

Supporting information

Pd-catalyzed Site-Selective C(sp²)–H Olefination and Alkynylation of Phenylalanine Residues in Peptides

Yong Zheng^a and Weibin Song^{b*}

^aShanghai Institute of Materia Medica, Chinese Academy of Sciences, 501 Haik Road, Shanghai 201203, China

^bJiangsu Key Laboratory for Functional Substances of Chinese Medicine, Stake Key Laboratory Cultivation Base for TCM Quality and Efficacy, School of Pharmacy, Nanjing University of Chinese Medicine, Nanjing 210023, China

Table of contents

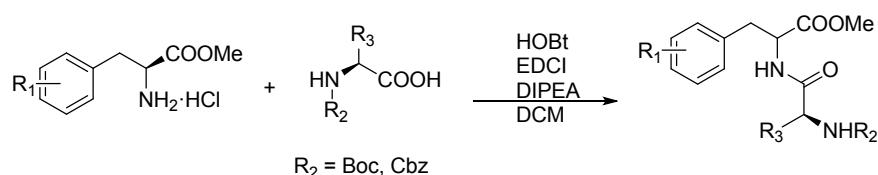
General information	2
General procedures for preparation of starting materials	2
Screening of reaction conditions	3
General procedure for C–H olefination	4
General procedure for C–H alkynylation	4
Characterization data of products	5-22
¹ H and ¹³ C NMR Spectra of products	24-66
HPLC analysis of ee value of 2a_{mono} and 2a_{di}	67

General information

All the reagents were used without further purification. ^1H and ^{13}C NMR spectra were recorded on a Bruker NMR spectrometer with CDCl_3 as the solvent and TMS as an internal standard. HRESIMS was measured on an Agilent G6224A TOF spectrometer. HPLC was performed on Chiralcel OD-H column ($i\text{-PrOH}$ in hexanes, 1 mL/min), $\lambda = 254$ nm. TLC was performed on pre-coated silica gel GF254 plates. Column chromatography was performed on silica gel (200–300 mesh). Visualization was carried out with UV254 or PMA staining.

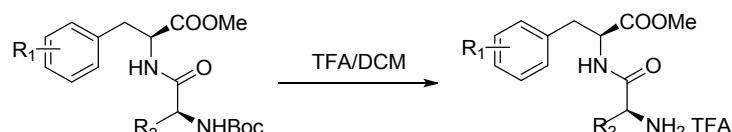
General procedures for preparation of starting materials:

Synthesis of dipeptides:

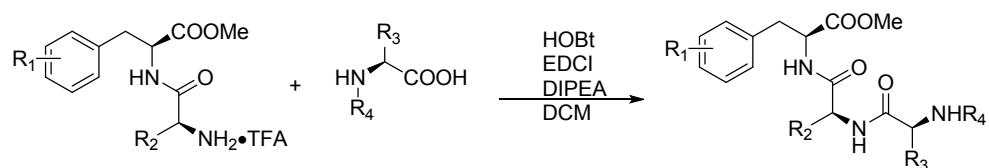


To a solution of protected-amino acid (1equiv) and phenylalanine methyl ester hydrochloride (1 equiv) in dry DCM (0.2 M) was added DIPEA (2 equiv), HOEt (1.1 equiv), and EDCI·HCl (1.2 equiv) at 0°C. After 1 h, the mixture was warmed to room temperature and stirred overnight. Water was added and the mixture was extracted with DCM. The combined organic layer was washed with 10% HCl, sat. NaHCO_3 , and brine, dried over anhydrous Na_2SO_4 , and concentrated. The resulting residue was purified by silica gel flash chromatography (hexanes/ethyl acetate) to give the dipeptide.

Synthesis of tripeptides:



The Boc-protected dipeptide in DCM was added TFA at 0°C. The reaction was allowed to stir at room temperature for 2h. The reaction was concentrated and used for the next step.



To a solution of dipeptide TFA salt (1equiv) and protected-amino acid (1 equiv) in dry DCM (0.2 M) was added DIPEA (2 equiv), HOEt (1.1 equiv), and EDCI·HCl (1.2 equiv) at 0°C. After 1 h, the mixture was warmed to room temperature and stirred overnight. Water was added and the mixture was extracted with DCM. The combined organic layer was washed with 10% HCl, sat. NaHCO_3 , and brine, dried over anhydrous Na_2SO_4 , and concentrated. The resulting residue was purified by silica gel flash chromatography (hexanes/ethyl acetate) to give the tripeptide.

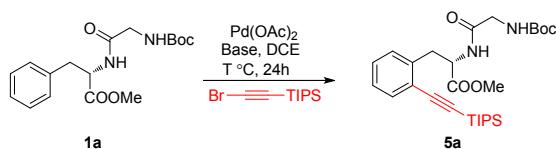
Table S1. Optimization of olefination Conditions^a



Entry	Catalyst	Base	Solvent	Yield(mono+di) ^b (%)
1	Pd(OAc) ₂	K ₂ CO ₃	DCE	10
2	Pd(OAc) ₂	Cu(OAc) ₂	DCE	5
3	Pd(OAc) ₂	KOAc	DCE	20
4	Pd(OAc) ₂	Cs ₂ CO ₃	DCE	12
5	Pd(OAc) ₂	Na ₂ S ₂ O ₈	DCE	5
6	Pd(OAc)₂	AgOAc	DCE	90
7	Pd(OAc) ₂	AgCO ₃	DCE	43
8	Pd(OAc) ₂	AgNO ₃	DCE	32
9	Pd(OAc) ₂	AgOAc	toluene	14
10	Pd(OAc) ₂	AgOAc	<i>t</i> -AmOH	60
11	Pd(OAc) ₂	AgOAc	THF	23
12	Pd(OAc) ₂	AgOAc	Dioxane	34
13	Pd(OAc) ₂	AgOAc	DMF	20
14	Pd(OAc) ₂	AgOAc	DMF	42
15	Pd(OAc) ₂	AgOAc	HFIP	<5
16 ^c	Pd(OAc) ₂	AgOAc	DCE	73
17 ^d	Pd(OAc) ₂	AgOAc	DCE	90
18	PdCl ₂	AgOAc	DCE	23
19	Pd(PPh ₃) ₂ Cl ₂	AgOAc	DCE	35
20	Pd(TFA) ₂	AgOAc	DCE	45
21		AgOAc	DCE	0
22	Pd(OAc) ₂		DCE	0

^aConditions: **1a** (0.3 mmol), methyl acrylate (0.9 mmol), base (0.6 mmol), Pd(OAc)₂ (10 mol %), solvent (2 mL), 120 °C, 20 h. ^bIsolated yields. ^c80 °C. ^d150 °C.

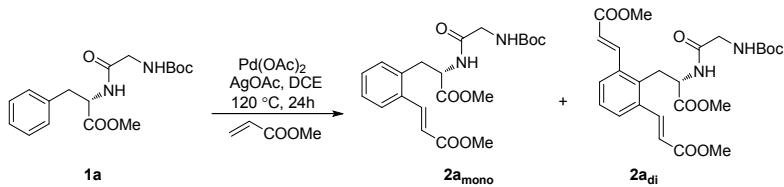
Table S2. Optimization of alkynylation Conditions^a



Entry	Catalyst	Base	Additive	Yield(mono+di) ^b (%)
1	Pd(OAc) ₂	K ₂ CO ₃		55
2	Pd(OAc) ₂	KHCO ₃		43
3	Pd(OAc) ₂	AgOAc		24
4	Pd(OAc) ₂	NaOAc		32
5	Pd(OAc) ₂	Cs ₂ CO ₃		26
6	Pd(OAc) ₂	<i>t</i> -BuOK		42
7	Pd(OAc)₂	K₂CO₃	PivOH	87
8	Pd(OAc) ₂	K ₂ CO ₃	AcOH	62
9	Pd(OAc) ₂	K ₂ CO ₃	<i>o</i> -PBA	80
10	Pd(OAc) ₂	K ₂ CO ₃	Boc-Gly	67
11	PdCl ₂	K ₂ CO ₃	PivOH	45
12	Pd(TFA) ₂	K ₂ CO ₃	PivOH	33
13	Pd(PPh ₃) ₂ Cl ₂	K ₂ CO ₃	PivOH	40
14		K ₂ CO ₃	PivOH	0
15	Pd(OAc) ₂		PivOH	0

^aConditions: **1a** (0.3 mmol), (bromoethynyl)-triisopropylsilane (0.9 mmol), base (0.6 mmol), Pd(OAc)₂ (10 mol %), additive (0.06 mmol), solvent (2 mL), 120 °C, 20 h. ^bIsolated yields.

General procedure for C–H olefination:



A mixture of peptide (0.3 mmol), methyl acrylate (0.9 mmol), AgOAc (0.6 mmol), Pd(OAc)₂ (10 % mol), and DCE (2 mL) in sealed tube was heated at 120 °C for 24 h. The reaction mixture was cooled to room temperature, filter with pad of Celite and concentrated. The resulting residue was purified by silica gel flash chromatography (hexanes/ethyl acetate) to give the desired products.

1 mmol scale (1a** as example):**

A mixture of peptide **1a** (1 mmol, 336 mg), methyl acrylate (3 mmol, 258 mg), AgOAc (2 mmol, 334 mg), Pd(OAc)₂ (10 % mol, 23 mg), and DCE (6 mL) in sealed tube was heated at 120 °C for 24 h. The reaction mixture was cooled to room temperature, filter with pad of Celite and concentrated. The resulting residue was purified by silica gel flash chromatography (hexanes/ethyl acetate) to give **2a_{mono}** (58%, 244 mg) and **2a_{di}** (101 mg, 20%).

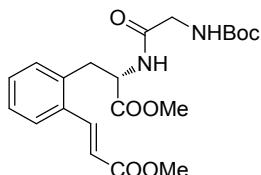
General procedure for C–H alkynylation:

A mixture of peptide (0.3 mmol), (bromoethynyl)-triisopropylsilane (0.9 mmol), K₂CO₃ (0.6 mmol), PivOH (0.06 mmol), Pd(OAc)₂ (10 % mol), and DCE (2 mL) in sealed tube was heated at 120 °C for 24 h. The reaction mixture was cooled to room temperature, filter with pad of Celite and concentrated. The resulting residue was purified by silica gel flash chromatography (hexanes/ethyl acetate) to give the products.

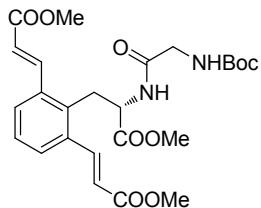
1 mmol scale (1a** as example):**

A mixture of peptide **1a** (1 mmol, 336 mg), (bromoethynyl)-triisopropylsilane (3 mmol, 780 mg), K₂CO₃ (2 mmol, 276 mg), PivOH (0.2 mmol, 21 mg), Pd(OAc)₂ (10 % mol, 23 mg), and DCE (6 mL) in sealed tube was heated at 120 °C for 24 h. The reaction mixture was cooled to room temperature, filter with pad of Celite and concentrated. The resulting residue was purified by silica gel flash chromatography (hexanes/ethyl acetate) to give **5a_{mono}** (50%, 258 mg) and **5b_{di}** (25%. 174 mg).

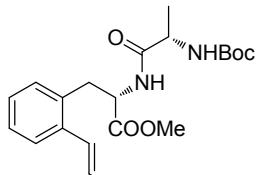
Characterization Data of products



(S,E)-methyl 3-(2-(2-((tert-butoxycarbonyl)amino)acetamido)-3-methoxy-3-oxopropyl)phenylacrylate.
 Yellow solid (78 mg, 65% yield). ¹H NMR (400 MHz, CDCl₃) δ 7.97 (d, *J* = 15.8 Hz, 1H), 7.60 (dd, *J* = 7.6, 1.3 Hz, 1H), 7.39 – 7.24 (m, 2H), 7.23 – 7.10 (m, 1H), 6.76 (d, *J* = 7.8 Hz, 1H), 6.41 (d, *J* = 15.8 Hz, 1H), 5.31 (t, *J* = 5.7 Hz, 1H), 4.87 (dd, *J* = 13.8, 6.2 Hz, 1H), 3.82 (s, 3H), 3.80 – 3.70 (m, 2H), 3.68 (s, 3H), 3.34 (dd, *J* = 14.3, 5.8 Hz, 1H), 3.30 – 3.17 (m, 1H), 1.43 (s, 9H).
¹³C NMR (101 MHz, CDCl₃) δ 171.45, 169.30, 167.36, 155.99, 141.67, 135.72, 133.63, 131.11, 130.22, 127.76, 126.76, 119.56, 80.14, 53.05, 52.48, 51.84, 44.13, 34.90, 28.27.
 HRMS (ESI): m/z [M + Na]⁺ calcd for C₂₁H₂₈N₂NaO₇, 443.1789; found, 443.1792.



(2E,2'E)-dimethyl 3,3'-(2-((S)-2-(2-((tert-butoxycarbonyl)amino)acetamido)-3-methoxy-3-oxopropyl)-1,3-phenylene) diacrylate.
 Yellow solid (38 mg, 25% yield). ¹H NMR (400 MHz, CDCl₃) δ 8.08 (t, *J* = 13.4 Hz, 2H), 7.61 (d, *J* = 7.8 Hz, 2H), 7.41 – 7.27 (m, 1H), 6.85 (d, *J* = 7.7 Hz, 1H), 6.40 (d, *J* = 15.7 Hz, 2H), 5.25 (br s, 1H), 4.79 (dd, *J* = 14.0, 7.8 Hz, 1H), 3.84 (s, 6H), 3.80 – 3.68 (m, 2H), 3.66 (s, 3H), 3.53 – 3.32 (m, 2H), 1.45 (s, 9H).
¹³C NMR (101 MHz, CDCl₃) δ 171.20, 169.12, 167.11, 155.88, 141.91, 135.32, 135.21, 128.64, 127.92, 121.06, 80.10, 52.87, 52.69, 51.94, 44.01, 31.59, 28.27.
 HRMS (ESI): m/z [M + Na]⁺ calcd for C₂₅H₃₂N₂NaO₉, 527.2000; found, 527.2007.



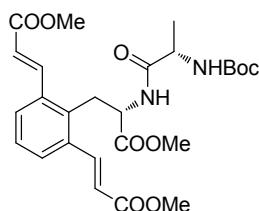
(E)-methyl 3-(2-((S)-2-((S)-2-((tert-butoxycarbonyl)amino)propanamido)-3-methoxy-3-oxopropyl)phenyl)acr

ylate.

White solid (82 mg, 63% yield). ^1H NMR (400 MHz, CDCl_3) δ 7.98 (d, $J = 15.8$ Hz, 1H), 7.59 (d, $J = 7.4$ Hz, 1H), 7.37 – 7.23 (m, 2H), 7.17 (dd, $J = 8.6, 7.3$ Hz, 1H), 6.82 (d, $J = 6.0$ Hz, 1H), 6.40 (d, $J = 15.8$ Hz, 1H), 5.15 (s, 1H), 4.89 – 4.77 (m, 1H), 4.15 (s, 1H), 3.81 (s, 3H), 3.68 (s, 3H), 3.32 (dd, $J = 14.3, 5.9$ Hz, 1H), 3.27 – 3.16 (m, 1H), 1.42 (s, 9H), 1.30 (d, $J = 6.9$ Hz, 3H).

^{13}C NMR (101 MHz, CDCl_3) δ 172.44, 171.49, 167.38, 155.40, 141.69, 135.80, 133.60, 131.13, 130.13, 127.69, 126.71, 119.66, 80.04, 53.04, 52.44, 51.82, 50.02, 34.94, 31.11, 28.26, 18.13.

HRMS (ESI): m/z [M + Na] $^+$ calcd for $\text{C}_{22}\text{H}_{30}\text{N}_2\text{NaO}_7$, 457.1945; found, 457.1945.



2b_{di}

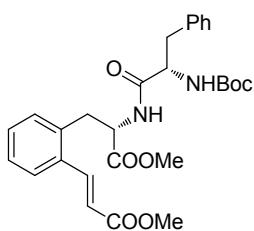
(2E,2'E)-dimethyl

3,3'-(2-((S)-2-((S)-2-((tert-butoxycarbonyl)amino)propanamido)-3-methoxy-3-oxopropyl)-1,3-phe nylene)diacrylate.

Yellow solid (36 mg, 23% yield). ^1H NMR (400 MHz, CDCl_3) δ 8.10 (d, $J = 15.7$ Hz, 2H), 7.61 (t, $J = 8.7$ Hz, 2H), 7.31 (t, $J = 7.8$ Hz, 1H), 6.89 (s, 1H), 6.46 – 6.34 (m, 2H), 5.14 (d, $J = 7.0$ Hz, 1H), 4.76 (dd, $J = 14.2, 7.3$ Hz, 1H), 4.11 (s, 1H), 3.90 – 3.81 (s, 6H), 3.68 (s, 3H), 3.47 – 3.30 (m, 2H), 1.45 (s, 9H), 1.26 (d, $J = 6.0$ Hz, 3H).

^{13}C NMR (101 MHz, CDCl_3) δ 172.30, 171.26, 167.09, 155.24, 141.97, 135.39, 135.22, 128.59, 127.87, 121.18, 80.02, 77.37, 77.05, 76.74, 52.87, 52.64, 51.92, 31.71, 28.27, 18.32.

HRMS (ESI): m/z [M + Na] $^+$ calcd for $\text{C}_{26}\text{H}_{34}\text{N}_2\text{NaO}_9$, 541.2157; found, 541.2171.



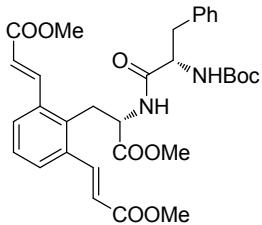
2c_{mono}

(E)-methyl

3-(2-((S)-2-((S)-2-((tert-butoxycarbonyl)amino)-3-phenylpropanamido)-3-methoxy-3-oxopropyl)p henyl)acrylate.

White solid (108 mg, 71% yield). ^1H NMR (400 MHz, CDCl_3) δ 7.96 (d, $J = 15.8$ Hz, 1H), 7.64 – 7.54 (m, 1H), 7.24 (m, 7H), 7.11 – 7.03 (m, 1H), 6.50 (d, $J = 6.8$ Hz, 1H), 6.38 (t, $J = 15.8$ Hz, 1H), 5.12 (s, 1H), 4.78 (d, $J = 6.6$ Hz, 1H), 4.34 (s, 1H), 3.82 (s, 3H), 3.63 (s, 3H), 3.26 (dd, $J = 14.2, 6.1$ Hz, 1H), 3.17 (dd, $J = 14.2, 6.6$ Hz, 1H), 3.08 (dd, $J = 13.8, 6.5$ Hz, 1H), 2.99 (s, 1H), 1.39 (s, 9H).

¹³C NMR (101 MHz, CDCl₃) δ 171.45, 169.30, 167.36, 155.99, 141.67, 135.72, 133.63, 131.11, 130.22, 127.76, 126.76, 119.56, 80.14, 53.05, 52.48, 51.84, 44.13, 34.90, 28.27.
 HRMS (ESI): m/z [M + Na]⁺ calcd for C₂₈H₃₄N₂NaO₇, 533.2258; found, 533.2252.



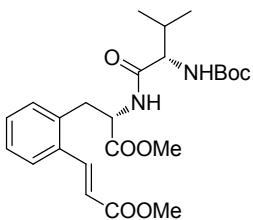
2c_{di}

(2E,2'E)-dimethyl
3,3'-(2-((S)-2-((S)-2-((tert-butoxycarbonyl)amino)-3-phenylpropanamido)-3-methoxy-3-oxopropyl)-1,3-phenylene)diacrylate.

Yellow solid (25 mg, 14% yield). ¹H NMR (400 MHz, CDCl₃) δ 8.07 (d, *J* = 15.7 Hz, 2H), 7.59 (t, *J* = 7.4 Hz, 2H), 7.36 – 7.12 (m, 6H), 6.70 (s, 1H), 6.40 (d, *J* = 15.7 Hz, 2H), 5.11 (s, 1H), 4.74 (dd, *J* = 14.6, 7.3 Hz, 1H), 4.32 (s, 1H), 3.90 – 3.82 (s, 6H), 3.64 (s, 3H), 3.39 – 3.25 (m, 2H), 3.03 (dd, *J* = 13.9, 6.1 Hz, 1H), 2.91 (s, 1H), 1.37 (s, 9H).

¹³C NMR (101 MHz, CDCl₃) δ 170.90, 167.05, 155.37, 141.88, 136.69, 135.31, 135.17, 129.31, 128.59, 128.56, 127.87, 126.82, 121.16, 80.06, 77.39, 77.07, 76.75, 52.90, 52.59, 51.91, 38.37, 31.87, 28.21.

HRMS (ESI): m/z [M + Na]⁺ calcd for C₃₂H₃₈N₂NaO₉, 617.2470; found, 617.2478.



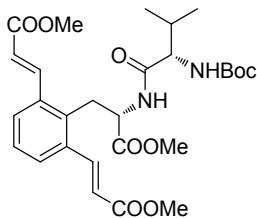
2d_{mono}

(E)-methyl
3-(2-((S)-2-((S)-2-((tert-butoxycarbonyl)amino)-3-methylbutanamido)-3-methoxy-3-oxopropyl)phenyl)acrylate.

Yellow solid (85 mg, 61% yield). ¹H NMR (400 MHz, CDCl₃) δ 7.99 (d, *J* = 15.8 Hz, 1H), 7.59 (d, *J* = 7.5 Hz, 1H), 7.39 – 7.25 (m, 2H), 7.19 (d, *J* = 7.3 Hz, 1H), 6.42 (dd, *J* = 15.7, 3.6 Hz, 2H), 5.09 (br s, 1H), 4.85 (dd, *J* = 13.8, 6.8 Hz, 1H), 3.99 – 3.88 (m, 1H), 3.83 (s, 3H), 3.68 (s, 3H), 3.27 (m, 2H), 2.11 (d, *J* = 6.4 Hz, 1H), 1.45 (s, 9H), 0.91 (d, *J* = 6.1 Hz, 3H), 0.87 (d, *J* = 6.1 Hz, 3H).

¹³C NMR (126 MHz, CDCl₃) δ 171.50, 171.28, 167.20, 155.71, 141.48, 135.58, 133.63, 131.06, 130.17, 127.75, 126.80, 119.90, 79.82, 59.83, 52.91, 52.46, 51.79, 35.00, 30.78, 28.30, 19.16, 17.62.

HRMS (ESI): m/z [M + Na]⁺ calcd for C₂₄H₃₄N₂NaO₇, 485.2258; found, 485.2269.



2d_{di}

(2E,2'E)-dimethyl

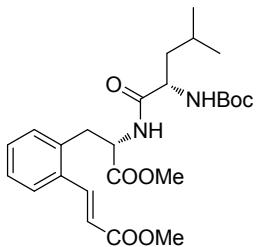
3,3'-(2-((S)-2-((S)-2-((tert-butoxycarbonyl)amino)-3-methylbutanamido)-3-methoxy-3-oxopropyl)-1,3-phenylene)diacrylate.

Yellow solid (34 mg, 21% yield). ¹H NMR (400 MHz, CDCl₃) δ 8.08 (d, *J* = 15.7 Hz, 2H), 7.58 (d, *J* = 7.8 Hz, 2H), 7.30 (dd, *J* = 10.7, 4.8 Hz, 1H), 6.66 – 6.50 (m, 1H), 6.39 (d, *J* = 15.7 Hz, 2H), 5.06 (d, *J* = 8.4 Hz, 1H), 4.75 (dd, *J* = 14.7, 8.2 Hz, 1H), 3.89 (dd, *J* = 14.6, 8.9 Hz, 1H), 3.83 (s, 6H), 3.65 (s, 3H), 3.49 – 3.26 (m, 2H), 2.16 – 2.06 (m, 1H), 1.43 (s, 9H), 0.87 (d, *J* = 6.8 Hz, 3H), 0.78 (d, *J* = 6.4 Hz, 3H).

¹³C NMR (126 MHz, CDCl₃) δ 171.25, 171.18, 166.93, 155.61, 141.75, 135.25, 135.12, 128.59,

127.88, 121.43, 79.68, 59.57, 52.83, 52.60, 51.86, 31.65, 30.88, 28.27, 19.06, 17.34.

HRMS (ESI): m/z [M + Na]⁺ calcd for C₂₈H₃₈N₂NaO₉, 569.2470; found, 569.2478.



2e_{mono}

(E)-methyl

3-(2-((S)-2-((S)-2-((tert-butoxycarbonyl)amino)-4-methylpentanamido)-3-methoxy-3-oxopropyl)phenyl)acrylate.

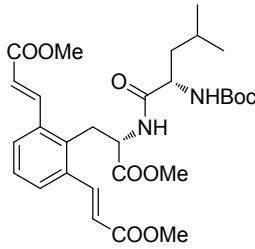
White solid (90 mg, 63% yield). ¹H NMR (400 MHz, CDCl₃) δ 7.97 (d, *J* = 15.8 Hz, 1H), 7.58 (d, *J* = 7.4 Hz, 1H), 7.34 – 7.21 (m, 2H), 7.16 (d, *J* = 7.4 Hz, 1H), 6.73 (d, *J* = 7.6 Hz, 1H), 6.39 (d, *J* = 15.8 Hz, 1H), 5.02 (d, *J* = 7.7 Hz, 1H), 4.82 (dd, *J* = 13.4, 6.5 Hz, 1H), 4.10 (br s, 1H), 3.80 (s, 3H), 3.66 (s, 3H), 3.31 (dd, *J* = 14.3, 5.9 Hz, 1H), 3.27 – 3.14 (m, 1H), 1.61 (dd, *J* = 17.5, 11.6 Hz, 2H), 1.41 (s, 9H), 1.40 (m, 1H), 0.90 (t, *J* = 6.2 Hz, 6H).

¹³C NMR (126 MHz, CDCl₃) δ 172.27, 171.44, 167.26, 155.55, 141.64, 135.76, 133.60, 131.17,

130.09, 127.66, 126.70, 119.71, 79.92, 52.93, 52.39, 51.75, 41.08, 34.95, 28.26, 24.66, 22.91,

21.86.

HRMS (ESI): m/z [M + Na]⁺ calcd for C₂₅H₃₆N₂NaO₇, 499.2415; found, 499.2429.



2e_{di}

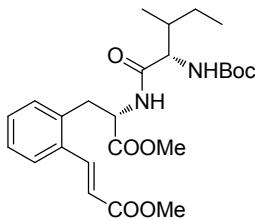
(2E,2'E)-dimethyl

3,3'-(2-((S)-2-((S)-2-((tert-butoxycarbonyl)amino)-4-methylpentanamido)-3-methoxy-3-oxopropyl)-1,3-phenylene)diacrylate.

White solid (39 mg, 23% yield). ¹H NMR (400 MHz, CDCl₃) δ 8.08 (t, *J* = 14.9 Hz, 2H), 7.60 (d, *J* = 7.8 Hz, 2H), 7.32 (t, *J* = 7.8 Hz, 1H), 6.76 (d, *J* = 6.5 Hz, 1H), 6.41 (d, *J* = 15.7 Hz, 2H), 4.98 (d, *J* = 7.1 Hz, 1H), 4.76 (dd, *J* = 14.2, 7.5 Hz, 1H), 4.04 (d, *J* = 12.8 Hz, 1H), 3.85 (s, 6H), 3.70 (s, 3H), 3.37 (qd, *J* = 14.7, 7.3 Hz, 2H), 1.66 – 1.50 (m, 2H), 1.46 (s, 9H), 0.93 – 0.86 (m, 6H).

¹³C NMR (126 MHz, CDCl₃) δ 172.20, 171.25, 167.03, 155.71, 141.96, 135.38, 135.22, 128.58, 127.86, 121.24, 80.15, 52.82, 52.62, 51.89, 41.25, 31.85, 28.27, 24.69, 22.98.

HRMS (ESI): m/z [M + Na]⁺ calcd for C₂₉H₄₀N₂NaO₉, 583.2626; found, 583.2633.



2f_{mono}

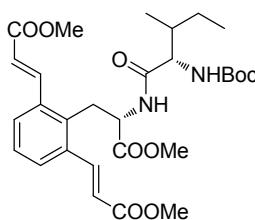
(E)-methyl

3-(2-((2S)-2-((2S)-2-((tert-butoxycarbonyl)amino)-3-methylpentanamido)-3-methoxy-3-oxopropyl)phenyl)acrylate.

Yellow solid (94 mg, 66% yield). ¹H NMR (400 MHz, CDCl₃) δ 7.99 (d, *J* = 15.8 Hz, 1H), 7.58 (d, *J* = 7.5 Hz, 1H), 7.36 – 7.23 (m, 2H), 7.23 – 7.13 (m, 1H), 6.54 (t, *J* = 13.1 Hz, 1H), 6.40 (d, *J* = 15.7 Hz, 1H), 5.18 – 5.01 (m, 1H), 4.91 – 4.78 (m, 1H), 3.95 (dd, *J* = 18.3, 11.3 Hz, 1H), 3.82 (s, 3H), 3.67 (s, 3H), 3.31 (dd, *J* = 14.3, 6.1 Hz, 1H), 3.21 (dd, *J* = 14.3, 6.9 Hz, 1H), 1.91 – 1.76 (m, 1H), 1.43 (s, 9H), 1.42 (m, 1H), 1.16 – 1.00 (m, 1H), 0.86 (t, *J* = 7.2 Hz, 6H).

¹³C NMR (101 MHz, CDCl₃) δ 171.50, 171.33, 167.20, 155.62, 141.49, 135.60, 133.60, 131.06, 130.15, 127.70, 126.77, 119.84, 79.78, 59.18, 52.88, 52.44, 51.78, 37.18, 34.93, 28.29, 24.60, 15.40, 11.42.

HRMS (ESI): m/z [M + Na]⁺ calcd for C₂₅H₃₆N₂NaO₇, 499.2415; found, 499.2407.



2f_{di}

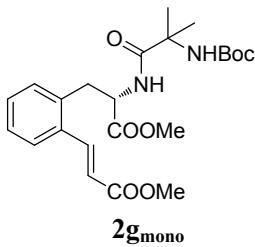
(*E,E*)-dimethyl

3,3'-(2-((2*S*)-2-((tert-butoxycarbonyl)amino)-2-methylpropanamido)-3-methoxy-3-oxopropyl)-1,3-phenylene)diacrylate.

Yellow solid (29 mg, 17% yield). ¹H NMR (400 MHz, CDCl₃) δ 8.08 (t, *J* = 13.9 Hz, 2H), 7.59 (d, *J* = 7.8 Hz, 2H), 7.31 (dd, *J* = 13.7, 5.9 Hz, 2H), 6.64 (d, *J* = 6.9 Hz, 1H), 6.41 (d, *J* = 15.7 Hz, 2H), 5.04 (d, *J* = 7.8 Hz, 1H), 4.85 – 4.71 (m, 1H), 3.91 (d, *J* = 6.7 Hz, 1H), 3.84 (s, 6H), 3.70 (s, 3H), 3.42 (dd, *J* = 14.6, 6.2 Hz, 1H), 3.33 (dd, *J* = 14.6, 8.6 Hz, 1H), 1.90 – 1.75 (m, 1H), 1.44 (s, 9H), 1.43 (m, 1H), 1.12 – 0.97 (m, 1H), 0.98 – 0.79 (m, 6H).

¹³C NMR (101 MHz, CDCl₃) δ 171.29, 171.22, 167.00, 155.40, 141.78, 135.26, 135.12, 128.60, 127.88, 121.41, 77.25, 59.15, 52.79, 52.64, 51.91, 37.41, 31.61, 28.29, 24.49, 15.32, 11.53.

HRMS (ESI): m/z [M + Na]⁺ calcd for C₂₉H₄₀N₂NaO₉, 583.2626; found, 583.2635.



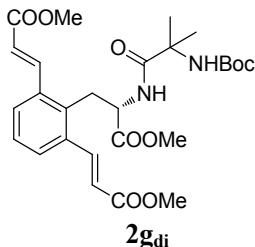
(*S,E*)-methyl

3-(2-(2-((tert-butoxycarbonyl)amino)-2-methylpropanamido)-3-methoxy-3-oxopropyl)phenyl)acrylate.

Yellow solid (79 mg, 59% yield). ¹H NMR (400 MHz, CDCl₃) δ 8.01 (d, *J* = 15.8 Hz, 1H), 7.61 (dd, *J* = 15.3, 8.0 Hz, 1H), 7.37 – 7.18 (m, 3H), 7.00 (s, 1H), 6.43 (t, *J* = 16.2 Hz, 1H), 4.96 (dd, *J* = 10.5, 6.9 Hz, 1H), 4.89 – 4.79 (m, 1H), 3.83 (s, 3H), 3.67 (s, 3H), 3.28 (qd, *J* = 14.3, 6.5 Hz, 2H), 1.46 (s, 3H), 1.42 (s, 12H).

¹³C NMR (126 MHz, CDCl₃) δ 174.40, 171.78, 167.17, 154.59, 141.64, 135.89, 133.68, 131.16, 130.02, 127.61, 126.73, 119.87, 81.52, 56.72, 53.19, 52.36, 51.75, 35.06, 28.26, 25.22.

HRMS (ESI): m/z [M + Na]⁺ calcd for C₂₃H₃₂N₂NaO₇, 471.2102; found, 471.2101.

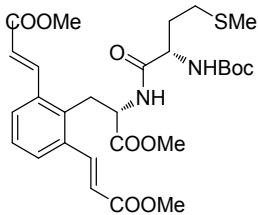


(*E,E*)-dimethyl

3,3'-(2-((*S*)-2-(2-((tert-butoxycarbonyl)amino)-2-methylpropanamido)-3-methoxy-3-oxopropyl)-1,3-phenylene)diacrylate.

Yellow solid (30 mg, 19% yield). ¹H NMR (400 MHz, CDCl₃) δ 8.12 (d, *J* = 15.7 Hz, 2H), 7.61 (t, *J* = 9.0 Hz, 2H), 7.38 – 7.28 (m, 2H), 6.46 – 6.35 (m, 2H), 5.04 – 4.89 (m, 1H), 4.73 (dd, *J* = 14.9, 7.5 Hz, 1H), 3.84 (s, 6H), 3.68 (s, 3H), 3.43 – 3.33 (m, 2H), 1.42 (s, 9H), 1.35 (s, 3H), 1.29 (s, 3H).

¹³C NMR (126 MHz, CDCl₃) δ 174.55, 171.53, 166.88, 154.50, 141.87, 135.32, 129.25, 128.59, 128.54, 127.82, 121.45, 80.16, 56.61, 53.20, 52.55, 51.84, 31.77, 29.70, 28.24.
 HRMS (ESI): m/z [M + Na]⁺ calcd for C₂₇H₃₆N₂NaO₉, 555.2313; found, 555.2302.



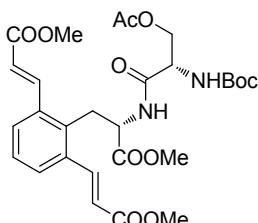
2h

(2E,2'E)-dimethyl
3,3'-{2-((S)-2-((S)-2-((tert-butoxycarbonyl)amino)-4-(methylthio)butanamido)-3-methoxy-3-oxopropyl}-1,3-phenylene)diacrylate.

Yellow solid (161 mg, 93% yield). ¹H NMR (400 MHz, CDCl₃) δ 8.08 (d, *J* = 15.7 Hz, 2H), 7.60 (d, *J* = 7.8 Hz, 2H), 7.37 – 7.25 (m, 1H), 6.84 (d, *J* = 8.2 Hz, 1H), 6.41 (dd, *J* = 15.7, 2.9 Hz, 2H), 5.25 (d, *J* = 6.5 Hz, 1H), 4.77 (dd, *J* = 14.3, 7.9 Hz, 1H), 4.17 (dd, *J* = 21.5, 6.4 Hz, 1H), 3.84 (s, 6H), 3.69 (s, 3H), 3.42 (dt, *J* = 14.4, 7.3 Hz, 1H), 3.34 (dd, *J* = 14.6, 8.3 Hz, 1H), 2.49 (t, *J* = 7.2 Hz, 2H), 2.08 (s, 3H), 1.99 (dt, *J* = 14.0, 6.8 Hz, 1H), 1.85 (t, *J* = 16.9 Hz, 1H), 1.45 (s, 9H).

¹³C NMR (101 MHz, CDCl₃) δ 171.13, 171.08, 166.99, 155.28, 141.80, 135.24, 135.19, 128.64, 127.92, 121.36, 80.00, 53.34, 52.87, 52.68, 51.91, 31.71, 31.63, 30.05, 28.28, 15.13.

HRMS (ESI): m/z [M + Na]⁺ calcd for C₂₈H₃₈N₂NaO₉S, 601.2190; found, 601.2189.



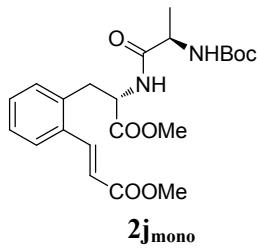
2i

(2E,2'E)-dimethyl
3,3'-{2-((S)-2-((S)-3-acetoxy-2-((tert-butoxycarbonyl)amino)propanamido)-3-methoxy-3-oxopropyl}-1,3-phenylene)diacrylate.

Yellow solid (147 mg, 85% yield). ¹H NMR (500 MHz, CDCl₃) δ 8.10 (d, *J* = 15.7 Hz, 2H), 7.61 (d, *J* = 7.8 Hz, 2H), 7.32 (t, *J* = 7.8 Hz, 1H), 7.09 (d, *J* = 7.7 Hz, 1H), 6.41 (d, *J* = 15.7 Hz, 2H), 5.40 (d, *J* = 7.0 Hz, 1H), 4.78 (dd, *J* = 14.7, 7.5 Hz, 1H), 4.38 (br s, 1H), 4.30 – 4.22 (m, 1H), 4.22 – 4.12 (m, 1H), 3.84 (s, 6H), 3.68 (s, 3H), 3.42 – 3.38 (m, 2H), 2.05 (s, 3H), 1.45 (s, 9H).

¹³C NMR (126 MHz, CDCl₃) δ 171.04, 170.66, 168.75, 167.08, 141.83, 135.22, 128.60, 127.97, 121.26, 80.39, 63.95, 53.00, 52.75, 51.97, 31.77, 28.25, 20.71.

HRMS (ESI): m/z [M + Na]⁺ calcd for C₂₈H₃₆N₂NaO₁₁, 599.2211; found, 599.2207.



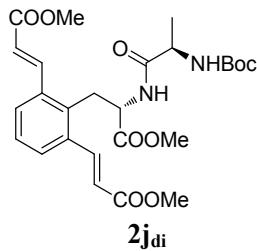
(E)-methyl

3-((S)-2-((R)-2-((tert-butoxycarbonyl)amino)propanamido)-3-methoxy-3-oxopropyl)phenyl)acrylate.

Yellow solid (72 mg, 55% yield). ¹H NMR (400 MHz, CDCl₃) δ 8.00 (d, *J* = 15.8 Hz, 1H), 7.60 (d, *J* = 7.5 Hz, 1H), 7.37 – 7.26 (m, 2H), 7.23 – 7.13 (m, 1H), 6.77 (br s, 1H), 6.41 (d, *J* = 15.7 Hz, 1H), 5.02 (br s, 1H), 4.90 – 4.76 (m, 1H), 4.17 (br s, 1H), 3.83 (s, 3H), 3.68 (s, 3H), 3.32 (m, 1H), 3.28 – 3.14 (m, 1H), 1.43 (s, 9H), 1.28 (d, *J* = 7.0 Hz, 3H).

¹³C NMR (126 MHz, CDCl₃) δ 172.32, 171.61, 167.13, 155.46, 141.49, 135.62, 133.69, 131.05, 130.09, 127.72, 126.83, 119.93, 80.08, 52.93, 52.46, 51.76, 49.82, 34.92, 28.29, 18.11.

HRMS (ESI): m/z [M + Na]⁺ calcd for C₂₂H₃₀N₂NaO₇, 457.1945; found, 457.1950.



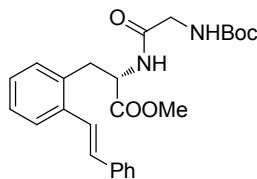
(2E,2'E)-dimethyl

3,3'-(2-((S)-2-((R)-2-((tert-butoxycarbonyl)amino)propanamido)-3-methoxy-3-oxopropyl)-1,3-phenylene)diacrylate.

Yellow solid (39 mg, 25% yield). ¹H NMR (400 MHz, CDCl₃) δ 8.07 (d, *J* = 15.7 Hz, 2H), 7.58 (d, *J* = 7.8 Hz, 2H), 7.34 – 7.25 (m, 1H), 6.89 (br s, 1H), 6.38 (d, *J* = 15.7 Hz, 2H), 5.03 (br s, 1H), 4.77 – 4.65 (m, 1H), 4.11 (d, *J* = 6.4 Hz, 1H), 3.81 (s, 6H), 3.65 (s, 3H), 3.38 (qd, *J* = 14.6, 7.4 Hz, 2H), 1.40 (s, 9H), 1.17 (dd, *J* = 16.4, 7.0 Hz, 3H).

¹³C NMR (126 MHz, CDCl₃) δ 172.34, 171.24, 166.85, 155.70, 141.74, 135.30, 135.21, 128.57, 127.86, 121.40, 79.97, 52.94, 52.62, 51.83, 49.59, 31.41, 28.26, 17.91.

HRMS (ESI): m/z [M + Na]⁺ calcd for C₂₆H₃₄N₂NaO₉, 541.2157; found, 541.2161.

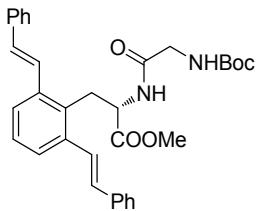


(S,E)-methyl 2-((tert-butoxycarbonyl)amino)acetamido)-3-(2-styrylphenyl)propanoate.

Yellow solid (75 mg, 57% yield). ¹H NMR (400 MHz, CDCl₃) δ 7.67 (d, *J* = 7.7 Hz, 1H), 7.59 (t, *J* = 9.5 Hz, 2H), 7.47 – 7.37 (m, 3H), 7.29 (dd, *J* = 10.3, 4.5 Hz, 2H), 7.22 (dd, *J* = 10.6, 4.1 Hz, 1H), 7.13 – 7.00 (m, 2H), 6.63 (d, *J* = 7.4 Hz, 1H), 4.96 (br s, 1H), 4.89 (dt, *J* = 16.8, 8.4 Hz, 1H),

3.79 – 3.58 (m, 2H), 3.59 (s, 3H), 3.39 (dd, J = 14.1, 6.3 Hz, 1H), 3.27 (dd, J = 14.1, 5.9 Hz, 1H), 1.45 (s, 9H).

^{13}C NMR (126 MHz, CDCl_3) δ 171.72, 169.11, 155.87, 137.20, 136.81, 133.73, 130.65, 130.62, 128.89, 127.98, 127.71, 127.73, 126.64, 125.92, 125.61, 80.18, 53.26, 52.48, 44.12, 35.16, 28.28.
HRMS (ESI): m/z [M + Na]⁺ calcd for $\text{C}_{25}\text{H}_{30}\text{N}_2\text{NaO}_5$, 461.2047; found, 461.2054.



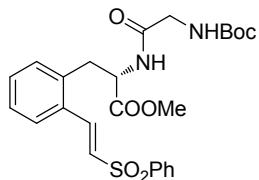
2k_{di}

(S)-methyl 2-(2-((tert-butoxycarbonyl)amino)acetamido)-3-(2,6-di((E)-styryl)phenyl)propanoate.

Yellow solid (45 mg, 28% yield). ^1H NMR (400 MHz, CDCl_3) δ 7.65–7.60 (m, 5H), 7.52 (d, J = 15.9 Hz, 2H), 7.42 (t, J = 7.6 Hz, 4H), 7.37 – 7.29 (m, 4H), 7.04 (d, J = 15.9 Hz, 2H), 6.63 (d, J = 7.5 Hz, 1H), 4.84 (m, 2H), 3.67 (d, J = 14.1 Hz, 2H), 3.56 (s, 3H), 3.48 (m, 2H), 1.46 (s, 9H).

^{13}C NMR (126 MHz, CDCl_3) δ 171.91, 168.89, 137.84, 137.22, 131.68, 128.87, 127.98, 127.67, 126.76, 126.17, 125.75, 80.39, 53.08, 52.69, 43.98, 31.56, 28.28.

HRMS (ESI): m/z [M + Na]⁺ calcd for $\text{C}_{33}\text{H}_{36}\text{N}_2\text{NaO}_5$, 563.2516; found, 563.2506.



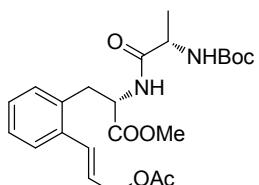
2l_{mono}

(S,E)-methyl

2-(2-((tert-butoxycarbonyl)amino)acetamido)-3-(2-(phenylsulfonyl)vinyl)phenylpropanoate.

Yellow solid (92 mg, 62% yield). ^1H NMR (400 MHz, CDCl_3) δ 8.05 – 7.93 (m, 3H), 7.71 – 7.61 (m, 1H), 7.61 – 7.54 (m, 2H), 7.47 (d, J = 7.7 Hz, 1H), 7.42 – 7.31 (m, 1H), 7.31 – 7.18 (m, 2H), 6.85 (m, 2H), 5.41 (t, J = 5.9 Hz, 1H), 4.87 (d, J = 6.4 Hz, 1H), 3.86 – 3.75 (m, 2H), 3.71 (s, 3H), 3.38 (dd, J = 14.3, 5.5 Hz, 1H), 3.23 (dd, J = 14.3, 6.5 Hz, 1H), 1.44 (s, 9H).

^{13}C NMR (101 MHz, CDCl_3) δ 171.24, 169.62, 156.13, 140.30, 139.60, 136.54, 133.56, 131.65, 131.35, 131.10, 129.44, 128.98, 127.85, 127.77, 127.25, 80.20, 53.28, 52.64, 44.22, 35.08, 28.27.
HRMS (ESI): m/z [M + Na]⁺ calcd for $\text{C}_{25}\text{H}_{30}\text{N}_2\text{NaO}_7\text{S}$, 525.1666; found, 525.1666.



2m

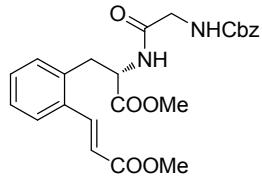
(S)-methyl

3-(2-((E)-3-acetoxyprop-1-en-1-yl)phenyl)-2-((S)-2-((tert-butoxycarbonyl)amino)propanamido)propanoate.

Yellow solid (82 mg, 61% yield). ^1H NMR (400 MHz, CDCl_3) δ 7.57 – 7.45 (m, 1H), 7.30 – 7.17 (m, 2H), 7.09 (dd, J = 10.3, 3.4 Hz, 1H), 6.95 (d, J = 15.7 Hz, 1H), 6.62 (d, J = 7.8 Hz, 1H), 6.23 (dt, J = 15.6, 6.2 Hz, 1H), 5.11 – 4.97 (m, 1H), 4.79 (m, 3H), 4.14 (dd, J = 14.2, 7.1 Hz, 1H), 3.69 (s, 3H), 3.23 (dd, J = 14.1, 6.5 Hz, 1H), 3.14 (dd, J = 14.1, 6.9 Hz, 1H), 2.14 (s, 3H), 1.44 (s, 9H), 1.31 (d, J = 7.1 Hz, 3H).

^{13}C NMR (101 MHz, CDCl_3) δ 172.25, 171.80, 170.91, 155.39, 135.70, 133.71, 130.85, 130.48, 128.06, 127.55, 126.38, 125.71, 80.09, 65.13, 53.05, 52.35, 50.14, 35.30, 28.28, 20.99, 18.21.

HRMS (ESI): m/z [M + Na] $^+$ calcd for $\text{C}_{23}\text{H}_{32}\text{N}_2\text{NaO}_7$, 471.2102; found, 471.2101.



2n_{mono}

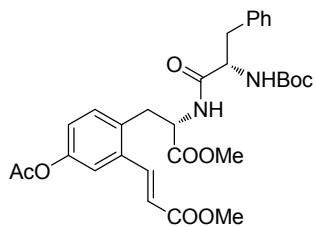
(S,E)-methyl

3-(2-(2-((benzyloxy)carbonyl)amino)acetamido)-3-methoxy-3-oxopropylphenylacrylate.

Yellow solid (21 mg, 45% yield). ^1H NMR (400 MHz, CDCl_3) δ 7.96 (d, J = 15.8 Hz, 1H), 7.58 (dd, J = 8.7, 6.8 Hz, 1H), 7.42 – 7.23 (m, 7H), 7.14 (d, J = 6.8 Hz, 1H), 6.73 (br s, 1H), 6.42 (t, J = 13.7 Hz, 1H), 5.65 (br s, 1H), 5.10 (s, 2H), 4.89 (dd, J = 13.3, 6.1 Hz, 1H), 3.86 (ddd, J = 19.3, 14.0, 5.7 Hz, 2H), 3.80 (s, 3H), 3.68 (s, 3H), 3.35 (dd, J = 14.2, 5.6 Hz, 1H), 3.21 (dd, J = 14.2, 6.3 Hz, 1H).

^{13}C NMR (126 MHz, CDCl_3) δ 171.43, 168.75, 167.37, 156.56, 141.62, 136.23, 135.69, 133.65, 131.13, 130.20, 128.53, 128.19, 128.06, 127.80, 126.78, 119.59, 67.12, 53.11, 52.51, 51.83, 44.38, 34.84.

HRMS (ESI): m/z [M + Na] $^+$ calcd for $\text{C}_{24}\text{H}_{26}\text{N}_2\text{NaO}_7$, 477.1632; found, 477.1641.



2o_{mono}

(E)-methyl

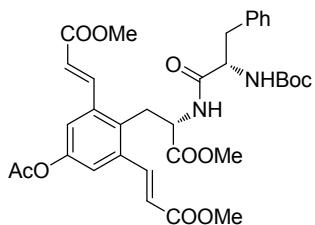
3-(5-acetoxy-2-((S)-2-((tert-butoxycarbonyl)amino)-3-phenylpropanamido)-3-methoxy-3-oxopropylphenylacrylate.

Yellow solid (97 mg, 57% yield). ^1H NMR (500 MHz, CDCl_3) δ 7.91 (d, J = 15.8 Hz, 1H), 7.34 – 7.27 (m, 3H), 7.24 (t, J = 4.8 Hz, 1H), 7.21 (t, J = 6.1 Hz, 2H), 7.09 (d, J = 8.4 Hz, 1H), 7.04 (dd, J = 8.4, 2.3 Hz, 1H), 6.44 (d, J = 7.6 Hz, 1H), 6.41 – 6.34 (m, 1H), 5.09 (br s, 1H), 4.78 (d, J = 6.6

Hz, 1H), 4.34 (br s, 1H), 3.86 (s, 3H), 3.65 (m, 3H), 3.25 (dd, $J = 14.3, 6.3$ Hz, 1H), 3.18 (dd, $J = 14.3, 6.5$ Hz, 1H), 3.09 (dd, $J = 13.9, 6.6$ Hz, 1H), 3.02 (s, 1H), 2.34 (s, 3H), 1.41 (s, 9H).

^{13}C NMR (126 MHz, CDCl_3) δ 171.03, 170.97, 169.19, 167.02, 155.59, 149.97, 140.66, 136.68, 134.89, 133.20, 132.22, 129.33, 128.64, 126.91, 123.30, 120.65, 119.55, 80.16, 55.81, 52.99, 52.47, 51.91, 38.17, 34.64, 28.23, 21.11.

HRMS (ESI): m/z [M + Na]⁺ calcd for $\text{C}_{30}\text{H}_{36}\text{N}_2\text{NaO}_9$, 591.2313; found, 591.2321.



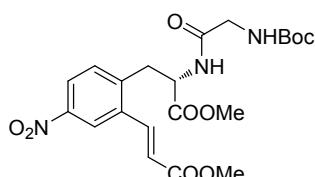
2o_{di}

(*E,E*)-dimethyl
3,3'-(5-acetoxy-2-((S)-2-((S)-2-((tert-butoxycarbonyl)amino)-3-phenylpropanamido)-3-methoxy-3-oxopropyl)-1,3-phenylene)diacrylate.

Yellow solid (55 mg, 28% yield). ^1H NMR (500 MHz, CDCl_3) δ 8.04 (d, $J = 15.6$ Hz, 2H), 7.34 (s, 2H), 7.31 – 7.21 (m, 3H), 7.17 (d, $J = 7.3$ Hz, 2H), 6.60 (d, $J = 7.4$ Hz, 1H), 6.39 – 6.33 (m, 2H), 5.12 (br s, 1H), 4.72 (dd, $J = 14.6, 7.2$ Hz, 1H), 4.33 (br s, 1H), 3.86 (s, 6H), 3.65 (s, 3H), 3.29 (d, $J = 6.9$ Hz, 2H), 3.05 (dd, $J = 13.9, 6.2$ Hz, 1H), 2.96 (br s, 1H), 2.34 (s, 3H), 1.41 (s, 9H).

^{13}C NMR (126 MHz, CDCl_3) δ 170.86, 170.80, 169.03, 166.76, 155.59, 149.83, 141.00, 136.68, 136.60, 132.81, 129.33, 128.59, 126.85, 122.03, 121.47, 80.39, 55.86, 52.81, 52.66, 52.00, 38.30, 31.69, 28.22, 21.10.

HRMS (ESI): m/z [M + Na]⁺ calcd for $\text{C}_{34}\text{H}_{40}\text{N}_2\text{NaO}_{11}$, 675.2524; found, 675.2532.



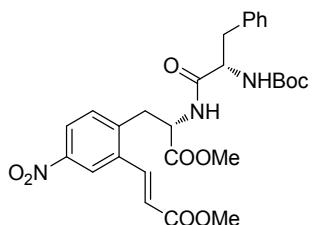
2p

(*S,E*)-methyl
3-(2-(2-((tert-butoxycarbonyl)amino)acetamido)-3-methoxy-3-oxopropyl)-5-nitrophenylacrylate.

Yellow solid (106 mg, 76% yield). ^1H NMR (400 MHz, CDCl_3) δ 8.44 (d, $J = 2.2$ Hz, 1H), 8.23 – 8.12 (m, 1H), 7.97 (d, $J = 15.8$ Hz, 1H), 7.38 (t, $J = 8.3$ Hz, 1H), 6.90 (d, $J = 7.6$ Hz, 1H), 6.56 (d, $J = 15.7$ Hz, 1H), 5.25 (br s, 1H), 4.90 (dd, $J = 13.5, 6.5$ Hz, 1H), 3.92 – 3.83 (s, 3H), 3.77 – 3.68 (m, 2H), 3.73 (s, 3H), 3.45 (dd, $J = 14.2, 5.8$ Hz, 1H), 3.36 – 3.25 (m, 1H), 1.44 (s, 9H).

^{13}C NMR (101 MHz, CDCl_3) δ 170.93, 169.56, 166.63, 156.04, 147.38, 142.74, 139.40, 135.29, 132.34, 124.11, 122.59, 121.66, 80.49, 52.79, 52.65, 52.14, 44.27, 35.17, 28.23.

HRMS (ESI): m/z [M + Na]⁺ calcd for $\text{C}_{21}\text{H}_{27}\text{N}_3\text{NaO}_9$, 488.1640; found, 488.1642.



2q

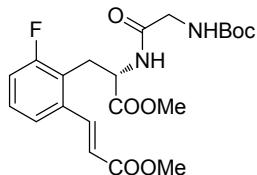
(*E*)-methyl

3-((S)-2-((tert-butoxycarbonyl)amino)-2-((tert-butoxycarbonyl)amino)-3-phenylpropanamido)-3-methoxy-3-oxopropyl)-5-nitrophenylacrylate.

Yellow solid (108 mg, 65% yield). ^1H NMR (400 MHz, CDCl_3) δ 8.41 (d, $J = 2.3$ Hz, 1H), 8.10 (ddd, $J = 8.4, 5.7, 2.9$ Hz, 1H), 7.94 (d, $J = 15.8$ Hz, 1H), 7.33 – 7.15 (m, 6H), 6.54 (m, 2H), 5.02 (s, 1H), 4.79 (d, $J = 6.7$ Hz, 1H), 4.32 (dd, $J = 14.5, 7.1$ Hz, 1H), 3.87 (s, 3H), 3.74 – 3.69 (m, 1H), 3.67 (s, 3H), 3.36 (dd, $J = 14.2, 6.1$ Hz, 1H), 3.24 (dd, $J = 14.2, 6.7$ Hz, 1H), 3.02 (t, $J = 10.6$ Hz, 2H), 1.42 (s, 9H).

^{13}C NMR (101 MHz, CDCl_3) δ 171.21, 170.57, 166.56, 155.68, 147.34, 142.67, 139.30, 136.41, 135.22, 132.31, 129.26, 128.69, 127.02, 124.00, 122.69, 121.63, 80.42, 52.70, 52.58, 52.12, 38.00, 35.24, 28.21.

HRMS (ESI): m/z [M + Na] $^+$ calcd for $\text{C}_{28}\text{H}_{33}\text{N}_3\text{NaO}_9$, 578.2109; found, 578.2122.



2r

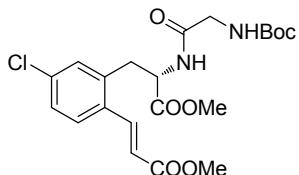
(*S,E*)-methyl

3-((2-((tert-butoxycarbonyl)amino)acetamido)-3-methoxy-3-oxopropyl)-3-fluorophenylacrylate.

Yellow solid (116 mg, 84% yield). ^1H NMR (400 MHz, CDCl_3) δ 7.96 (d, $J = 15.8$ Hz, 1H), 7.41 (d, $J = 7.8$ Hz, 1H), 7.34 – 7.22 (m, 1H), 7.09 (t, $J = 8.7$ Hz, 1H), 6.67 (d, $J = 8.0$ Hz, 1H), 6.44 (d, $J = 15.7$ Hz, 1H), 5.16 (br s, 1H), 4.85 (dd, $J = 13.9, 7.2$ Hz, 1H), 3.84 (s, 3H), 3.80 – 3.75 (m, 1H), 3.74 (s, 3H), 3.68 (dd, $J = 10.5, 7.2$ Hz, 1H), 3.37 (ddd, $J = 14.2, 5.9, 1.7$ Hz, 1H), 3.27 (ddd, $J = 14.3, 7.1, 1.5$ Hz, 1H), 1.46 (s, 9H).

^{13}C NMR (126 MHz, CDCl_3) δ 171.36, 169.19, 166.98, 161.73 (d, $J = 244.7$ Hz), 140.41, 136.09, 136.06, 128.89 (d, $J = 9.2$ Hz), 123.11 (d, $J = 15.7$ Hz), 122.50, 121.15, 116.54 (d, $J = 23.7$ Hz), 80.00, 52.70, 52.21, 52.00, 44.05, 28.29, 27.76, 27.74.

HRMS (ESI): m/z [M + Na] $^+$ calcd for $\text{C}_{21}\text{H}_{27}\text{FN}_2\text{NaO}_7$, 461.1695; found, 461.1695.

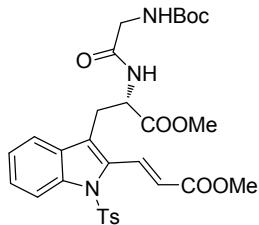


2s*(S,E)-methyl**3-(2-(2-((tert-butoxycarbonyl)amino)acetamido)-3-methoxy-3-oxopropyl)-4-chlorophenyl)acrylate.*

Yellow solid (94 mg, 69% yield). ^1H NMR (500 MHz, CDCl_3) δ 7.89 (d, $J = 15.8$ Hz, 1H), 7.53 (d, $J = 8.5$ Hz, 1H), 7.25 (dd, $J = 8.4, 2.1$ Hz, 1H), 7.17 (t, $J = 5.0$ Hz, 1H), 6.79 (d, $J = 6.8$ Hz, 1H), 6.38 (d, $J = 15.8$ Hz, 1H), 5.23 (d, $J = 27.3$ Hz, 1H), 4.83 (dt, $J = 20.9, 6.6$ Hz, 1H), 3.82 (s, 3H), 3.81 – 3.74 (m, 2H), 3.70 (s, 3H), 3.32 (dd, $J = 14.2, 5.8$ Hz, 1H), 3.23 – 3.12 (m, 1H), 1.44 (s, 9H).

^{13}C NMR (126 MHz, CDCl_3) δ 171.16, 169.40, 169.33, 167.16, 140.45, 137.62, 135.94, 132.19, 131.04, 128.02, 127.37, 119.98, 80.40, 53.02, 52.60, 52.49, 51.94, 44.23, 37.57, 34.86, 28.26.

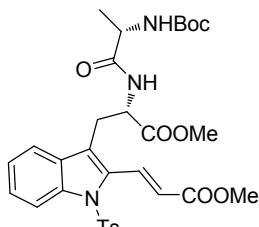
HRMS (ESI): m/z [M + Na]⁺ calcd for $\text{C}_{21}\text{H}_{27}\text{ClN}_2\text{NaO}_7$, 477.1399; found, 477.1403.

**2t***(S,E)-methyl**3-(3-(2-((tert-butoxycarbonyl)amino)acetamido)-3-methoxy-3-oxopropyl)-1-tosyl-1H-indol-2-yl)acrylate.*

Yellow solid (125 mg, 68% yield). ^1H NMR (400 MHz, CDCl_3) δ 8.19 (d, $J = 8.4$ Hz, 1H), 8.10 (t, $J = 16.2$ Hz, 1H), 7.54 (m, 3H), 7.42 – 7.33 (m, 1H), 7.34 – 7.23 (m, 1H), 7.14 (t, $J = 8.3$ Hz, 2H), 6.85 (d, $J = 7.2$ Hz, 1H), 6.26 (d, $J = 16.2$, 1H), 5.28 (s, 1H), 4.85 – 4.72 (m, 1H), 3.87 (s, 3H), 3.71 (dd, $J = 12.9, 5.7$ Hz, 2H), 3.67 – 3.57 (m, 1H), 3.42 (s, 3H), 3.27 (d, $J = 6.7$ Hz, 2H), 2.31 (s, 3H), 1.46 (s, 9H).

^{13}C NMR (101 MHz, CDCl_3) δ 171.30, 169.39, 166.69, 156.05, 145.09, 136.99, 134.77, 134.29, 133.36, 130.40, 129.68, 126.69, 126.58, 124.31, 122.58, 121.21, 119.83, 115.45, 80.38, 52.45, 52.15, 52.11, 28.25, 27.72, 21.53.

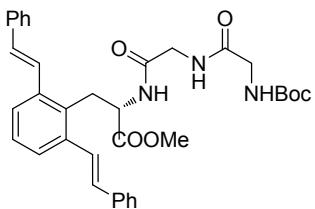
HRMS (ESI): m/z [M + Na]⁺ calcd for $\text{C}_{30}\text{H}_{35}\text{N}_3\text{NaO}_9\text{S}$, 636.1986; found, 636.1986.

**2u***(E)-methyl**3-(3-((S)-2-((S)-2-((tert-butoxycarbonyl)amino)propanamido)-3-methoxy-3-oxopropyl)-1-tosyl-1H-indol-2-yl)acrylate.*

Yellow solid (107 mg, 57% yield). ^1H NMR (500 MHz, CDCl_3) δ 8.20 (d, $J = 8.4$ Hz, 1H), 8.18 – 8.07 (m, 1H), 7.64 – 7.50 (m, 3H), 7.44 – 7.35 (m, 1H), 7.33 – 7.27 (m, 1H), 7.18 (t, $J = 18.1$ Hz, 2H), 6.85 (t, $J = 19.2$ Hz, 1H), 6.26 (dd, $J = 16.2, 7.5$ Hz, 1H), 5.11 (br s, 1H), 4.77 (d, $J = 6.5$ Hz, 1H), 4.11 (dt, $J = 23.4, 6.9$ Hz, 1H), 3.88 (s, 3H), 3.45 (s, 3H), 3.33 – 3.22 (m, 2H), 2.32 (s, 3H), 1.45 (s, 9H).

^{13}C NMR (126 MHz, CDCl_3) δ 172.38, 171.32, 166.64, 155.58, 145.06, 136.98, 134.78, 134.42, 133.32, 130.51, 129.88, 129.69, 129.56, 126.79, 126.71, 126.57, 124.28, 122.49, 121.35, 120.05, 115.43, 80.37, 52.43, 52.23, 52.10, 50.00, 28.26, 27.95, 21.55, 18.17, 17.76.

HRMS (ESI): m/z [M + Na] $^+$ calcd for $\text{C}_{31}\text{H}_{37}\text{N}_3\text{NaO}_9\text{S}$, 650.2143; found, 650.2147.



4a

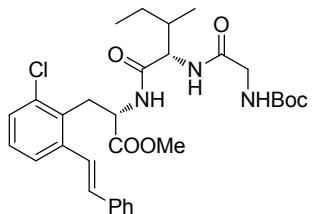
(*S*)-methyl

12-(2,6-di((E)-styryl)benzyl)-2,2-dimethyl-4,7,10-trioxo-3-oxa-5,8,11-triazatridecan-13-oate

Red solid (88 mg, 49% yield). ^1H NMR (300 MHz, CDCl_3) δ 7.55–7.63 (m, 5H), 7.48 (d, $J = 16.1$ Hz, 2H), 7.44–7.36 (t, $J = 7.4$ Hz, 4H), 7.36–7.26 (dd, $J = 10.1, 4.5$ Hz, 4H), 7.02 (d, $J = 16.0$ Hz, 2H), 6.54 (br s, 1H), 6.36 (br s, 1H), 4.99 (br s, 1H), 4.78 (d, $J = 6.9$ Hz, 1H), 3.83 – 3.68 (m, 2H), 3.68–3.60 (d, $J = 5.1$ Hz, 2H), 3.54 (s, 3H), 3.51 (d, $J = 6.7$ Hz, 2H), 1.45 (s, 9H).

^{13}C NMR (75 MHz, CDCl_3) δ 171.9, 169.7, 168.2, 138.0, 137.4, 132.1, 131.7, 129.0, 128.1, 127.8, 126.9, 126.4, 126.0, 80.4, 53.3, 52.9, 42.8, 31.3, 28.5.

HRMS (ESI): m/z [M + Na] $^+$ calcd for $\text{C}_{35}\text{H}_{39}\text{N}_3\text{O}_6\text{Na}$, 620.2731; found, 620.2747.



4b

(*9S,12S*)-methyl

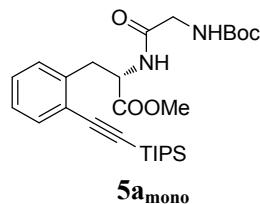
9-(sec-butyl)-12-(2-chloro-6-((E)-styryl)benzyl)-2,2-dimethyl-4,7,10-trioxo-3-oxa-5,8,11-triazatridiecan-13-oate

Yellow solid (107 mg, 58% yield). ^1H NMR (300 MHz, CDCl_3) δ 7.62 (d, $J = 7.4$ Hz, 2H), 7.54 (d, $J = 7.4$ Hz, 1H), 7.48 (d, $J = 16.0$ Hz, 1H), 7.40 (t, $J = 7.4$ Hz, 2H), 7.31 (dd, $J = 7.0, 4.2$ Hz, 2H), 7.21 (t, $J = 7.8$ Hz, 1H), 7.05 (d, $J = 16.0$ Hz, 1H), 6.62 (d, $J = 7.4$ Hz, 1H), 6.56 (d, $J = 8.8$ Hz, 1H), 5.10 (s, 1H), 4.85 (dd, $J = 15.1, 7.7$ Hz, 1H), 4.31 (dd, $J = 8.7, 6.0$ Hz, 1H), 3.75 – 3.72 (m, 1H), 3.71 (s, 3H), 3.55 – 3.31 (m, 2H), 1.82 (s, 1H), 1.46 (s, 9H), 1.34–1.32 (m, 1H), 1.09–1.06 (m, 1H), 0.93 – 0.73 (m, 6H).

^{13}C NMR (75 MHz, CDCl_3) δ 171.9, 170.8, 169.4, 156.2, 139.7, 137.1, 135.6, 133.4, 132.1, 129.1,

128.9, 128.7, 128.6, 127.3, 125.4, 125.2, 80.6, 57.6, 53.0, 52.6, 44.7, 37.9, 32.4, 28.2, 24.9, 15.4, 11.7.

HRMS (ESI): m/z [M + Na]⁺ calcd for C₃₁H₄₀ClN₃O₆Cl, 608.2498; found, 608.2499.



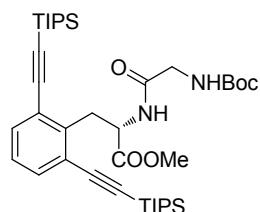
(S)-methyl

2-(2-((tert-butoxycarbonyl)amino)acetamido)-3-(2-((triisopropylsilyl)ethynyl)phenyl)propanoate.

Yellow solid (81 mg, 52% yield). ¹H NMR (400 MHz, CDCl₃) δ 7.49 (d, J = 7.1 Hz, 1H), 7.32 – 7.16 (m, 3H), 6.67 (d, J = 7.6 Hz, 1H), 5.21 (br s, 1H), 4.89 (dd, J = 14.1, 8.7 Hz, 1H), 3.78 – 3.69 (m, 2H), 3.67 (s, 3H), 3.49 – 3.38 (m, 1H), 3.25 – 3.13 (m, 1H), 1.45 (s, 9H), 1.22 – 1.10 (m, 2H).

¹³C NMR (126 MHz, CDCl₃) δ 171.90, 168.97, 138.13, 133.18, 129.37, 128.77, 127.04, 123.62, 105.16, 95.42, 80.06, 53.03, 52.38, 43.96, 36.44, 28.28, 18.69, 11.33.

HRMS (ESI): m/z [M + Na]⁺ calcd for C₂₈H₄₄N₂NaO₅Si, 539.2912; found, 539.2909.



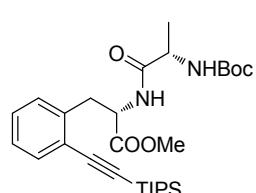
(S)-methyl

3-(2,6-bis((triisopropylsilyl)ethynyl)phenyl)-2-(2-((tert-butoxycarbonyl)amino)acetamido)propanoate.

Yellow solid (25 mg, 35% yield). ¹H NMR (400 MHz, CDCl₃) δ 7.47 (d, J = 7.7 Hz, 2H), 7.18 (t, J = 7.7 Hz, 1H), 6.35 (d, J = 8.1 Hz, 1H), 5.17 – 5.06 (m, 1H), 5.01 (m, 1H), 3.77 (s, 3H), 3.67 (dt, J = 13.1, 8.7 Hz, 3H), 3.43 (t, J = 12.7 Hz, 1H), 1.42 (s, 9H), 1.24 – 1.13 (m, 41H).

¹³C NMR (126 MHz, CDCl₃) δ 171.71, 168.61, 140.12, 133.29, 127.00, 124.23, 104.62, 96.37, 79.75, 52.49, 52.25, 34.89, 28.30, 18.70, 18.55, 11.30.

HRMS (ESI): m/z [M + Na]⁺ calcd for C₃₉H₆₄N₂NaO₅Si₂, 719.4246; found, 719.4231.



(S)-methyl

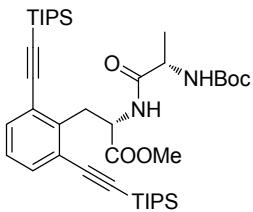
2-((S)-2-((tert-butoxycarbonyl)amino)propanamido)-3-(2-((triisopropylsilyl)ethynyl)phenyl)propa

noate.

Yellow solid (73 mg, 46% yield). ^1H NMR (400 MHz, CDCl_3) δ 7.52–7.49 (m, 1H), 7.35 – 7.15 (m, 3H), 6.54 (d, $J = 7.9$ Hz, 1H), 5.01 – 4.83 (m, 2H), 4.10 (br s, 1H), 3.71 (s, 3H), 3.42 (dd, $J = 13.7, 5.5$ Hz, 1H), 3.20 (dd, $J = 13.7, 9.7$ Hz, 1H), 1.43 (s, 9H), 1.25 (d, $J = 5.9$ Hz, 3H), 1.21 – 1.12 (m, 21H).

^{13}C NMR (126 MHz, CDCl_3) δ 172.13, 171.84, 138.26, 133.13, 129.39, 128.68, 126.94, 123.67, 105.21, 95.34, 80.03, 52.86, 52.32, 36.53, 28.30, 18.70, 18.50, 11.33.

HRMS (ESI): m/z [M + Na] $^+$ calcd for $\text{C}_{29}\text{H}_{46}\text{N}_2\text{NaO}_5\text{Si}$, 553.3068; found, 553.3068.



5b_{di}

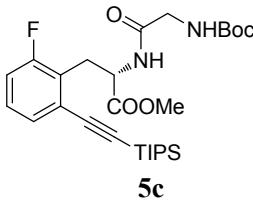
(S)-methyl

3-(2,6-bis((triisopropylsilyl)ethynyl)phenyl)-2-((S)-2-((tert-butoxycarbonyl)amino)propanamido)propoanoate.

Yellow solid (60 mg, 28% yield). ^1H NMR (400 MHz, CDCl_3) δ 7.46 (d, $J = 7.7$ Hz, 2H), 7.16 (t, $J = 7.8$ Hz, 1H), 6.43 (d, $J = 8.3$ Hz, 1H), 5.22 – 5.11 (m, 1H), 4.98 (d, $J = 19.1$ Hz, 1H), 4.07 – 3.92 (m, 1H), 3.76 (s, 3H), 3.72 – 3.62 (m, 1H), 3.43 (t, $J = 12.6$ Hz, 1H), 1.43 (s, 9H), 1.23 – 1.12 (m, 45H).

^{13}C NMR (126 MHz, CDCl_3) δ 171.97, 171.76, 154.86, 140.16, 133.27, 126.88, 124.30, 104.74, 96.14, 52.22, 51.95, 35.08, 29.73, 28.31, 19.33, 18.72, 18.61, 11.30.

HRMS (ESI): m/z [M + Na] $^+$ calcd for $\text{C}_{40}\text{H}_{66}\text{N}_2\text{NaO}_5\text{Si}_2$, 733.4402; found, 733.4403.



5c

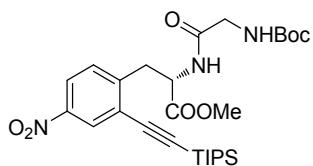
(S)-methyl

2-((tert-butoxycarbonyl)amino)acetamido)-3-(2-fluoro-6-((triisopropylsilyl)ethynyl)phenyl)propoanoate.

Yellow solid (113 mg, 71% yield). ^1H NMR (500 MHz, CDCl_3) δ 7.29 (d, $J = 7.4$ Hz, 1H), 7.18 (td, $J = 8.0, 5.7$ Hz, 1H), 7.02 (t, $J = 8.7$ Hz, 1H), 6.48 (d, $J = 8.3$ Hz, 1H), 5.05 (br s, 1H), 4.92 (tt, $J = 8.6, 7.4$ Hz, 1H), 3.73 (s, 3H), 3.69 (dd, $J = 16.8, 5.4$ Hz, 1H), 3.50 – 3.39 (m, 1H), 3.24 (td, $J = 12.9, 2.3$ Hz, 1H), 1.44 (s, 9H), 1.21 – 1.11 (m, 21H).

^{13}C NMR (126 MHz, CDCl_3) δ 171.69, 169.00, 161.25 (d, $J = 245.0$ Hz), 155.68, 129.05 (d, $J = 2.6$ Hz), 128.55 (d, $J = 9.4$ Hz), 125.78 (d, $J = 5.6$ Hz), 125.40 (d, $J = 17.1$ Hz), 115.80 (d, $J = 22.9$ Hz), 103.66, 96.67, 80.00, 52.48, 51.94, 43.79, 30.02, 28.29, 27.20, 18.70, 18.67, 11.26, 11.03.

HRMS (ESI): m/z [M + Na] $^+$ calcd for $\text{C}_{28}\text{H}_{43}\text{FN}_2\text{NaO}_5\text{Si}$, 557.2817; found, 557.2824.



5d

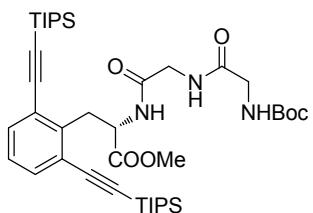
(*S*)-methyl

2-(2-((tert-butoxycarbonyl)amino)acetamido)-3-(4-nitro-2-((triisopropylsilyl)ethynyl)phenyl)propanoate.

Yellow solid (93 mg, 55% yield). ^1H NMR (400 MHz, CDCl_3) δ 8.29 (t, $J = 6.6$ Hz, 1H), 8.10 (dd, $J = 8.5, 2.4$ Hz, 1H), 7.43 (d, $J = 8.5$ Hz, 1H), 6.74 (d, $J = 7.4$ Hz, 1H), 5.10 (br s, 1H), 4.96 (dt, $J = 14.3, 7.2$ Hz, 1H), 3.83 – 3.68 (m, 2H), 3.73 (s, 3H), 3.55 (dd, $J = 13.6, 5.6$ Hz, 1H), 3.24 (dd, $J = 13.6, 9.4$ Hz, 1H), 1.43 (s, 9H), 1.22 – 1.11 (m, 21H).

^{13}C NMR (126 MHz, CDCl_3) δ 171.32, 169.21, 146.73, 145.52, 130.58, 127.73, 125.18, 123.12, 102.47, 98.78, 80.43, 52.67, 52.19, 44.17, 36.87, 28.25, 18.66, 11.23.

HRMS (ESI): m/z [M + Na] $^+$ calcd for $\text{C}_{28}\text{H}_{43}\text{N}_3\text{NaO}_7\text{Si}$, 584.2762; found, 584.2769.



6a

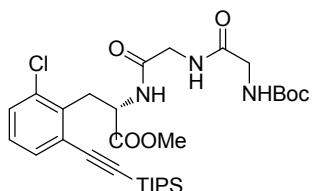
(*S*)-methyl

12-(2,6-bis((triisopropylsilyl)ethynyl)benzyl)-2,2-dimethyl-4,7,10-trioxo-3-oxa-5,8,11-triazatridecan-13-oate

Yellow solid (127 mg, 56% yield). ^1H NMR (300 MHz, CDCl_3) δ 7.47 (d, $J = 7.7$ Hz, 2H), 7.19 (t, $J = 7.7$ Hz, 1H), 6.46 (br s, 1H), 6.37 (d, $J = 8.2$ Hz, 1H), 5.16 – 4.92 (m, 2H), 3.89 (dd, $J = 17.0, 4.4$ Hz, 1H), 3.80 (dd, $J = 11.4, 5.9$ Hz, 2H), 3.76 (s, 3H), 3.66 (dd, $J = 13.2, 4.1$ Hz, 1H), 3.42 (t, $J = 12.7$ Hz, 1H), 1.44 (s, 9H), 1.20–1.03 (m, 42H).

^{13}C NMR (75 MHz, CDCl_3) δ 171.7, 169.4, 168.1, 156.0, 140.2, 133.6, 127.4, 124.4, 104.8, 96.8, 80.3, 53.0, 52.6, 44.1, 42.2, 34.9, 28.5, 18.0, 11.1.

HRMS (ESI): m/z [M + Na] $^+$ calcd for $\text{C}_{41}\text{H}_{67}\text{N}_3\text{O}_6\text{Si}_2\text{Na}$, 776.4461; found, 776.4464.



6b

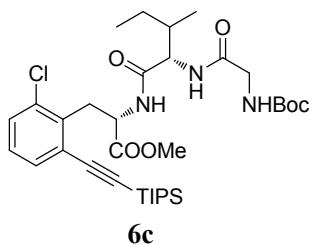
(S)-methyl

12-(2-chloro-6-((triisopropylsilyl)ethynyl)benzyl)-2,2-dimethyl-4,7,10-trioxo-3-oxa-5,8,11-triazatridecan-13-oate

Yellow solid (128 mg, 70% yield). ^1H NMR (300 MHz, CDCl_3) δ 7.43 (d, $J = 7.2$ Hz, 1H), 7.35 (d, $J = 7.9$ Hz, 1H), 7.17 (t, $J = 7.9$ Hz, 1H), 6.55 (br s, 1H), 6.40 (d, $J = 8.2$ Hz, 1H), 5.14 – 4.98 (m, 2H), 3.87 (dd, $J = 16.6, 4.7$ Hz, 2H), 3.83 – 3.78 (m, 2H), 3.76 (s, 3H), 3.56 (dd, $J = 13.5, 5.0$ Hz, 1H), 3.48 – 3.34 (m, 1H), 1.44 (s, 9H), 1.16 (m, 21H).

^{13}C NMR (75 MHz, CDCl_3) δ 171.8, 169.9, 168.5, 156.2, 136.3, 135.1, 132.1, 130.2, 128.4, 126.0, 104.5, 97.3, 80.4, 52.8, 52.2, 44.2, 42.6, 34.2, 28.5, 18.0, 11.5.

HRMS (ESI): m/z [M + Na] $^+$ calcd for $\text{C}_{30}\text{H}_{46}\text{ClN}_3\text{O}_6\text{SiNa}$, 630.2737; found, 630.2737.



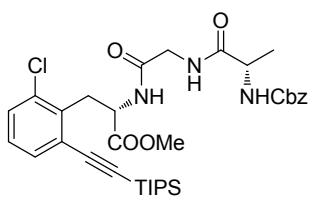
(9S,12S)-methyl

9-(sec-butyl)-12-(2-chloro-6-((triisopropylsilyl)ethynyl)benzyl)-2,2-dimethyl-4,7,10-trioxo-3-oxa-5,8,11-triazatridecan-13-oate

White solid (133 mg, 67% yield). ^1H NMR (300 MHz, CDCl_3) δ 7.41 (d, $J = 7.6$ Hz, 1H), 7.32 (d, $J = 8.0$ Hz, 1H), 7.14 (t, $J = 7.9$ Hz, 1H), 6.43 (d, $J = 8.5$ Hz, 1H), 6.32 (d, $J = 8.1$ Hz, 1H), 5.14 – 4.92 (m, 2H), 4.27 (dd, $J = 8.5, 5.8$ Hz, 1H), 3.73 (s, 3H), 3.72 (m, 1H), 3.55 (dd, $J = 13.5, 5.3$ Hz, 1H), 3.39 (dd, $J = 13.3, 11.3$ Hz, 1H), 1.78–1.76 (m, 1H), 1.43 (s, 9H), 1.24–1.22 (m, 2H), 1.18 – 1.00 (m, 21H), 0.86 (t, $J = 7.1$ Hz, 6H).

^{13}C NMR (75 MHz, CDCl_3) δ 171.7, 170.8, 169.0, 156.1, 136.2, 135.0, 132.2, 130.2, 128.3, 126.2, 104.5, 97.3, 80.4, 57.5, 52.7, 52.0, 44.5, 38.3, 34.1, 24.7, 18.0, 15.3, 11.7.

HRMS (ESI): m/z [M + Na] $^+$ calcd for $\text{C}_{34}\text{H}_{54}\text{ClN}_3\text{O}_6\text{SiNa}$, 686.3363; found, 686.3376.



(5S,11S)-methyl

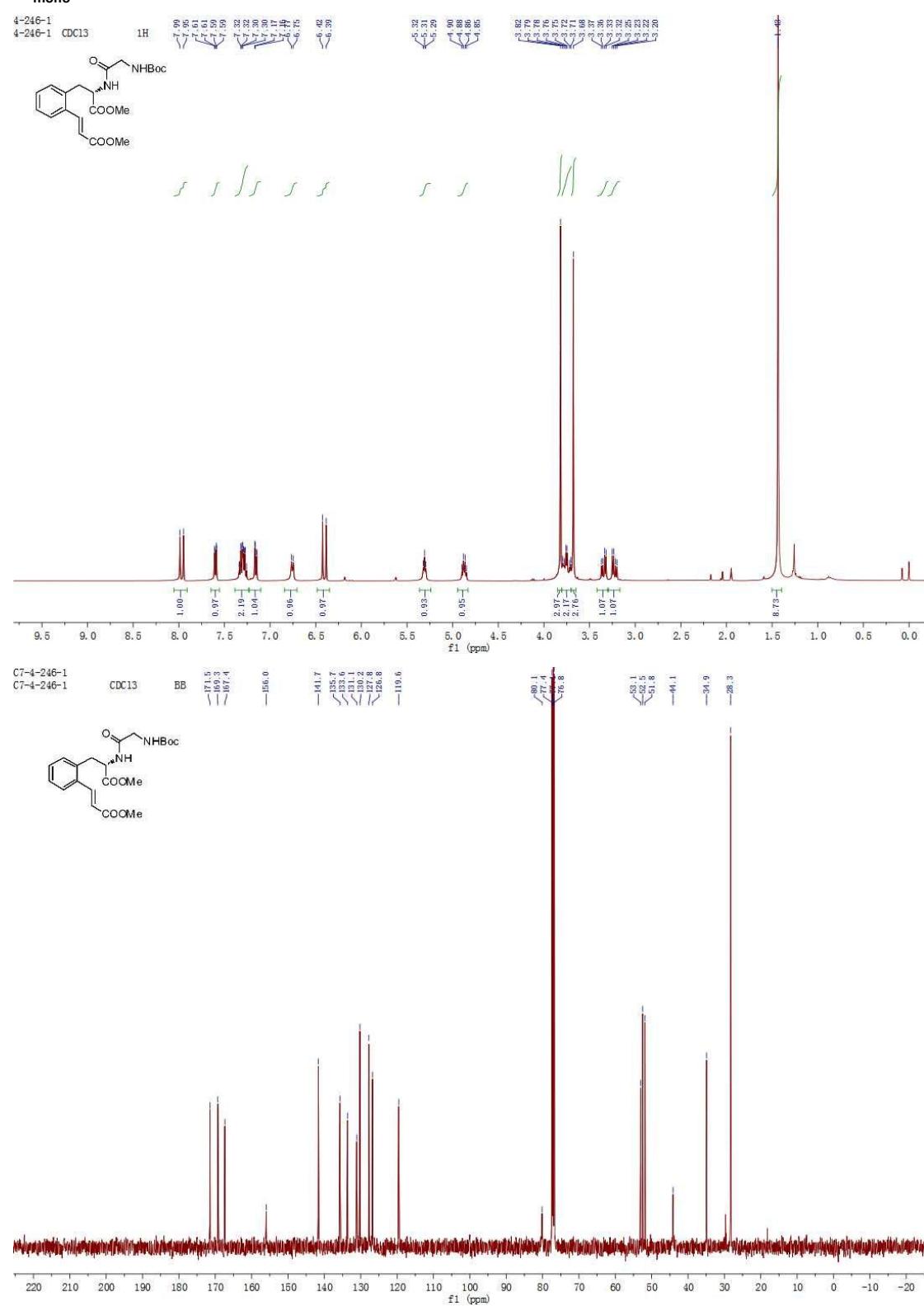
11-(2-chloro-6-((triisopropylsilyl)ethynyl)benzyl)-5-methyl-3,6,9-trioxo-1-phenyl-2-oxa-4,7,10-triazadodecan-12-oate

Yellow solid (126 mg, 64% yield). ^1H NMR (300 MHz, CDCl_3) δ 7.43 – 7.38 (m, 1H), 7.37 – 7.28 (m, 6H), 7.18 – 7.07 (m, 1H), 6.92 (br s, 1H), 6.75 (d, $J = 7.9$ Hz, 1H), 5.65 (d, $J = 7.0$ Hz, 1H), 5.08 – 4.93 (m, 2H), 4.35 – 4.17 (m, 1H), 4.07 – 3.91 (m, 1H), 3.75 (dd, $J = 10.4, 4.7$ Hz, 1H), 3.70 (s, 3H), 3.54 (dd, $J = 13.5, 5.6$ Hz, 1H), 3.46 – 3.32 (m, 1H), 1.35 (d, $J = 7.0$ Hz, 3H), 1.18 (m, 21H).

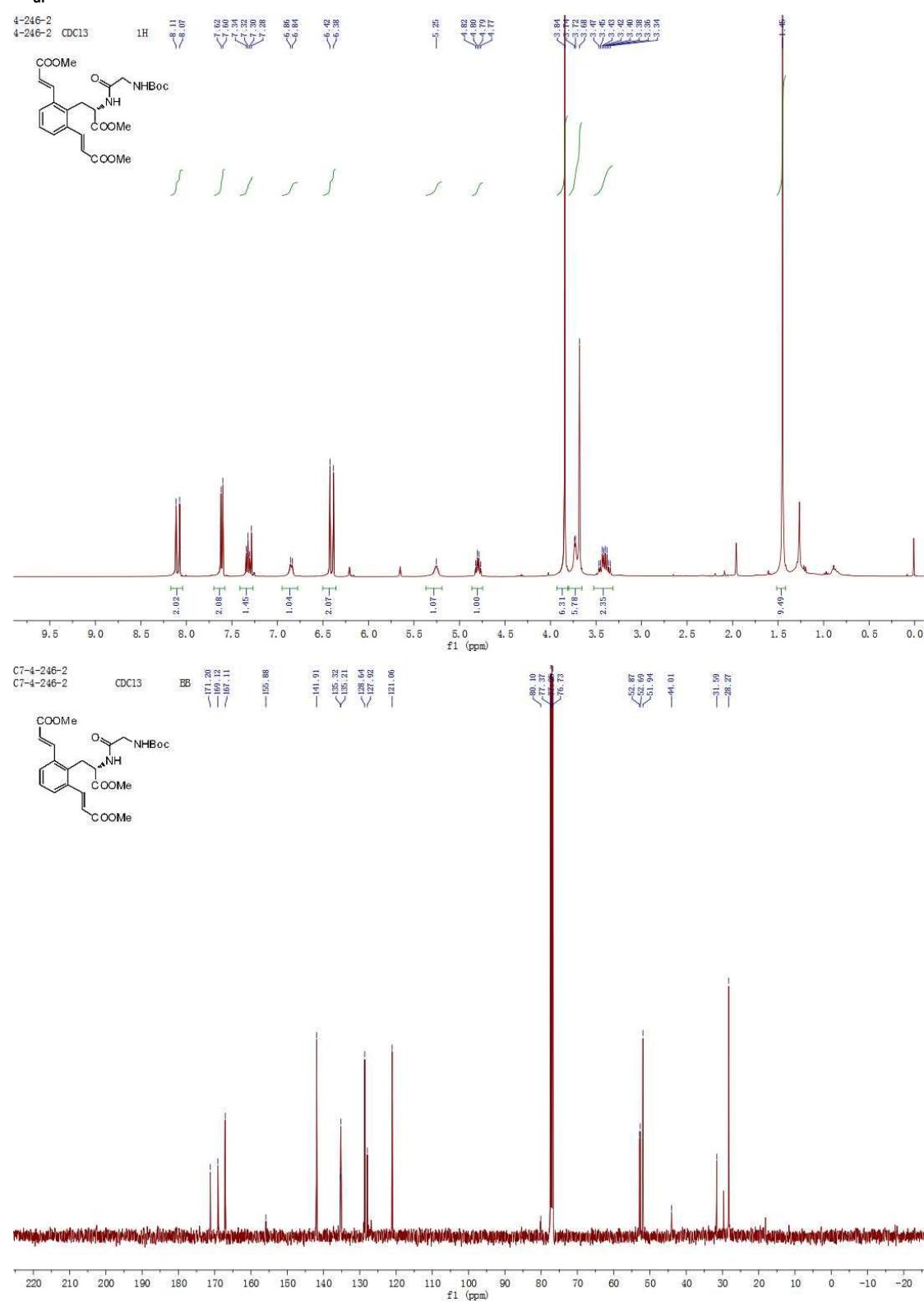
^{13}C NMR (75 MHz, CDCl_3) δ 172.8, 171.8, 168.5, 156.2, 136.4, 136.3, 135.1, 132.1, 130.2, 128.7,

128.4, 128.3, 126.0, 104.9, 97.3, 67.2, 52.8, 52.2, 50.8, 42.7, 34.3, 18.0, 11.5.
HRMS (ESI): m/z [M + Na]⁺ calcd for C₃₄H₄₆ClN₃O₆Na, 678.2737; found, 678.2751.

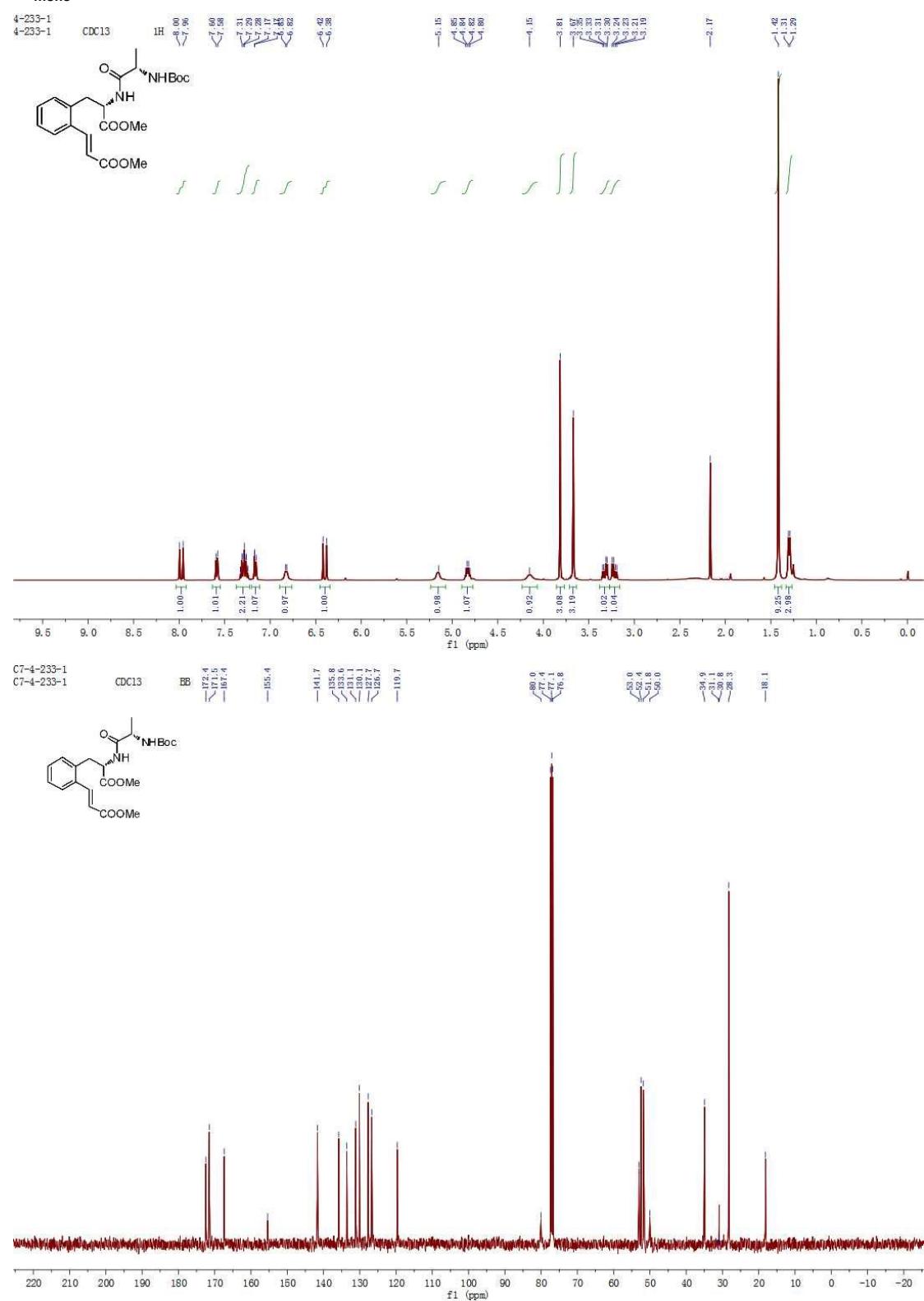
2a_{mono}



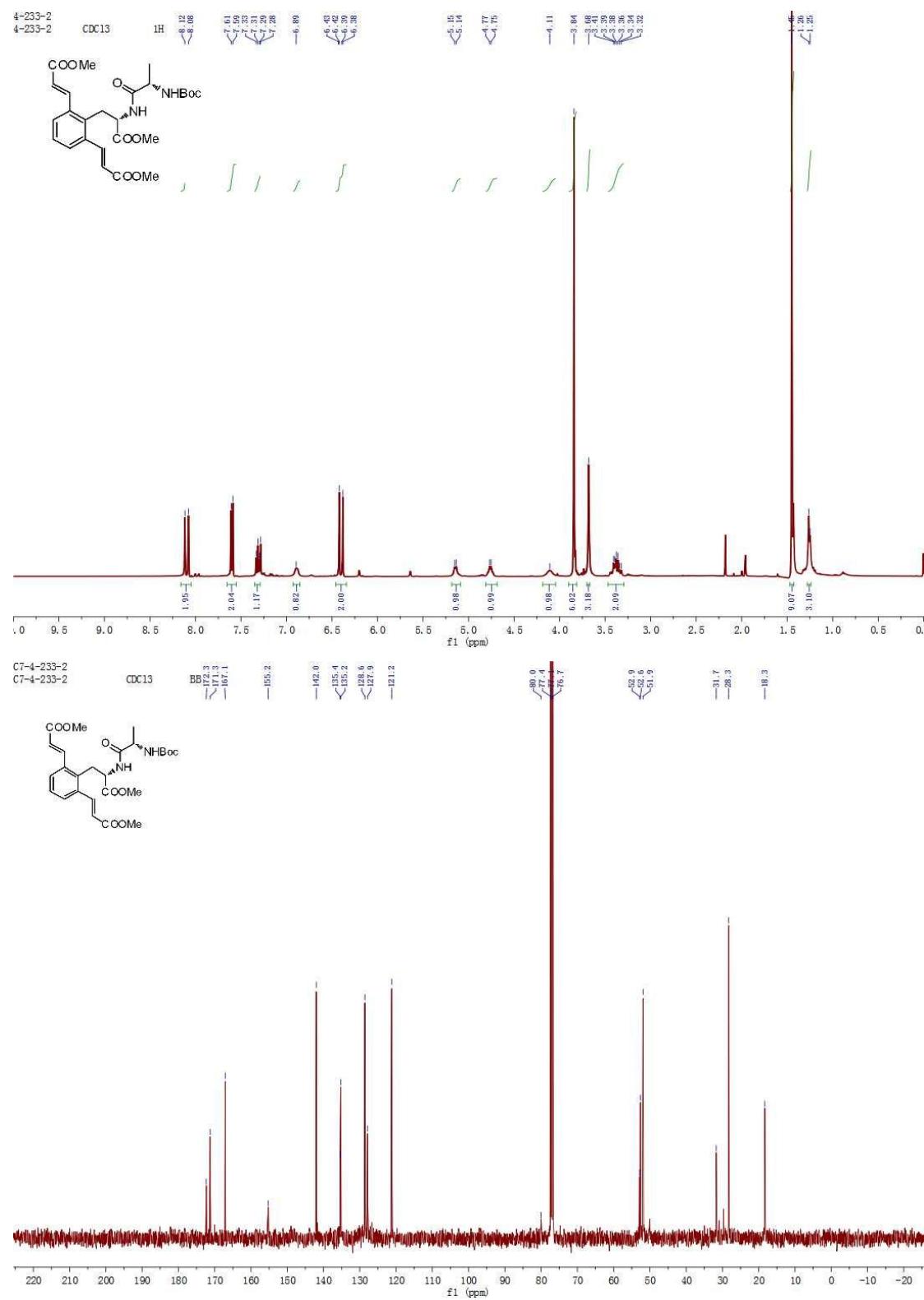
2a_{di}



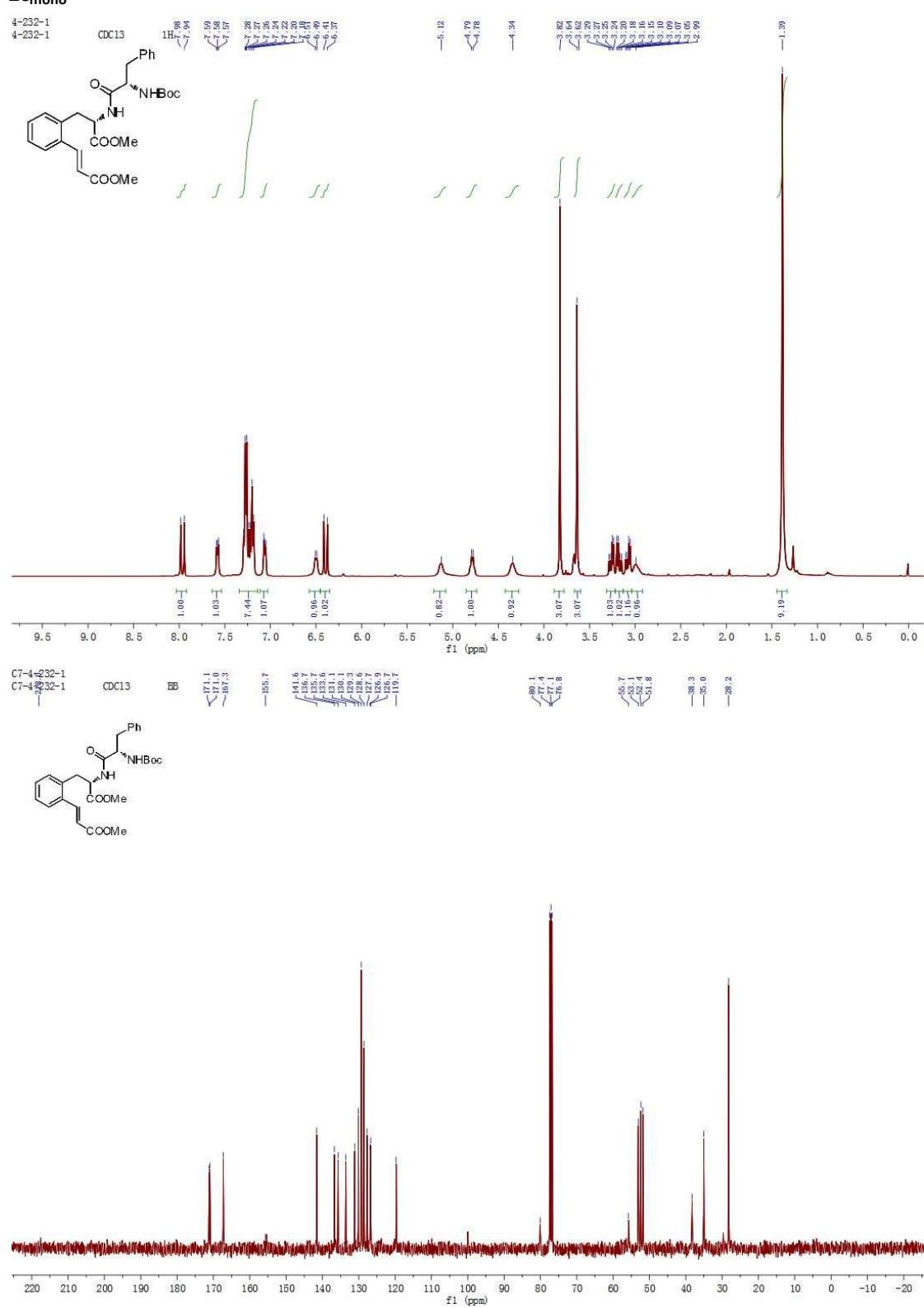
2b_{mono}



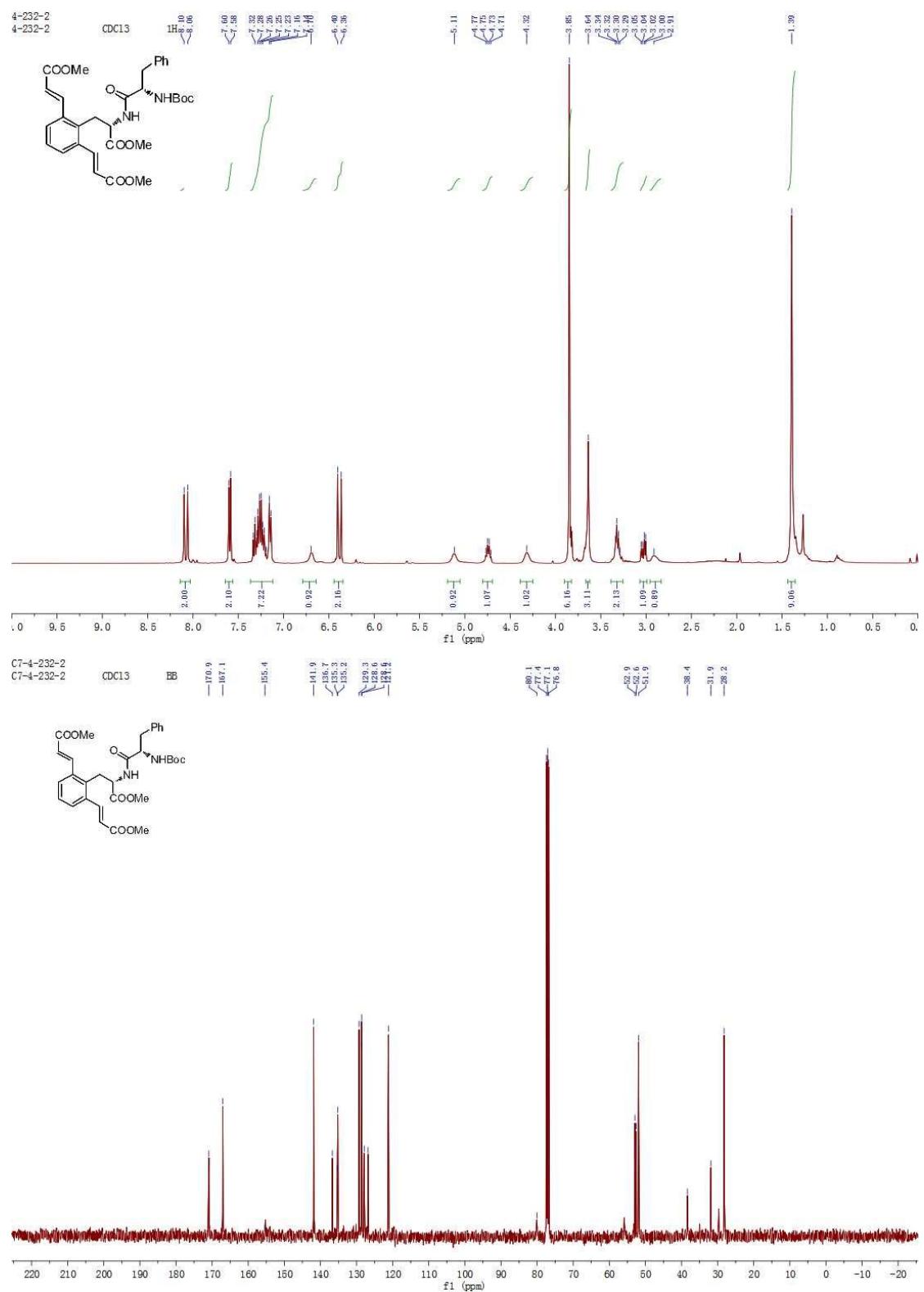
2b_{di}



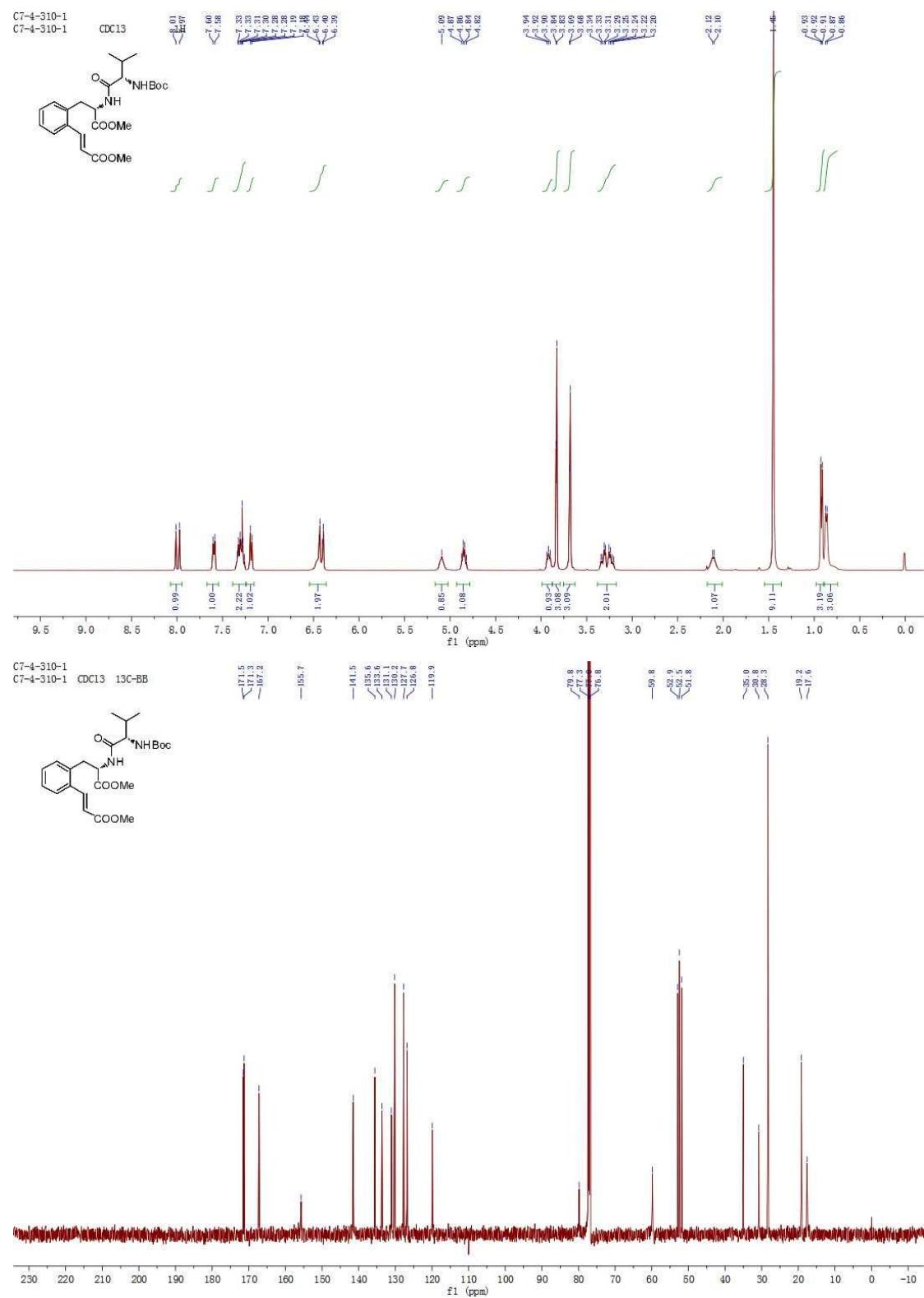
2c_{mono}

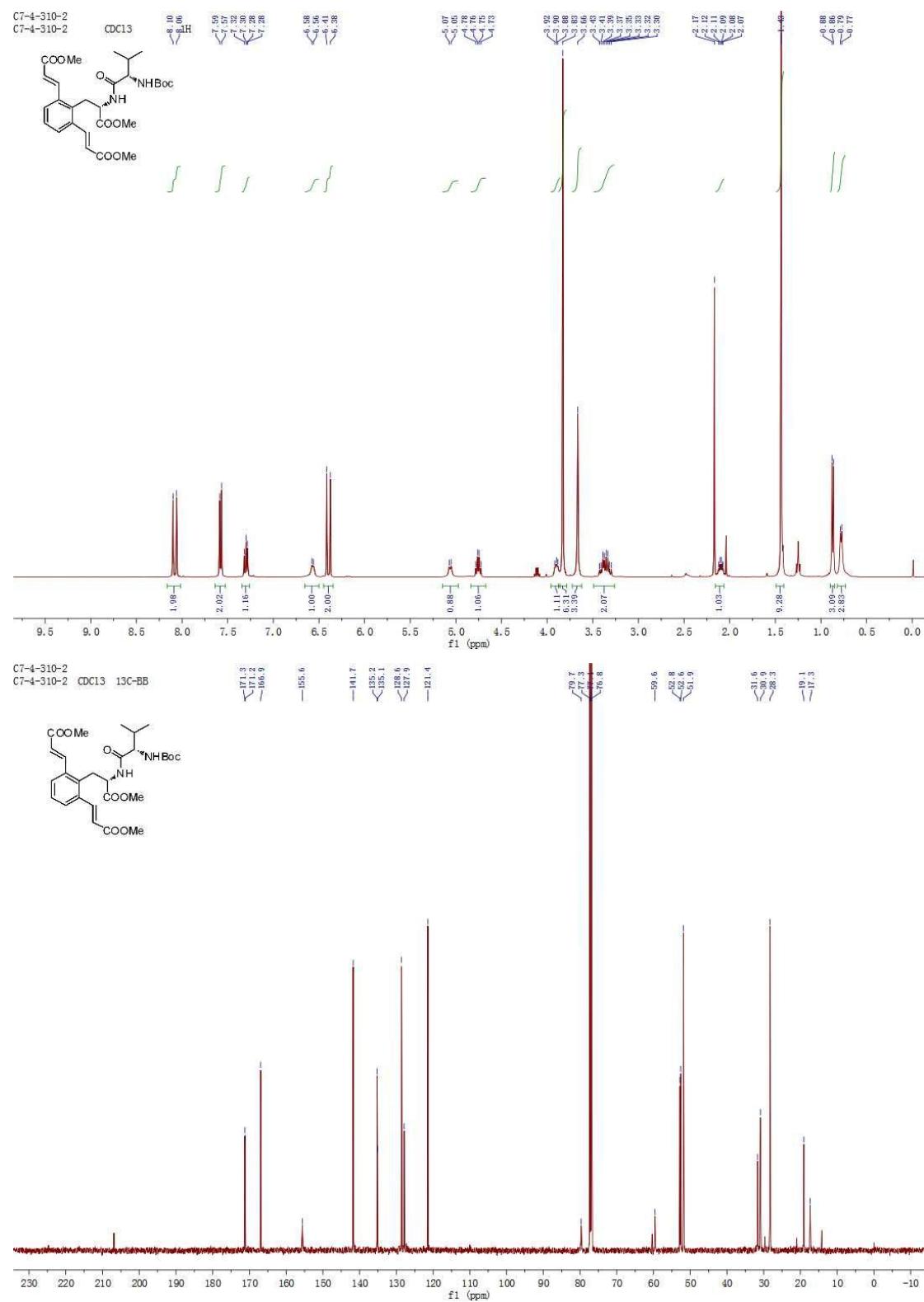


2c_{di}



2d_{mono}

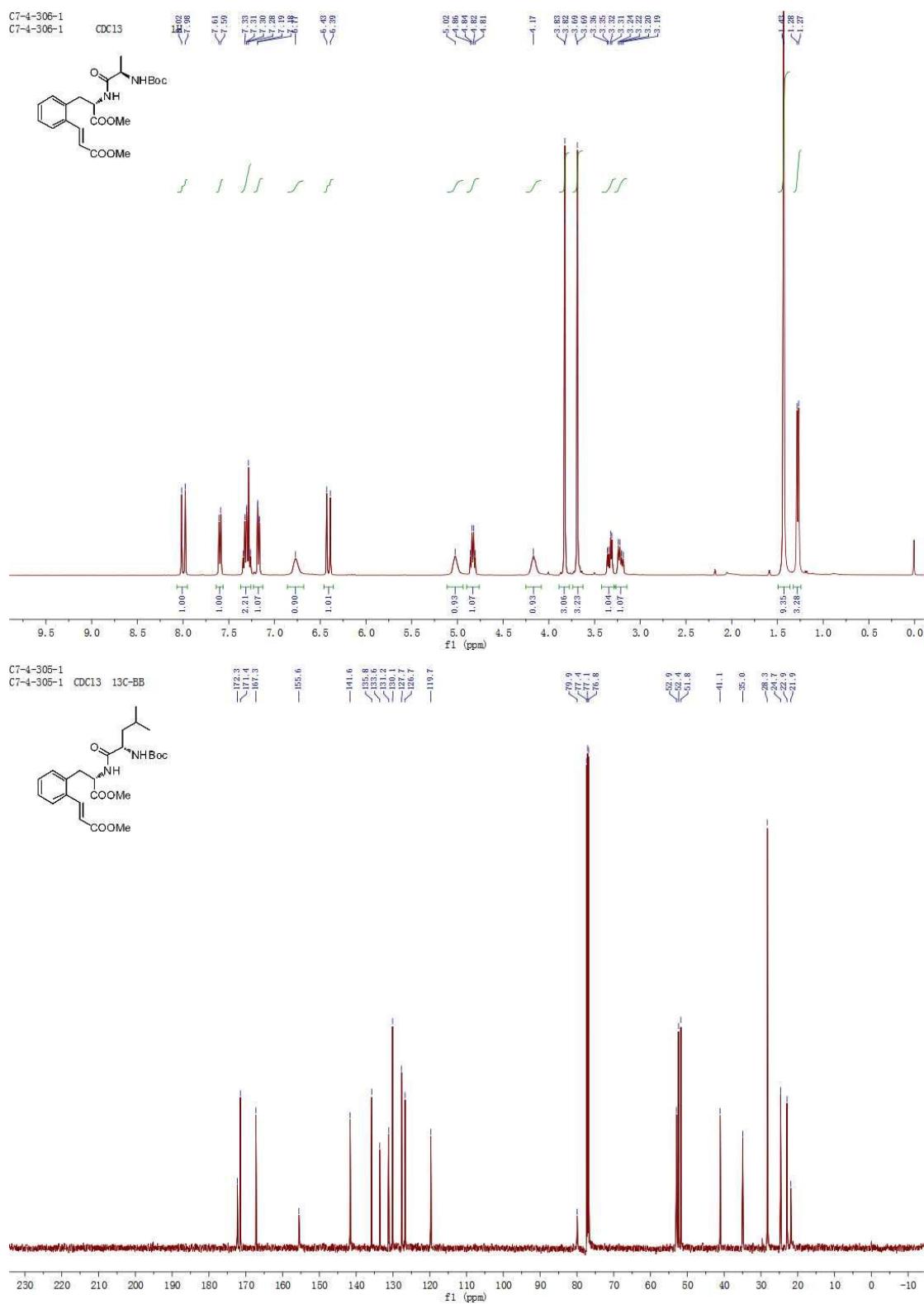


2d_{di}

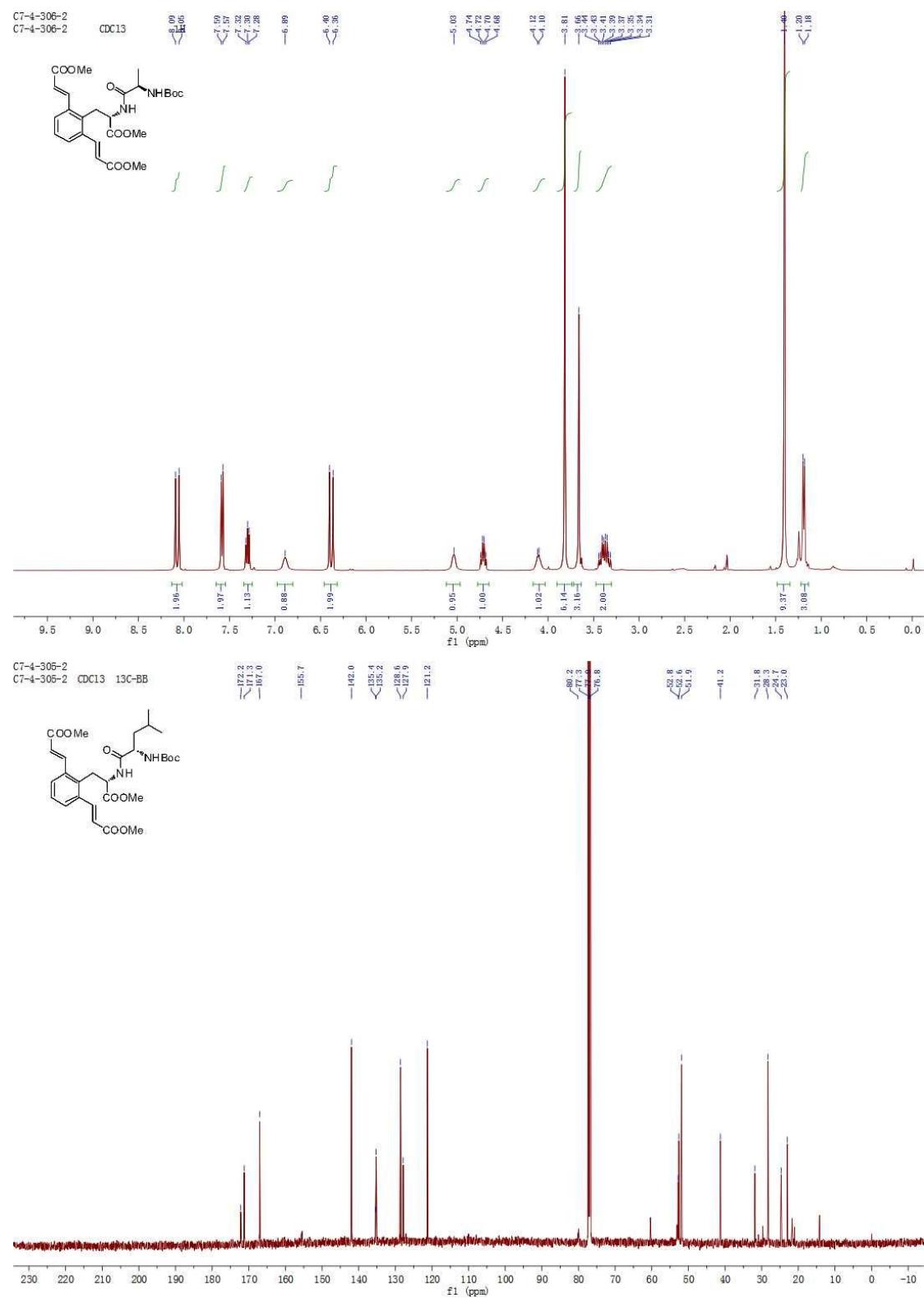
2e_{mono}

C7-4-306-1
C7-4-306-1

C7-4-306-1
C7-4-306-1



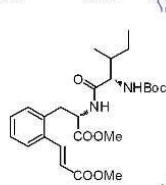
2e_{di}



2f_{mono}

c7-4-266-1
c7-4-266-1

CDCl₃

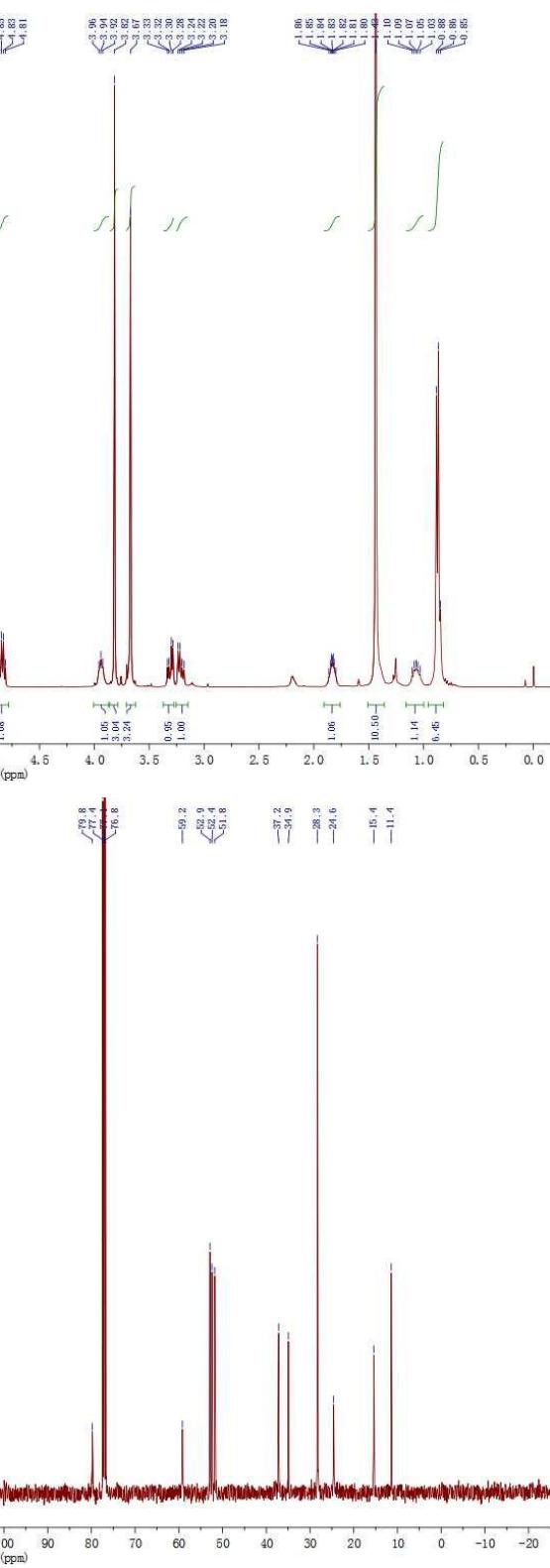


c7-4-266-1
c7-4-266-1

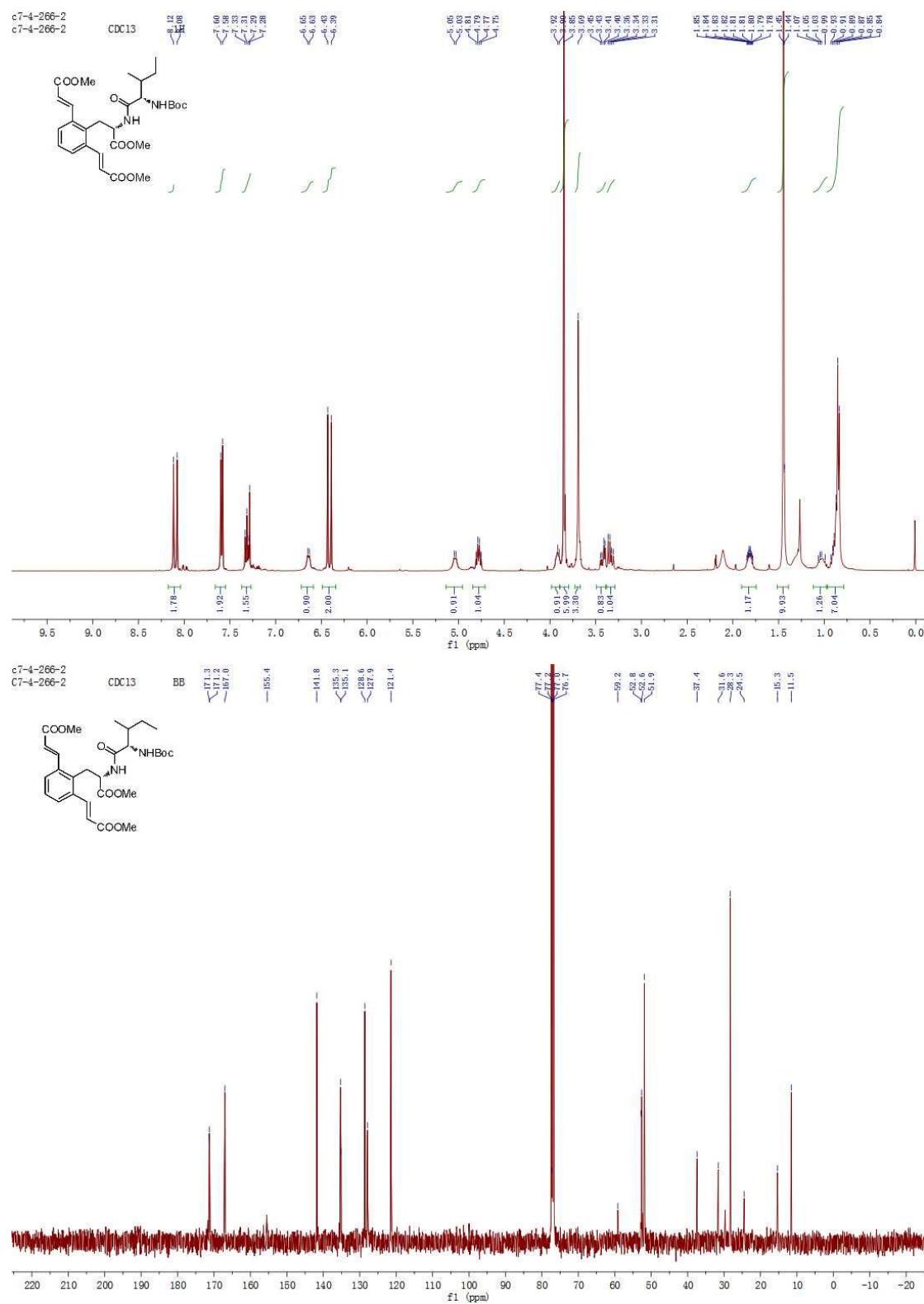
CDCl₃

BB 171.5
171.3
161.2
—155.6

—141.5
—135.9
—133.6
—131.1
—130.7
—127.7
—126.6
—119.6

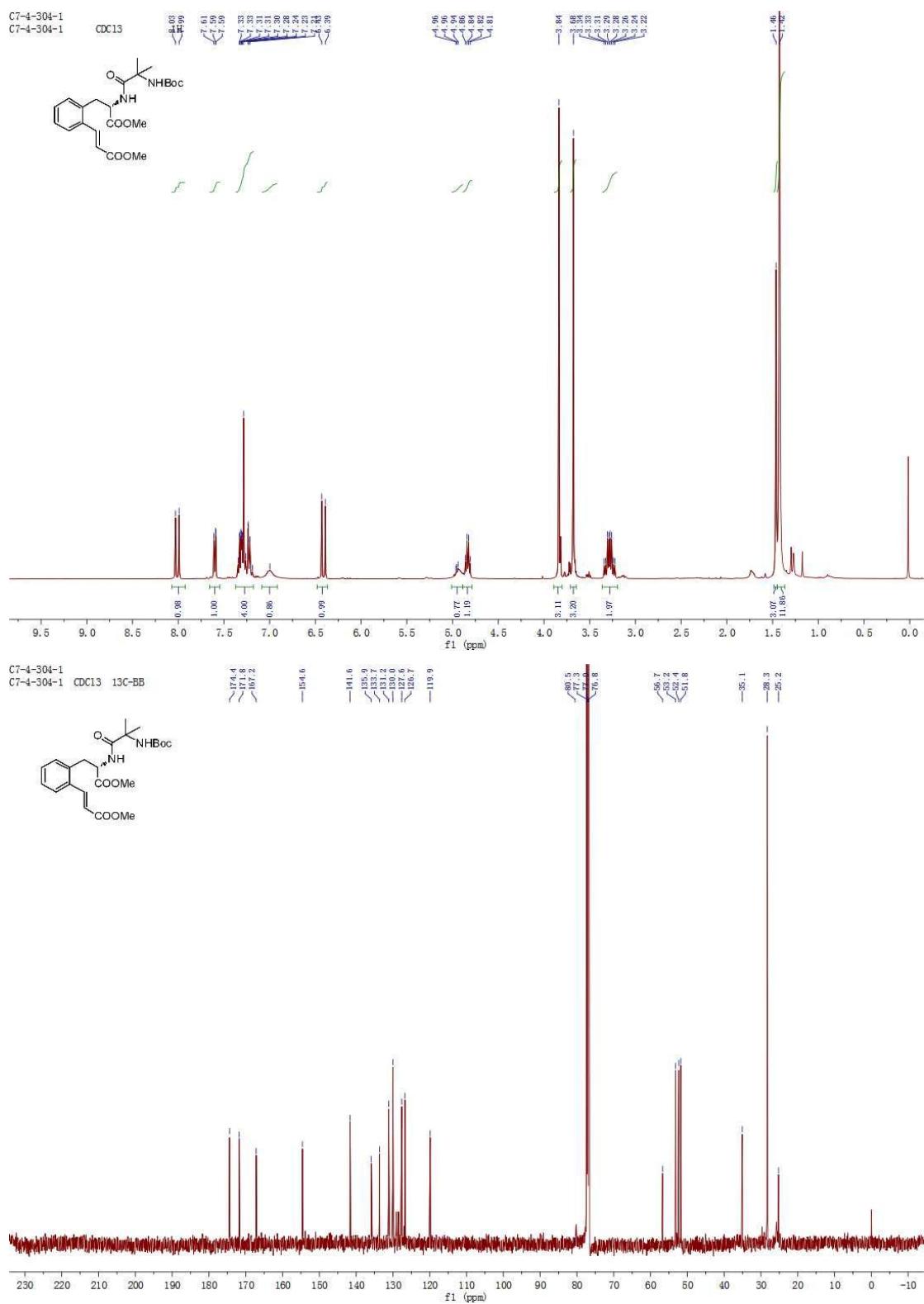


$$2f_{di}$$

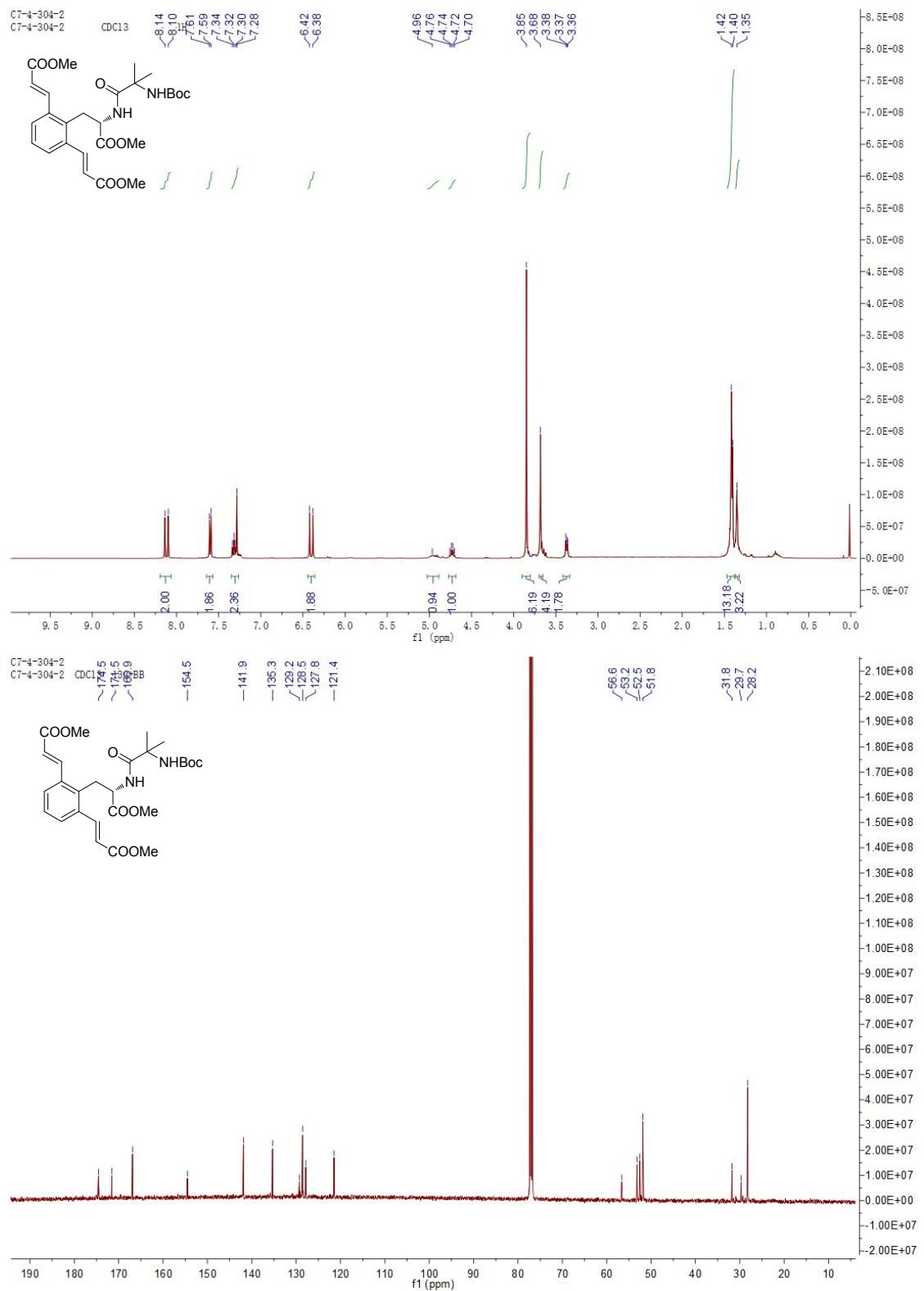


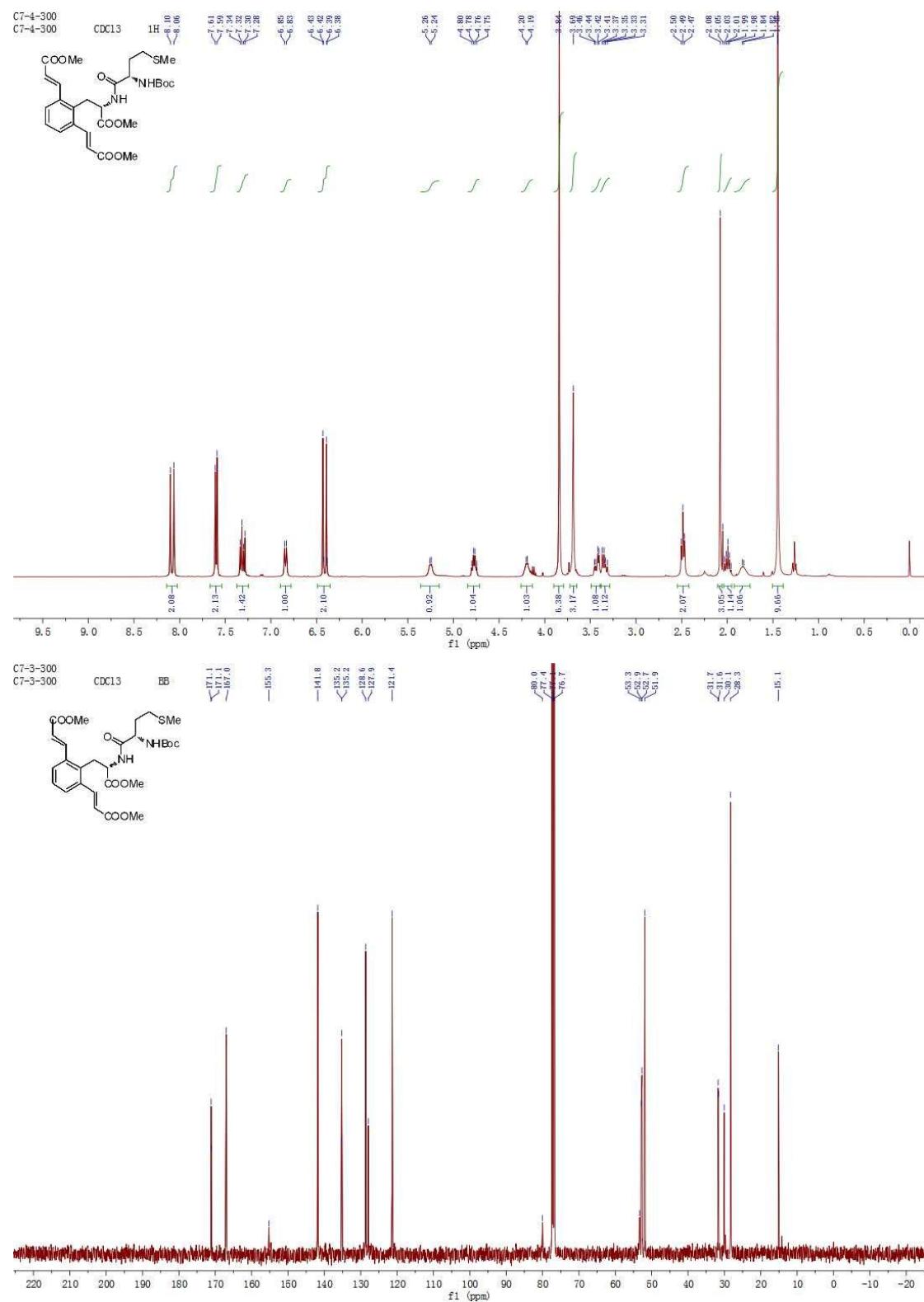
2g_{mono}

C7-4-304-1
C7-4-304-1

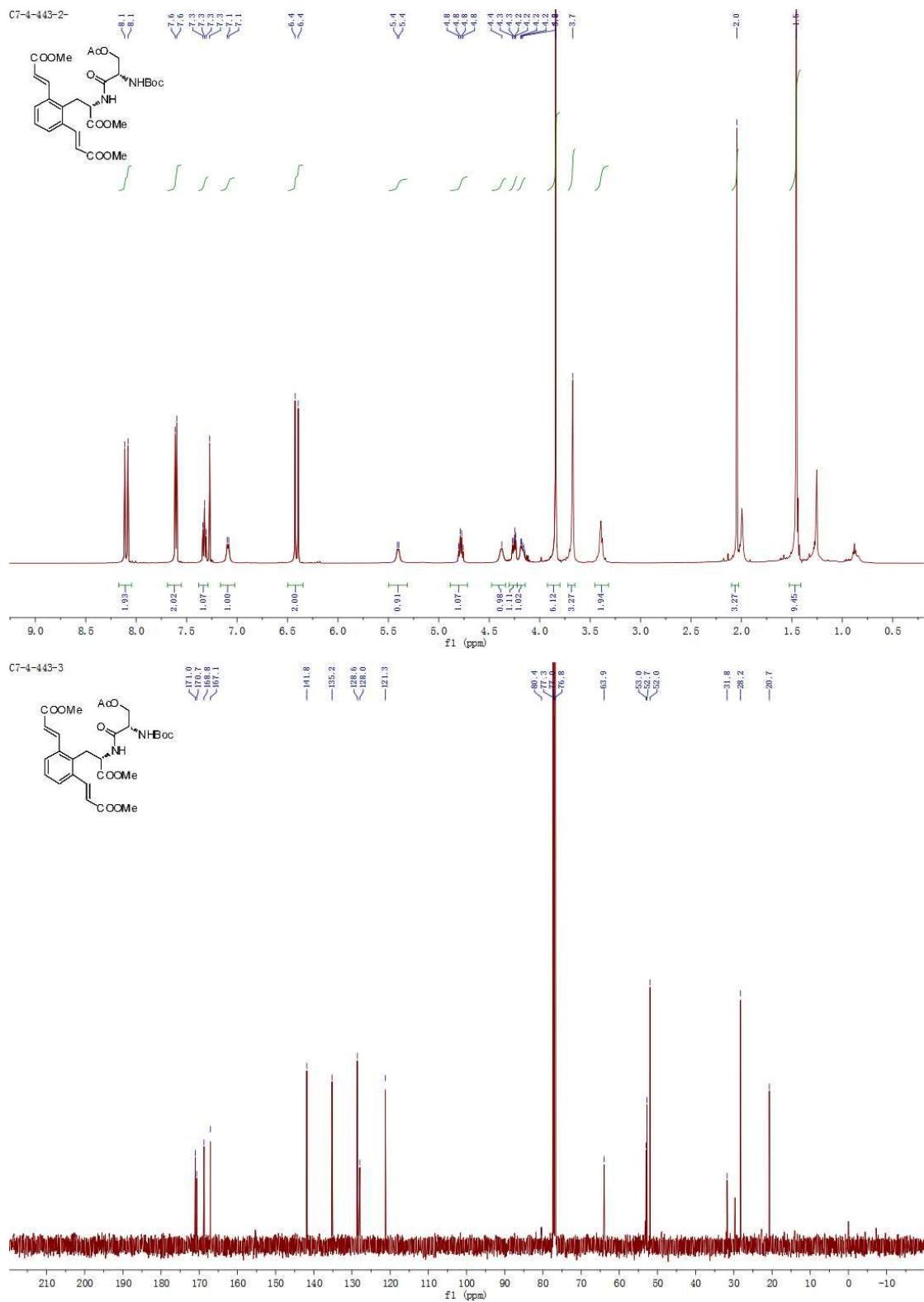


2g_{di}

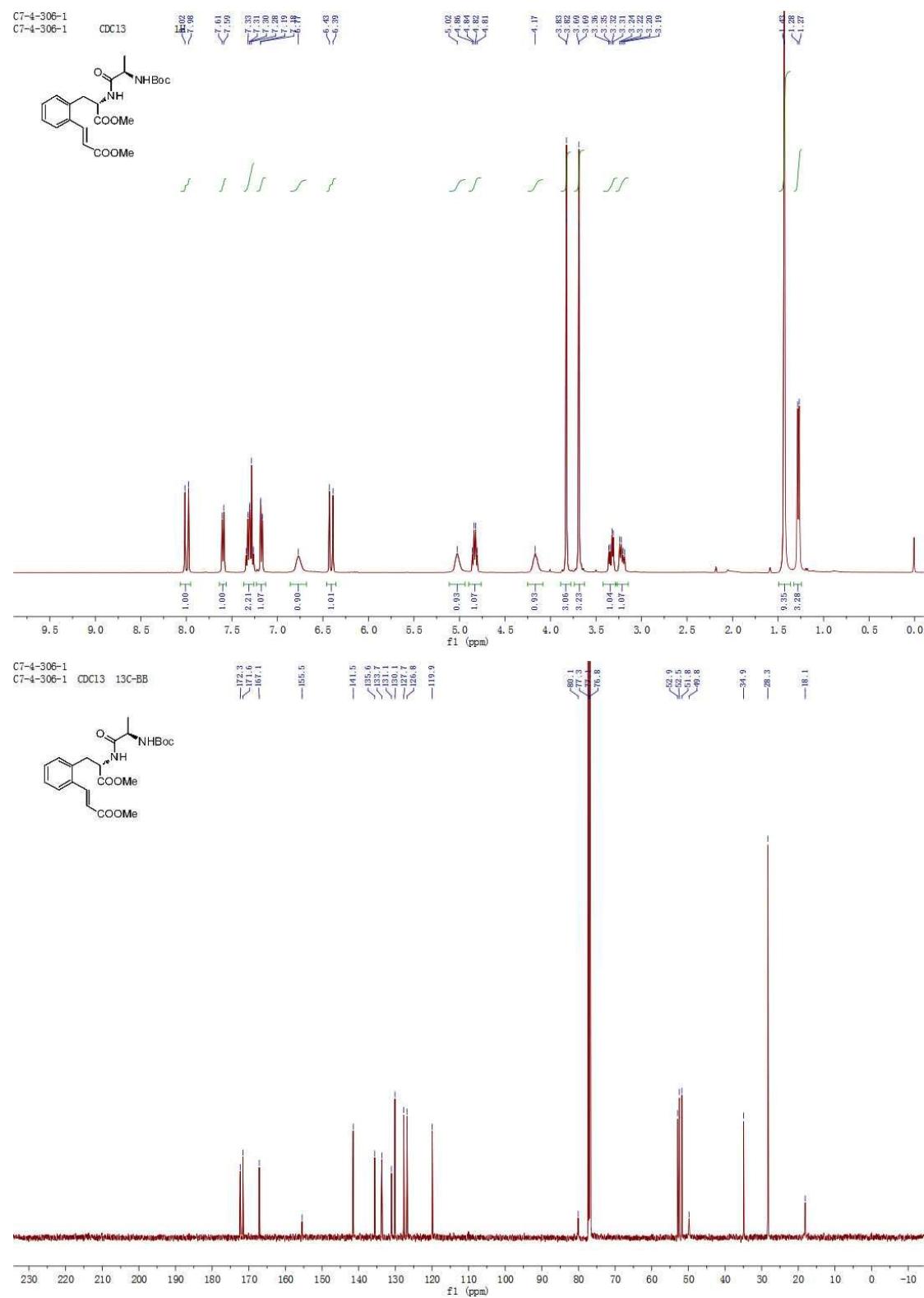


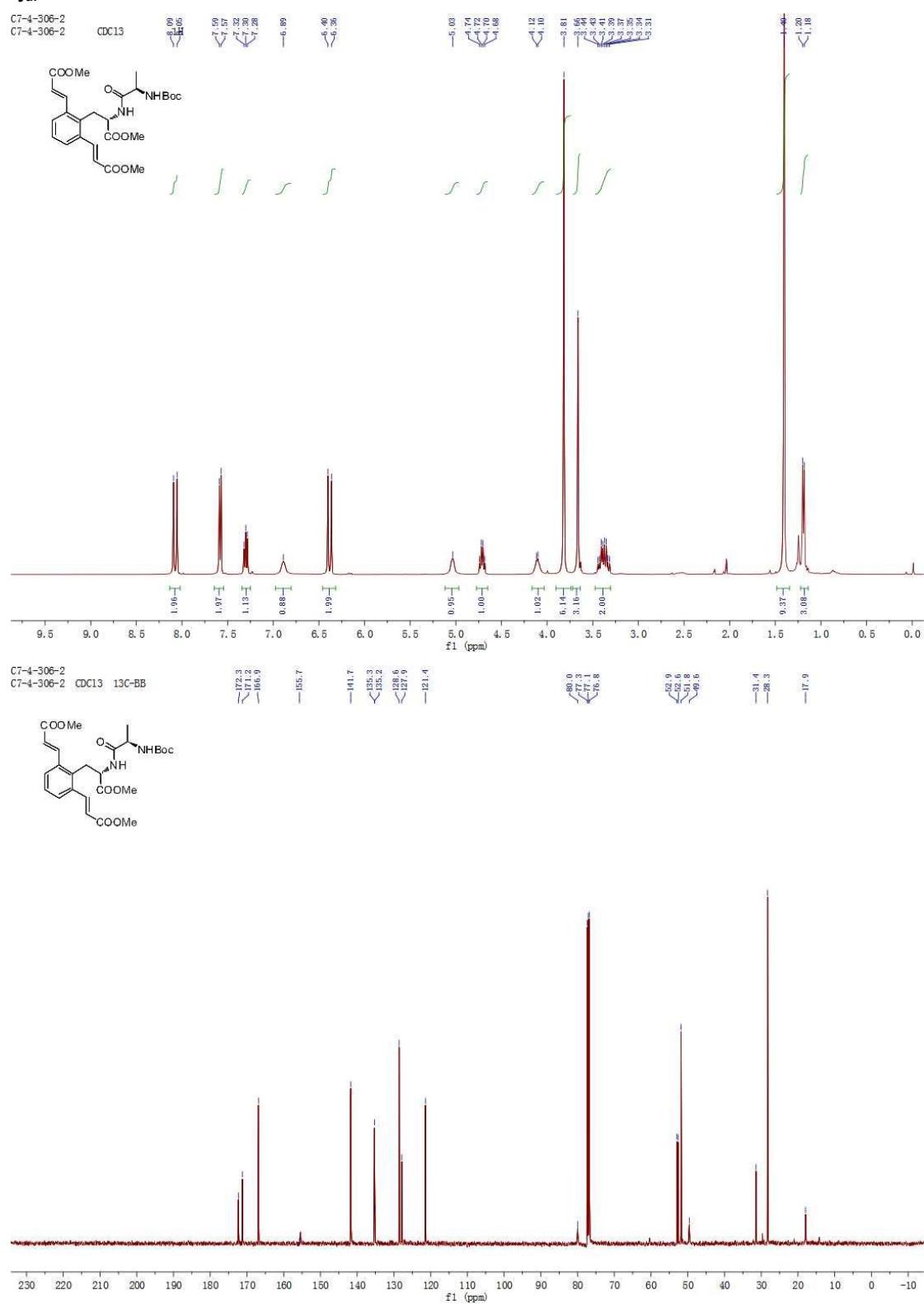
2h

2i

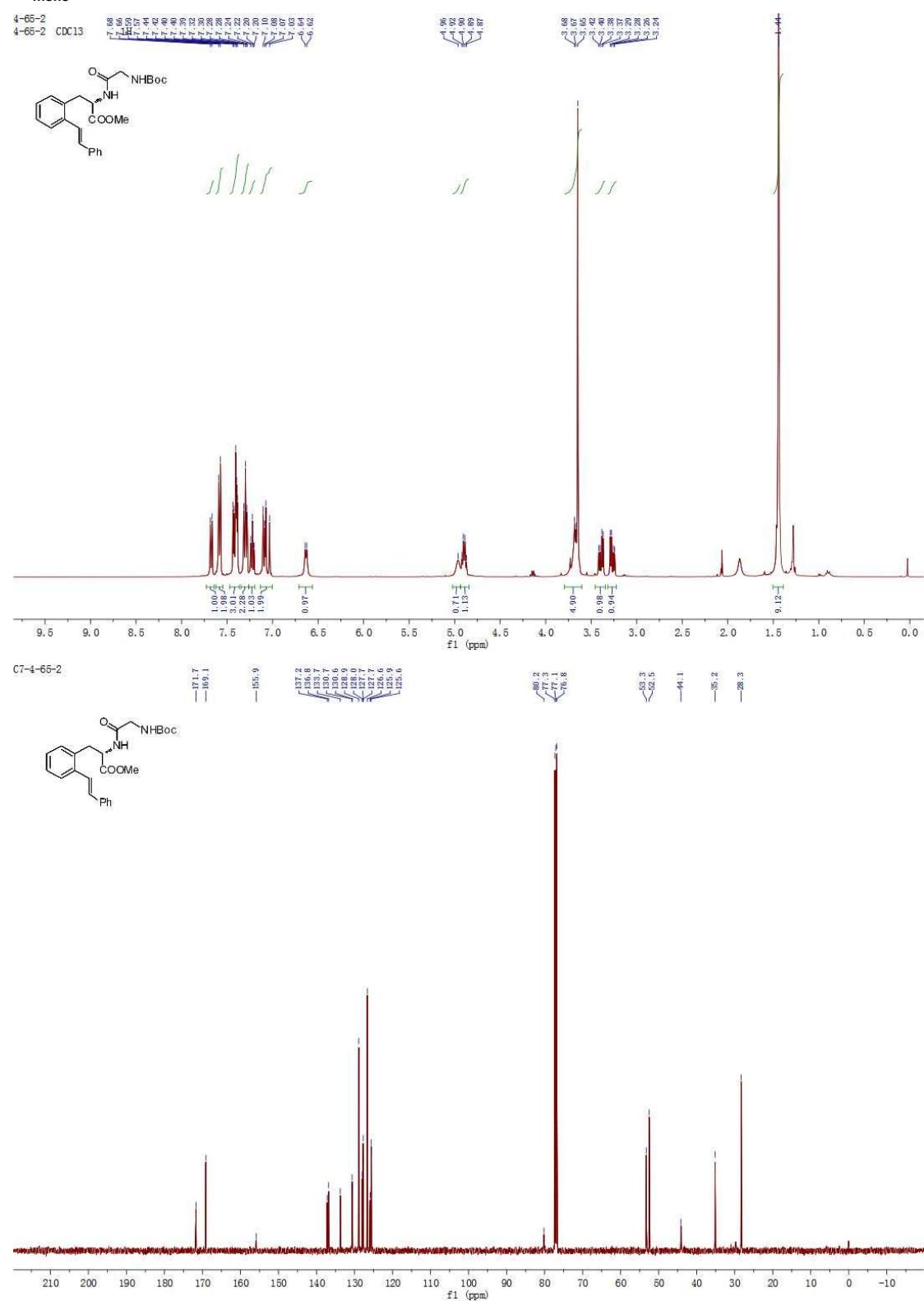


2jmono

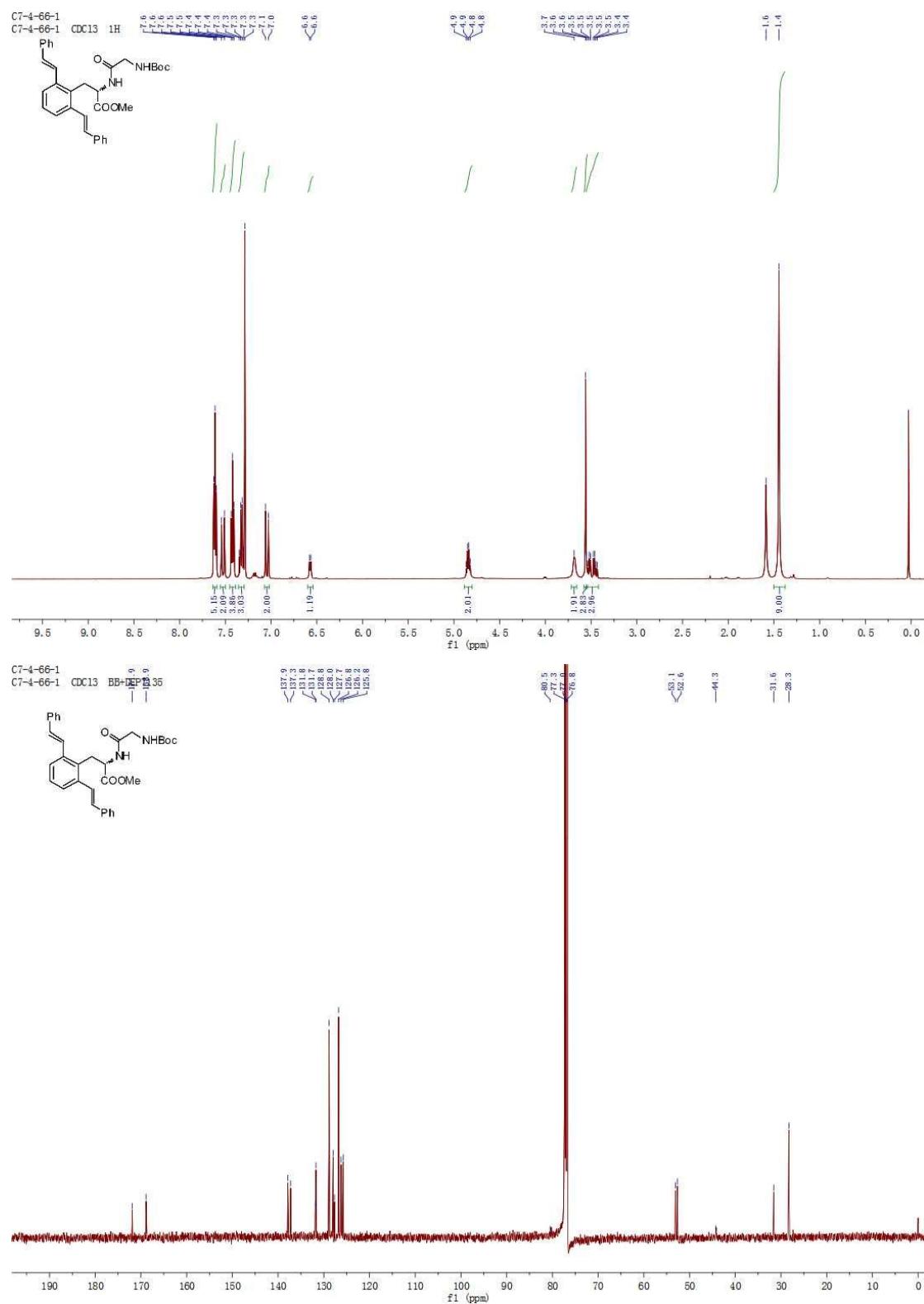


2j_{di}

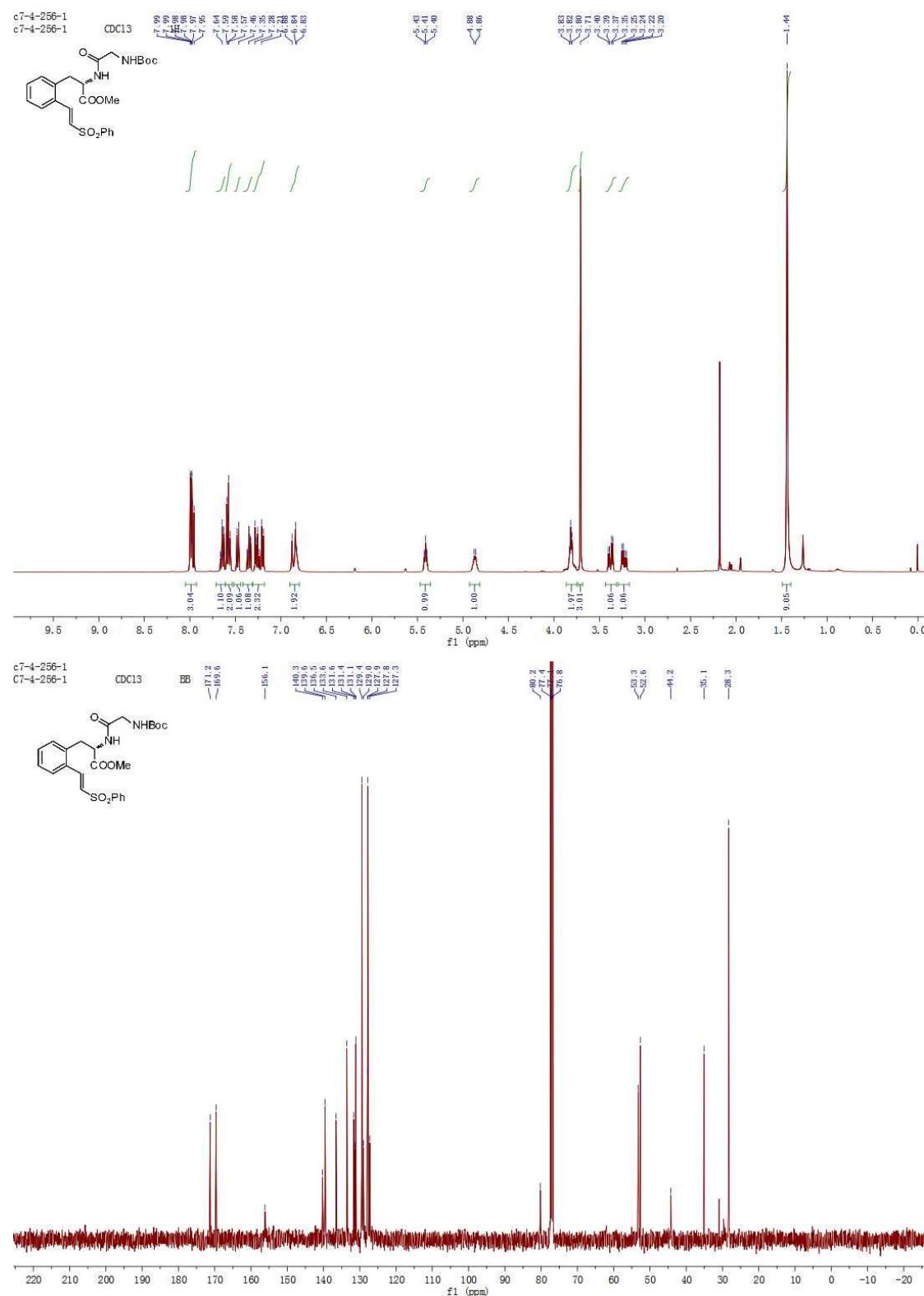
2k_{mono}



$$2k_{di}$$



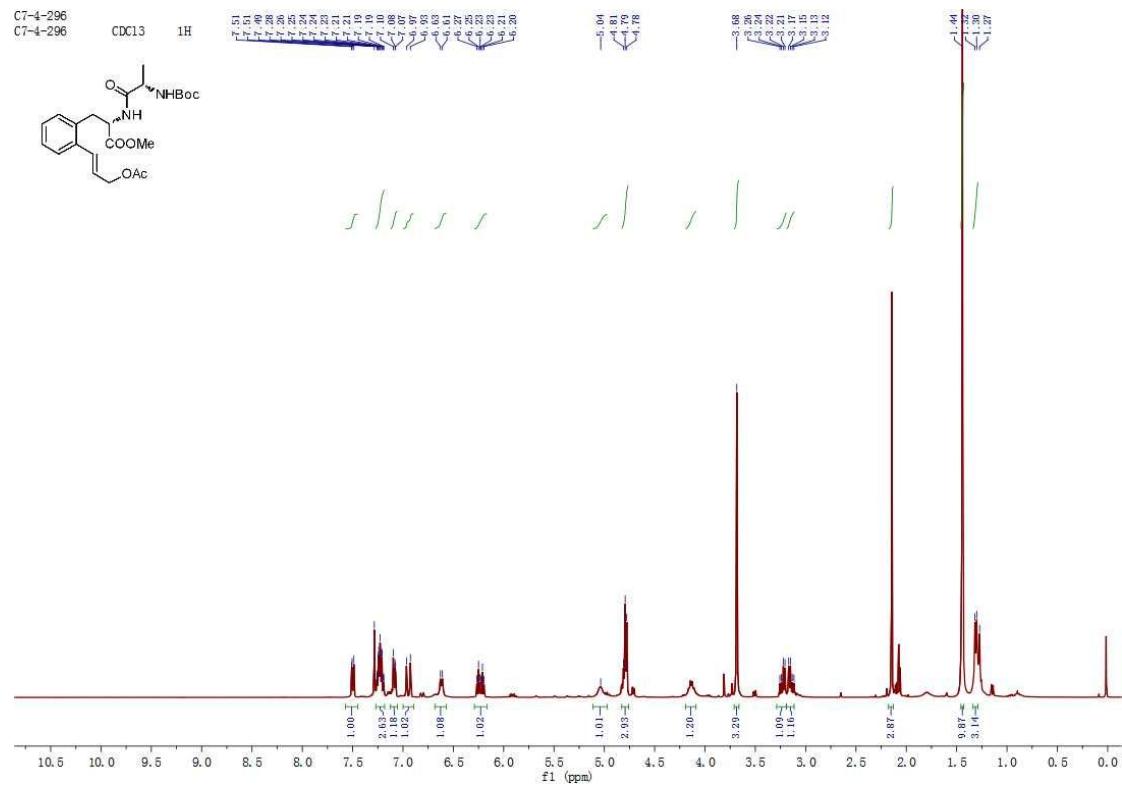
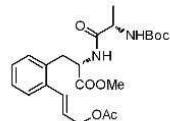
2I_{mono}



2m

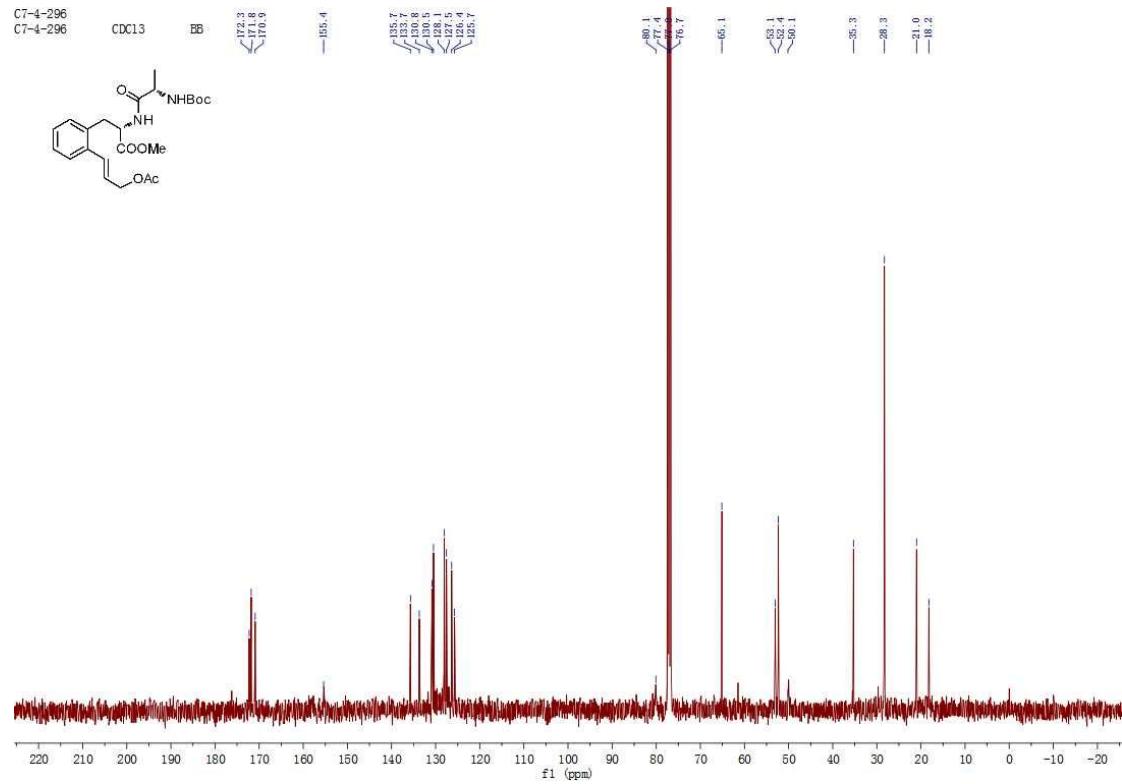
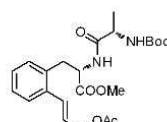
C7-4-296

C7-4-296

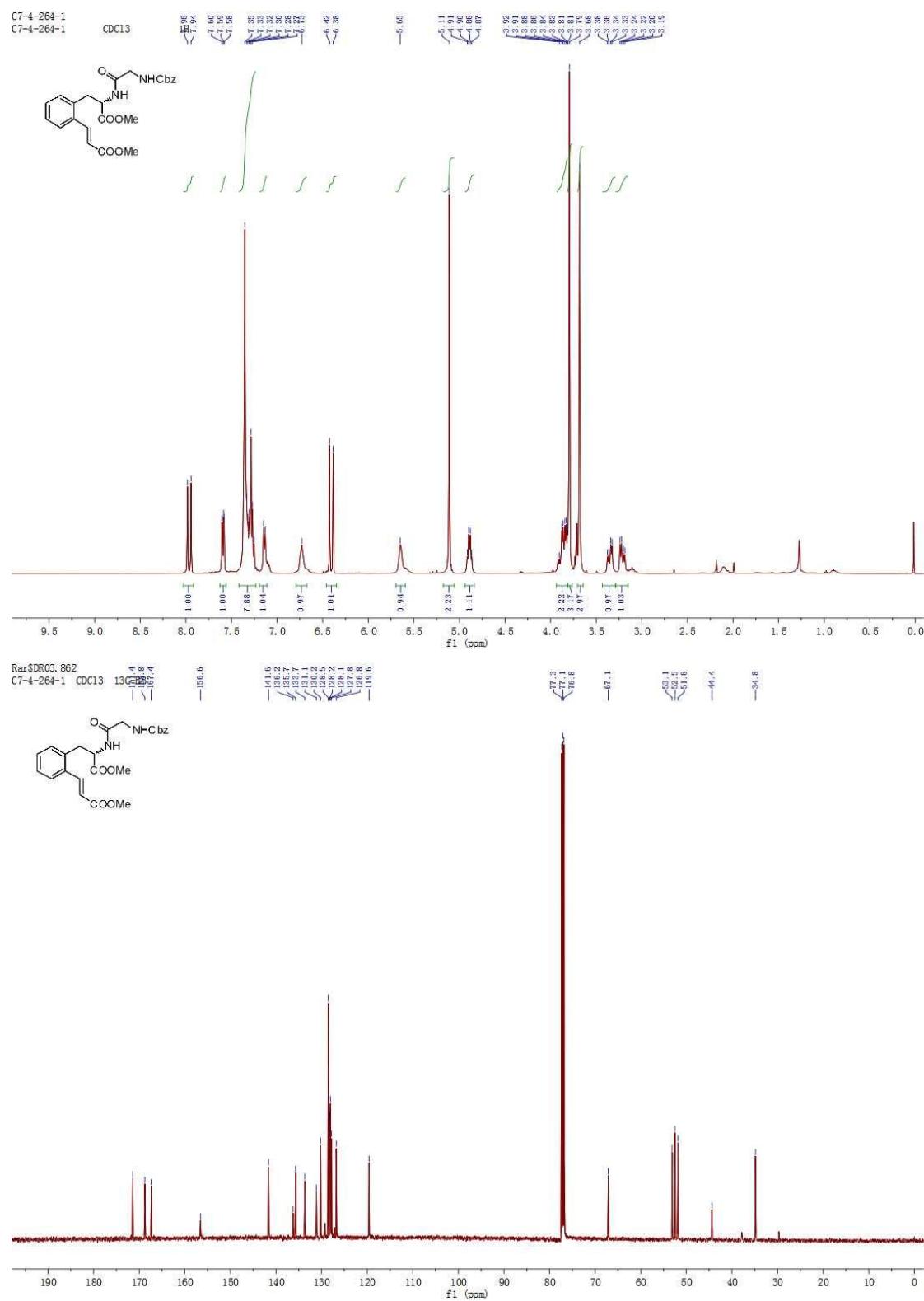


C7-4-296
C7-4-296

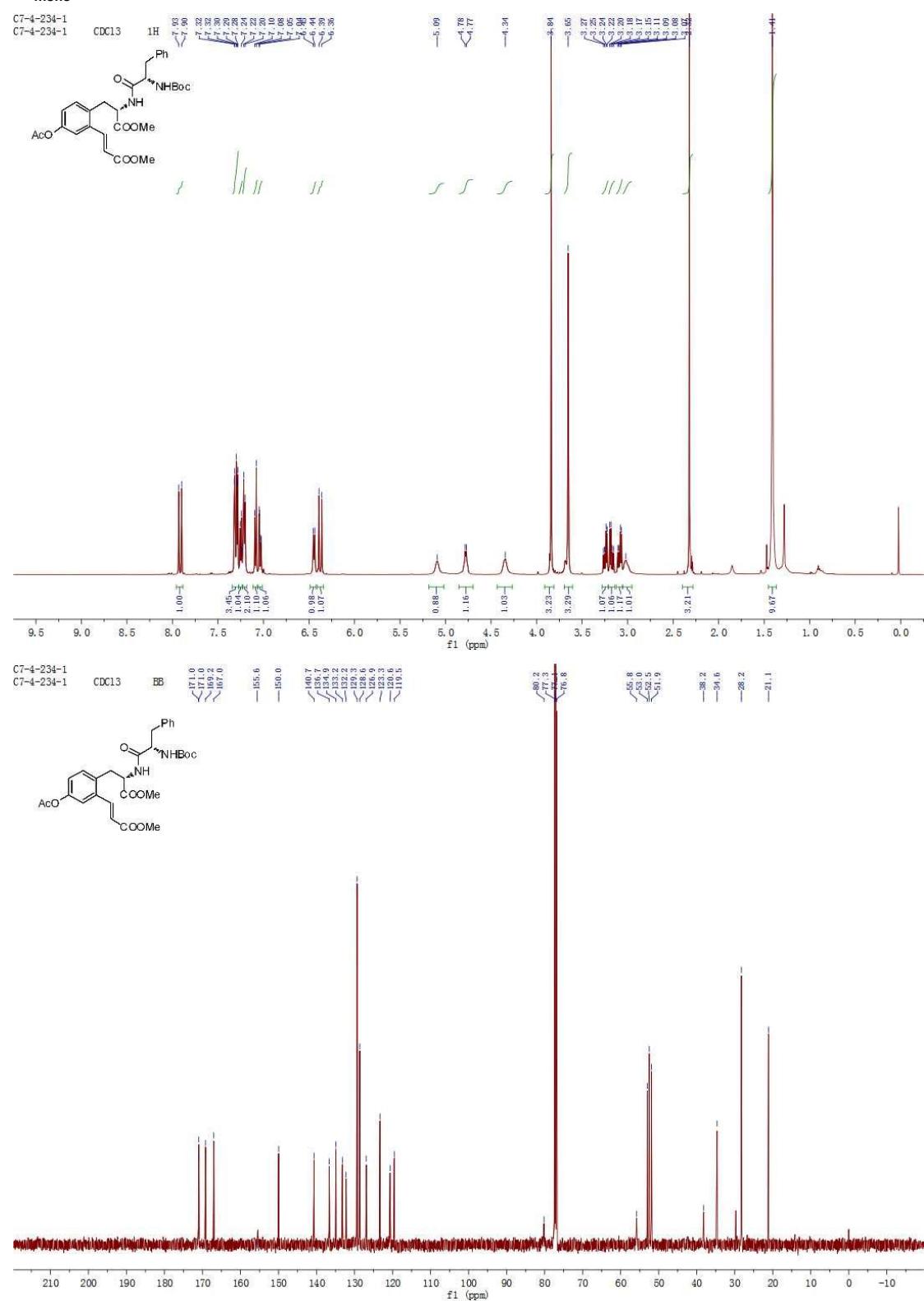
C7-4-296 C7-4-296 CDC13 B



2n



2O_{mono}



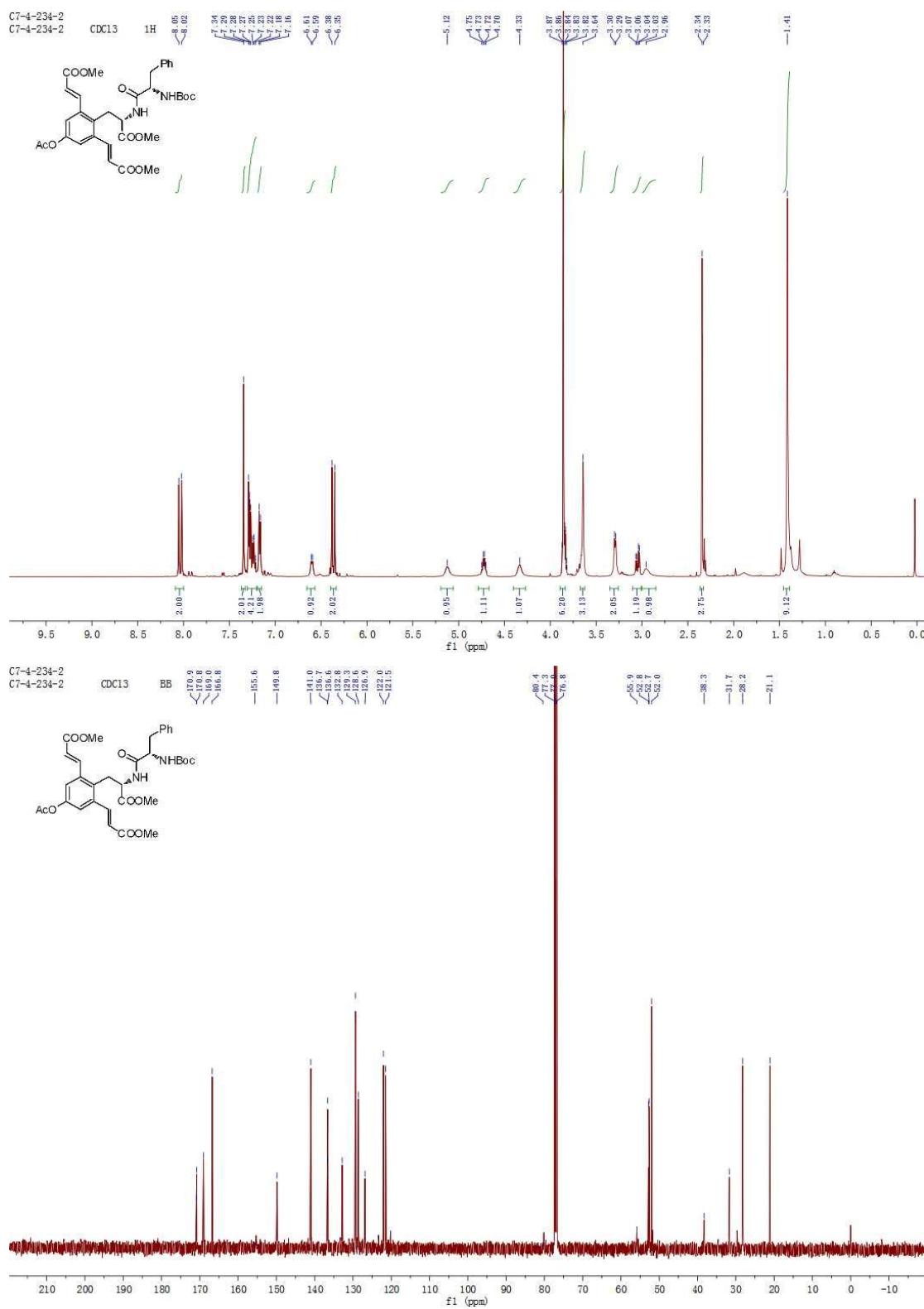
$2o_{di}$

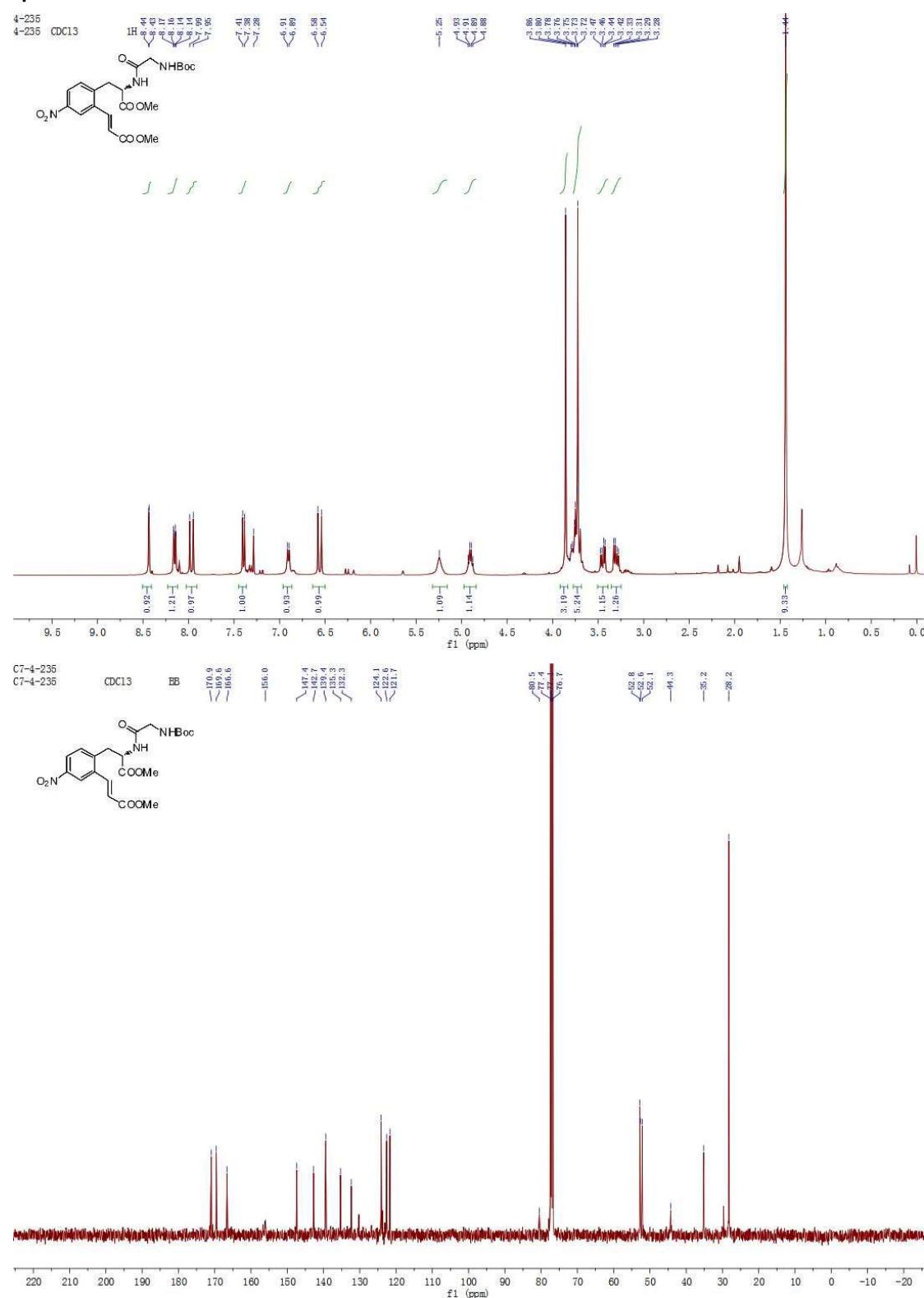
C7-4-234-2

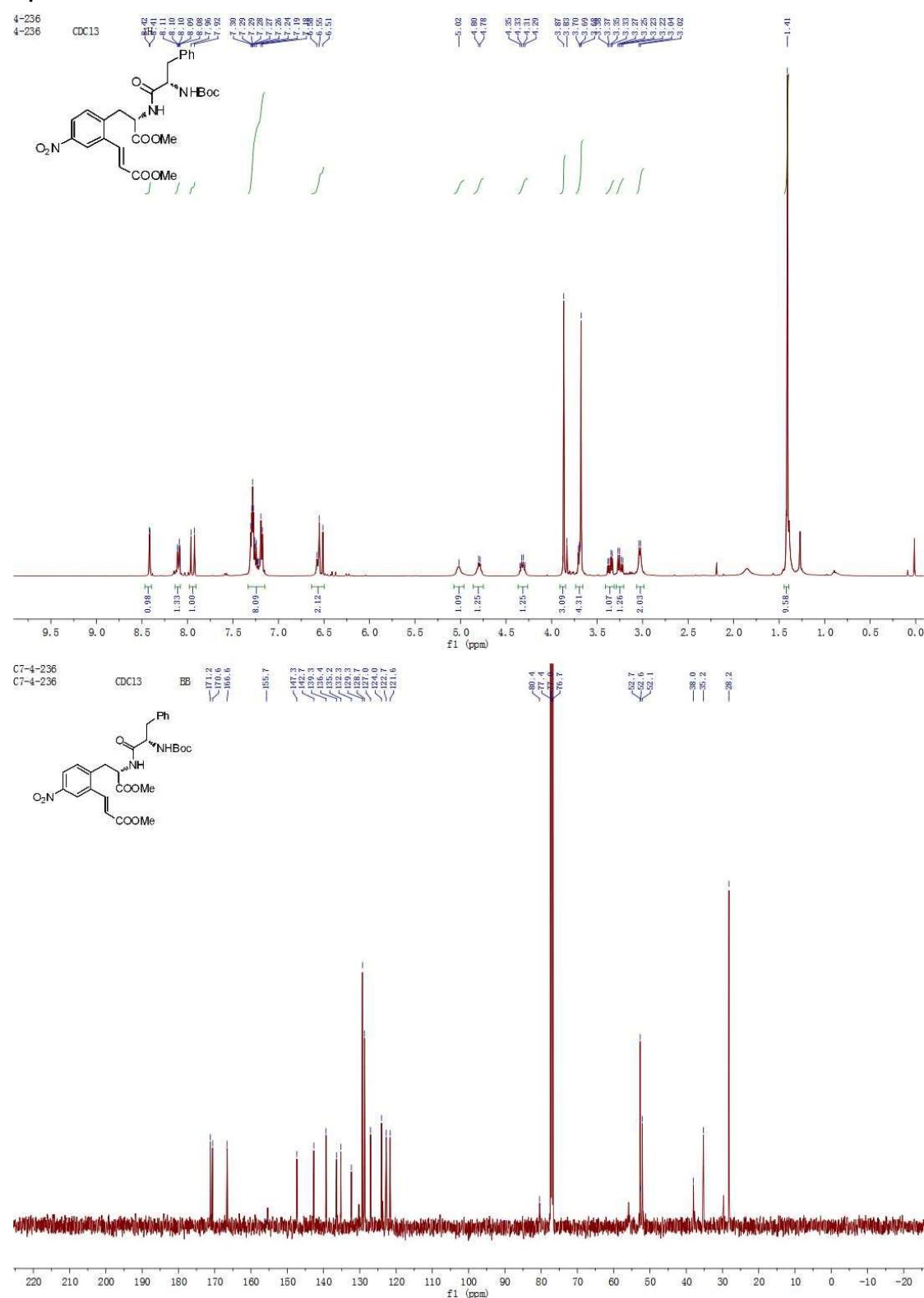
CDC13

1

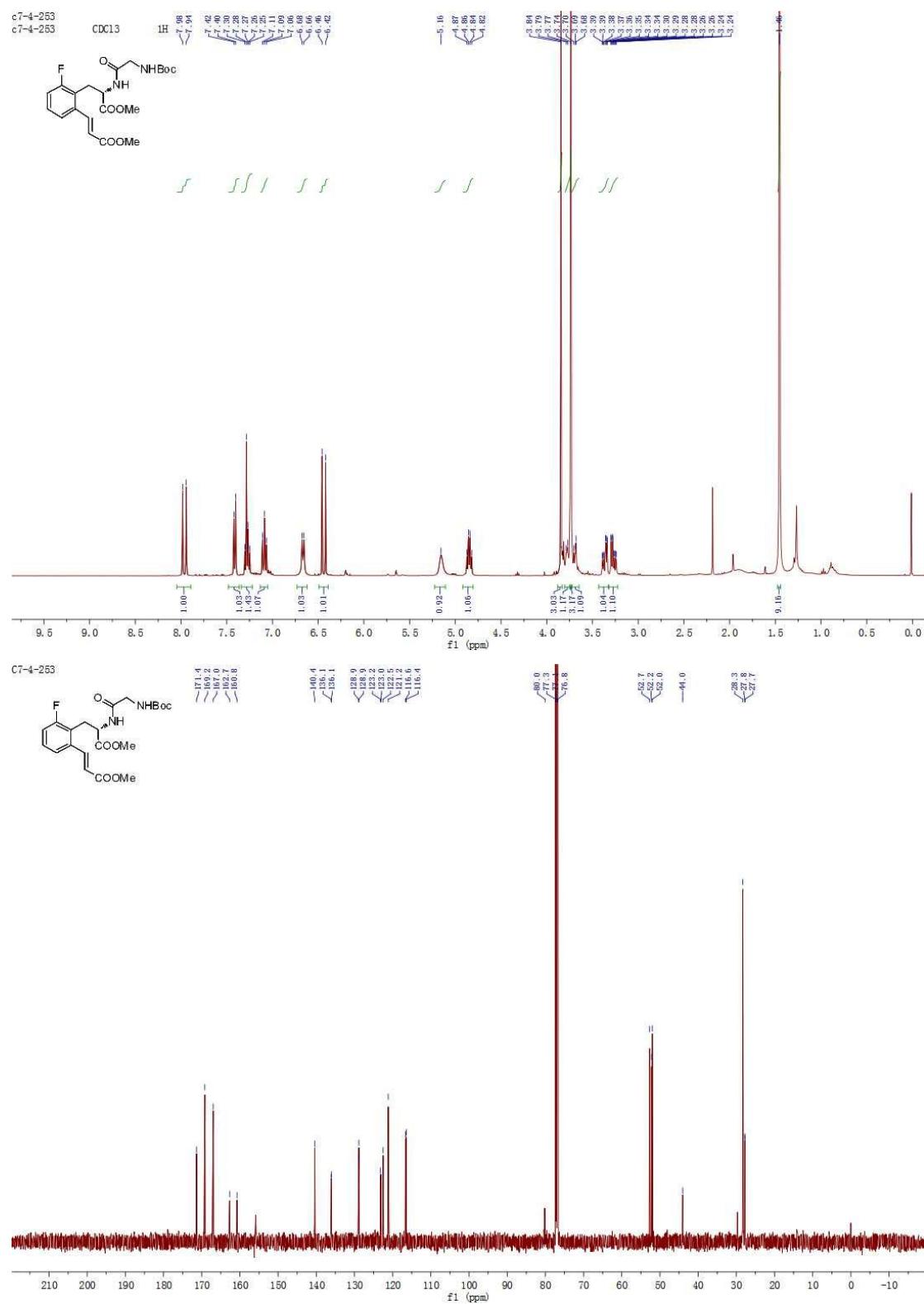
-8.05



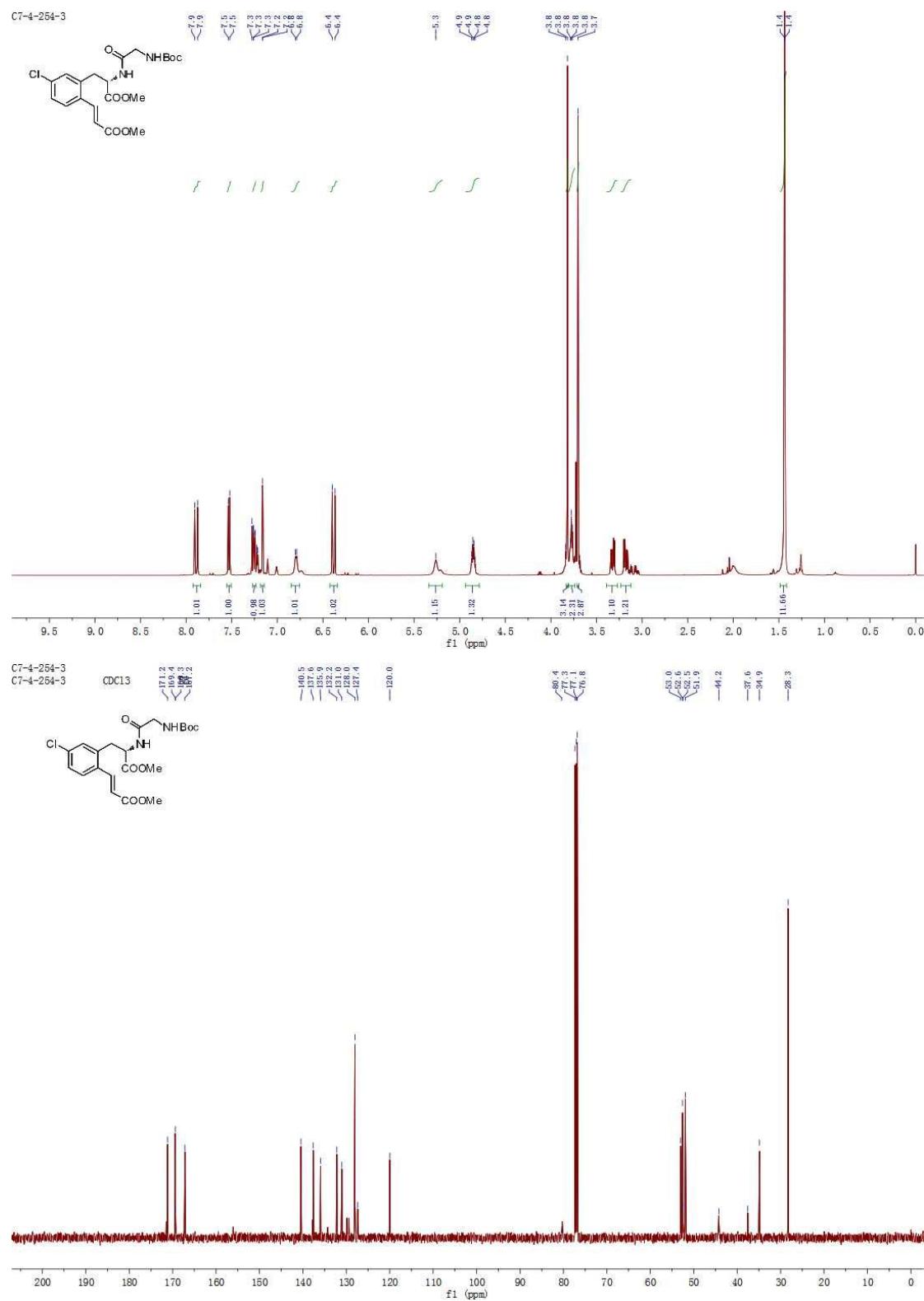
2p

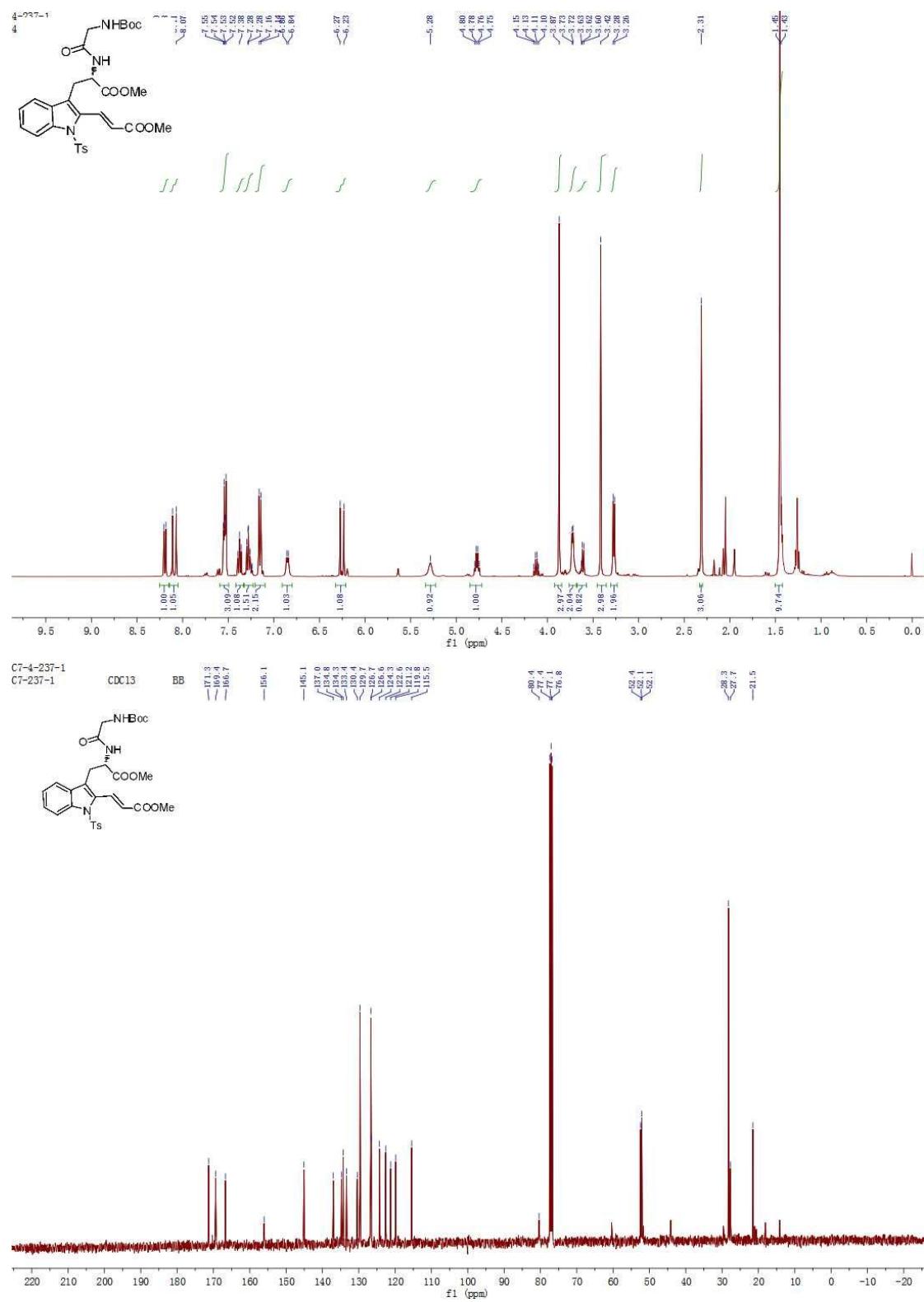
2q

2r

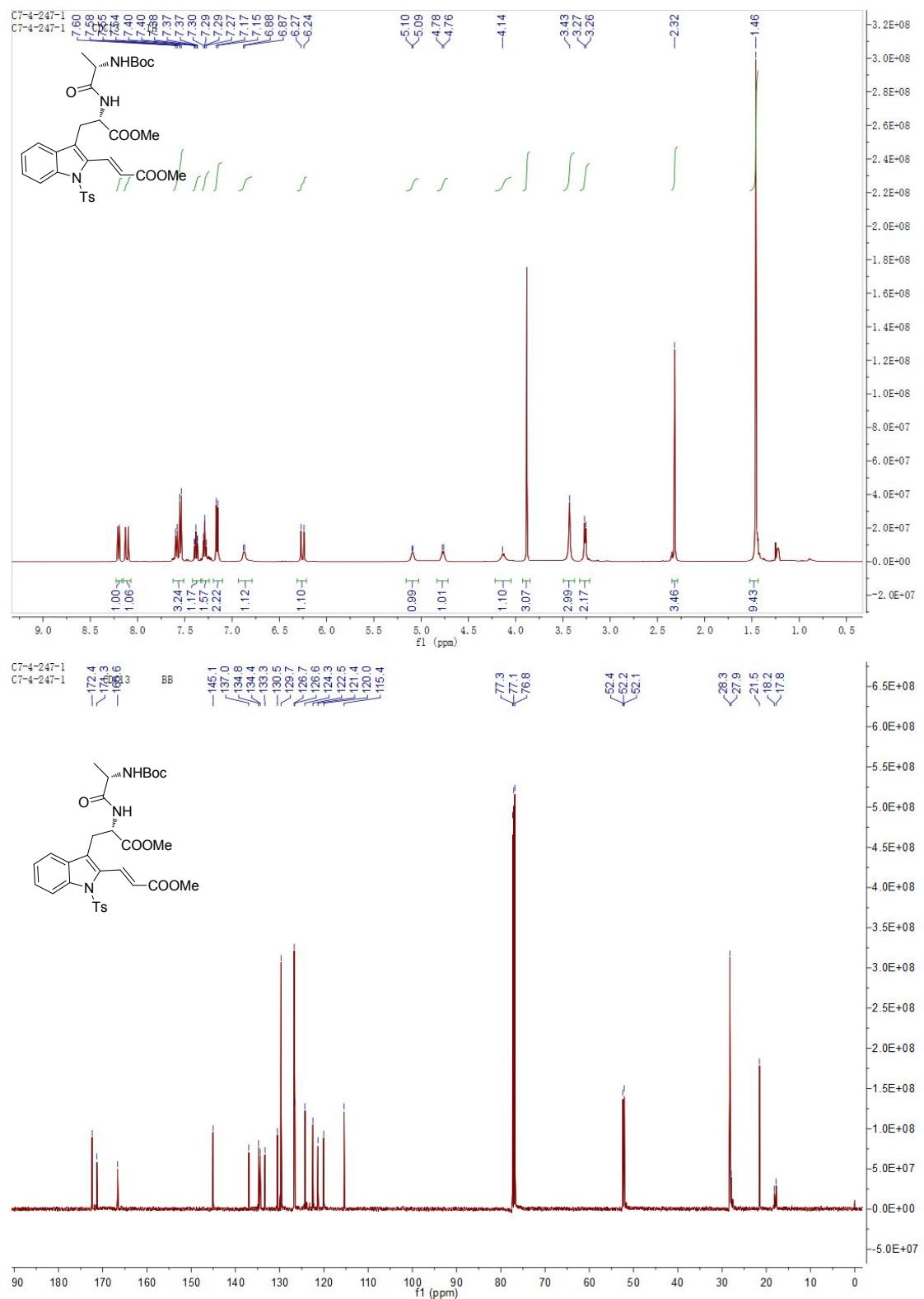


2s

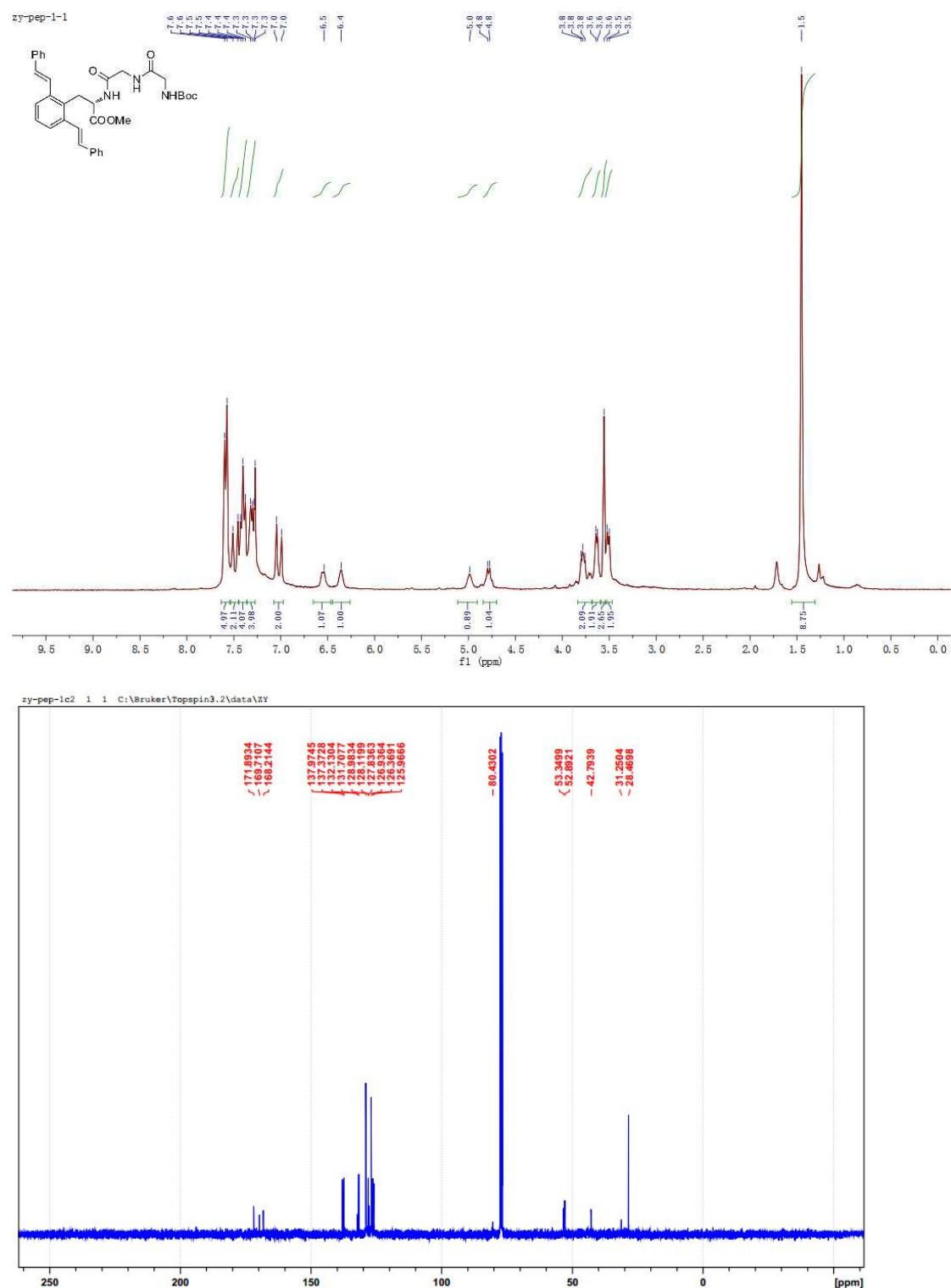


2t

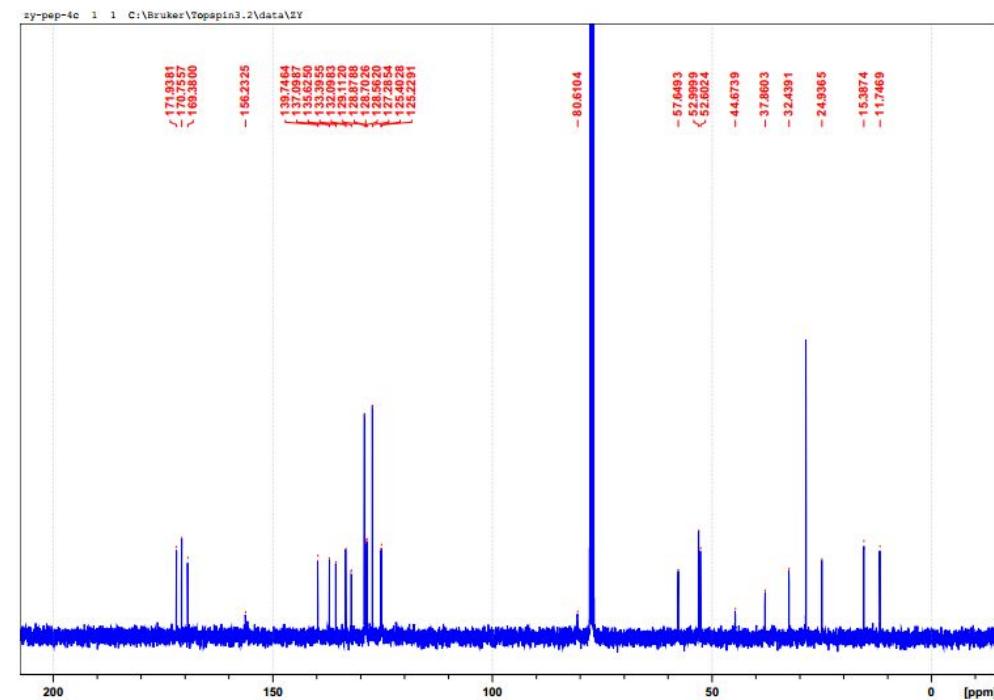
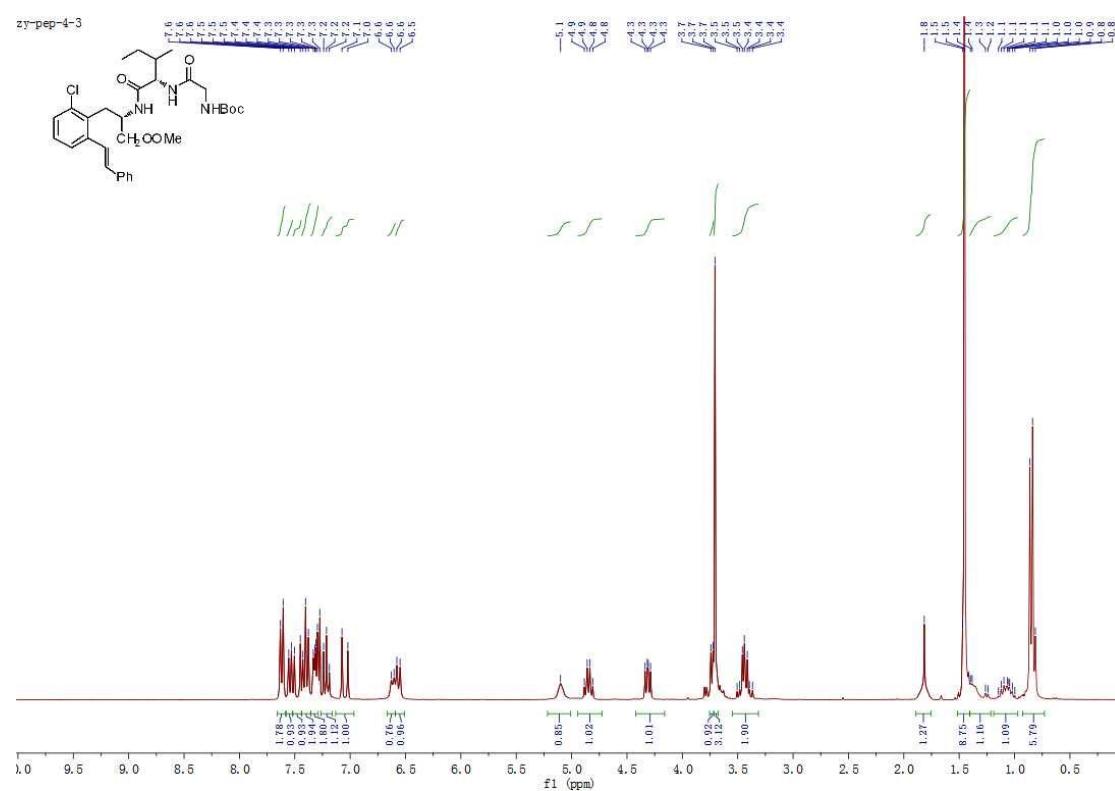
2u



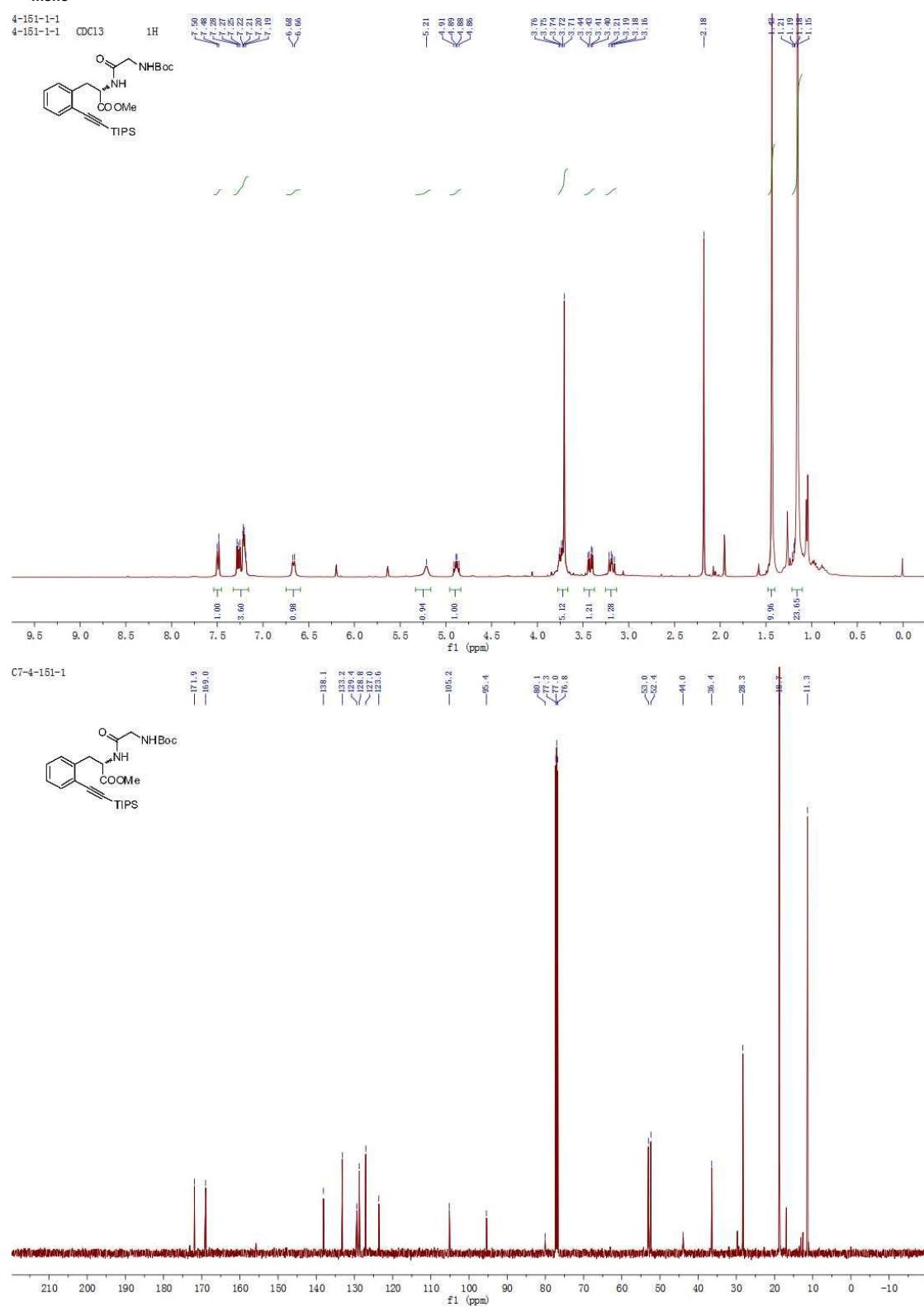
4a



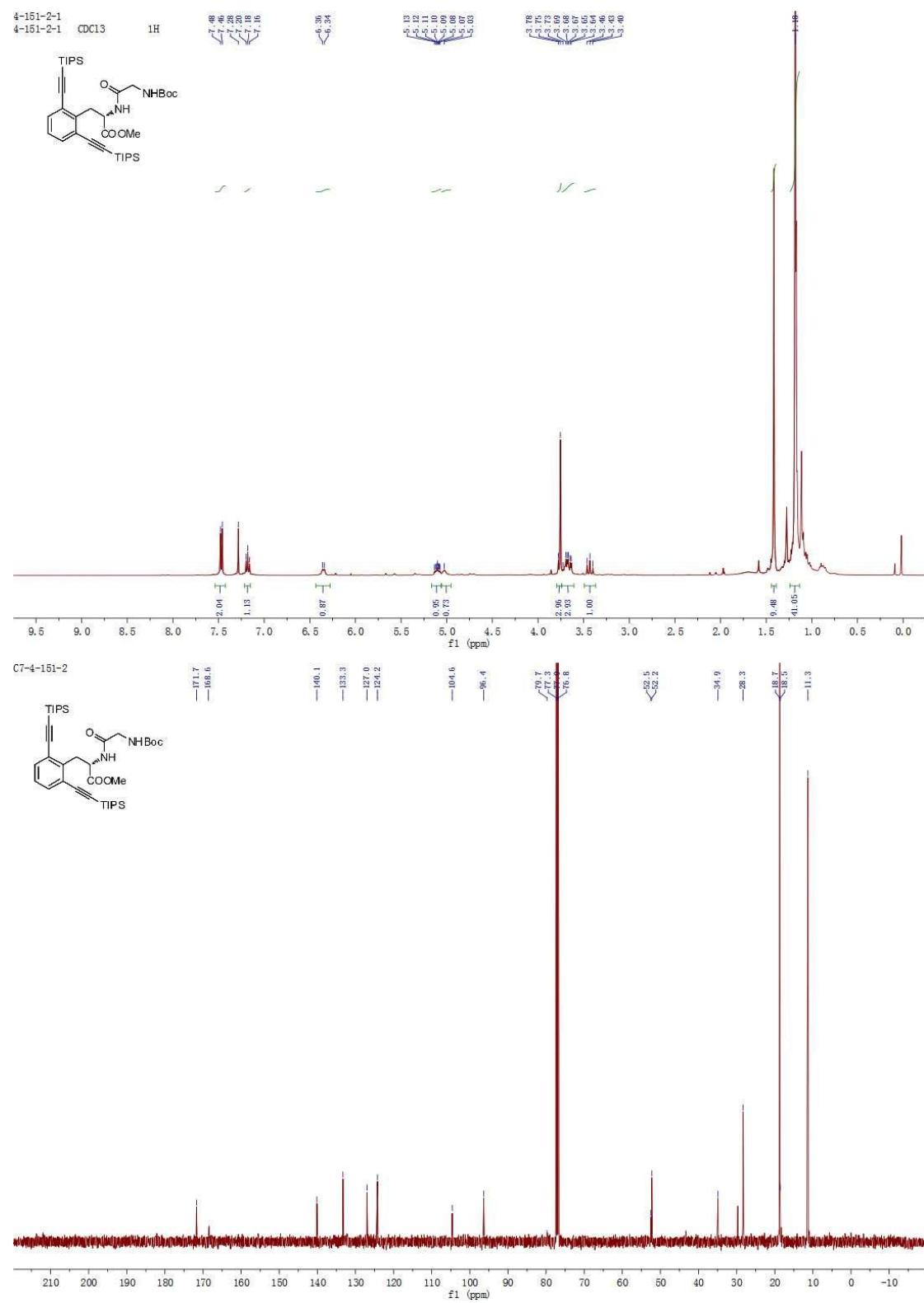
4b



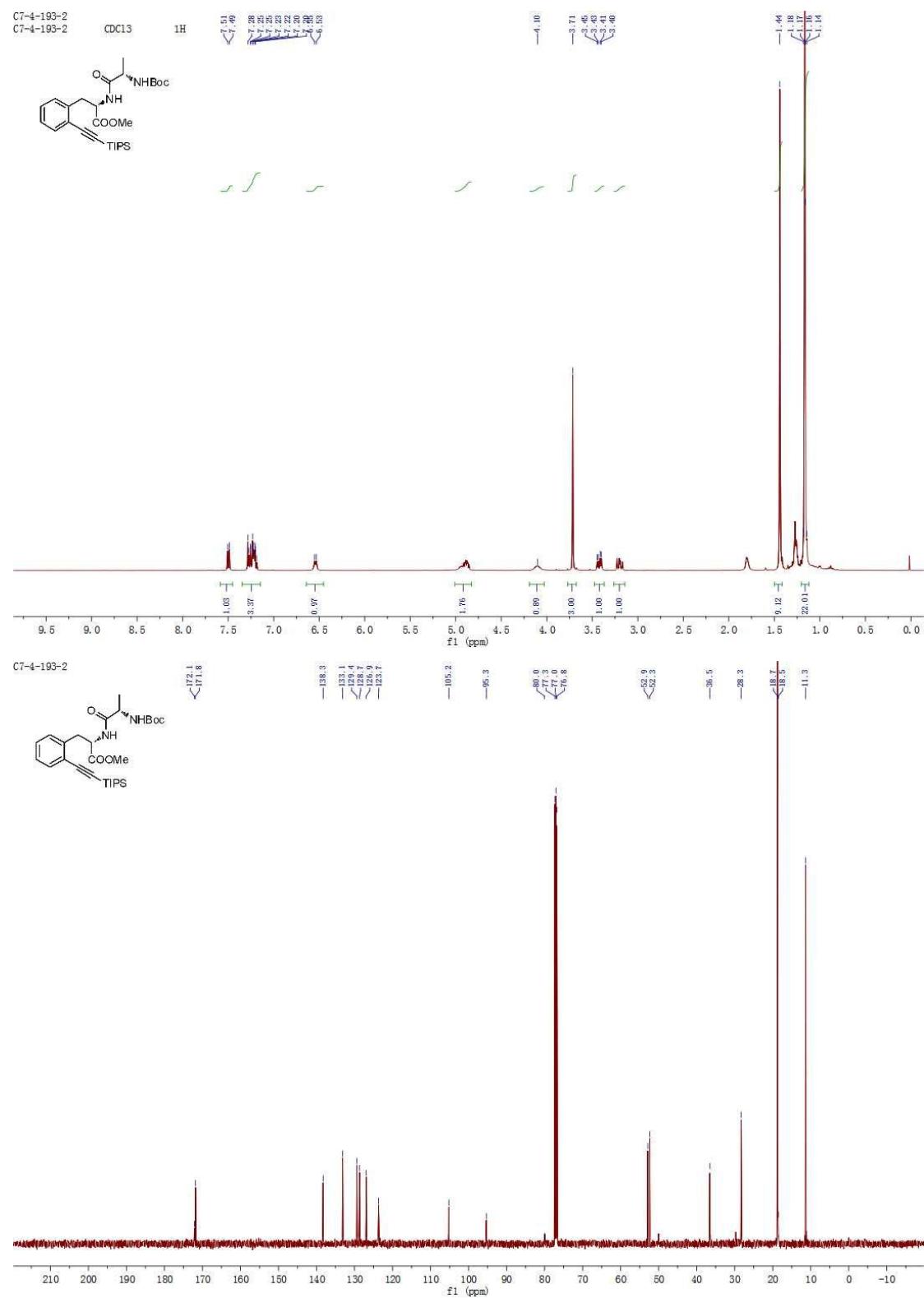
5a_{mono}



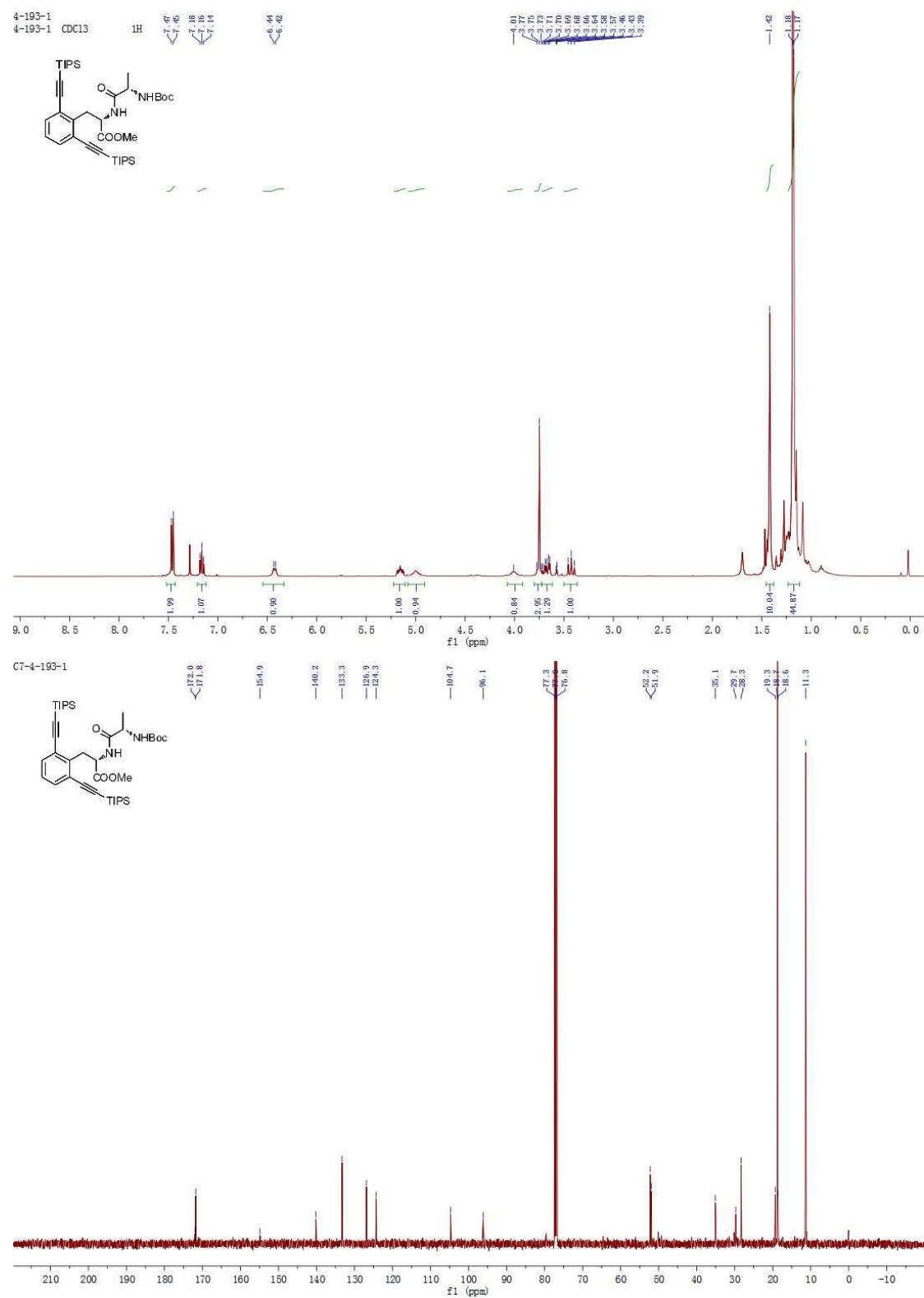
5a_{di}



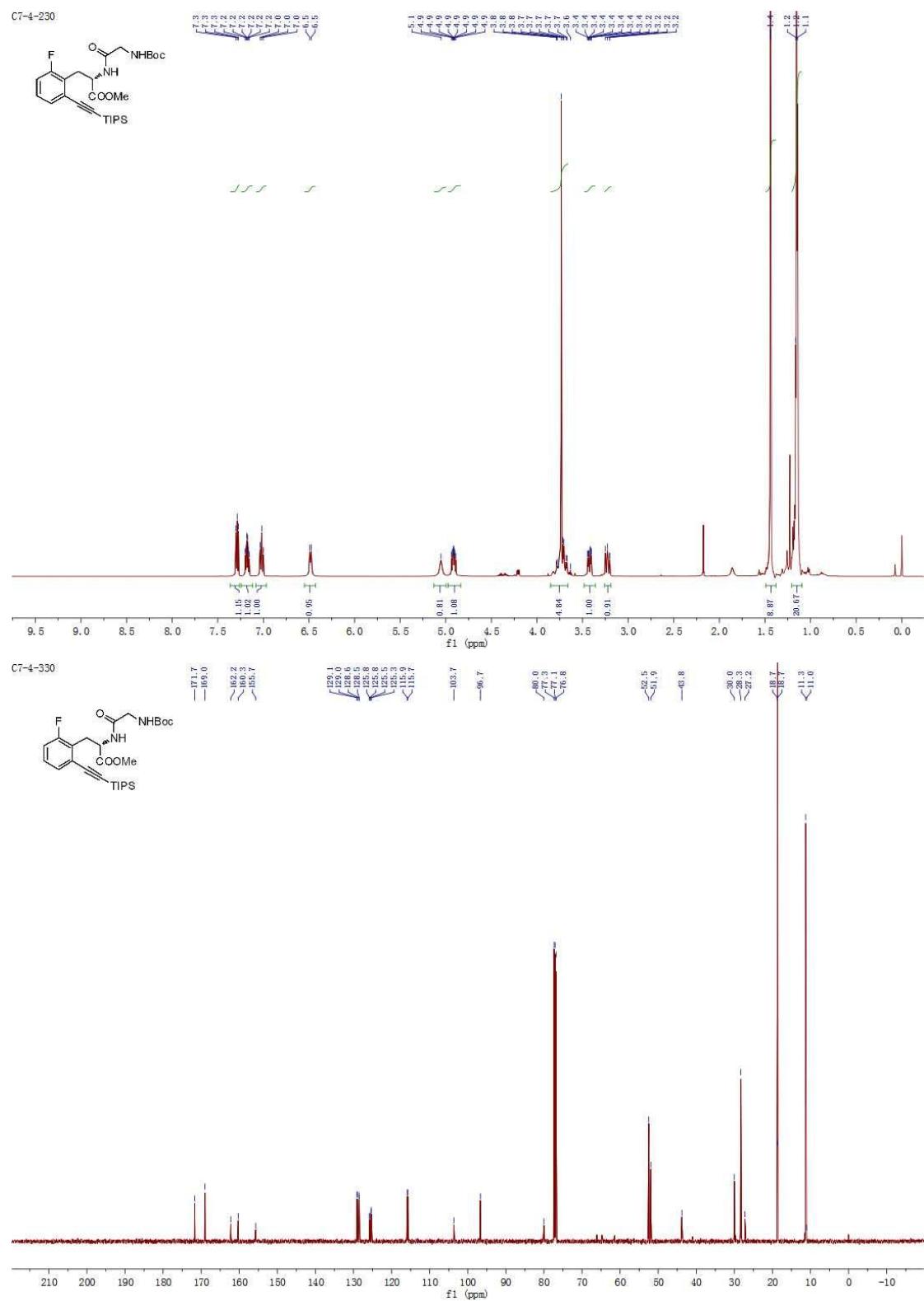
5b_{mono}



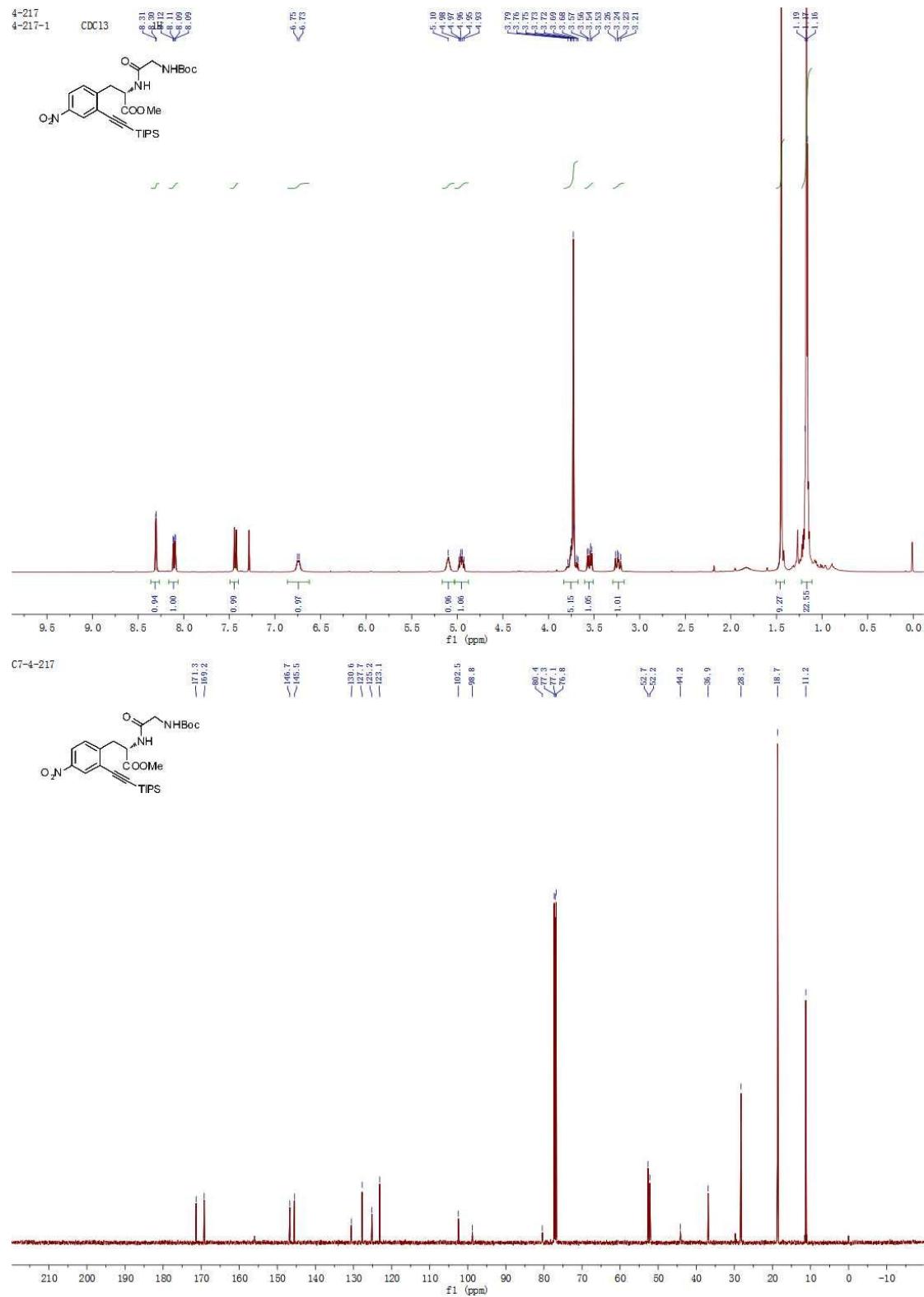
5b_{di}



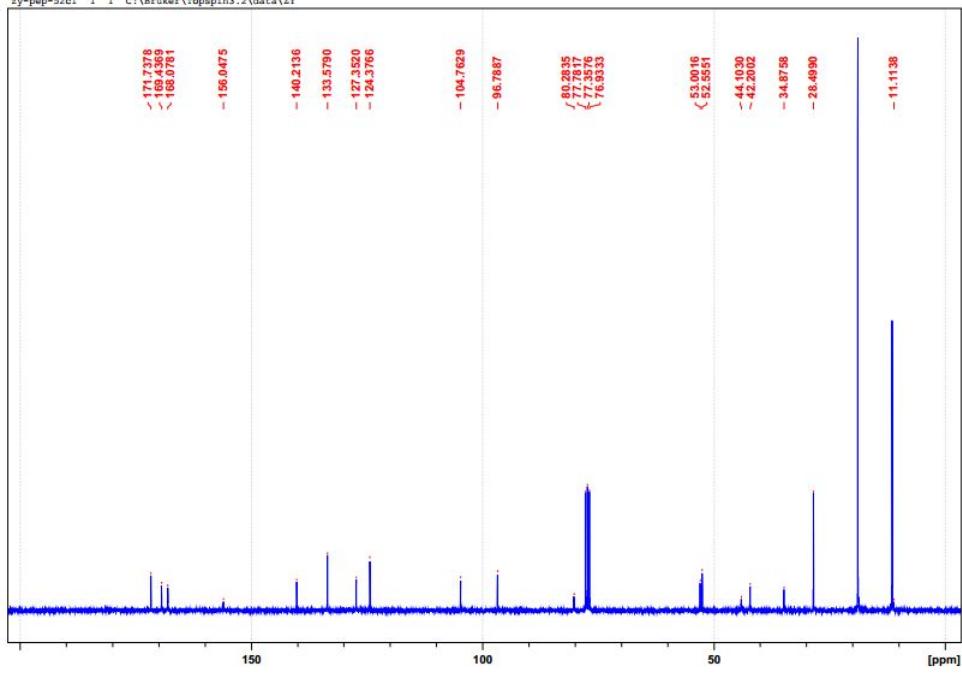
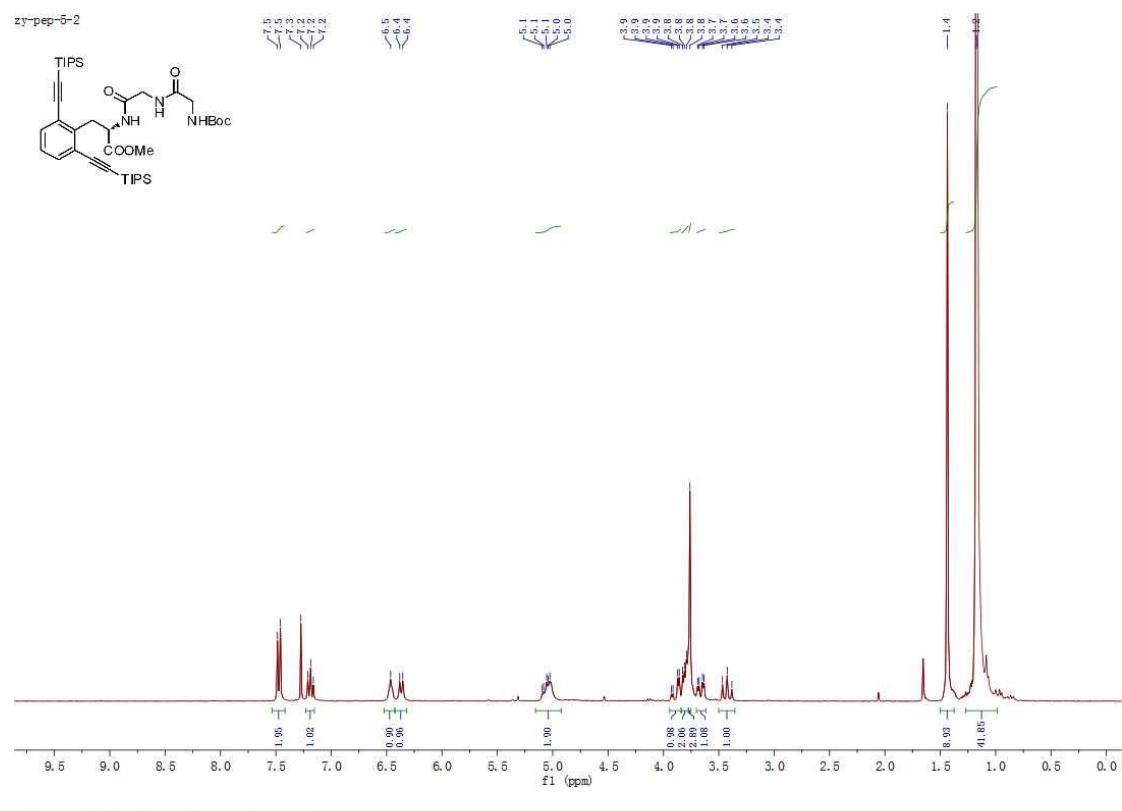
5c



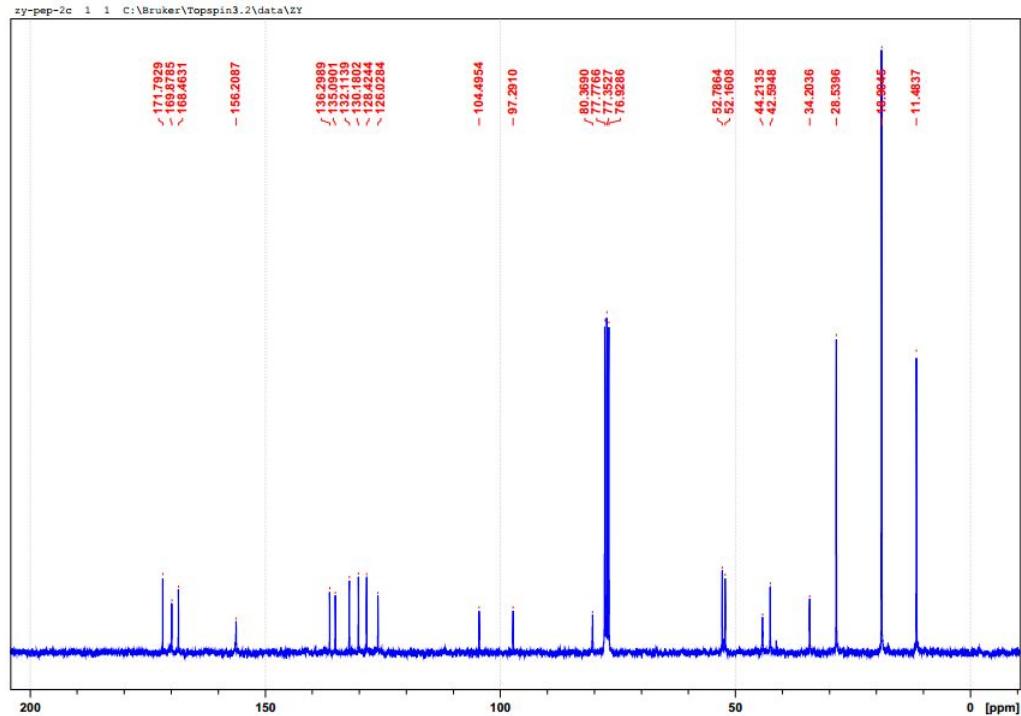
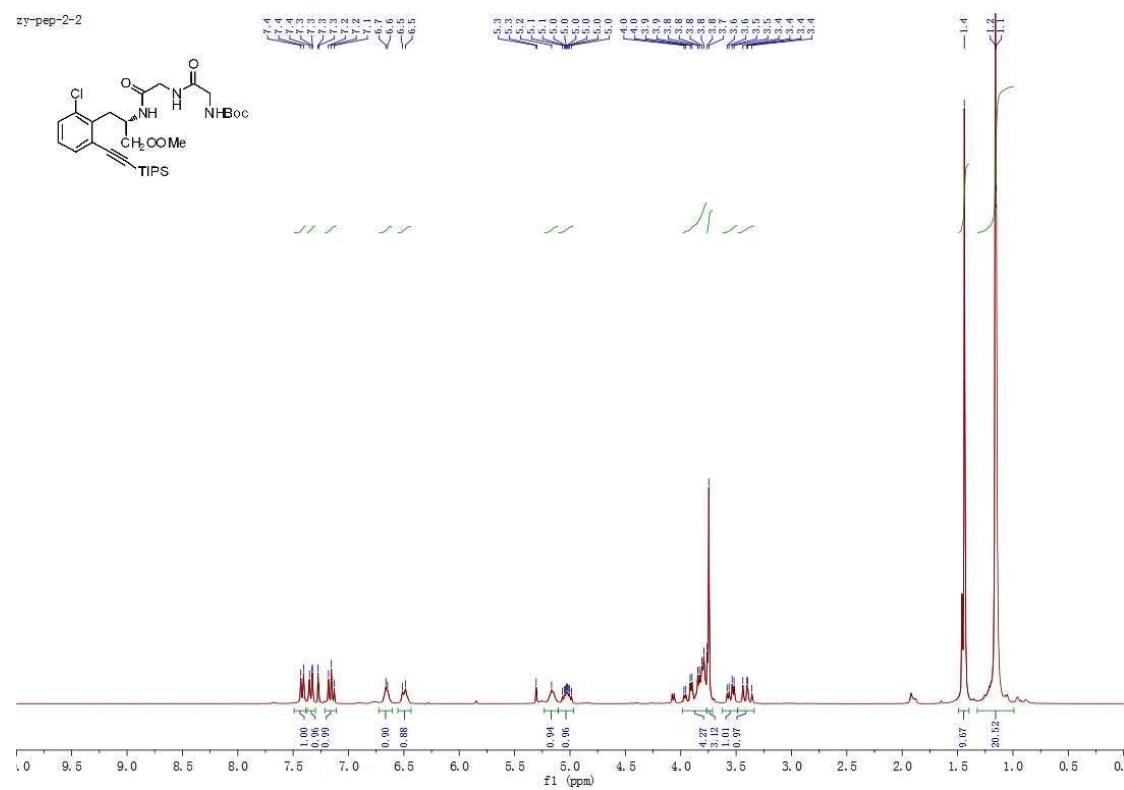
5d



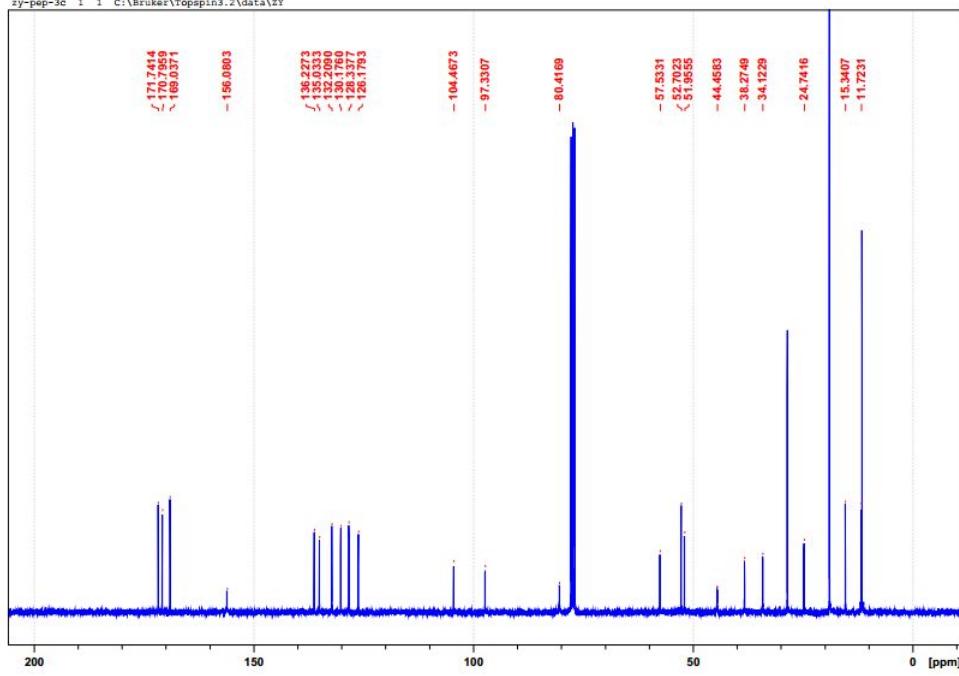
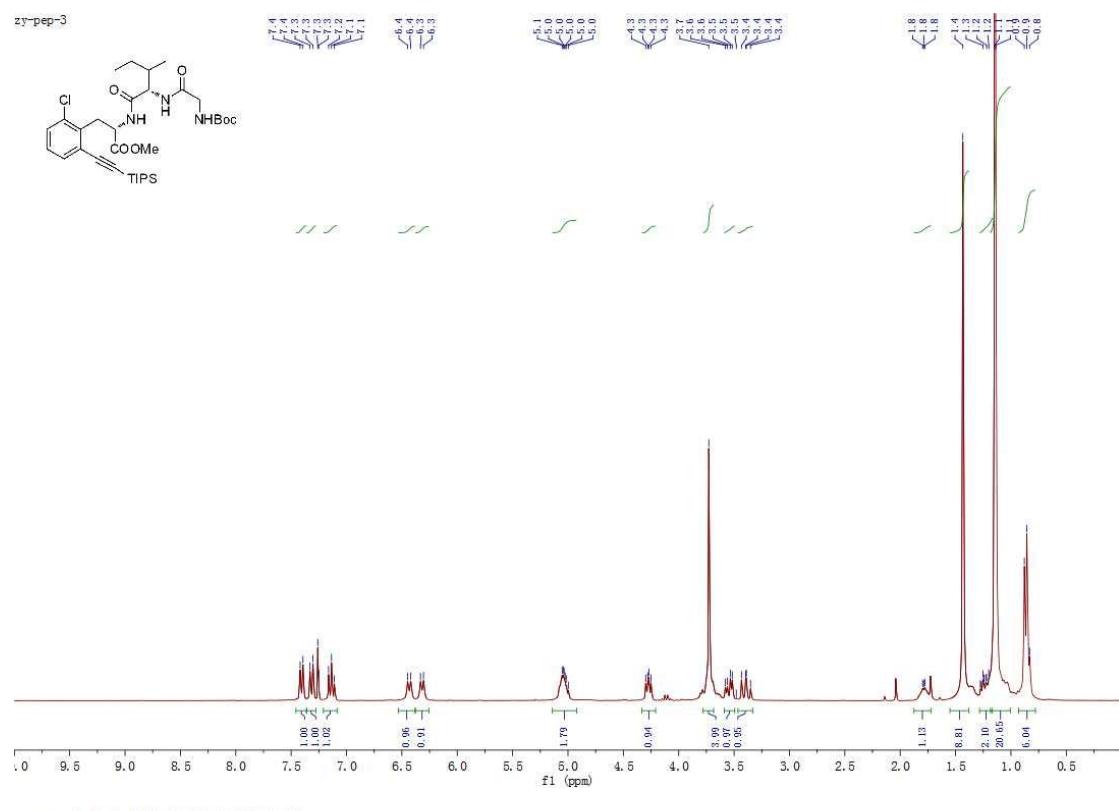
6a

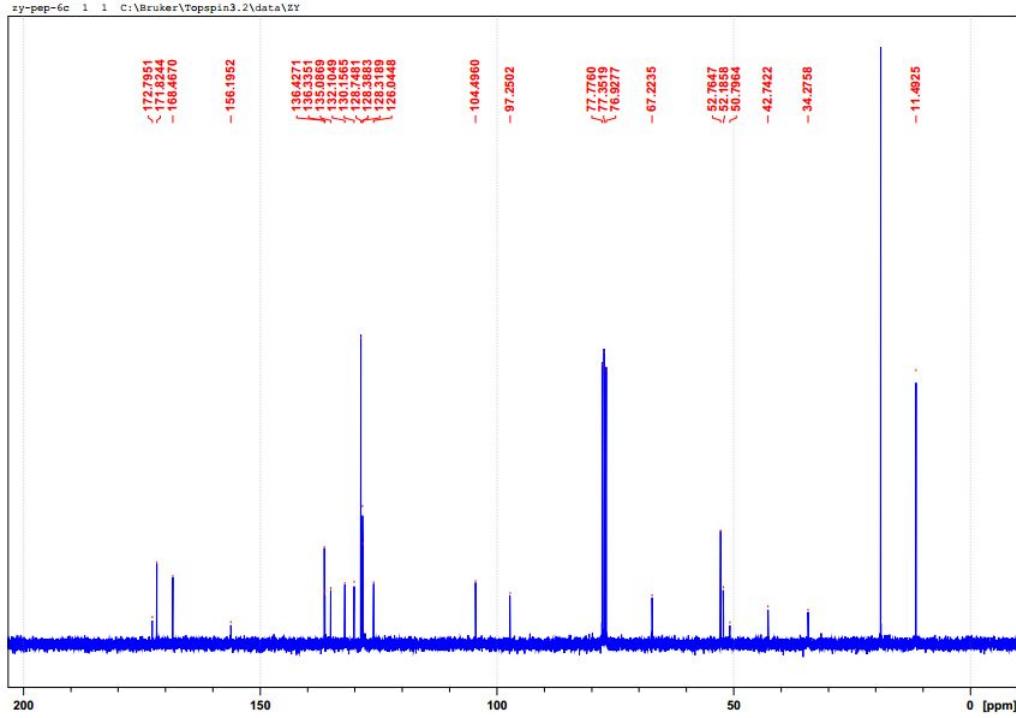
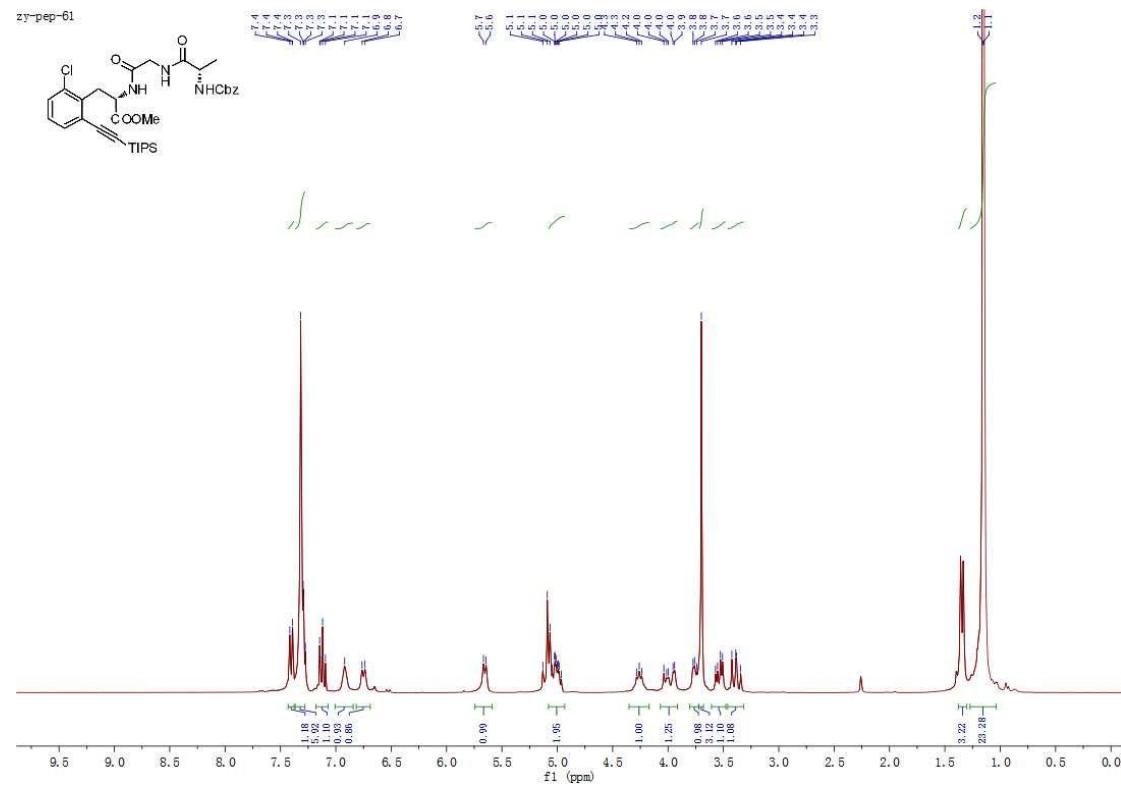


6b



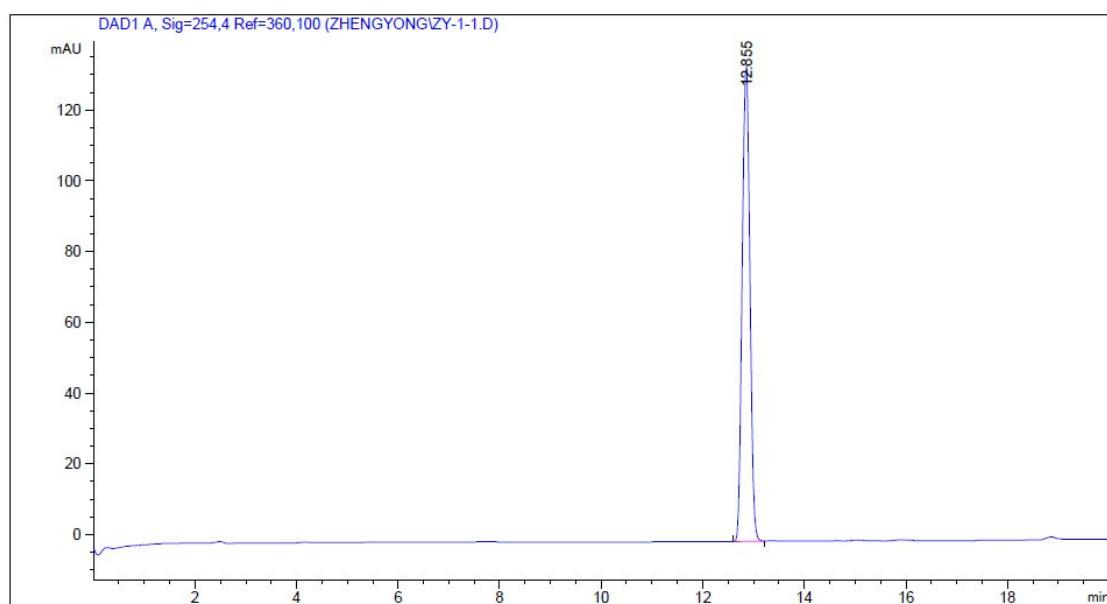
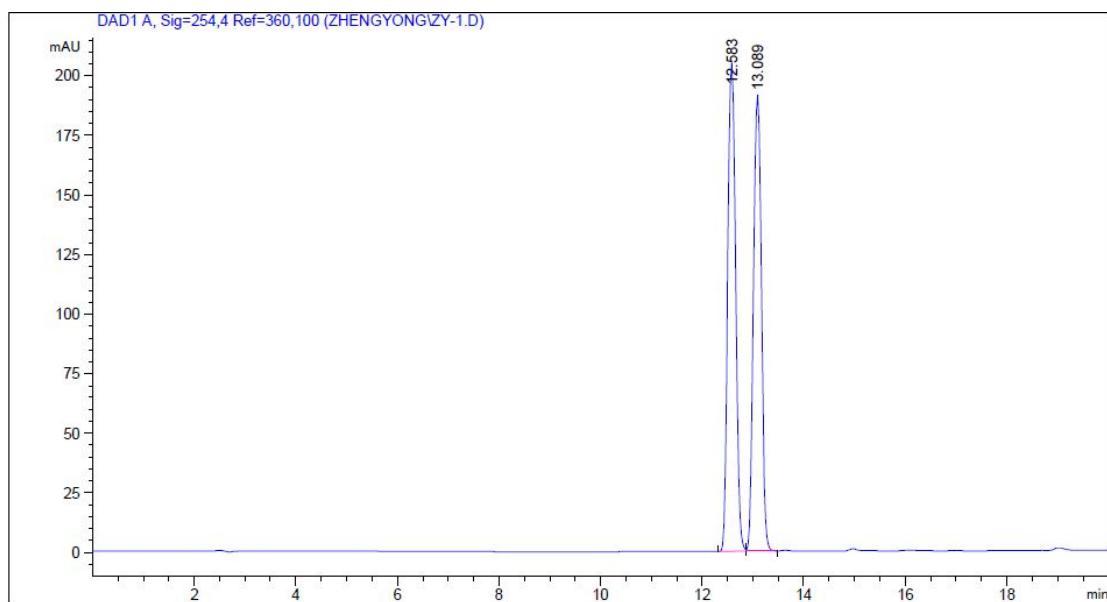
6c



6d

The ee value was determined by HPLC analysis on a Chiralcel OD-H column (15% *i*-PrOH in hexanes, 0.6 mL/min), $\lambda = 254$ nm.

2a_{mono}:



2a_{di}

