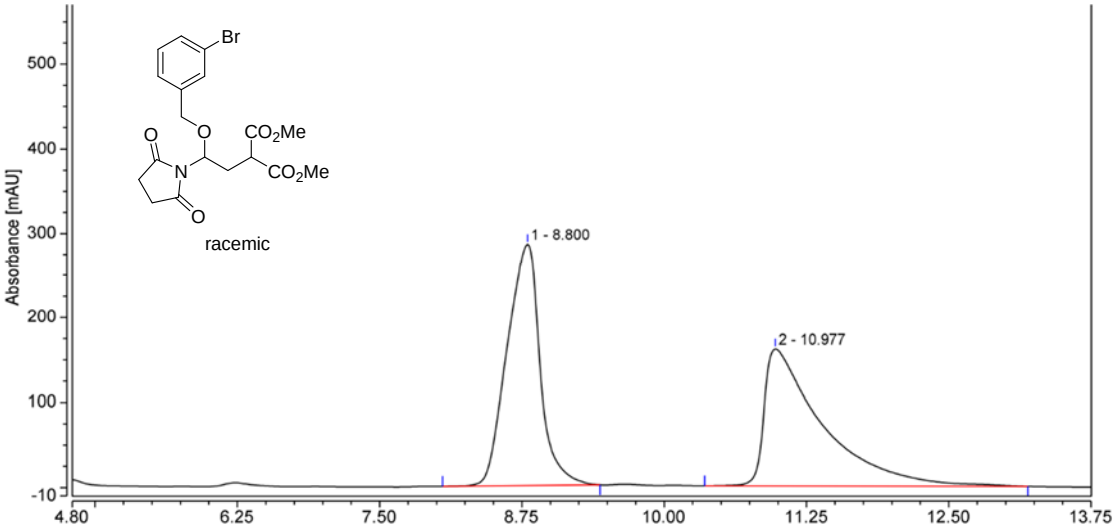
Peak	Retention Time min	Area mAU*min	Height mAU	Area %	Height %
1	11.832	120.338	266.776	50.12	59.07
2	14.450	119.781	184.872	49.88	40.93
Total:		**240.119**	**451.649**	**100.00**	**100.00**

HPLC Spectrum of (*S*)-**3ag**



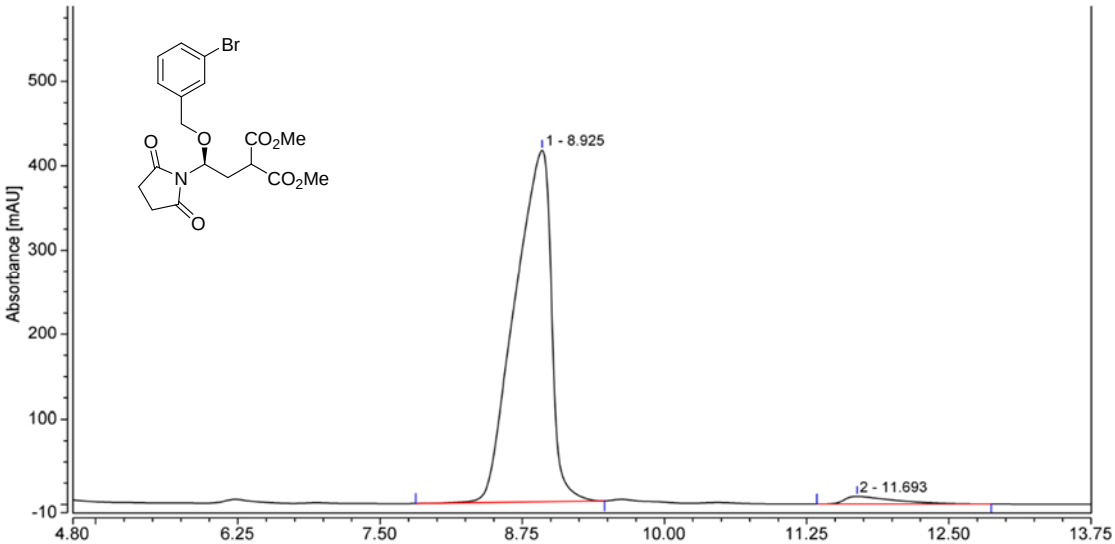
Peak	Retention Time min	Area mAU*min	Height mAU	Area %	Height %
1	11.843	132.671	303.866	96.51	97.00
2	15.030	4.796	9.413	3.49	3.00
Total:		**137.467**	**313.279**	**100.00**	**100.00**

HPLC Spectrum of (±)-**3ah**



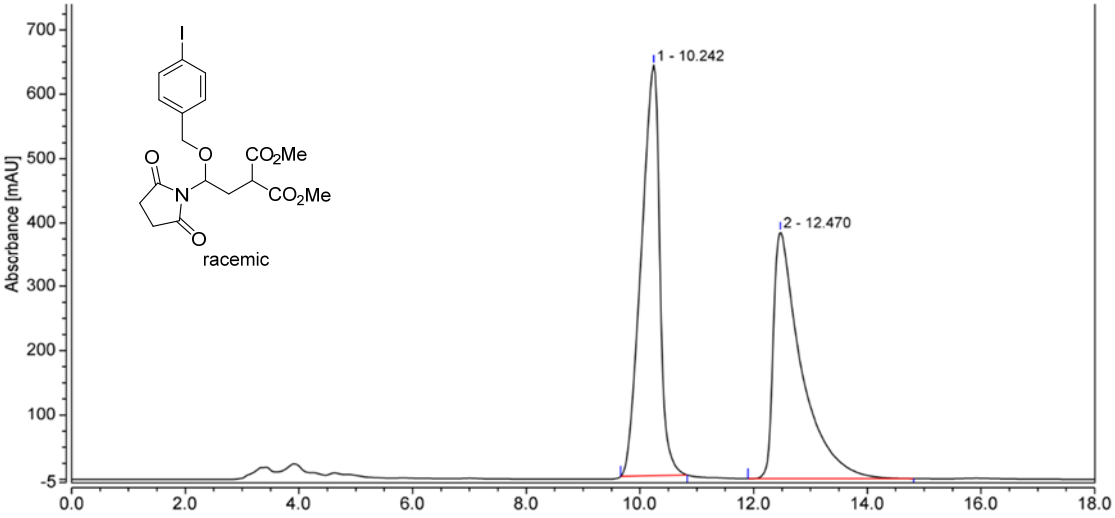
Peak	Retention Time min	Area mAU*min	Height mAU	Area %	Height %
1	8.800	95.664	284.998	50.12	63.94
2	10.977	95.218	160.738	49.88	36.06
Total:		**190.881**	**445.735**	**100.00**	**100.00**

HPLC Spectrum of (*S*)-**3ah**



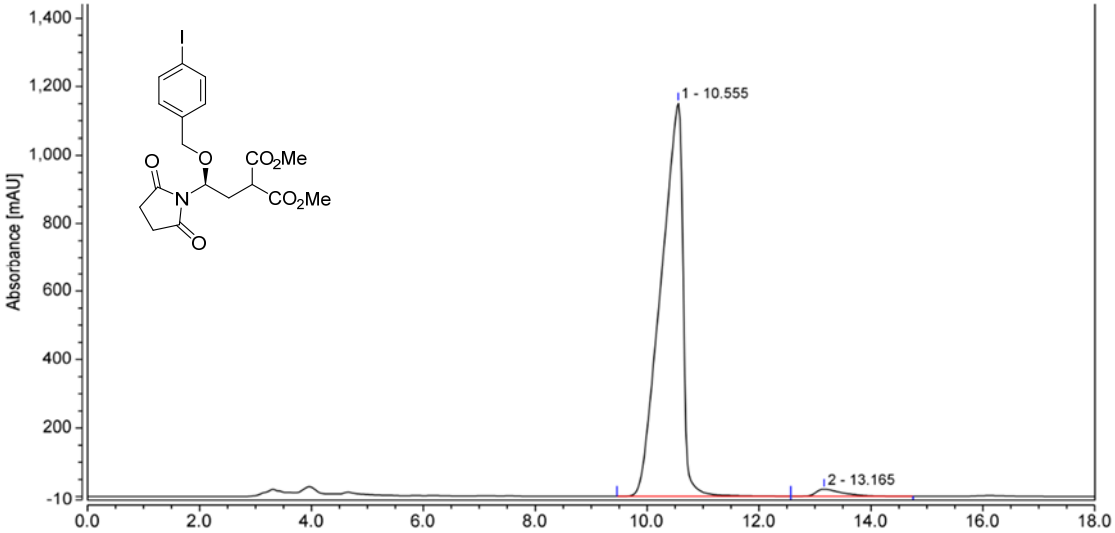
Peak	Retention Time min	Area mAU*min	Height mAU	Area %	Height %
1	8.925	153.681	415.577	97.12	97.88
2	11.693	4.558	8.996	2.88	2.12
Total:		**158.240**	**424.573**	**100.00**	**100.00**

HPLC Spectrum of (±)-**3ai**



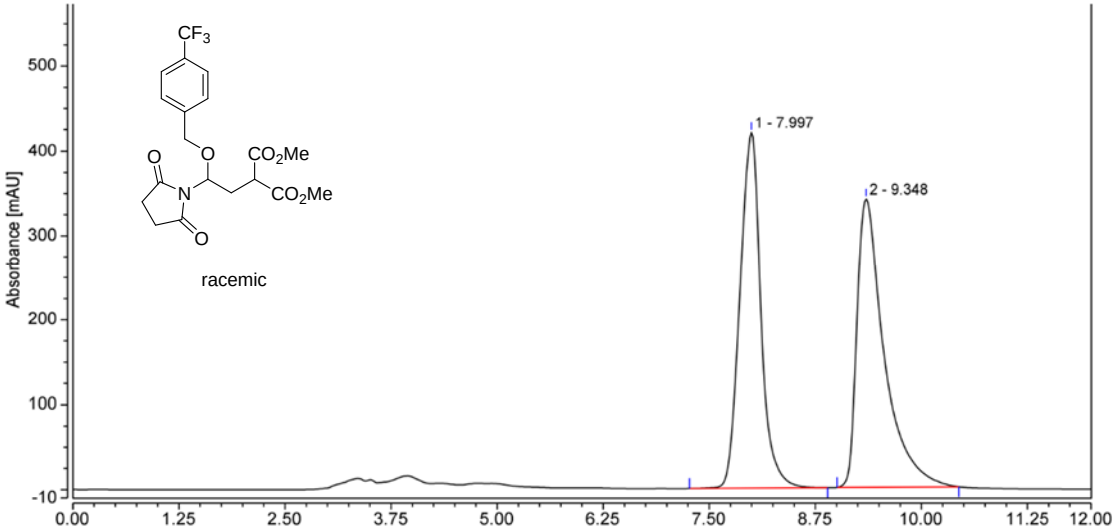
Peak	Retention Time min	Area mAU*min	Height mAU	Area %	Height %
1	10.242	240.671	639.324	52.45	62.44
2	12.470	218.204	384.623	47.55	37.56
Total:		**458.875**	**1023.947**	**100.00**	**100.00**

HPLC Spectrum of (*S*)-**3ai**



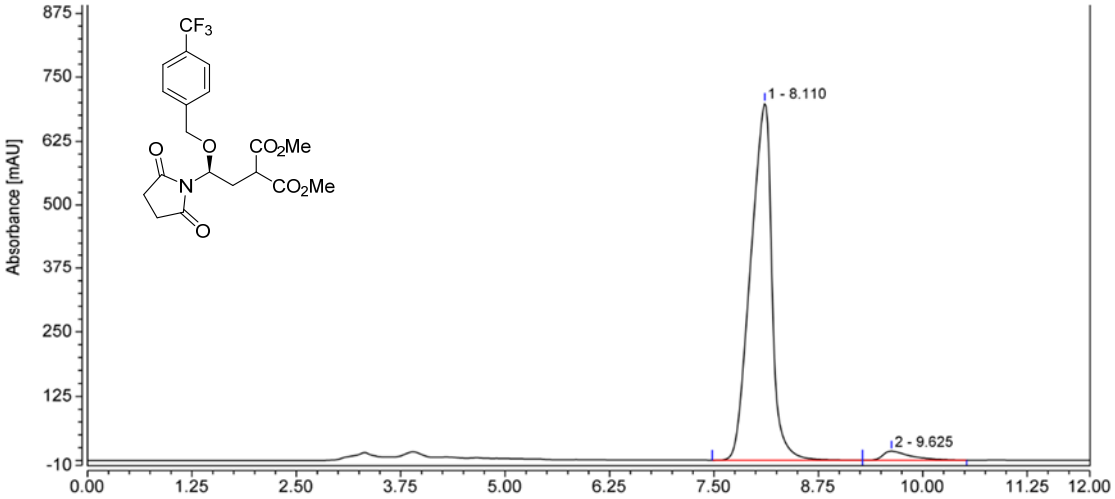
Peak	Retention Time min	Area mAU*min	Height mAU	Area %	Height %
1	10.555	522.670	1151.427	97.82	98.23
2	13.165	11.629	20.765	2.18	1.77
Total:		**534.298**	**1172.192**	**100.00**	**100.00**

HPLC Spectrum of (±)-**3aj**



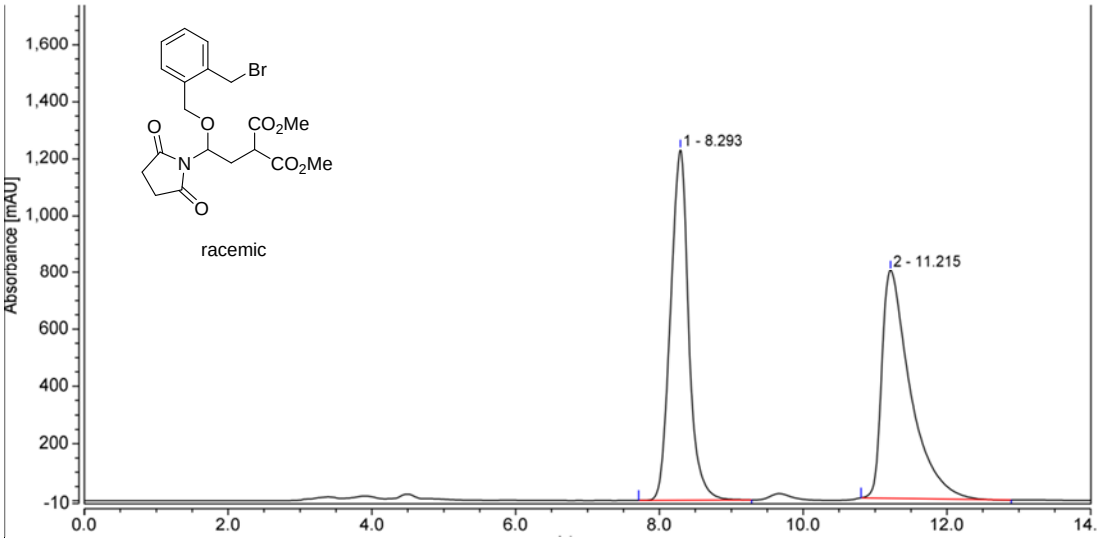
Peak	Retention Time min	Area mAU*min	Height mAU	Area %	Height %
1	7.997	119.942	419.912	48.66	55.19
2	9.348	126.526	340.975	51.34	44.81
Total:		**246.468**	**760.887**	**100.00**	**100.00**

HPLC Spectrum of (*S*)-**3aj**



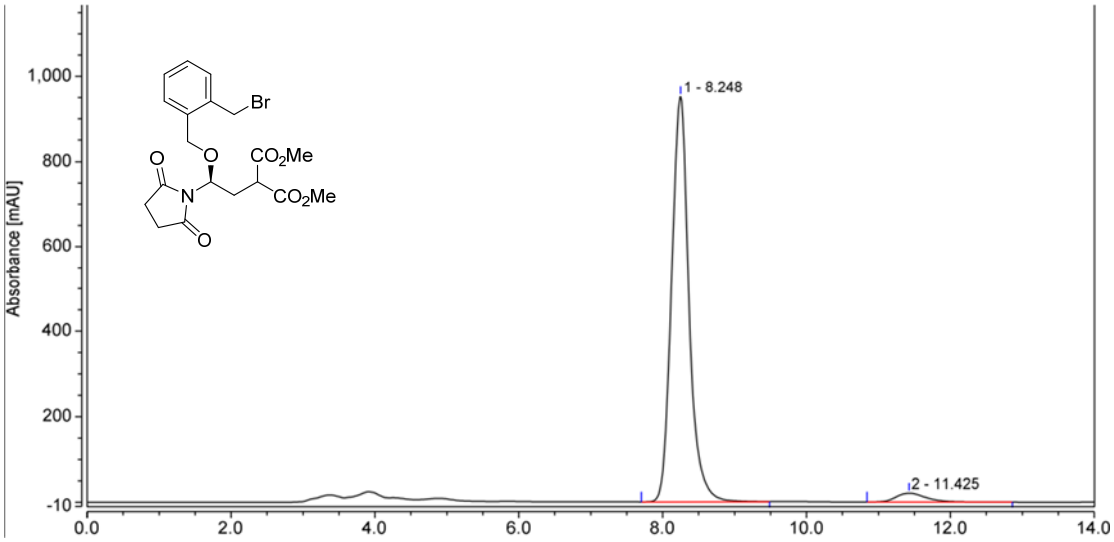
Peak	Retention Time min	Area mAU*min	Height mAU	Area %	Height %
1	8.110	206.329	698.109	96.83	97.53
2	9.625	6.748	17.711	3.17	2.47
Total:		**213.078**	**715.820**	**100.00**	**100.00**

HPLC Spectrum of (±)-**3al**



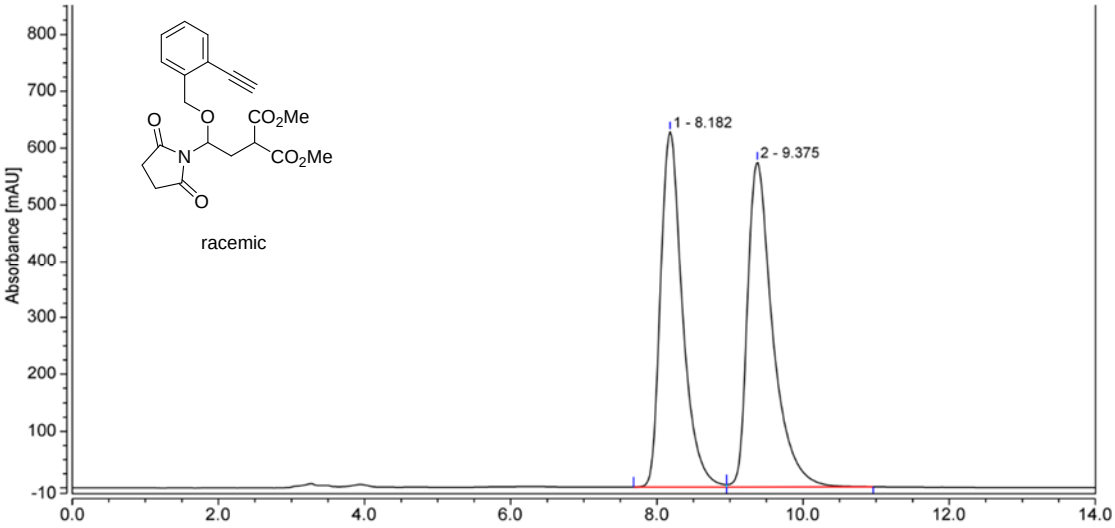
Peak	Retention Time min	Area mAU*min	Height mAU	Area %	Height %
1	8.293	359.286	1229.329	49.55	60.64
2	11.215	365.855	797.943	50.45	39.36
Total:		**725.140**	**2027.272**	**100.00**	**100.00**

HPLC Spectrum of (*S*)-**3al**



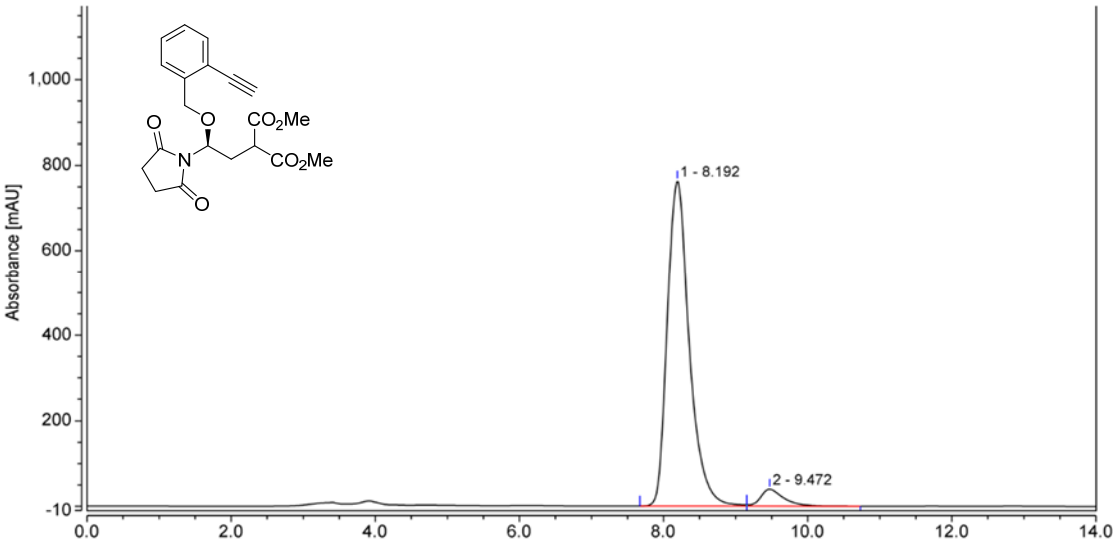
Peak	Retention Time min	Area mAU*min	Height mAU	Area %	Height %
1	8.248	267.026	951.499	96.39	97.87
2	11.425	9.992	20.682	3.61	2.13
Total:		**277.018**	**972.181**	**100.00**	**100.00**

HPLC Spectrum of (±)-**3am**



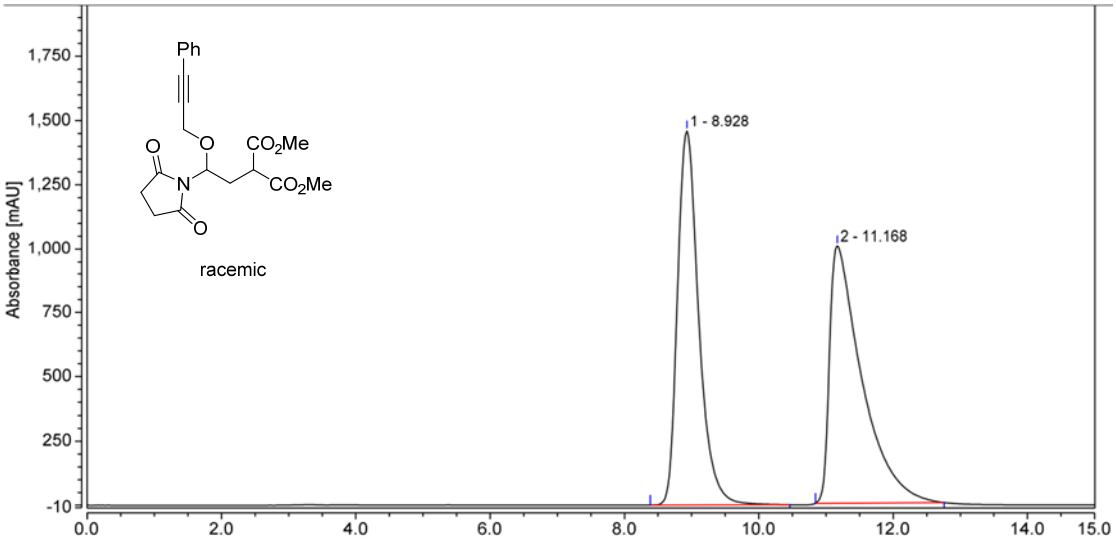
Peak	Retention Time min	Area mAU*min	Height mAU	Area %	Height %
1	8.182	217.711	627.202	48.77	52.24
2	9.375	228.709	573.319	51.23	47.76
Total:		**446.420**	**1200.521**	**100.00**	**100.00**

HPLC Spectrum of (*S*)-**3am**



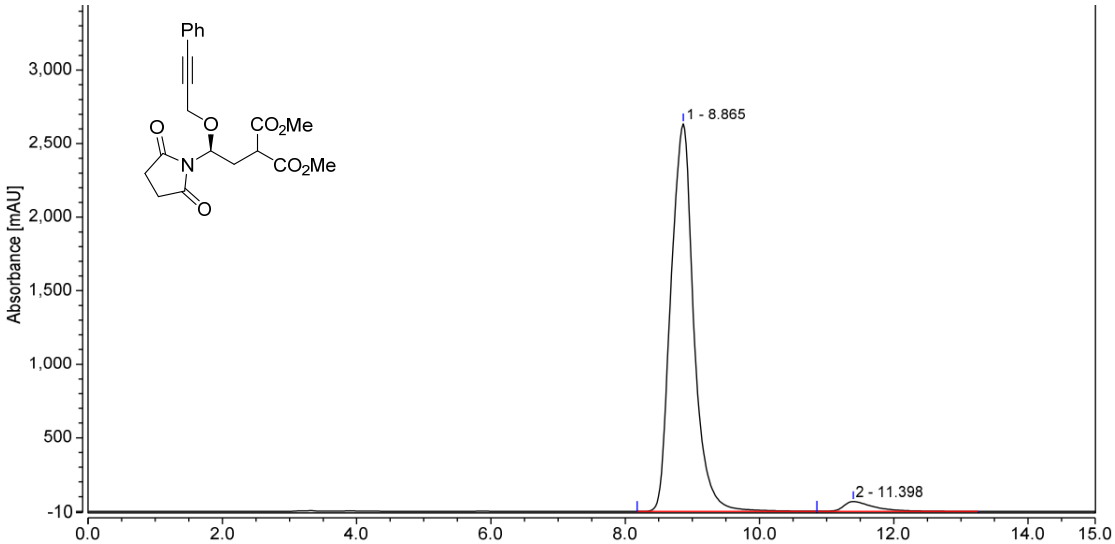
Peak	Retention Time min	Area mAU*min	Height mAU	Area %	Height %
1	8.192	269.554	763.255	94.78	95.04
2	9.472	14.851	39.807	5.22	4.96
Total:		**284.405**	**803.063**	**100.00**	**100.00**

HPLC Spectrum of (±)-**3an**



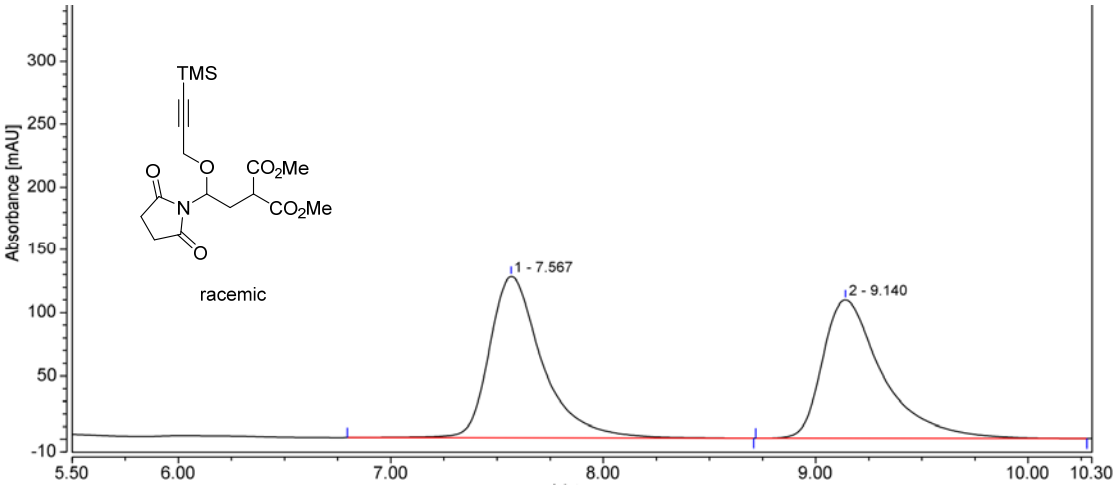
Peak	Retention Time min	Area mAU*min	Height mAU	Area %	Height %
1	8.928	535.819	1459.000	49.09	59.21
2	11.168	555.709	1004.964	50.91	40.79
Total:		**1091.528**	**2463.965**	**100.00**	**100.00**

HPLC Spectrum of (*S*)-**3an**



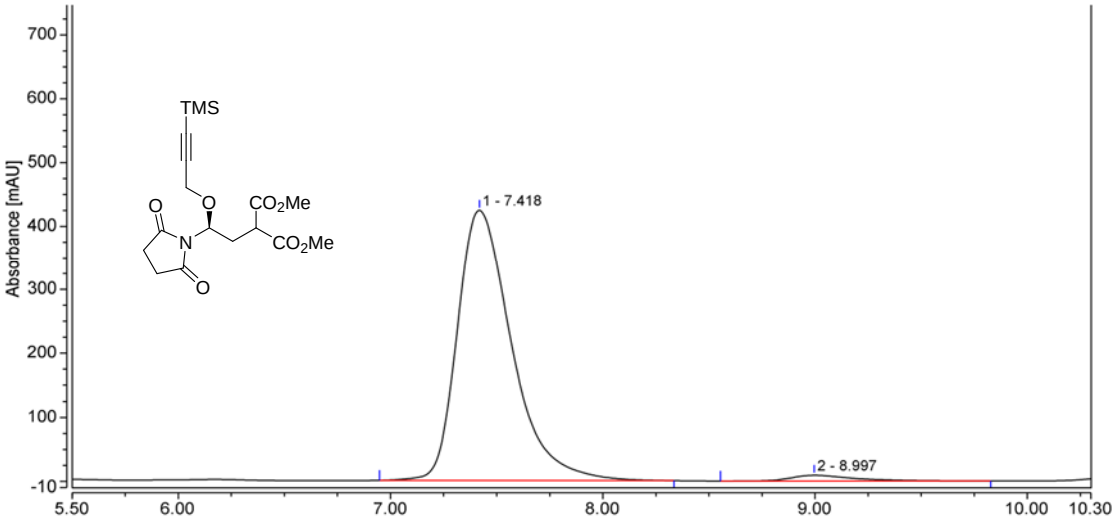
Peak	Retention Time min	Area mAU*min	Height mAU	Area %	Height %
1	8.865	1036.188	2635.931	96.66	97.52
2	11.398	35.860	67.048	3.34	2.48
Total:		**1072.048**	**2702.979**	**100.00**	**100.00**

HPLC Spectrum of (±)-**3ao**



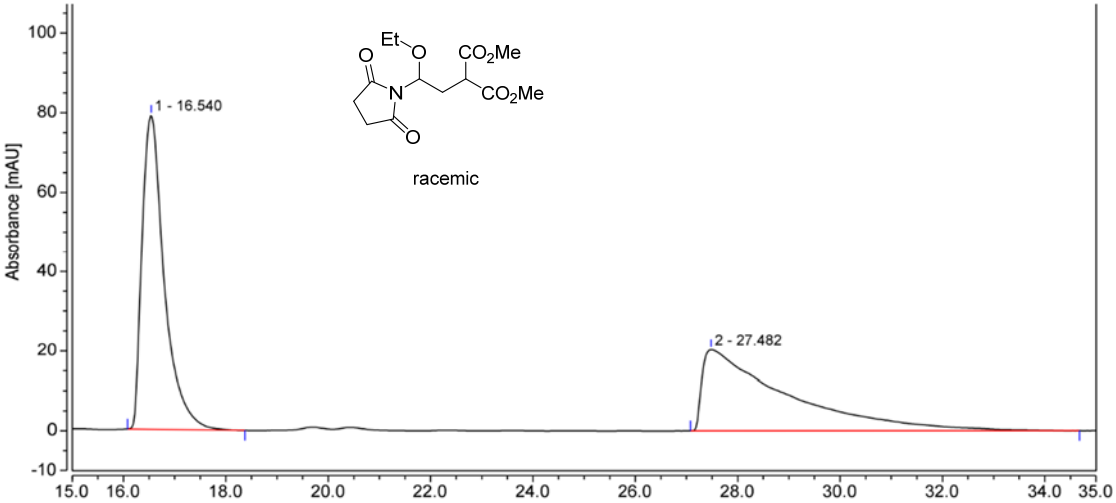
Peak	Retention Time min	Area mAU*min	Height mAU	Area %	Height %
1	7.567	36.862	127.354	50.69	53.84
2	9.140	35.853	109.201	49.31	46.16
Total:		**72.715**	**236.555**	**100.00**	**100.00**

HPLC Spectrum of (*S*)-**3ao**



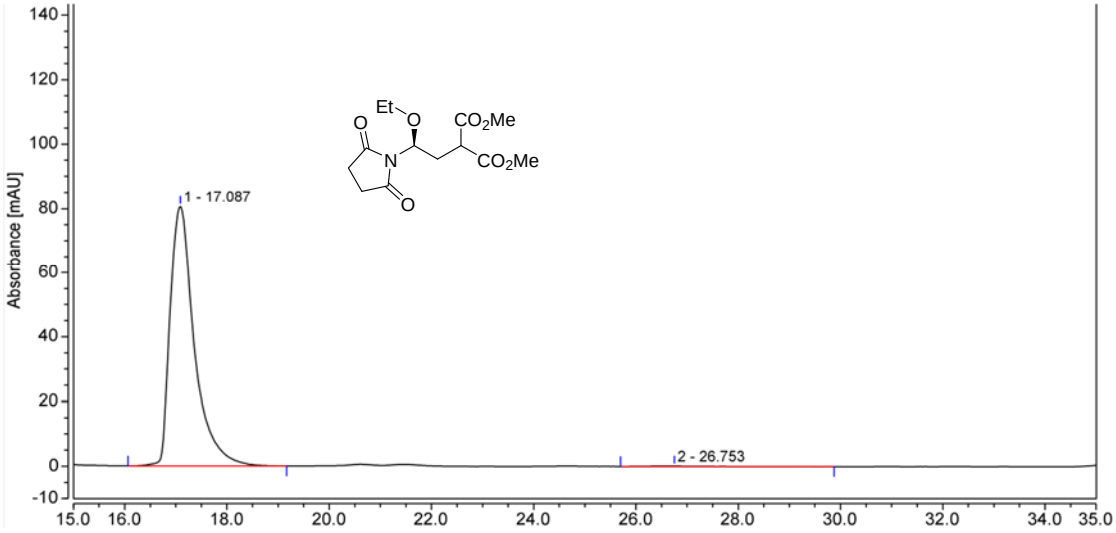
Peak	Retention Time min	Area mAU*min	Height mAU	Area %	Height %
1	7.418	125.259	423.820	97.58	97.94
2	8.997	3.105	8.927	2.42	2.06
Total:		**128.365**	**432.747**	**100.00**	**100.00**

HPLC Spectrum of (±)-**3ap**



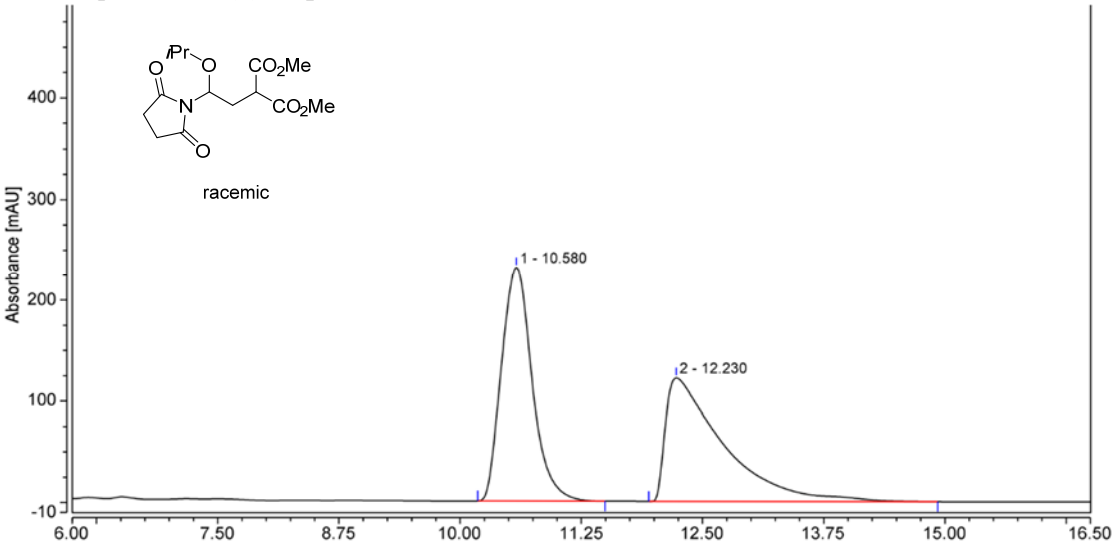
Peak	Retention Time min	Area mAU*min	Height mAU	Area %	Height %
1	16.540	39.640	78.977	50.81	79.57
2	27.482	38.380	20.281	49.19	20.43
Total:		**78.020**	**99.258**	**100.00**	**100.00**

HPLC Spectrum of (*S*)-**3ap**



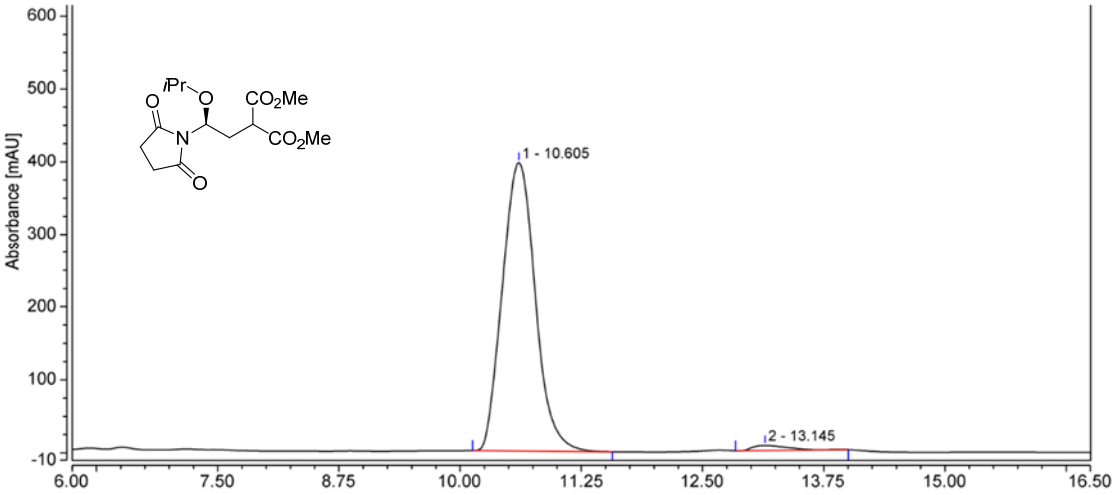
Peak	Retention Time min	Area mAU*min	Height mAU	Area %	Height %
1	17.087	44.155	80.640	99.60	99.82
2	26.753	0.179	0.146	0.40	0.18
Total:		**44.333**	**80.786**	**100.00**	**100.00**

HPLC Spectrum of (±)-**3aq**



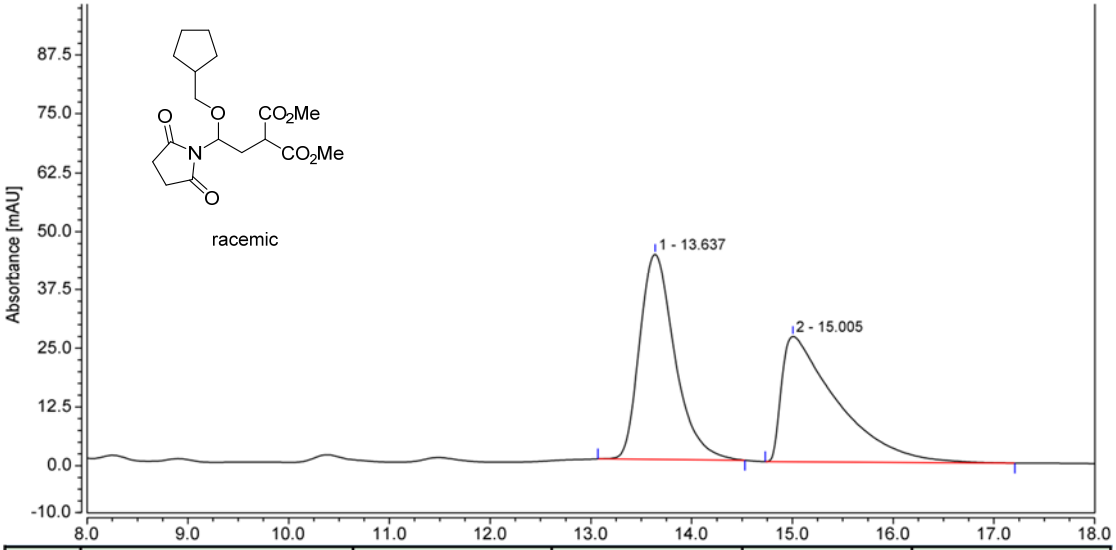
Peak	Retention Time min	Area mAU*min	Height mAU	Area %	Height %
1	10.580	84.931	231.594	50.28	65.53
2	12.230	83.988	121.847	49.72	34.47
Total:		**168.918**	**353.441**	**100.00**	**100.00**

HPLC Spectrum of (*S*)-**3aq**



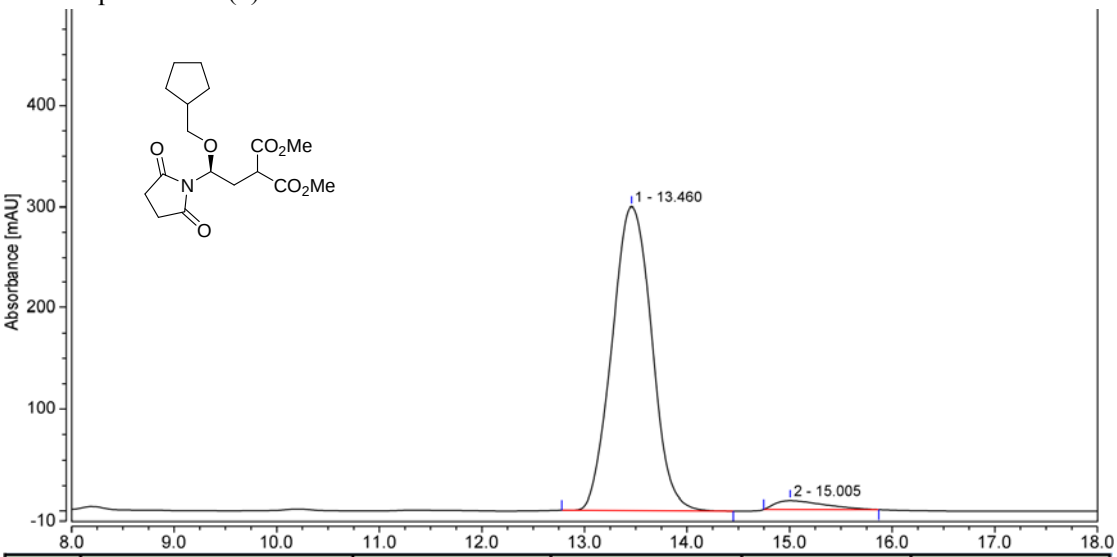
Peak	Retention Time min	Area mAU*min	Height mAU	Area %	Height %
1	10.605	155.866	396.252	98.18	98.31
2	13.145	2.897	6.824	1.82	1.69
Total:		**158.763**	**403.076**	**100.00**	**100.00**

HPLC Spectrum of (±)-**3ar**



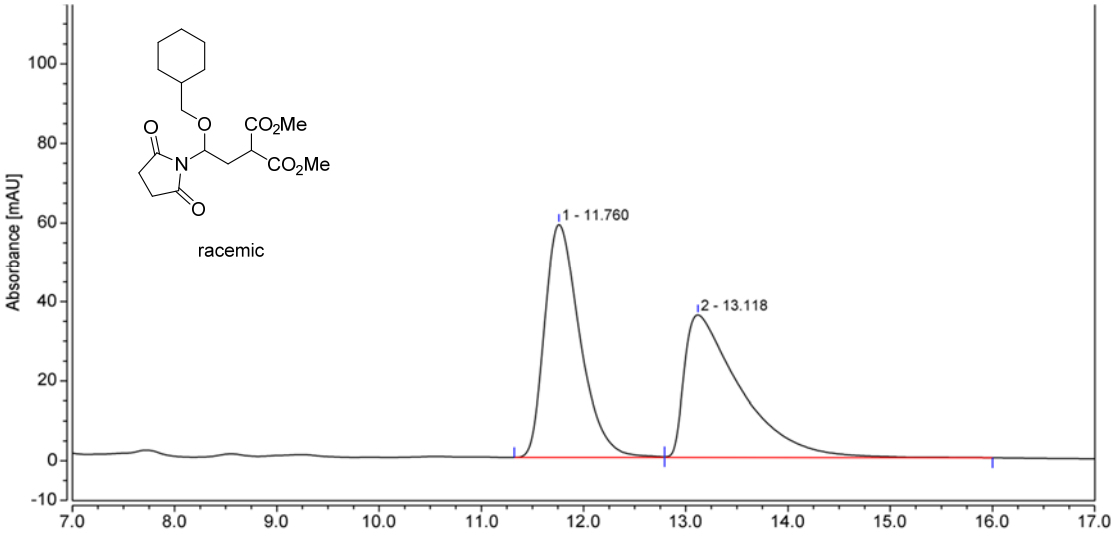
Peak	Retention Time min	Area mAU*min	Height mAU	Area %	Height %
1	13.637	17.744	43.866	51.03	62.18
2	15.005	17.031	26.676	48.97	37.82
Total:		**34.775**	**70.542**	**100.00**	**100.00**

HPLC Spectrum of (*S*)-**3ar**



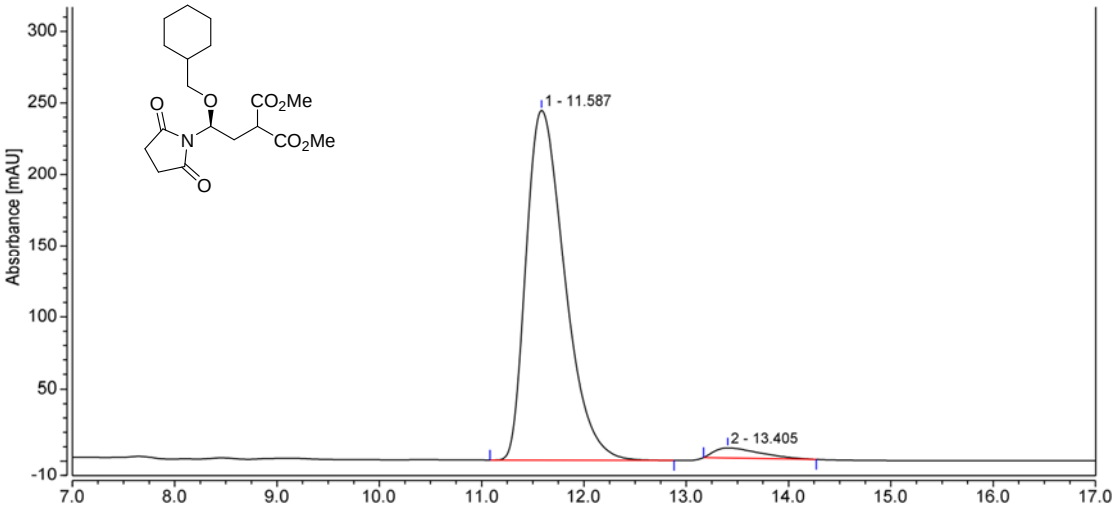
Peak	Retention Time min	Area mAU*min	Height mAU	Area %	Height %
1	13.460	134.130	300.124	96.41	97.11
2	15.005	5.000	8.934	3.59	2.89
Total:		**139.130**	**309.058**	**100.00**	**100.00**

HPLC Spectrum of (±)-**3as**



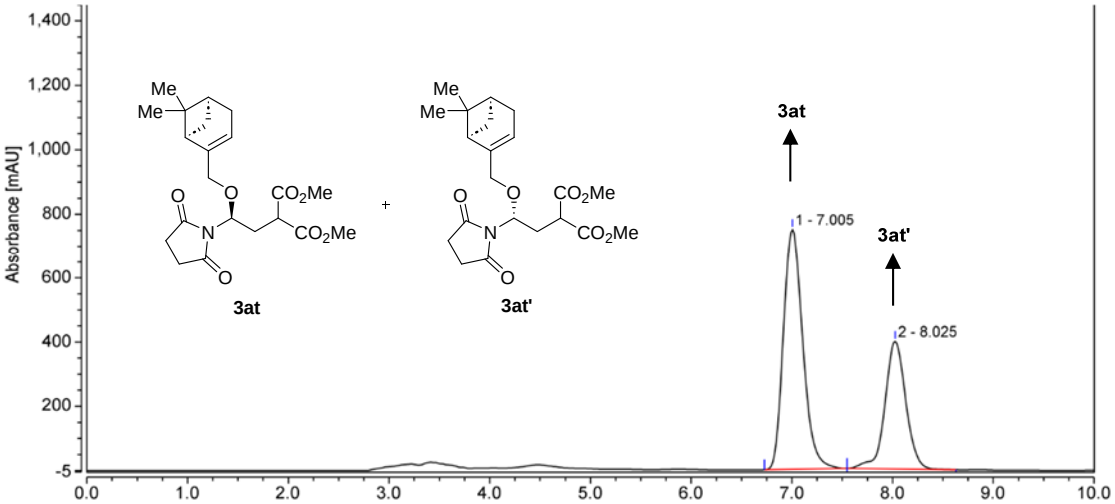
Peak	Retention Time min	Area mAU*min	Height mAU	Area %	Height %
1	11.760	23.605	58.826	50.76	62.14
2	13.118	22.903	35.844	49.24	37.86
Total:		**46.508**	**94.670**	**100.00**	**100.00**

HPLC Spectrum of (*S*)-**3as**



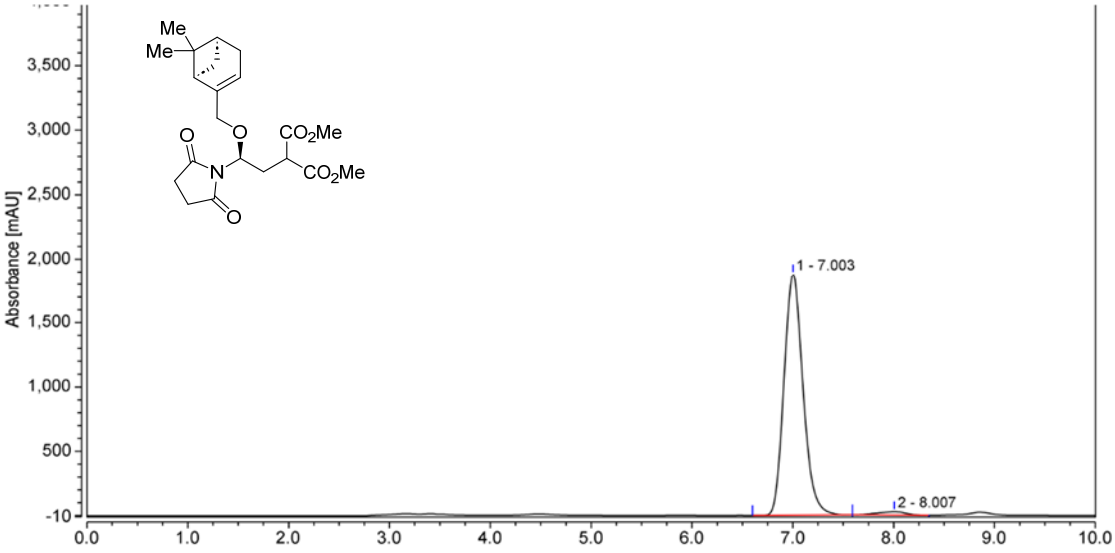
Peak	Retention Time min	Area mAU*min	Height mAU	Area %	Height %
1	11.587	106.615	244.190	96.72	97.22
2	13.405	3.618	6.984	3.28	2.78
Total:		**110.234**	**251.174**	**100.00**	**100.00**

HPLC Spectrum for the mixture of **3at** and **3at'**



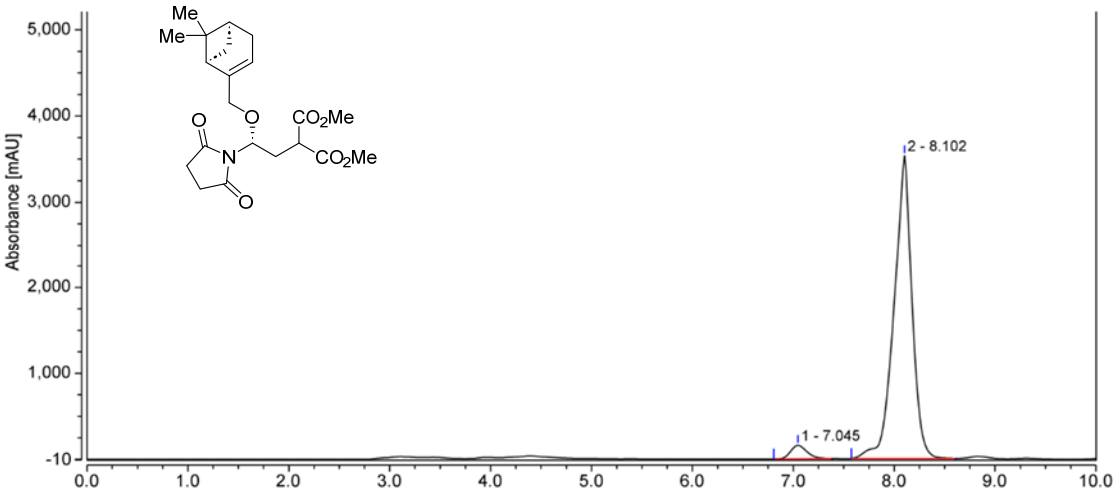
Peak	Retention Time min	Area mAU*min	Height mAU	Area %	Height %
1	7.005	167.187	749.375	63.58	65.33
2	8.025	95.754	397.710	36.42	34.67
Total:		**262.941**	**1147.086**	**100.00**	**100.00**

HPLC Spectrum of (*S*, 1*R*, 5*S*)-**3at**



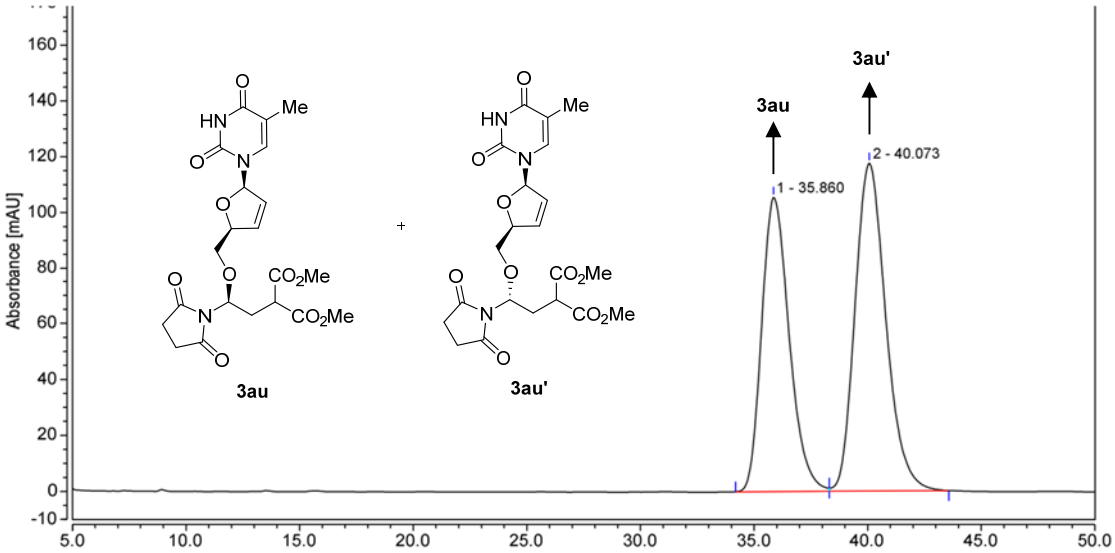
Peak	Retention Time min	Area mAU*min	Height mAU	Area %	Height %
1	7.003	409.501	1876.324	97.97	98.62
2	8.007	8.469	26.324	2.03	1.38
Total:		**417.970**	**1902.647**	**100.00**	**100.00**

HPLC Spectrum of (*R*, 1*R*, 5*S*)-**3at'**



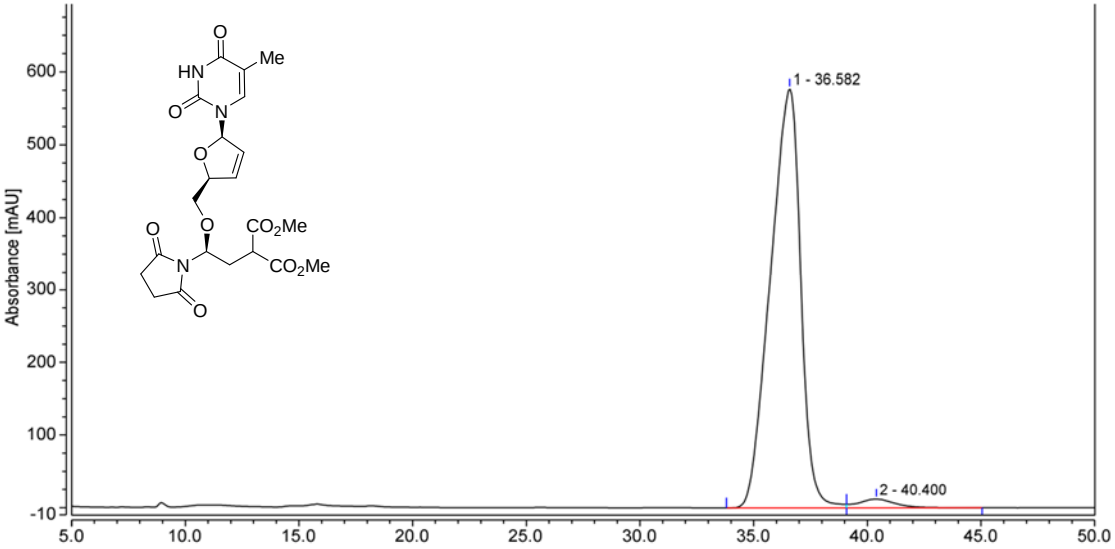
Peak	Retention Time min	Area mAU*min	Height mAU	Area %	Height %
1	7.045	28.965	156.823	3.83	4.25
2	8.102	727.550	3532.511	96.17	95.75
Total:		**756.515**	**3689.334**	**100.00**	**100.00**

HPLC Spectrum for the mixture of **3au** and **3au'**



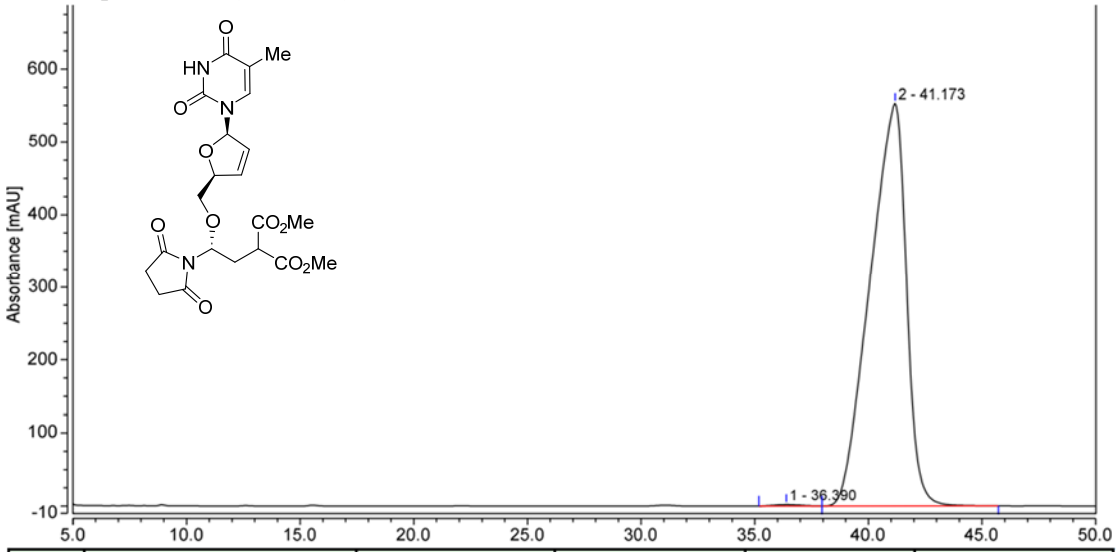
Peak	Retention Time min	Area mAU*min	Height mAU	Area %	Height %
1	35.860	147.625	105.646	44.45	47.31
2	40.073	184.522	117.679	55.55	52.69
Total:		**332.146**	**223.325**	**100.00**	**100.00**

HPLC Spectrum of (S, 2*S*, 5*R*)-**3au**



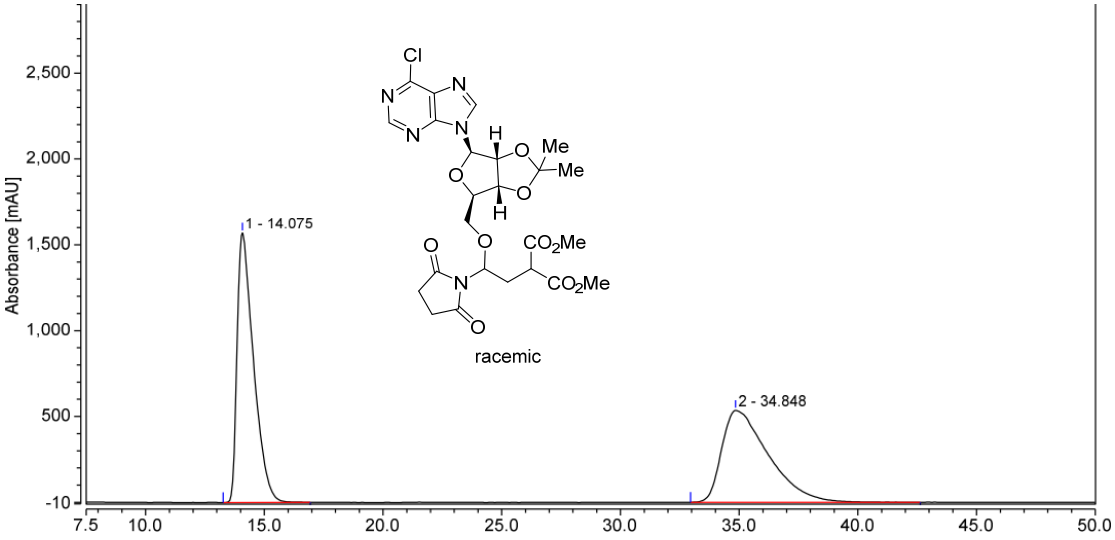
Peak	Retention Time min	Area mAU*min	Height mAU	Area %	Height %
1	36.582	889.357	576.893	97.57	97.99
2	40.400	22.142	11.824	2.43	2.01
Total:		**911.499**	**588.717**	**100.00**	**100.00**

HPLC Spectrum of (*R*, 2*S*, 5*R*)-**3au'**



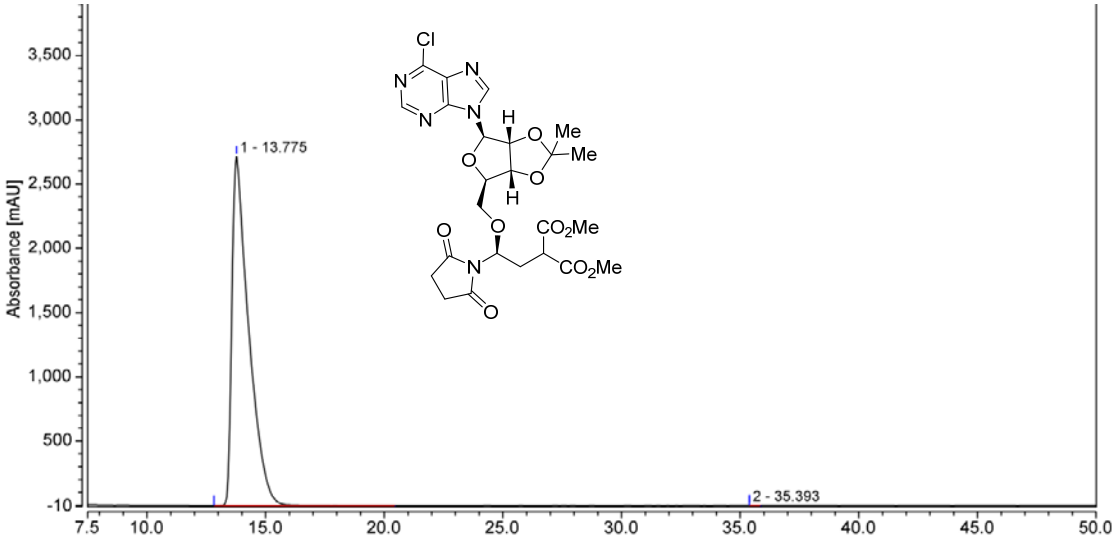
Peak	Retention Time min	Area mAU*min	Height mAU	Area %	Height %
1	36.390	2.543	1.880	0.25	0.34
2	41.173	1019.635	552.814	99.75	99.66
Total:		**1022.178**	**554.694**	**100.00**	**100.00**

HPLC Spectrum of (±)-**3av**



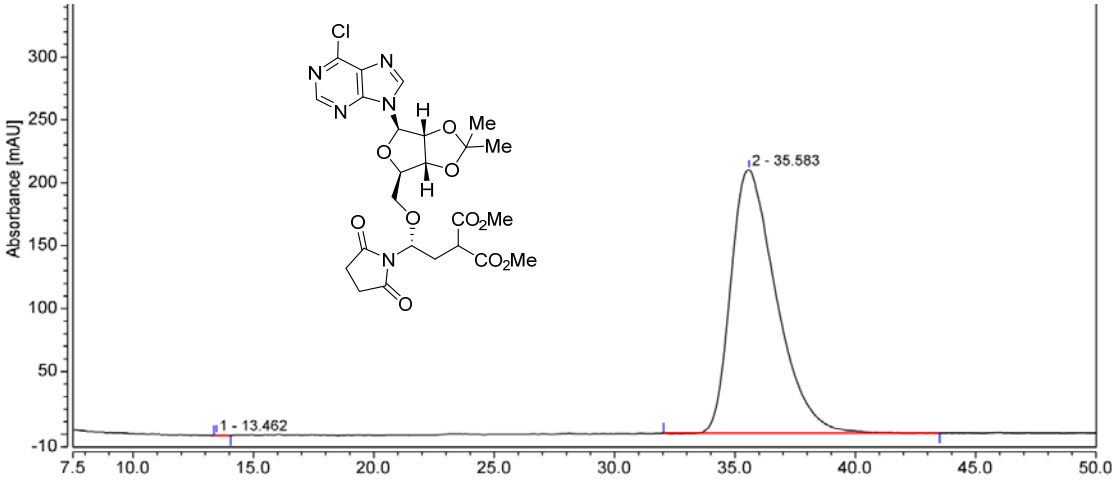
Peak	Retention Time min	Area mAU*min	Height mAU	Area %	Height %
1	14.075	1257.438	1569.705	50.88	74.57
2	34.848	1213.890	535.415	49.12	25.43
Total:		**2471.328**	**2105.120**	**100.00**	**100.00**

HPLC Spectrum of (*S*, 3a*R*, 4*R*, 6*R*, 6a*R*)-**3av**



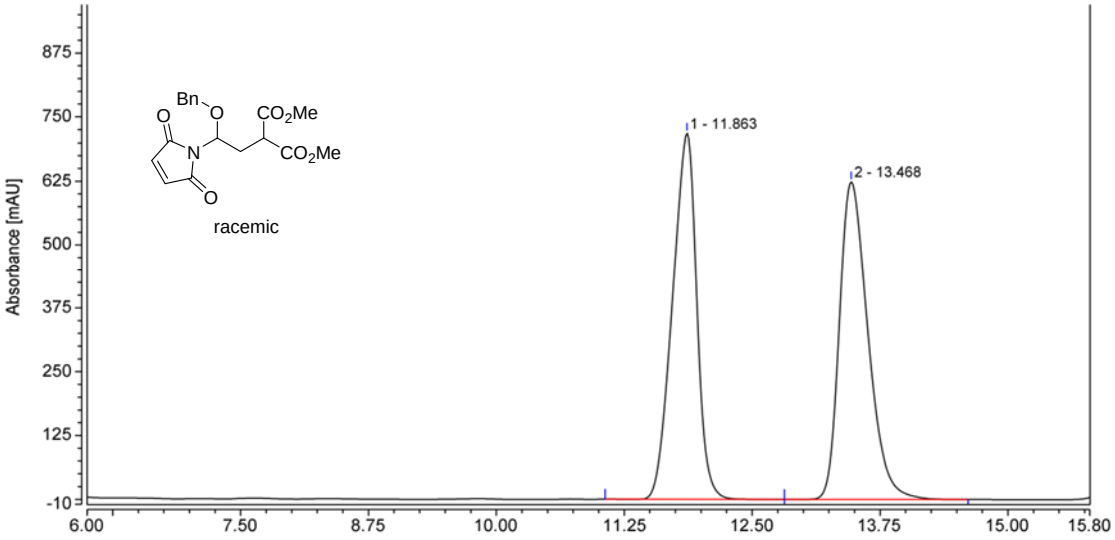
Peak	Retention Time min	Area mAU*min	Height mAU	Area %	Height %
1	13.775	2215.293	2715.555	100.00	100.00
2	35.393	0.014	0.002	0.00	0.00
Total:		**2215.307**	**2715.556**	**100.00**	**100.00**

HPLC Spectrum of (*R*, 3a*R*, 4*R*, 6*R*, 6a*R*)-**3av'**



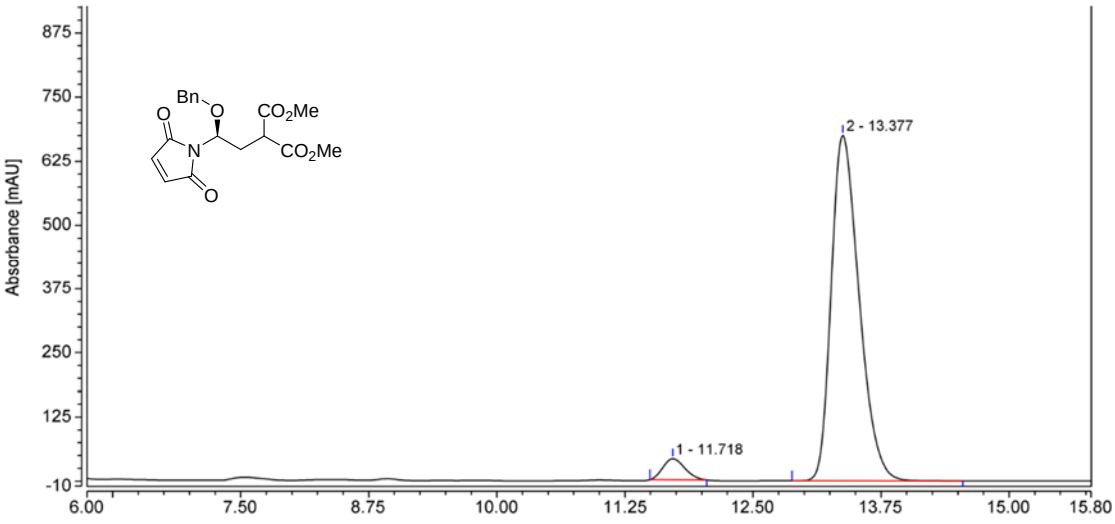
Peak	Retention Time min	Area mAU*min	Height mAU	Area %	Height %
1	13.462	0.079	0.202	0.02	0.10
2	35.583	458.041	209.353	99.98	99.90
Total:		**458.120**	**209.555**	**100.00**	**100.00**

HPLC Spectrum of (±)-**3ba**



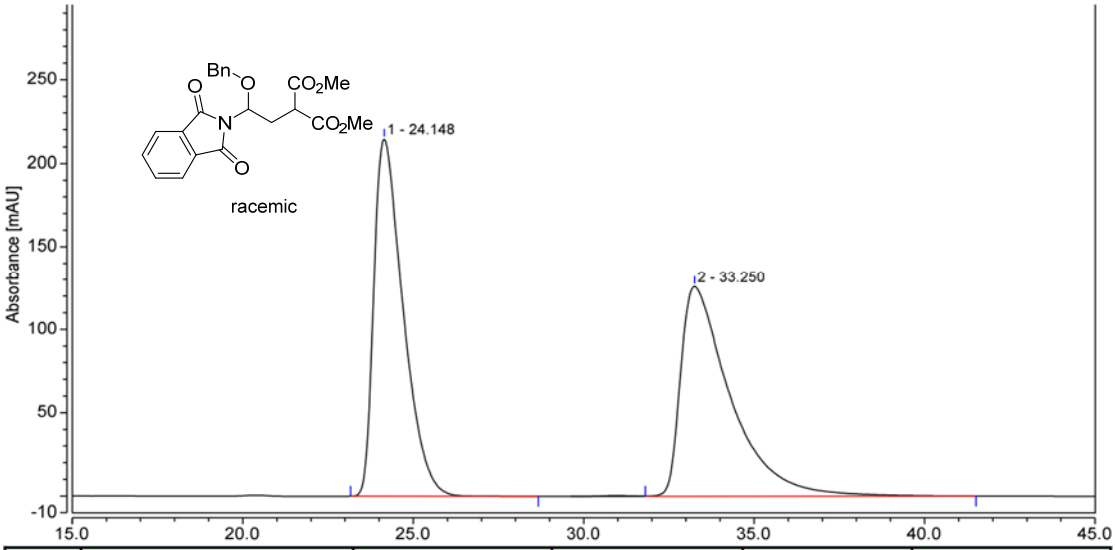
Peak	Retention Time min	Area mAU*min	Height mAU	Area %	Height %
1	11.863	196.402	718.073	49.45	53.50
2	13.468	200.793	624.230	50.55	46.50
Total:		**397.195**	**1342.303**	**100.00**	**100.00**

HPLC Spectrum of (*S*)-**3ba**



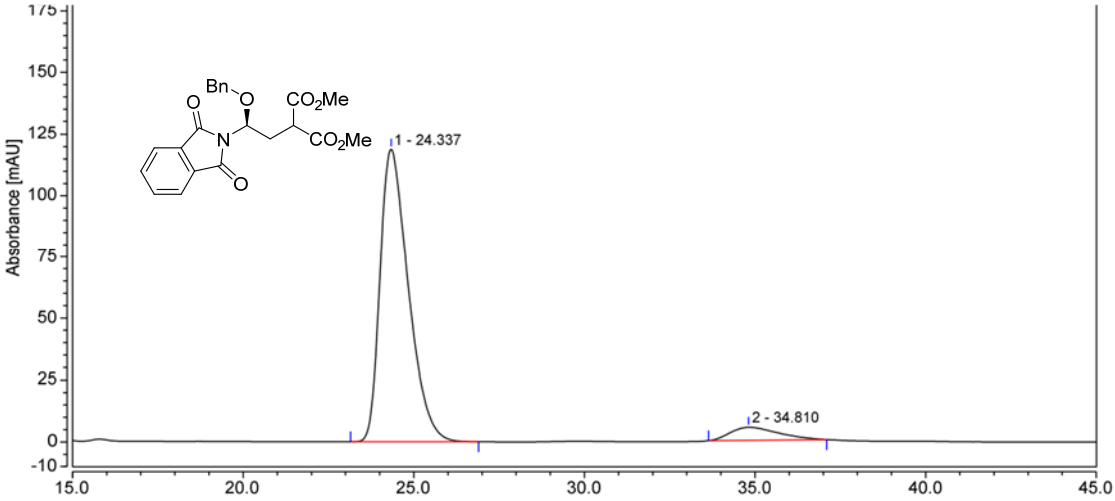
Peak	Retention Time min	Area mAU*min	Height mAU	Area %	Height %
1	11.718	10.217	41.187	4.60	5.75
2	13.377	211.804	675.094	95.40	94.25
Total:		**222.021**	**716.280**	**100.00**	**100.00**

HPLC Spectrum of (±)-**3ca**



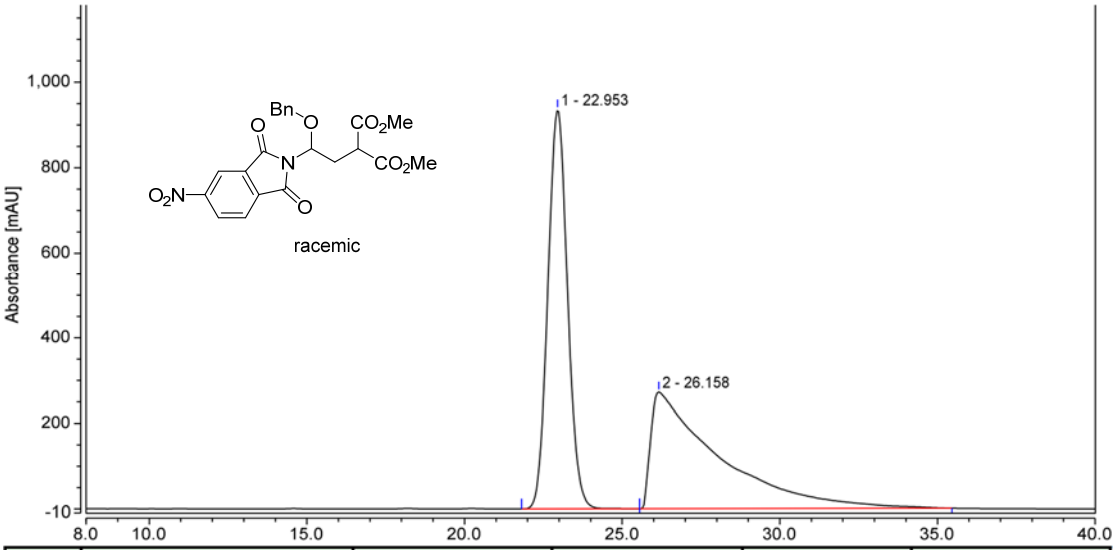
Peak	Retention Time min	Area mAU*min	Height mAU	Area %	Height %
1	24.148	213.934	214.463	50.01	62.98
2	33.250	213.829	126.044	49.99	37.02
Total:		**427.764**	**340.508**	**100.00**	**100.00**

HPLC Spectrum of (*S*)-**3ca**



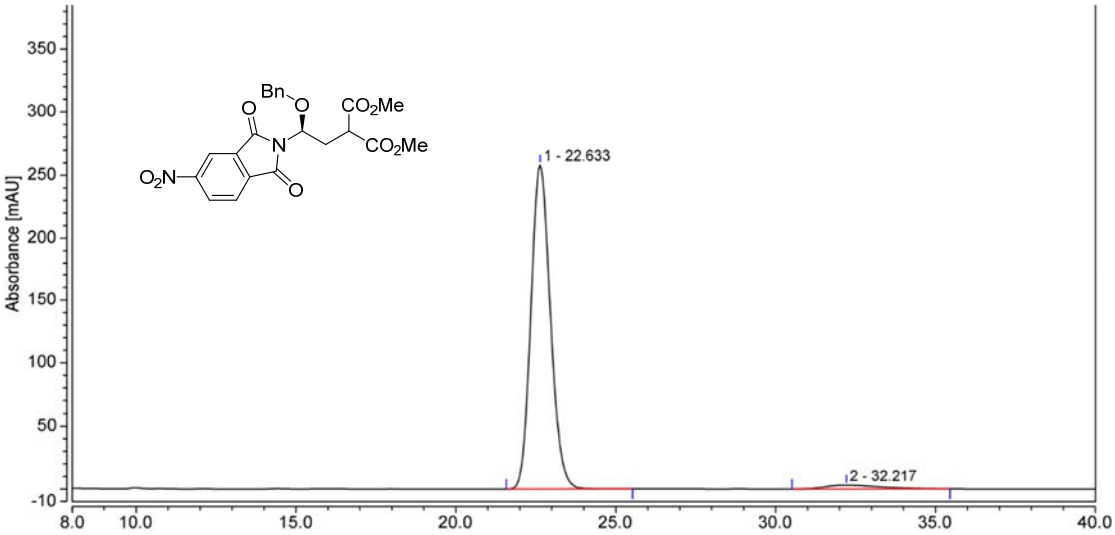
Peak	Retention Time min	Area mAU*min	Height mAU	Area %	Height %
1	24.337	113.906	118.982	93.02	95.77
2	34.810	8.548	5.261	6.98	4.23
Total:		**122.454**	**124.243**	**100.00**	**100.00**

HPLC Spectrum of (±)-**3da**



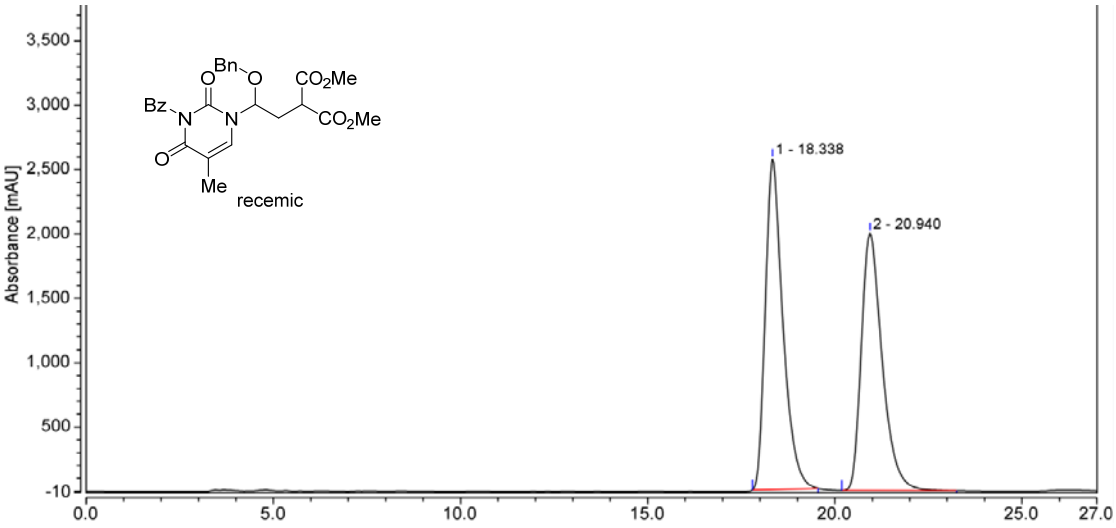
Peak	Retention Time min	Area mAU*min	Height mAU	Area %	Height %
1	22.953	675.722	935.491	49.96	77.46
2	26.158	676.786	272.206	50.04	22.54
Total:		**1352.508**	**1207.697**	**100.00**	**100.00**

HPLC Spectrum of (*S*)-**3da**



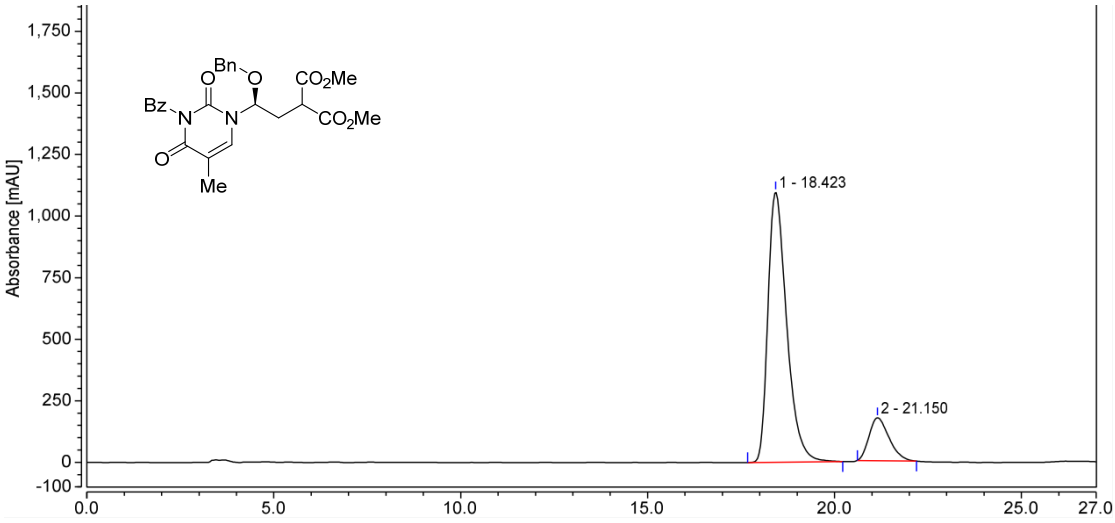
Peak	Retention Time min	Area mAU*min	Height mAU	Area %	Height %
1	22.633	182.258	258.294	96.68	98.83
2	32.217	6.266	3.062	3.32	1.17
Total:		**188.524**	**261.357**	**100.00**	**100.00**

HPLC Spectrum of (±)-**3ea**



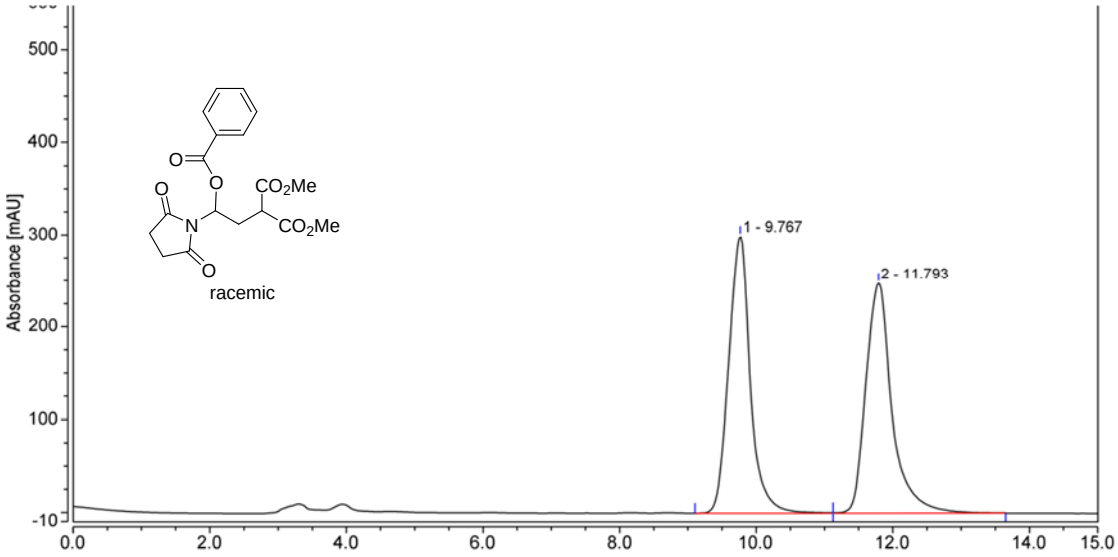
Peak	Retention Time min	Area mAU*min	Height mAU	Area %	Height %
1	18.338	1392.359	2568.448	51.89	56.22
2	20.940	1291.037	2000.224	48.11	43.78
Total:		**2683.396**	**4568.672**	**100.00**	**100.00**

HPLC Spectrum of (*S*)-**3ea**



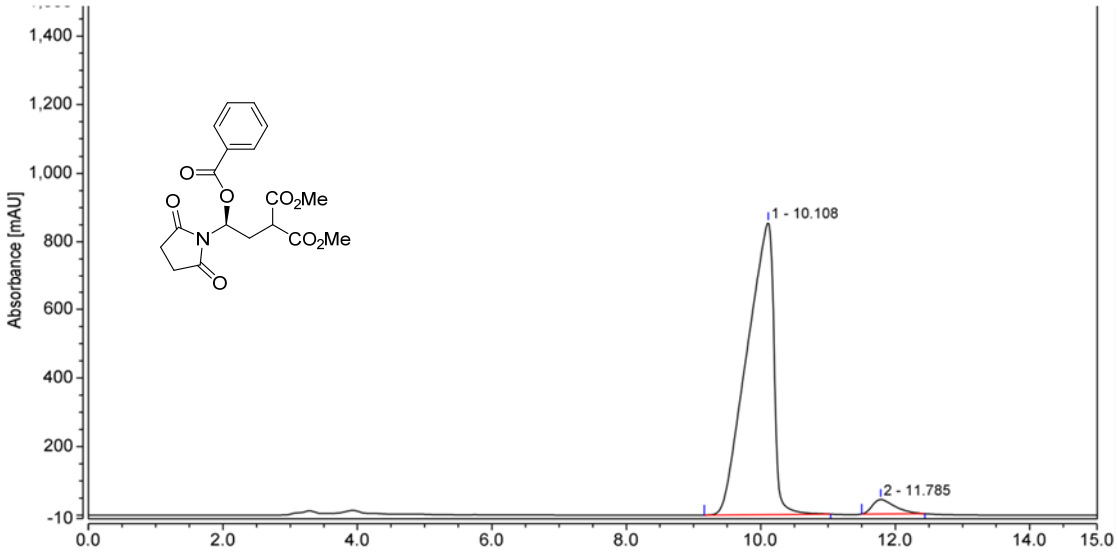
Peak	Retention Time min	Area mAU*min	Height mAU	Area %	Height %
1	18.423	637.871	1098.539	85.48	86.30
2	21.150	108.333	174.431	14.52	13.70
Total:		**746.204**	**1272.971**	**100.00**	**100.00**

HPLC Spectrum of (±)-**5aa**



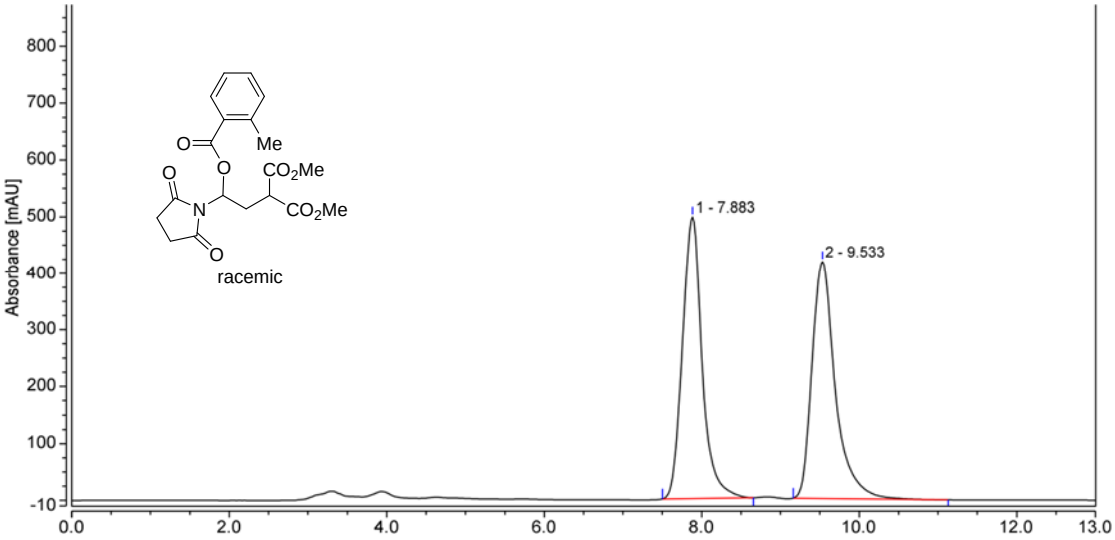
Peak	Retention Time min	Area mAU*min	Height mAU	Area %	Height %
1	9.767	109.473	299.279	49.93	54.67
2	11.793	109.791	248.119	50.07	45.33
Total:		**219.265**	**547.399**	**100.00**	**100.00**

HPLC Spectrum of (*S*)-**5aa**



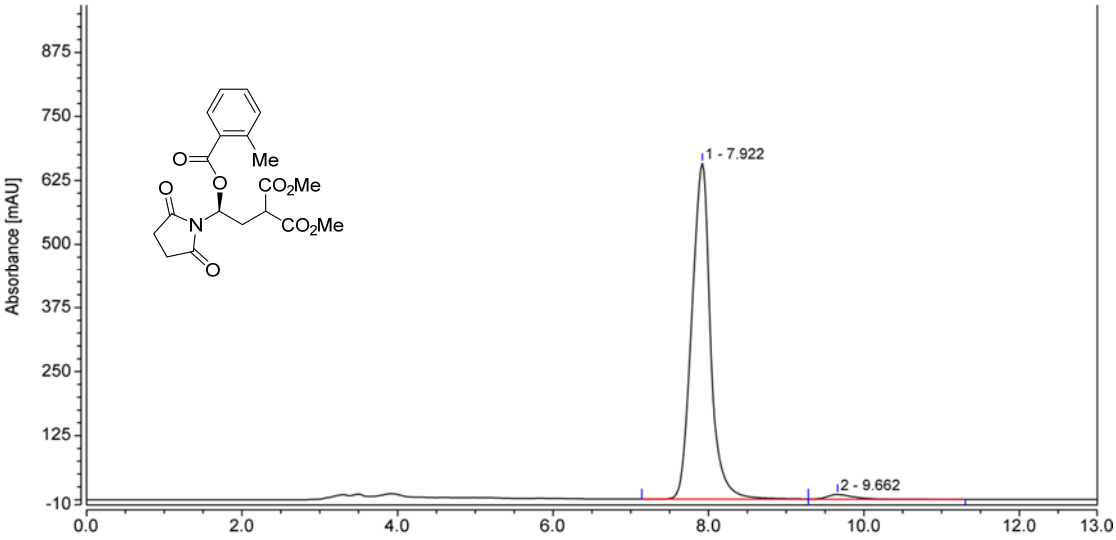
Peak	Retention Time min	Area mAU*min	Height mAU	Area %	Height %
1	10.108	393.022	854.344	96.00	95.32
2	11.785	16.388	41.924	4.00	4.68
Total:		**409.410**	**896.268**	**100.00**	**100.00**

HPLC Spectrum of (±)-**5ab**



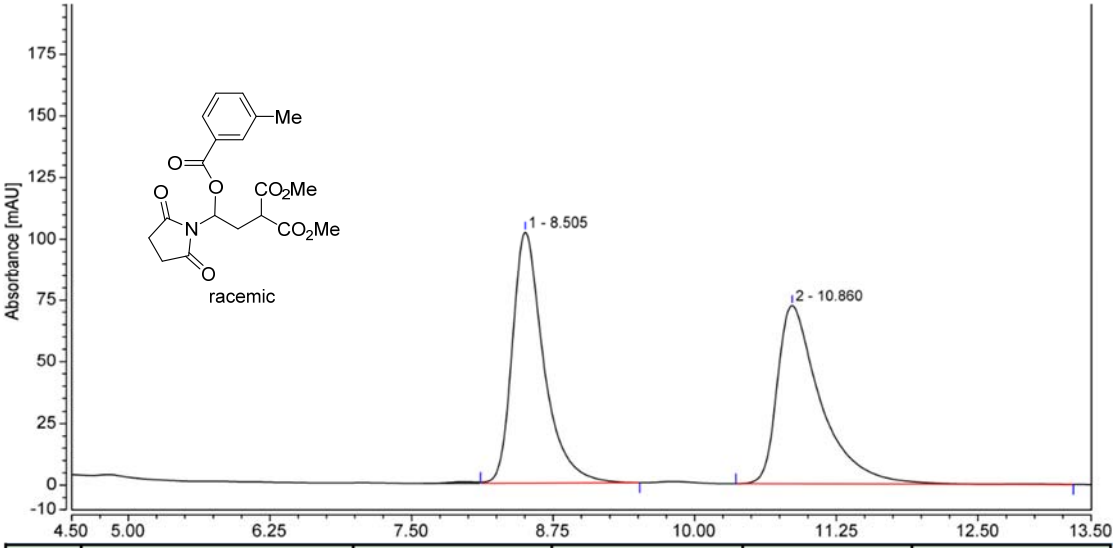
Peak	Retention Time min	Area mAU*min	Height mAU	Area %	Height %
1	7.883	143.492	496.909	50.04	54.33
2	9.533	143.275	417.677	49.96	45.67
Total:		**286.767**	**914.586**	**100.00**	**100.00**

HPLC Spectrum of (*S*)-**5ab**



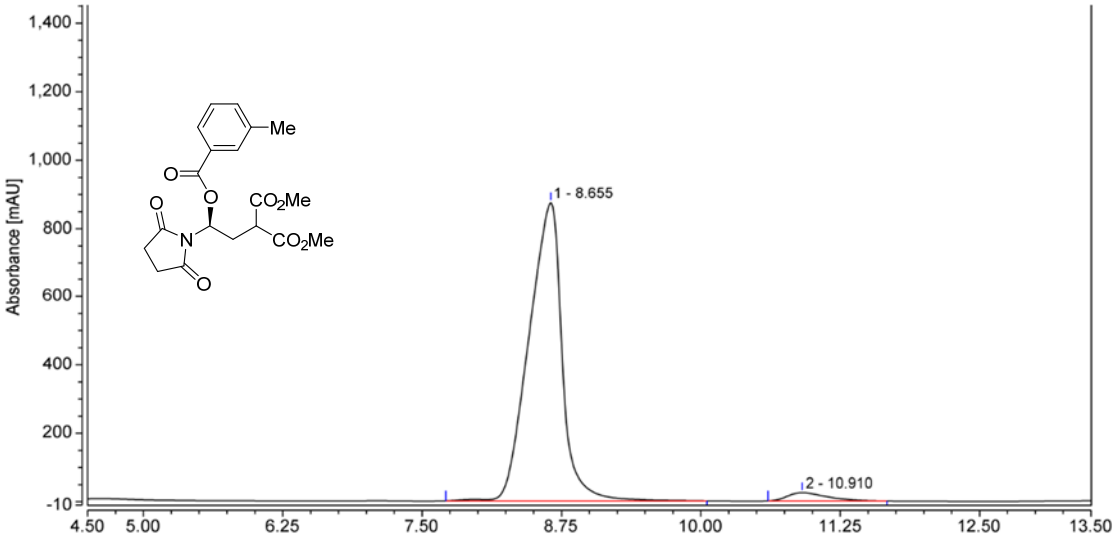
Peak	Retention Time min	Area mAU*min	Height mAU	Area %	Height %
1	7.922	184.303	657.403	97.90	98.60
2	9.662	3.958	9.312	2.10	1.40
Total:		**188.261**	**666.716**	**100.00**	**100.00**

HPLC Spectrum of (±)-**5ac**



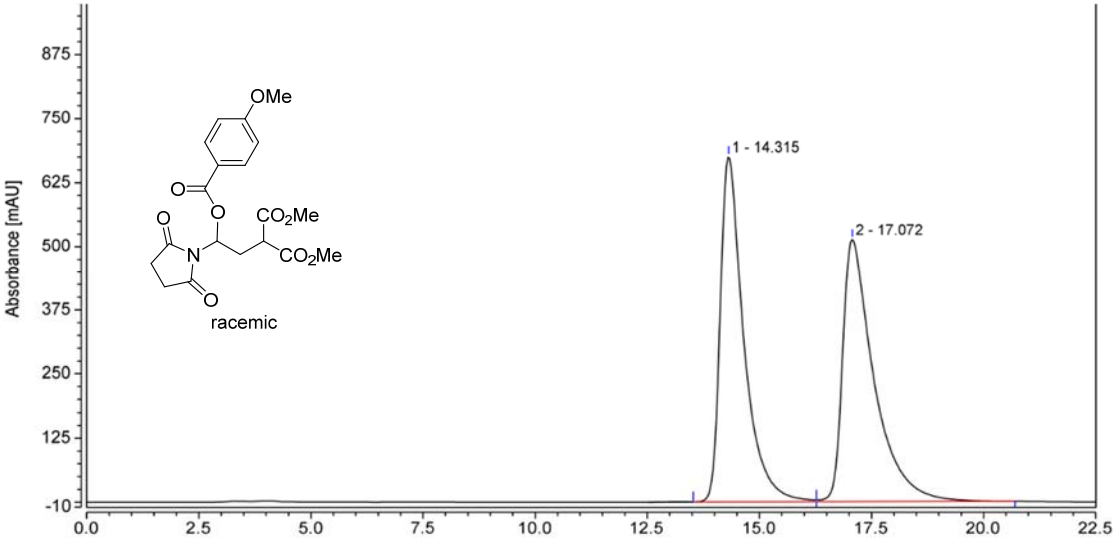
Peak	Retention Time min	Area mAU*min	Height mAU	Area %	Height %
1	8.505	32.761	102.129	50.47	58.58
2	10.860	32.146	72.224	49.53	41.42
Total:		**64.907**	**174.353**	**100.00**	**100.00**

HPLC Spectrum of (*S*)-**5ac**



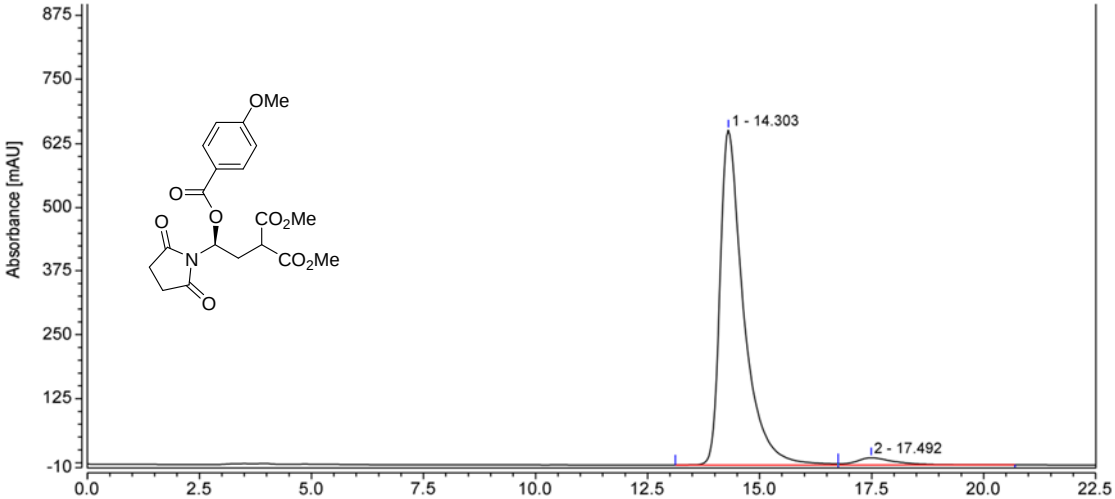
Peak	Retention Time min	Area mAU*min	Height mAU	Area %	Height %
1	8.655	300.638	873.580	96.82	97.30
2	10.910	9.861	24.212	3.18	2.70
Total:		**310.499**	**897.792**	**100.00**	**100.00**

HPLC Spectrum of (±)-**5ad**



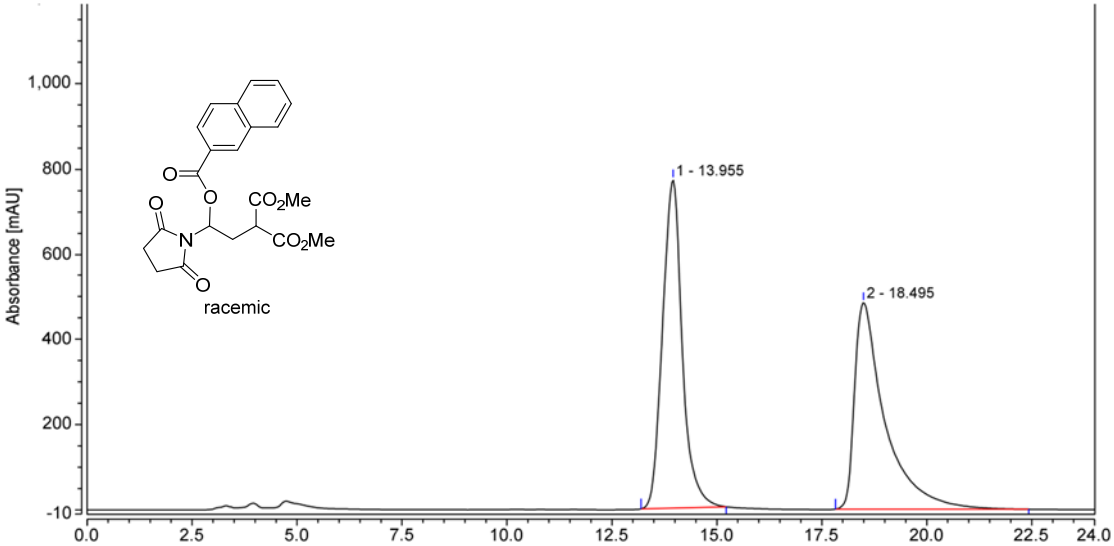
Peak	Retention Time min	Area mAU*min	Height mAU	Area %	Height %
1	14.315	411.803	675.637	49.80	56.81
2	17.072	415.152	513.630	50.20	43.19
Total:		**826.954**	**1189.268**	**100.00**	**100.00**

HPLC Spectrum of (*S*)-**5ad**



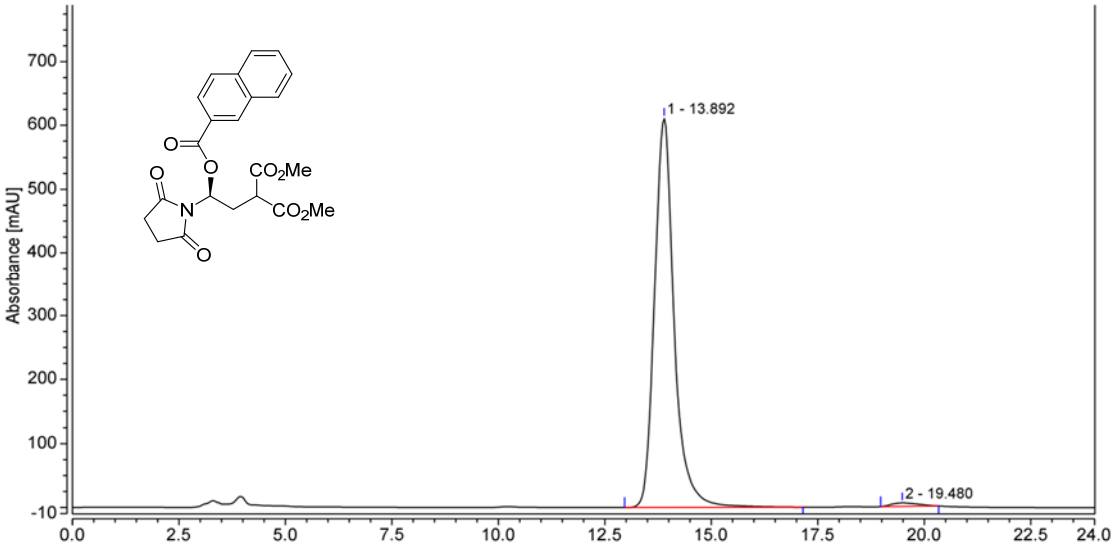
Peak	Retention Time min	Area mAU*min	Height mAU	Area %	Height %
1	14.303	398.799	654.861	96.60	97.92
2	17.492	14.023	13.891	3.40	2.08
Total:		**412.822**	**668.752**	**100.00**	**100.00**

HPLC Spectrum of (±)-**5ae**



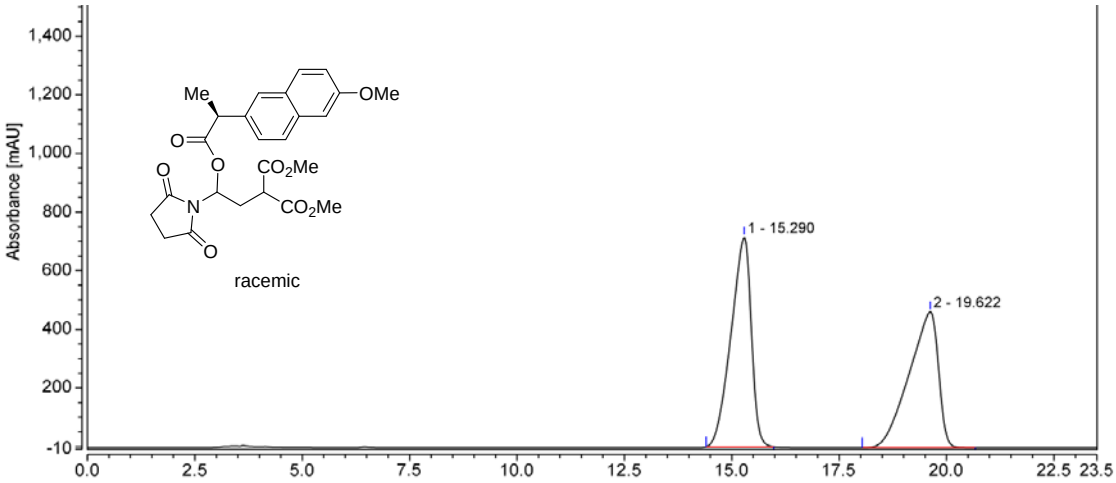
Peak	Retention Time min	Area mAU*min	Height mAU	Area %	Height %
1	13.955	418.248	771.544	50.70	61.46
2	18.495	406.711	483.875	49.30	38.54
Total:		**824.959**	**1255.419**	**100.00**	**100.00**

HPLC Spectrum of (*S*)-**5ae**



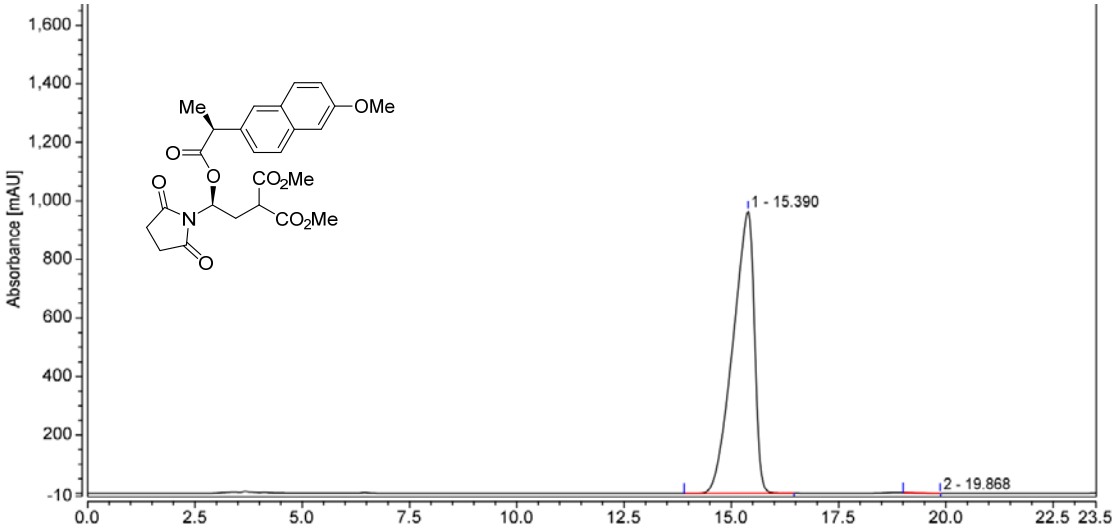
Peak	Retention Time min	Area mAU*min	Height mAU	Area %	Height %
1	13.892	326.327	610.888	98.79	99.11
2	19.480	4.001	5.504	1.21	0.89
Total:		**330.328**	**616.392**	**100.00**	**100.00**

HPLC Spectrum of (±)-**5af**



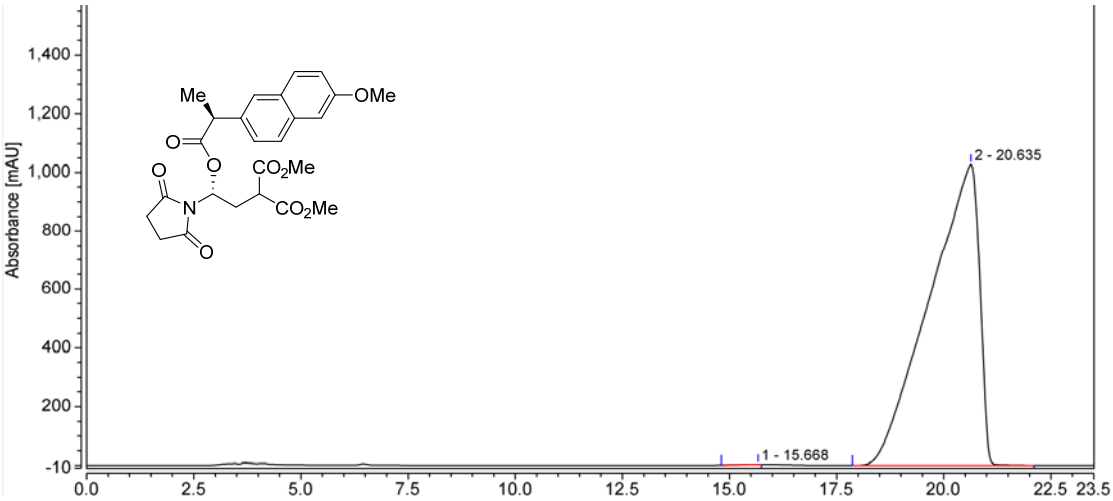
Peak	Retention Time min	Area mAU*min	Height mAU	Area %	Height %
1	15.290	390.642	715.218	51.65	60.65
2	19.622	365.702	464.017	48.35	39.35
Total:		**756.343**	**1179.236**	**100.00**	**100.00**

HPLC Spectrum of (*S*, *S*)-**5af**



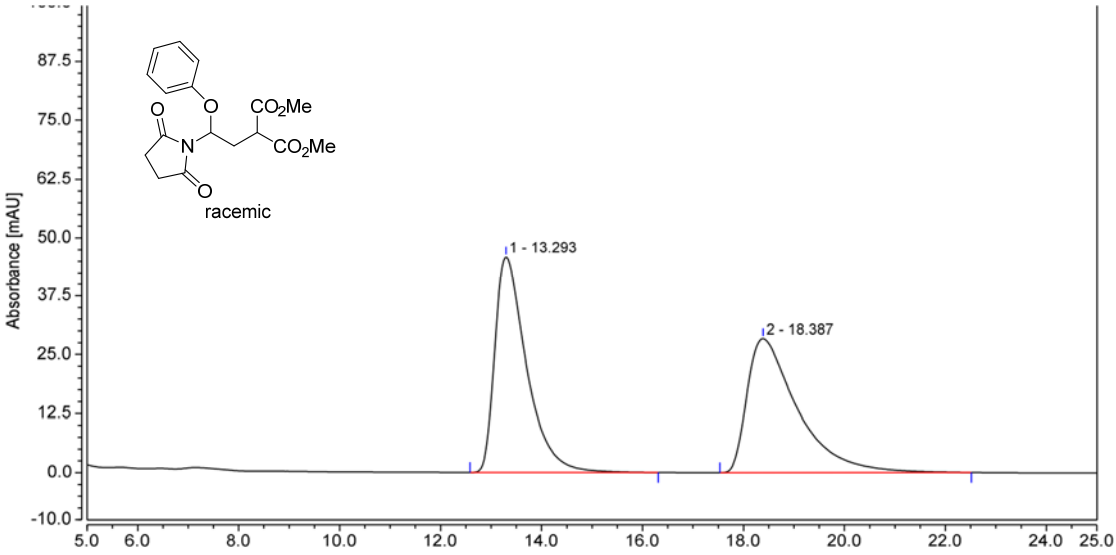
Peak	Retention Time min	Area mAU*min	Height mAU	Area %	Height %
1	15.390	555.933	964.693	99.91	100.00
2	19.868	0.475	0.040	0.09	0.00
Total:		**556.408**	**964.734**	**100.00**	**100.00**

HPLC Spectrum of (*R*, *S*)-**5af'**



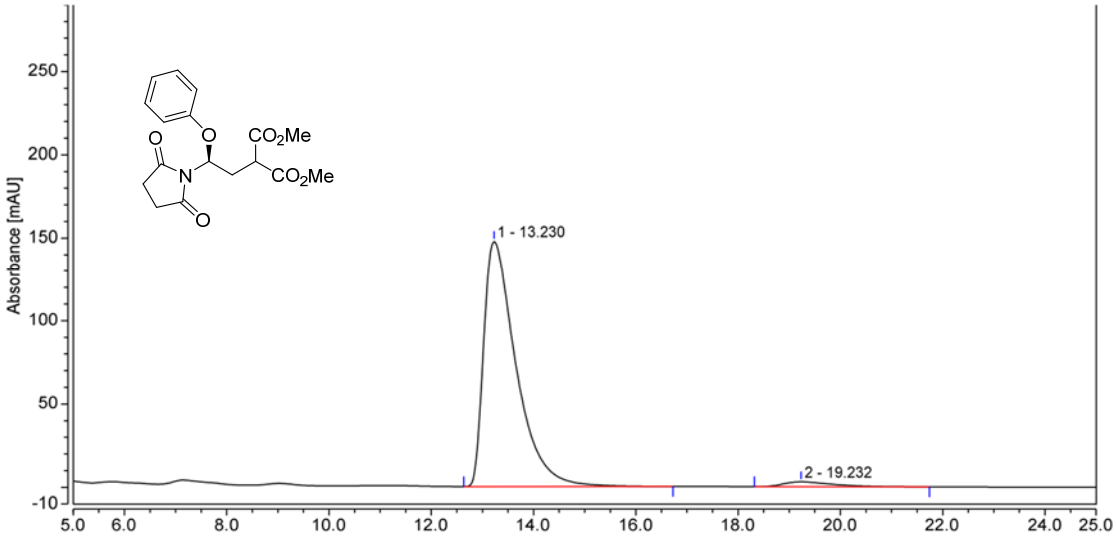
Peak	Retention Time min	Area mAU*min	Height mAU	Area %	Height %
1	15.668	0.214	0.196	0.02	0.02
2	20.635	1375.984	1027.453	99.98	99.98
Total:		**1376.198**	**1027.650**	**100.00**	**100.00**

HPLC Spectrum of (±)-**7aa**



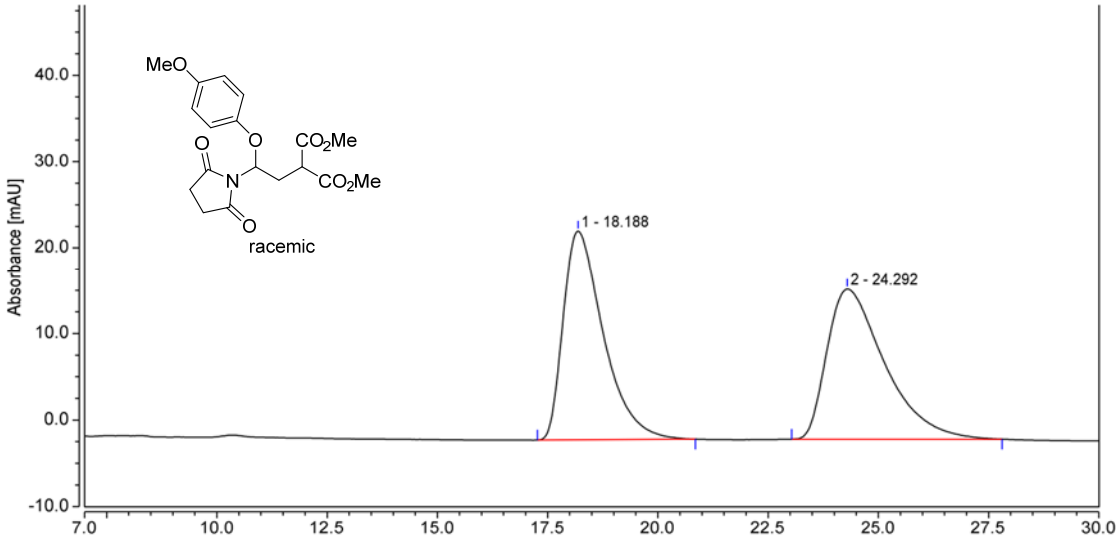
Peak	Retention Time min	Area mAU*min	Height mAU	Area %	Height %
1	13.293	33.331	45.892	50.38	61.82
2	18.387	32.825	28.337	49.62	38.18
Total:		**66.156**	**74.229**	**100.00**	**100.00**

HPLC Spectrum of *R*-**7aa**



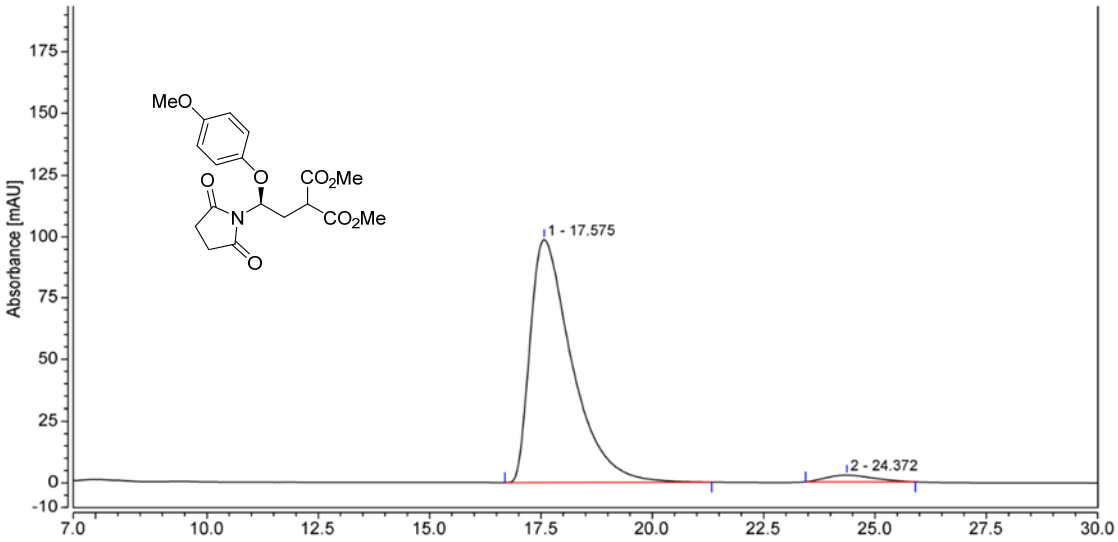
Peak	Retention Time min	Area mAU*min	Height mAU	Area %	Height %
1	13.230	107.917	147.610	97.09	98.06
2	19.232	3.234	2.914	2.91	1.94
Total:		**111.151**	**150.525**	**100.00**	**100.00**

HPLC Spectrum of (±)-**7ab**



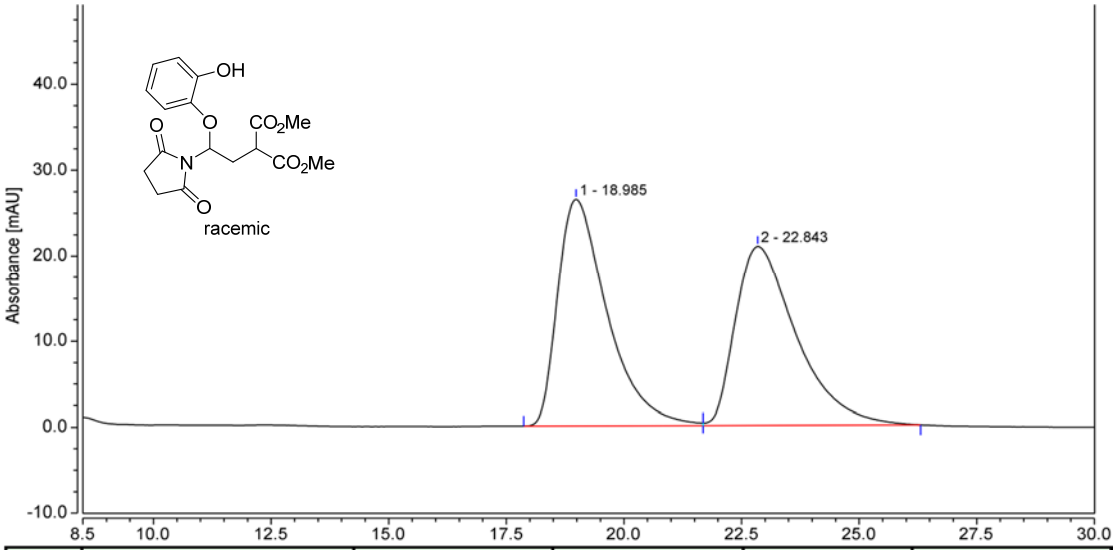
Peak	Retention Time min	Area mAU*min	Height mAU	Area %	Height %
1	18.188	25.517	24.250	49.28	58.29
2	24.292	26.266	17.352	50.72	41.71
Total:		**51.782**	**41.602**	**100.00**	**100.00**

HPLC Spectrum of (*S*)-**7ab**



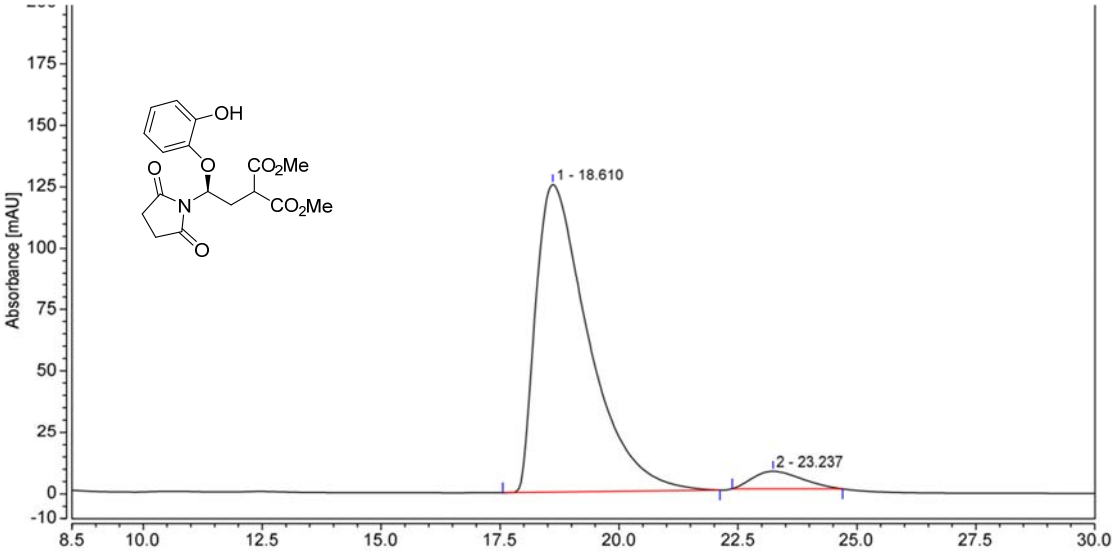
Peak	Retention Time min	Area mAU*min	Height mAU	Area %	Height %
1	17.575	107.036	98.816	97.00	97.34
2	24.372	3.309	2.701	3.00	2.66
Total:		**110.344**	**101.516**	**100.00**	**100.00**

HPLC Spectrum of (±)-**7ac**



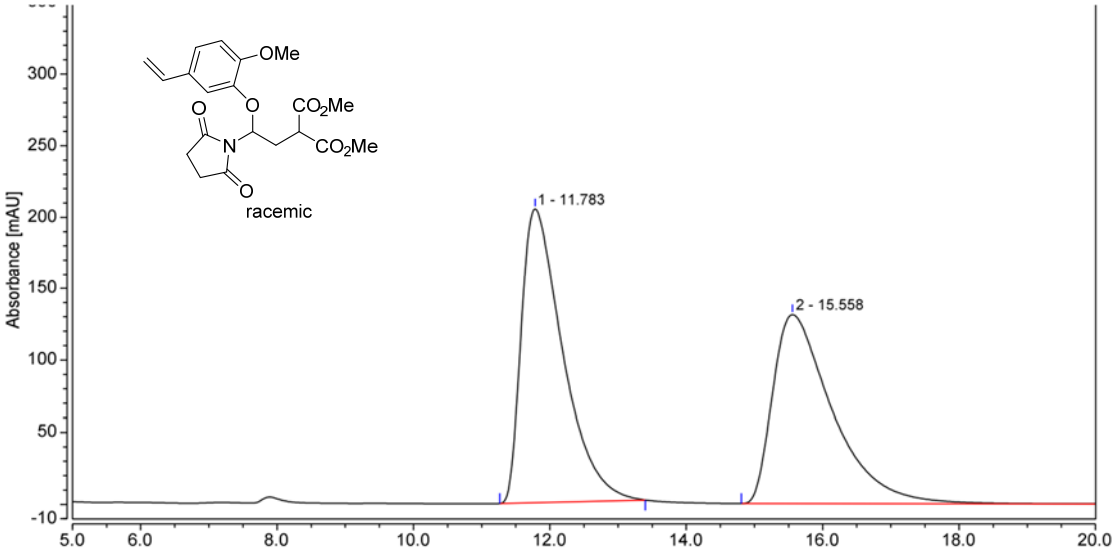
Peak	Retention Time min	Area mAU*min	Height mAU	Area %	Height %
1	18.985	32.227	26.457	50.71	55.86
2	22.843	31.323	20.910	49.29	44.14
Total:		**63.550**	**47.367**	**100.00**	**100.00**

HPLC Spectrum of (*S*)-**7ac**



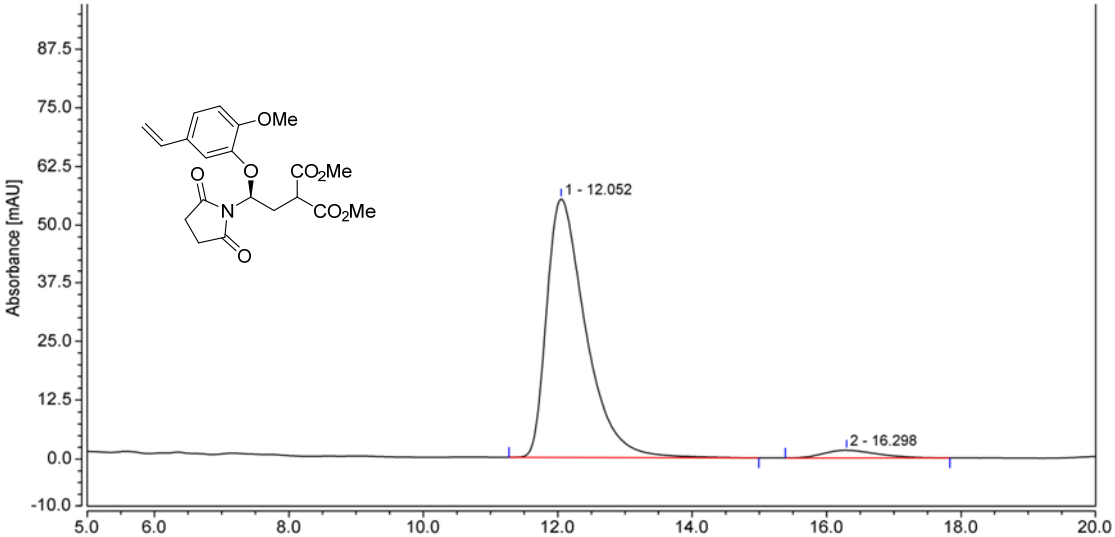
Peak	Retention Time min	Area mAU*min	Height mAU	Area %	Height %
1	18.610	161.090	125.201	94.99	94.64
2	23.237	8.495	7.096	5.01	5.36
Total:		**169.585**	**132.297**	**100.00**	**100.00**

HPLC Spectrum of (±)-**7ad**



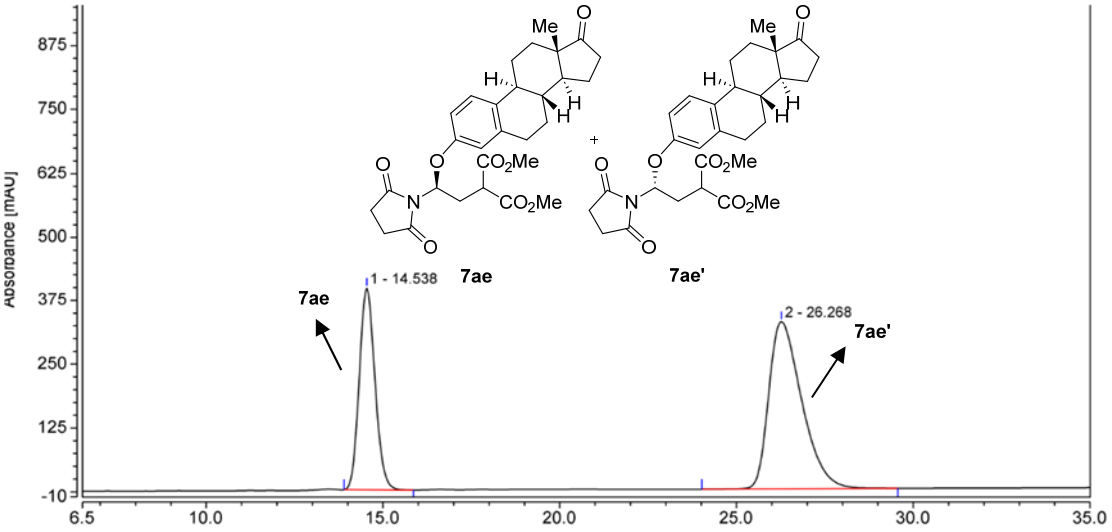
Peak	Retention Time min	Area mAU*min	Height mAU	Area %	Height %
1	11.783	143.745	204.711	51.86	60.99
2	15.558	133.421	130.916	48.14	39.01
Total:		**277.166**	**335.627**	**100.00**	**100.00**

HPLC Spectrum of (*S*)-**7ad**



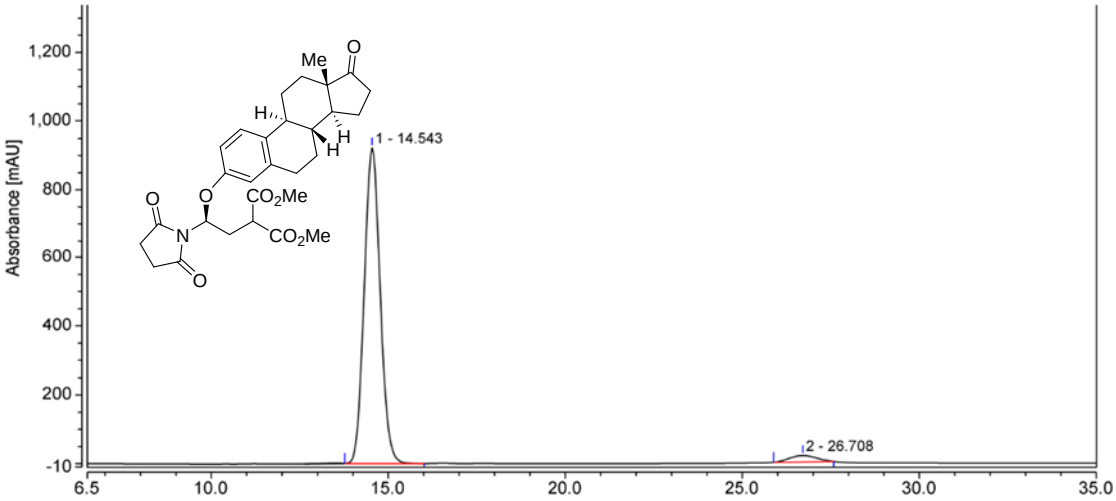
Peak	Retention Time min	Area mAU*min	Height mAU	Area %	Height %
1	12.052	37.029	55.233	96.05	97.11
2	16.298	1.523	1.641	3.95	2.89
Total:		**38.552**	**56.874**	**100.00**	**100.00**

HPLC Spectrum for the mixture of **7ae** and **7ae'**



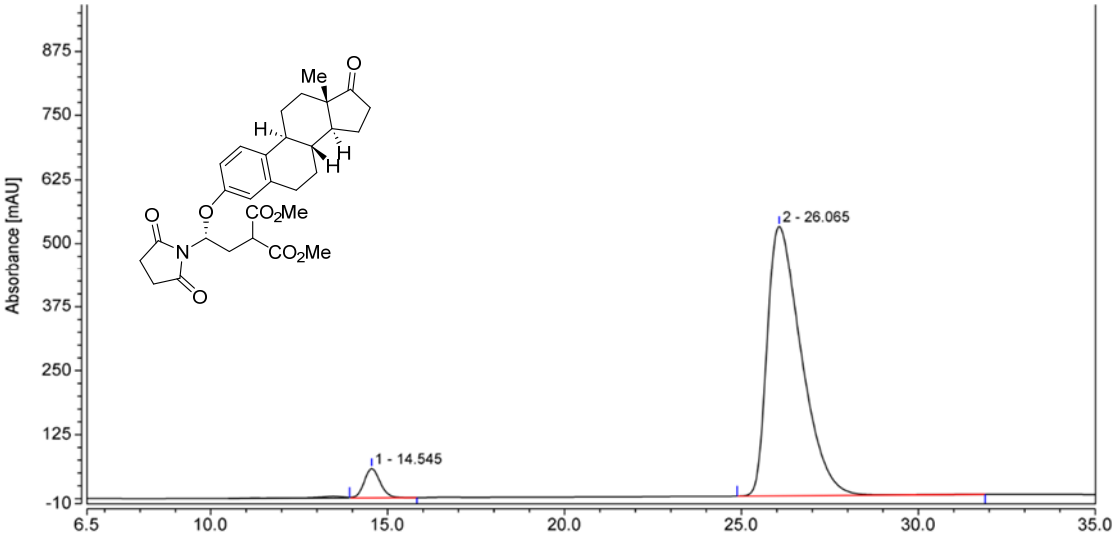
Peak	Retention Time min	Area mAU*min	Height mAU	Area %	Height %
1	14.538	203.980	394.743	36.55	54.66
2	26.268	354.148	327.494	63.45	45.34
Total:		**558.127**	**722.237**	**100.00**	**100.00**

HPLC Spectrum of (*S*, 8*R*, 9*S*, 13*S*, 14*S*)-**7ae**



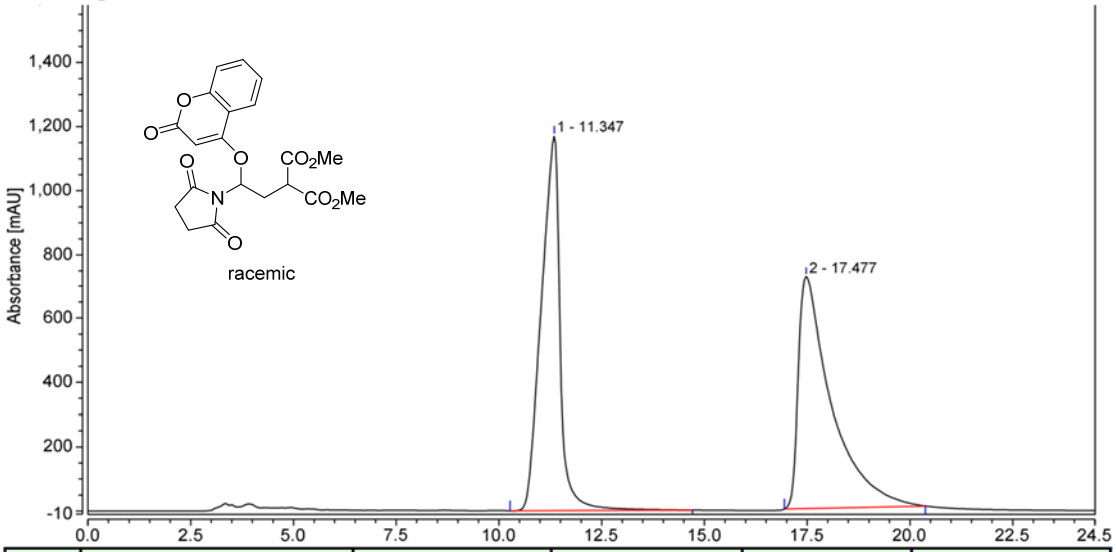
Peak	Retention Time min	Area mAU*min	Height mAU	Area %	Height %
1	14.543	482.562	922.436	96.71	98.01
2	26.708	16.407	18.687	3.29	1.99
Total:		**498.969**	**941.123**	**100.00**	**100.00**

HPLC Spectrum of (*R*, 8*R*, 9*S*, 13*S*, 14*S*)-**7ae'**



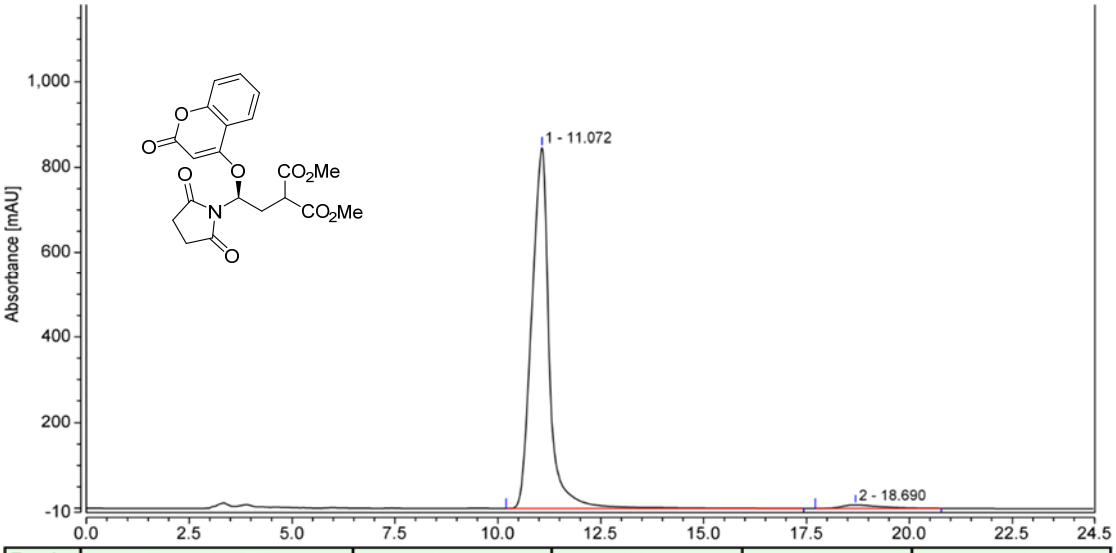
Peak	Retention Time min	Area mAU*min	Height mAU	Area %	Height %
1	14.545	29.877	57.145	4.83	9.76
2	26.065	588.790	528.422	95.17	90.24
Total:		**618.666**	**585.567**	**100.00**	**100.00**

HPLC Spectrum of (±)-**9aa**



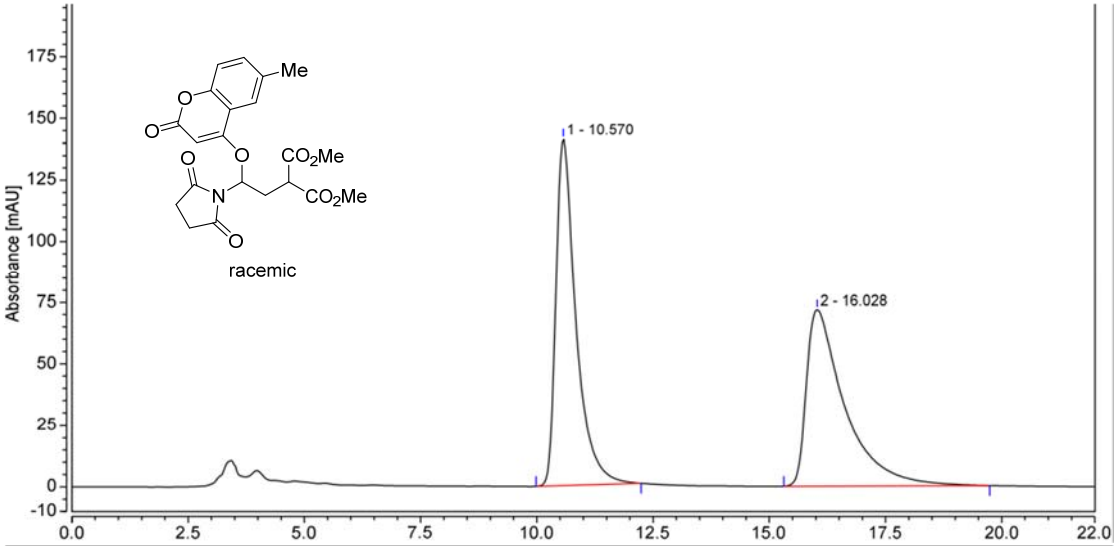
Peak	Retention Time min	Area mAU*min	Height mAU	Area %	Height %
1	11.347	620.521	1168.894	48.02	61.82
2	17.477	671.605	721.917	51.98	38.18
Total:		**1292.125**	**1890.811**	**100.00**	**100.00**

HPLC Spectrum of (*S*)-**9aa**



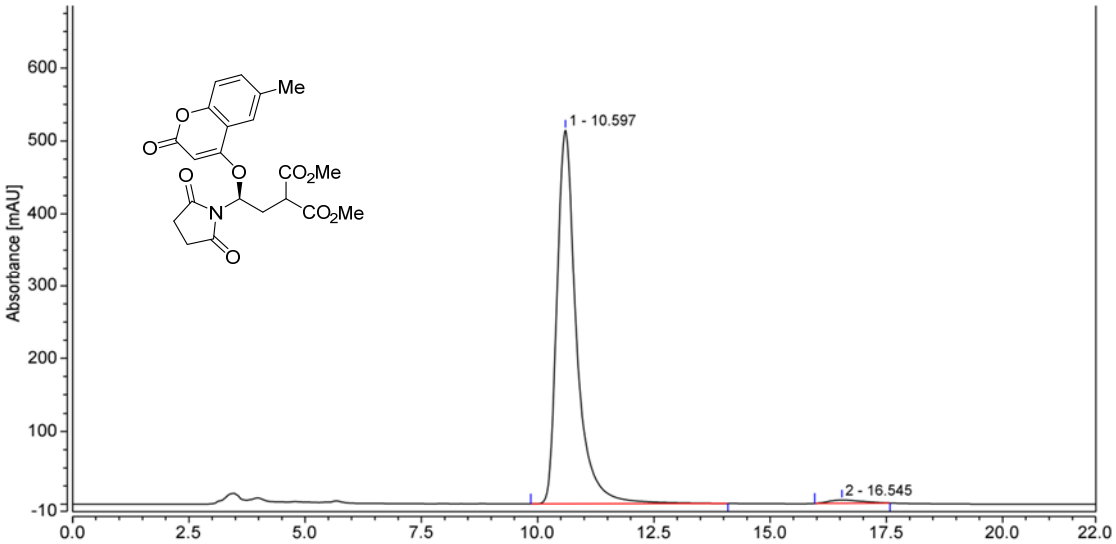
Peak	Retention Time min	Area mAU*min	Height mAU	Area %	Height %
1	11.072	419.165	847.277	97.93	99.07
2	18.690	8.874	7.950	2.07	0.93
Total:		**428.039**	**855.227**	**100.00**	**100.00**

HPLC Spectrum of (±)-**9ab**



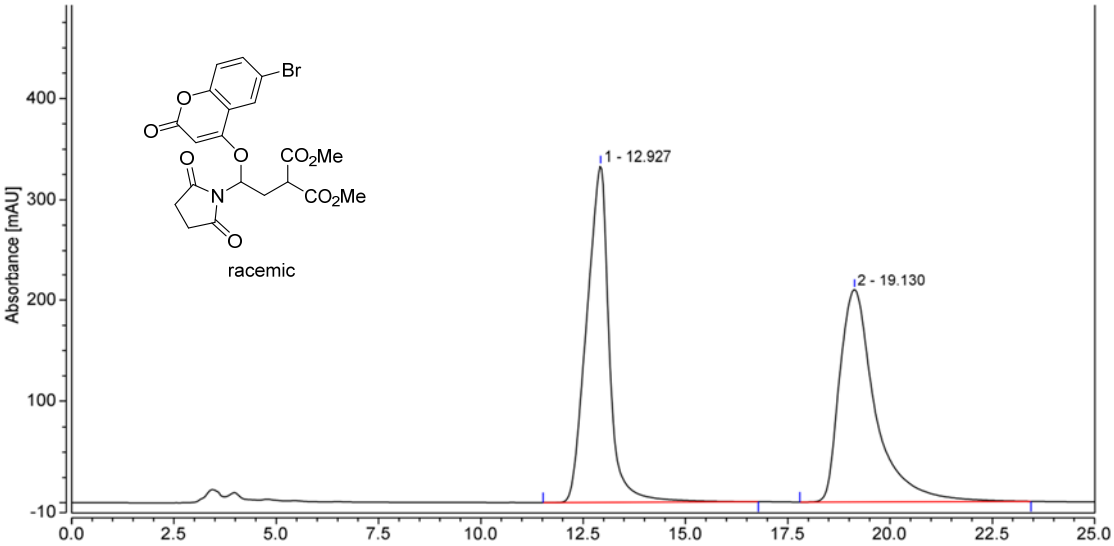
Peak	Retention Time min	Area mAU*min	Height mAU	Area %	Height %
1	10.570	70.423	141.062	50.68	66.30
2	16.028	68.529	71.687	49.32	33.70
Total:		**138.952**	**212.749**	**100.00**	**100.00**

HPLC Spectrum of (*S*)-**9ab**



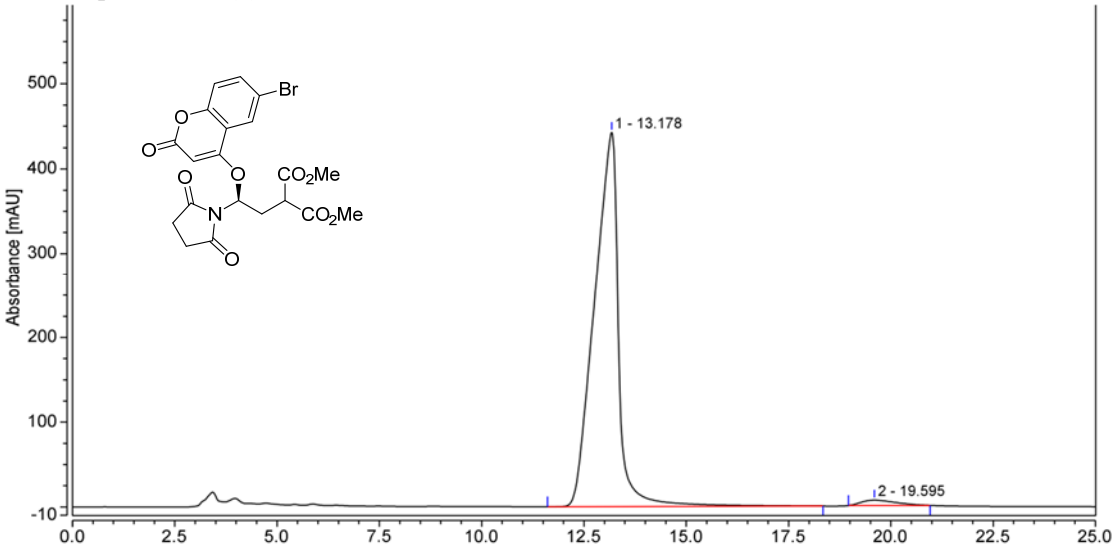
Peak	Retention Time min	Area mAU*min	Height mAU	Area %	Height %
1	10.597	250.503	514.392	98.52	99.13
2	16.545	3.762	4.524	1.48	0.87
Total:		**254.266**	**518.916**	**100.00**	**100.00**

HPLC Spectrum of (±)-**9ac**



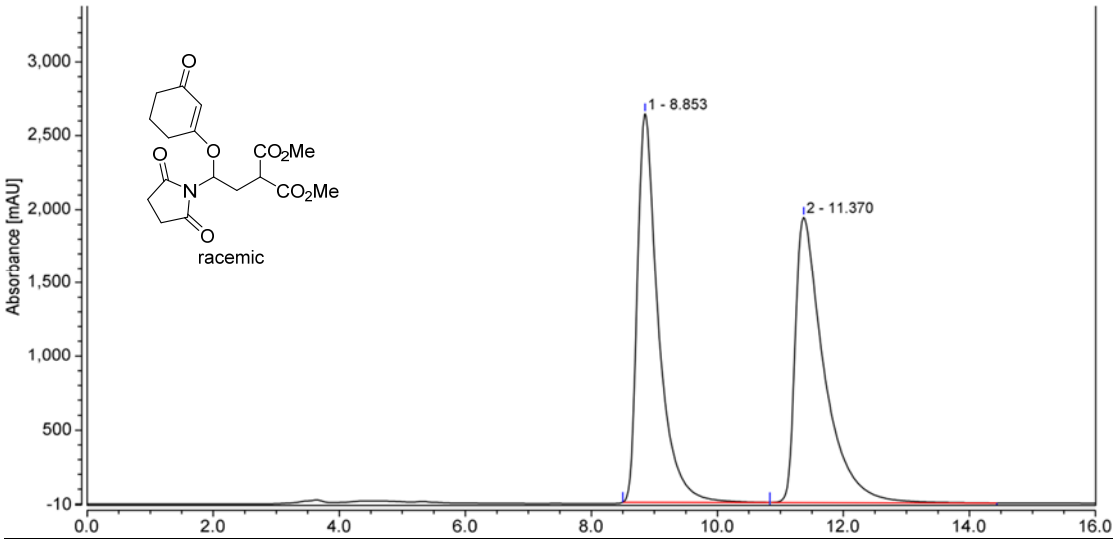
Peak	Retention Time min	Area mAU*min	Height mAU	Area %	Height %
1	12.927	212.621	333.182	50.02	61.37
2	19.130	212.416	209.740	49.98	38.63
Total:		**425.038**	**542.922**	**100.00**	**100.00**

HPLC Spectrum of (*S*)-**9ac**



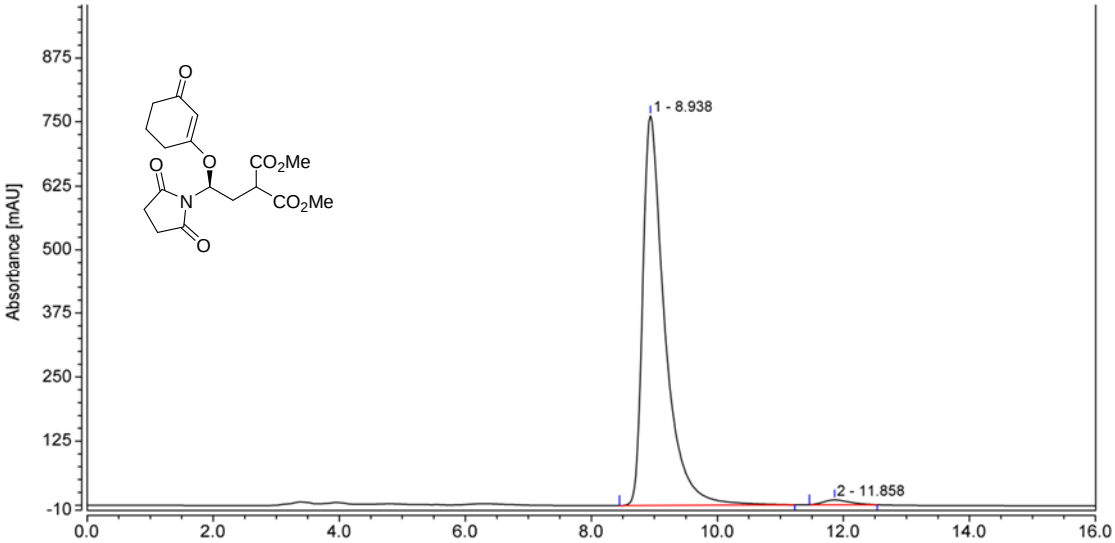
Peak	Retention Time min	Area mAU*min	Height mAU	Area %	Height %
1	13.178	302.011	442.195	98.00	98.60
2	19.595	6.152	6.269	2.00	1.40
Total:		**308.163**	**448.464**	**100.00**	**100.00**

HPLC Spectrum of (±)-**11aa**



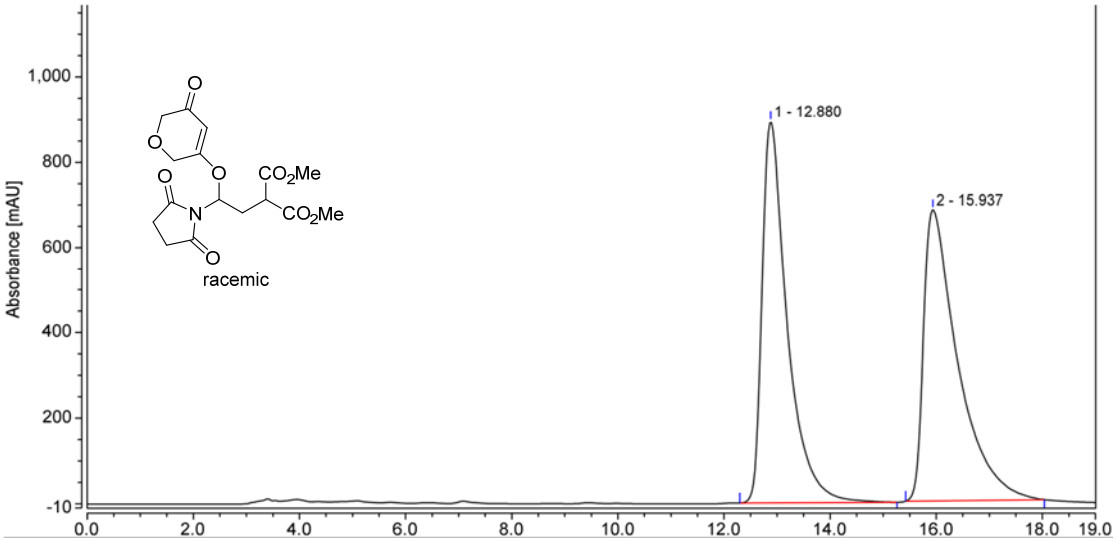
Peak	Retention Time min	Area mAU*min	Height mAU	Area %	Height %
1	8.853	1019.754	2639.118	49.84	57.61
2	11.370	1026.428	1942.203	50.16	42.39
Total:		**2046.182**	**4581.321**	**100.00**	**100.00**

HPLC Spectrum of (*S*)-**11aa**



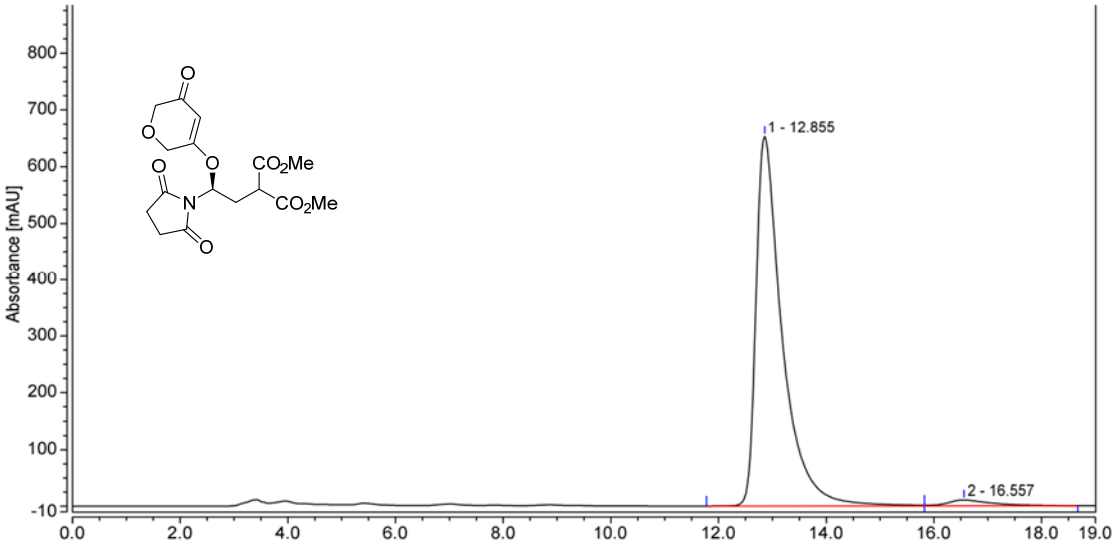
Peak	Retention Time min	Area mAU*min	Height mAU	Area %	Height %
1	8.938	308.408	762.208	98.56	98.80
2	11.858	4.510	9.266	1.44	1.20
Total:		**312.918**	**771.473**	**100.00**	**100.00**

HPLC Spectrum of (±)-**11ab**



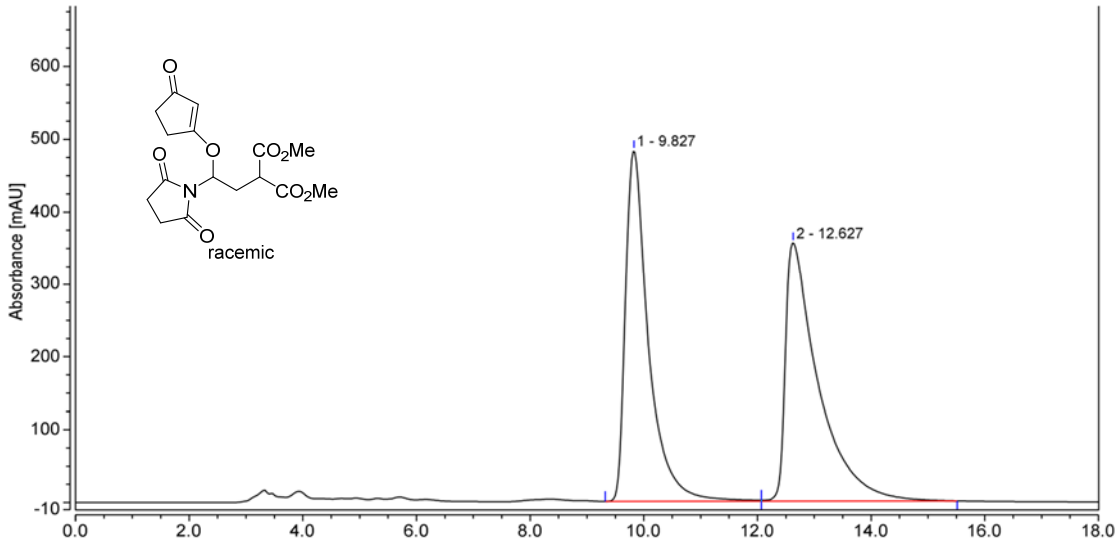
Peak	Retention Time min	Area mAU*min	Height mAU	Area %	Height %
1	12.880	488.988	893.640	49.08	56.70
2	15.937	507.310	682.472	50.92	43.30
Total:		**996.298**	**1576.111**	**100.00**	**100.00**

HPLC Spectrum of (*S*)-**11ab**



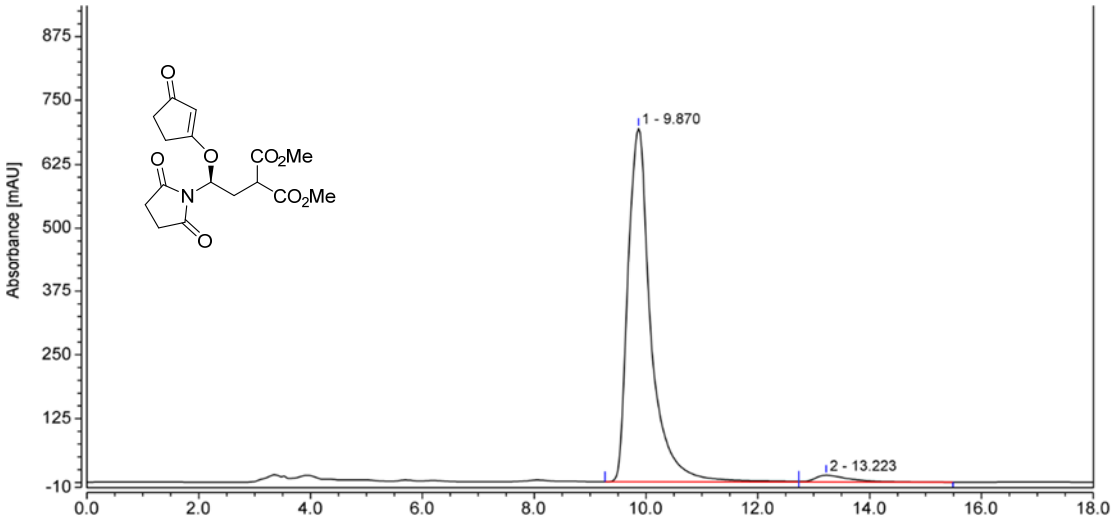
Peak	Retention Time min	Area mAU*min	Height mAU	Area %	Height %
1	12.855	369.023	652.972	97.32	98.43
2	16.557	10.146	10.402	2.68	1.57
Total:		**379.169**	**663.374**	**100.00**	**100.00**

HPLC Spectrum of (±)-**11ac**



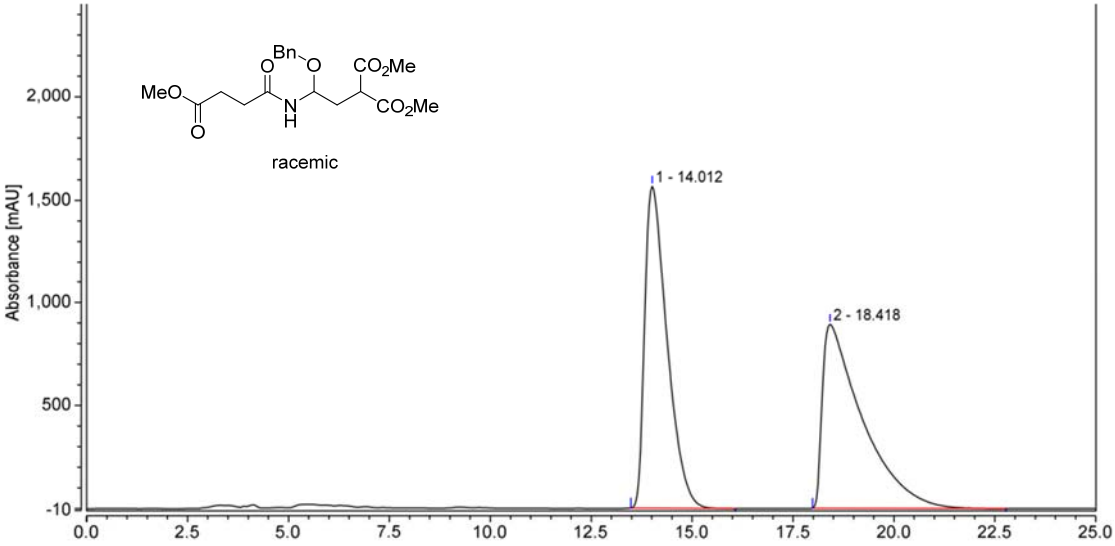
Peak	Retention Time min	Area mAU*min	Height mAU	Area %	Height %
1	9.827	227.389	483.129	48.88	57.55
2	12.627	237.815	356.436	51.12	42.45
Total:		**465.205**	**839.565**	**100.00**	**100.00**

HPLC Spectrum of (*S*)-**11ac**



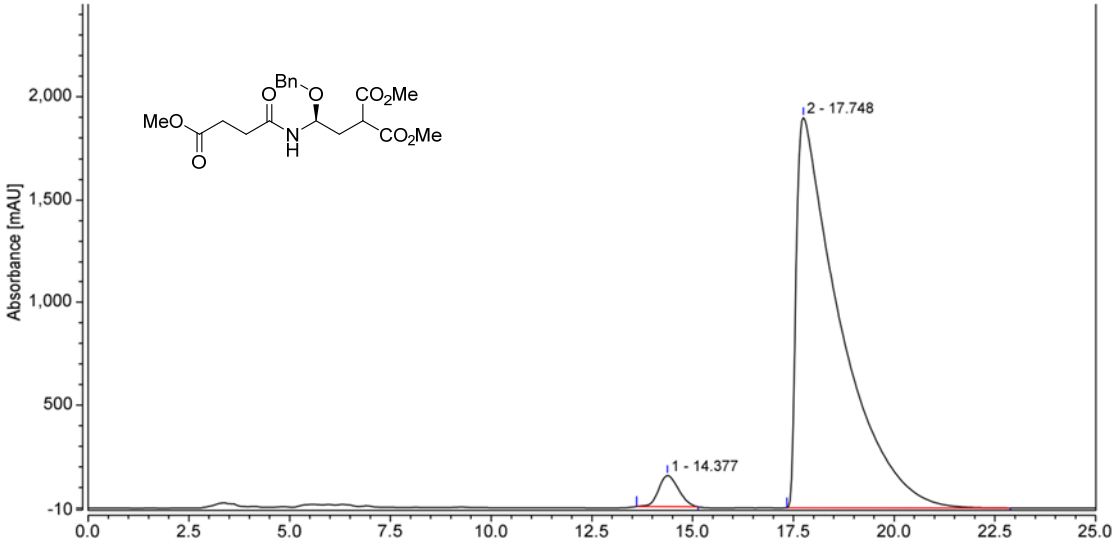
Peak	Retention Time min	Area mAU*min	Height mAU	Area %	Height %
1	9.870	329.273	693.753	97.08	98.10
2	13.223	9.897	13.456	2.92	1.90
Total:		**339.170**	**707.209**	**100.00**	**100.00**

HPLC Spectrum of (±)-**12aa**



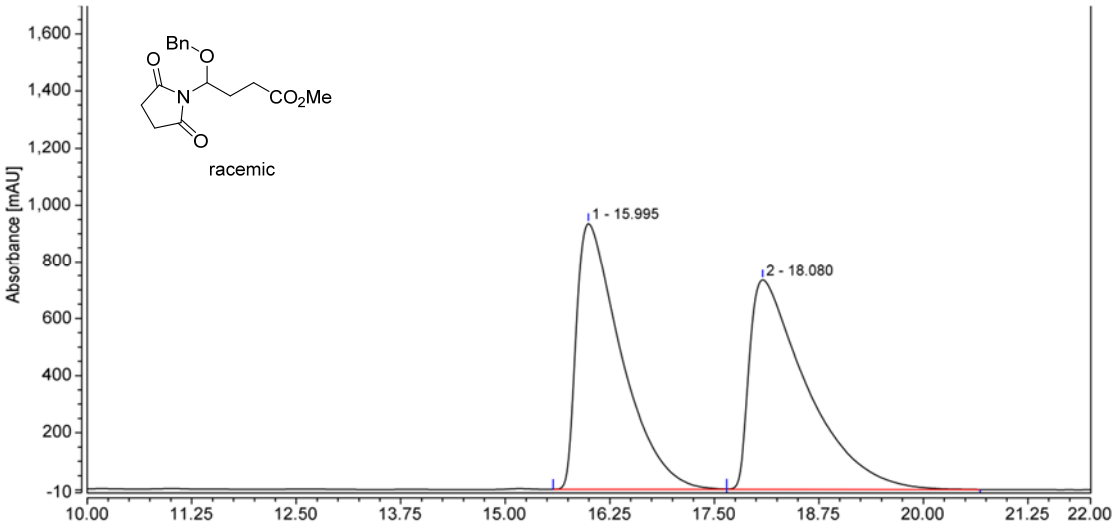
Peak	Retention Time min	Area mAU*min	Height mAU	Area %	Height %
1	14.012	1004.415	1566.749	49.54	63.73
2	18.418	1023.112	891.822	50.46	36.27
Total:		**2027.527**	**2458.571**	**100.00**	**100.00**

HPLC Spectrum of (*S*)-**12aa**



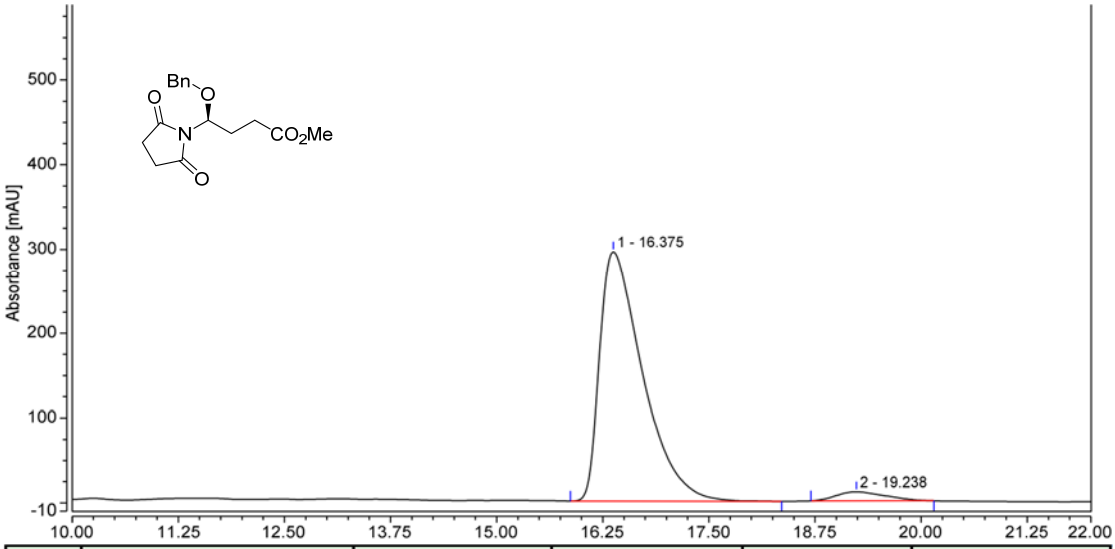
Peak	Retention Time min	Area mAU*min	Height mAU	Area %	Height %
1	14.377	86.179	150.522	3.50	7.35
2	17.748	2376.056	1896.139	96.50	92.65
Total:		**2462.235**	**2046.661**	**100.00**	**100.00**

HPLC Spectrum of (±)-**13aa**



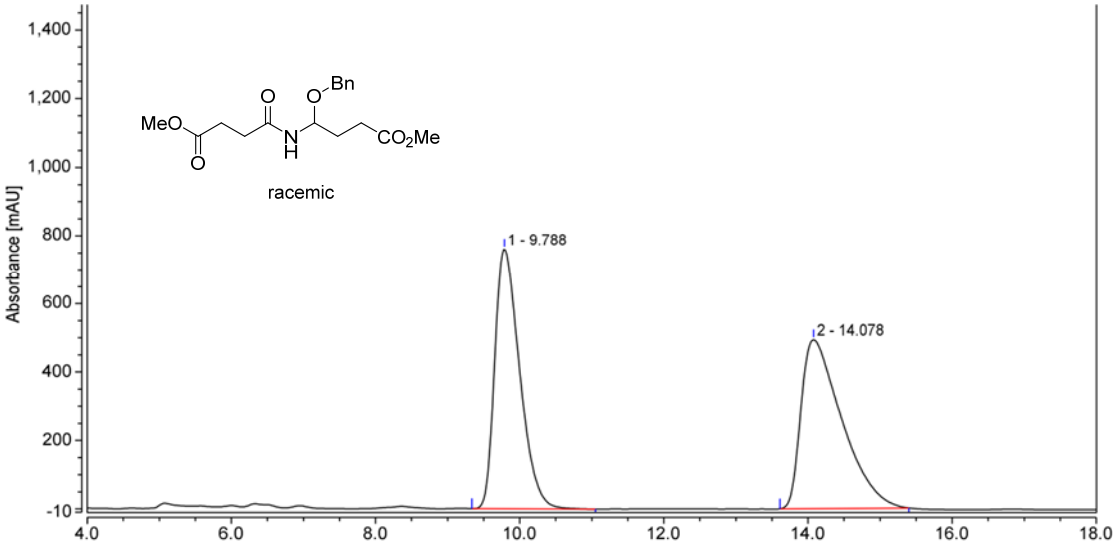
Peak	Retention Time min	Area mAU*min	Height mAU	Area %	Height %
1	15.995	580.862	933.844	49.91	56.02
2	18.080	582.934	733.016	50.09	43.98
Total:		**1163.796**	**1666.860**	**100.00**	**100.00**

HPLC Spectrum of (*S*)-**13aa**



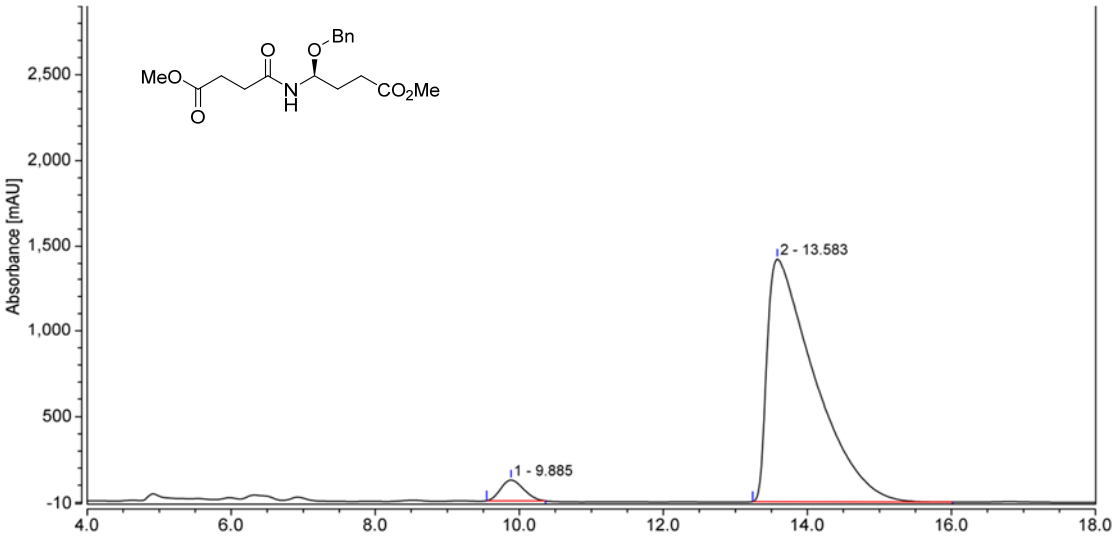
Peak	Retention Time min	Area mAU*min	Height mAU	Area %	Height %
1	16.375	173.541	295.318	96.07	96.52
2	19.238	7.105	10.655	3.93	3.48
Total:		**180.646**	**305.973**	**100.00**	**100.00**

HPLC Spectrum of (±)-**14aa**



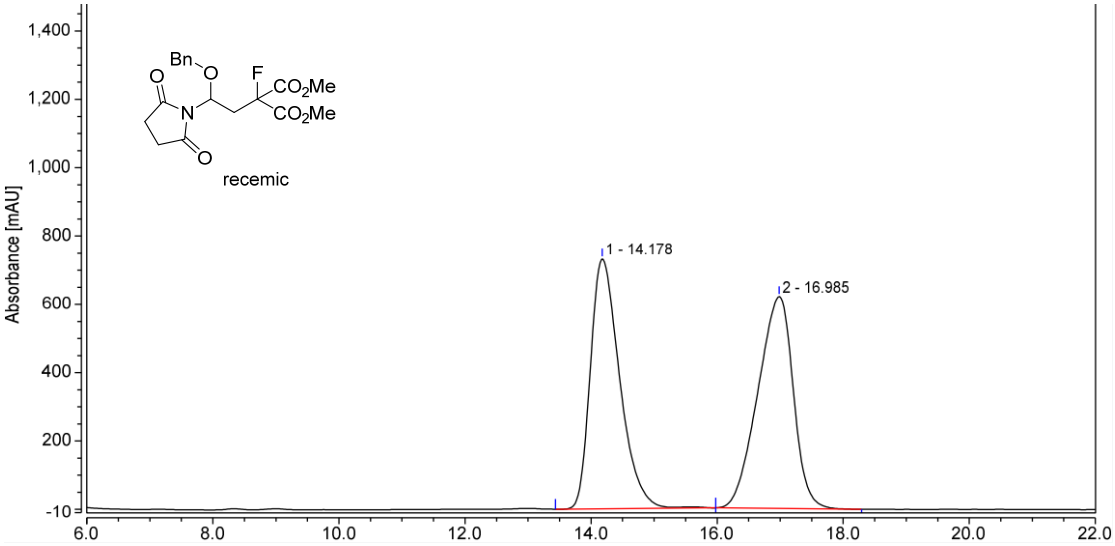
Peak	Retention Time min	Area mAU*min	Height mAU	Area %	Height %
1	9.788	304.478	760.311	48.48	60.64
2	14.078	323.581	493.500	51.52	39.36
Total:		**628.059**	**1253.812**	**100.00**	**100.00**

HPLC Spectrum of (*S*)-**14aa**



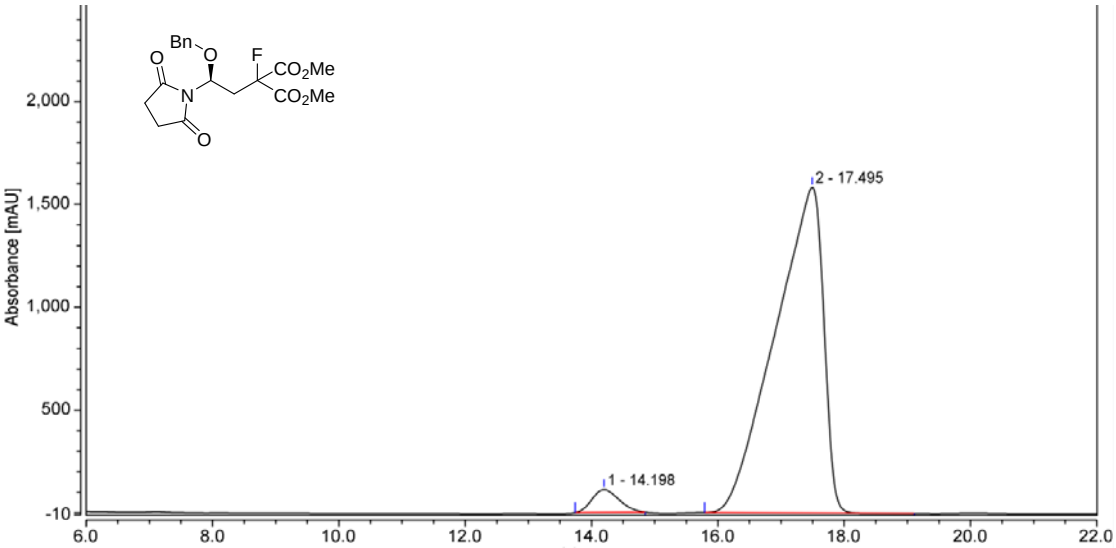
Peak	Retention Time min	Area mAU*min	Height mAU	Area %	Height %
1	9.885	44.787	121.171	3.97	7.86
2	13.583	1083.532	1420.693	96.03	92.14
Total:		**1128.319**	**1541.864**	**100.00**	**100.00**

HPLC Spectrum of (±)-**15aa**



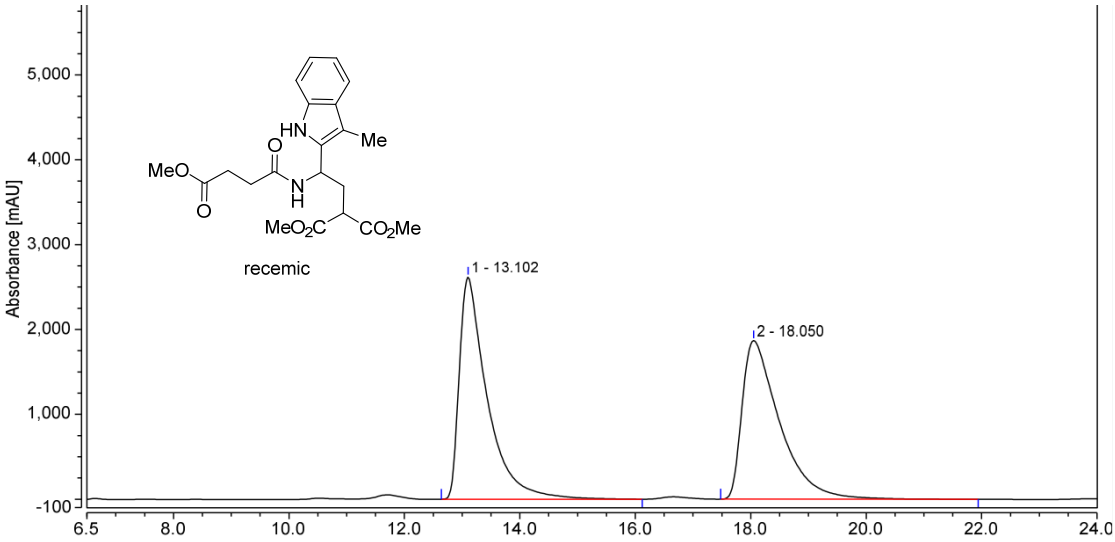
Peak	Retention Time min	Area mAU*min	Height mAU	Area %	Height %
1	14.178	393.759	731.821	49.38	54.14
2	16.985	403.605	619.797	50.62	45.86
Total:		**797.364**	**1351.618**	**100.00**	**100.00**

HPLC Spectrum of (*S*)-**15aa**



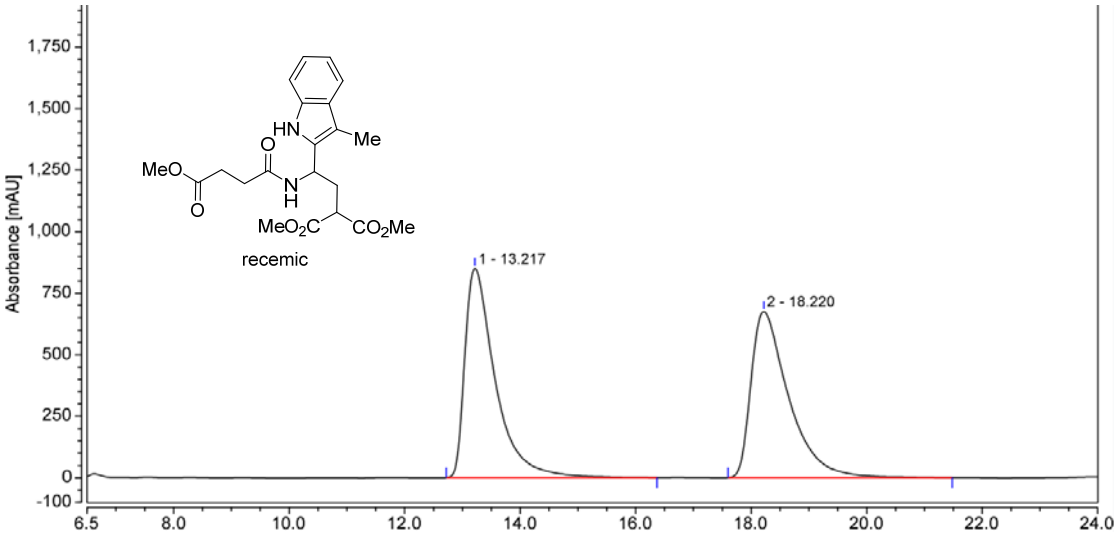
Peak	Retention Time min	Area mAU*min	Height mAU	Area %	Height %
1	14.198	55.656	111.480	3.81	6.57
2	17.495	1406.487	1584.538	96.19	93.43
Total:		**1462.143**	**1696.018**	**100.00**	**100.00**

HPLC Spectrum of (±)-**16aa** from (±)-**12aa**



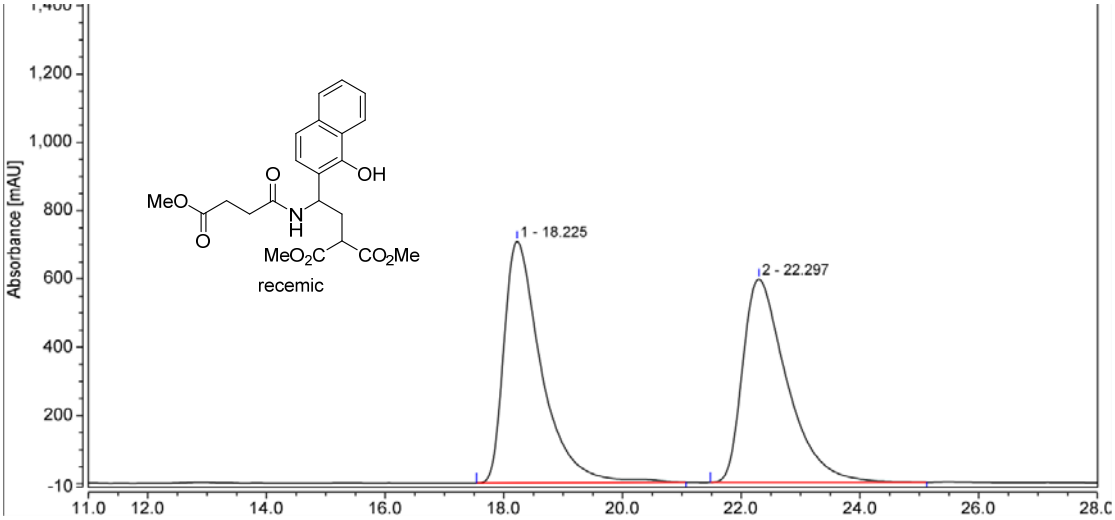
Peak	Retention Time min	Area mAU*min	Height mAU	Area %	Height %
1	13.102	1463.872	2619.185	51.00	58.37
2	18.050	1406.218	1867.839	49.00	41.63
Total:		**2870.090**	**4487.024**	**100.00**	**100.00**

HPLC Spectrum of (±)-**16aa** from (*S*)-**12aa** (92% ee)



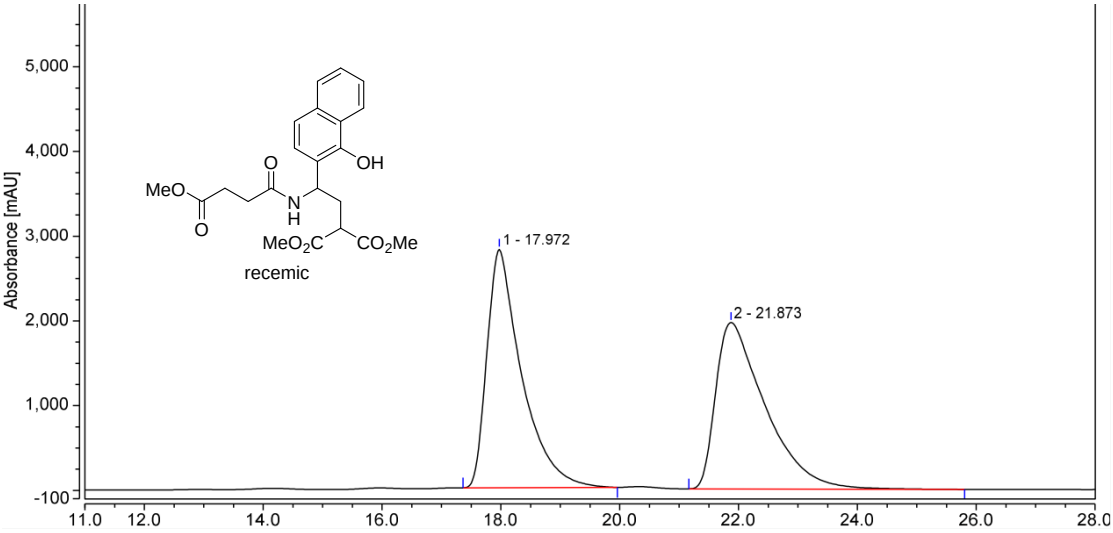
Peak	Retention Time min	Area mAU*min	Height mAU	Area %	Height %
1	13.217	518.791	850.106	50.44	55.74
2	18.220	509.761	674.917	49.56	44.26
Total:		**1028.551**	**1525.023**	**100.00**	**100.00**

HPLC Spectrum of (±)-**17aa** from (±)-**12aa**



Peak	Retention Time min	Area mAU*min	Height mAU	Area %	Height %
1	18.225	515.790	707.699	50.16	54.33
2	22.297	512.414	594.844	49.84	45.67
Total:		**1028.204**	**1302.543**	**100.00**	**100.00**

HPLC Spectrum of (±)-**17aa** from (*S*)-**12aa** (92% ee)



Peak	Retention Time min	Area mAU*min	Height mAU	Area %	Height %
1	17.972	1897.670	2816.278	50.09	58.90
2	21.873	1890.761	1965.317	49.91	41.10
Total:		**3788.431**	**4781.595**	**100.00**	**100.00**

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