Electronic Supplementary Material (ESI) for Chemical Science.

Supporting Information

Peptide Late-Stage C(sp^3)–H Arylation By Native Asparagine Assistance Without Exogenous Driecting Group

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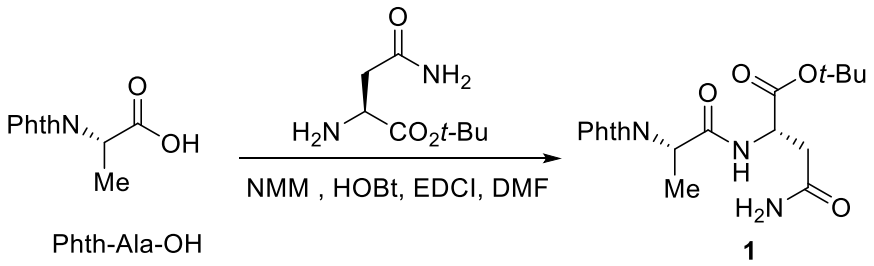
General Remarks

All commercial materials were used as received unless otherwise noted. Commercially available chemicals were obtained from Energy Chemical, Bidepharm and Aladdin. The Phth-Ala-OH was prepared according to literature procedure.[1] Iodo-BODIPY were synthesized according to a literature procedure.[2] 1, 2-Dichloroethane (DCE) was distilled from CaH_2 before use. Reactions in DCE were performed using standard Schlenk techniques. TLC analysis was performed using precoated glass plates, ^{I}H NMR was recorded on 400 MHz NMR spectrometer or 600 MHz NMR spectrometer. Chemical shifts were reported in ppm referenced to the appropriate solvent peak or 2.50 ppm for DMSO-d_6, or 7.26 ppm for $CDCl_3$. The following abbreviations were used to describe peak splitting patterns when appropriate: s = singlet, d = doublet, t = triplet, q = quartet, m = multiplet, dd = doublet of doublet. Coupling constants, *J*, were reported in Hertz unit (Hz). ^{13}C NMR was recorded on 100 MHz NMR spectrometer or 150 MHz NMR spectrometer, and fully decoupled by broad band proton decoupling. Chemical shifts were reported in ppm referenced to the central line of a multiplet at 39.52 ppm of DMSO-d_6, or that of a triplet at 77.16 ppm of $CDCl_3$. Mass spectra were measured with a Thermo Finnigan LCQ-Advantage. High resolution mass spectral (HRMS) analysis was performed on a Bruker micr OTOF-Q II instrument using ESI techniques. Melting points (m. p.) were obtained on a digital melting point apparatus and are uncorrected. HPLC were performed with Agilent 1100 using ZORBAX 300SB-C18 (5um, 4.6 × 250mm). Linear gradients using A: H_2O (0.1% TFA) and B: MeCN were run over varying periods time. Peptide centrifugation was performed with Cence TDZ5-WS. Semi preparative HPLC was carried out on Tong Heng Innovation LC3000 using 20NRAN C18 (10 um, 30 × 250 mm).

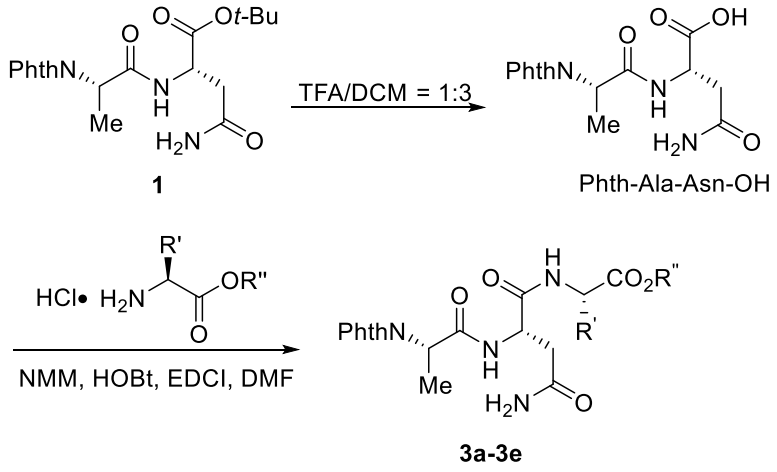
Synthesis of Starting Materials

Synthesis of Dipeptide 1



A solution of (*L*)-asparagine *tert*-butyl ester (3.76 g, 20 mmol), Phth-Ala-OH (4.38 g, 20 mmol), HOBt (2.97 g, 22 mmol), and NMM (3.44 g, 34 mmol) in DMF (50 mL) was cooled in an ice bath and subsequently treated with EDCI (4.6 g, 24 mmol). After 1 h at 0 °C, the mixture was warmed to room temperature, and stirred for 2 h. Then H_2O (50 mL) was added and the mixture was extracted with EtOAc (2 x 50 mL). The organic phase was washed with H_2O (50 mL) and brine (50 mL), concentrated *in vacuo*. The resulting residue was purified by flash chromatography yielding the dipeptide **1** (6.22 g, 80% yield).

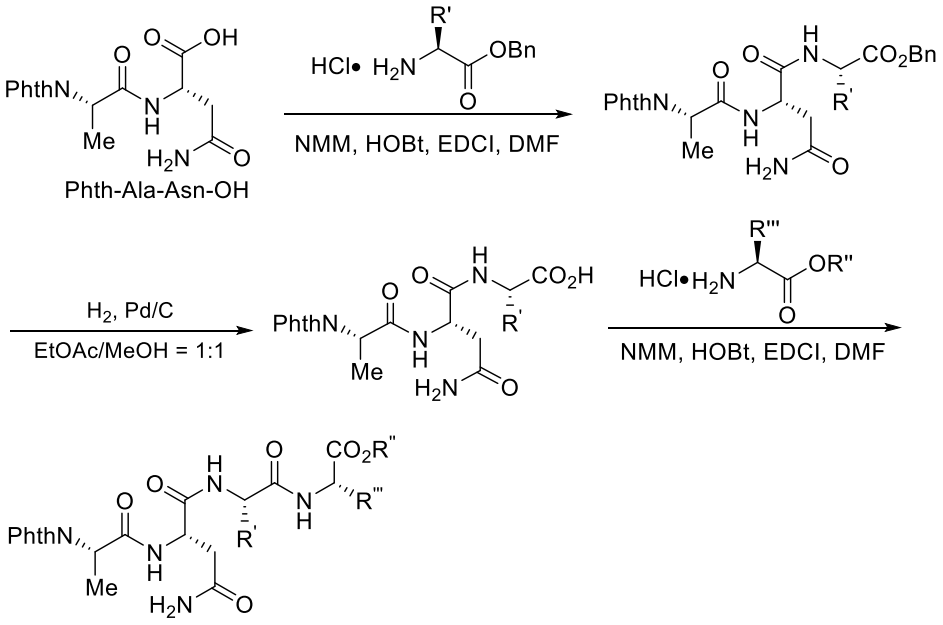
Synthesis of Tripeptides 3a-3e



A suspension of dipeptide **1** (3.89 g, 10 mmol) in CH_2Cl_2 (20 mL) was treated with trifluoroacetic acid (7 mL) for 4 h and then concentrated *in vacuo*. The resulting residue was recrystallized from EtOAc/hexanes (50 mL, 1/1, v/v) to give Phth-Ala-Asn-OH (2.33 g, 70%), which was then mixed with (*L*)-amino acid methyl ester hydrochloride or benzyl ester hydrochloride, or *tert*-butyl ester hydrochloride (8.4 mmol), HOBt (7.7 mmol), and NMM (11.9 mmol) in DMF (20 mL). The mixture was cooled in an ice bath and subsequently treated with EDCI (8.4 mmol). After 1 h at 0 °C, the mixture was warmed to room temperature and stirred

for 2 h. Then H_2O (20 mL) was added and the mixture was extracted with EtOAc (2 x 20 mL). The organic phase was washed with H_2O (20 mL) and brine (20 mL), concentrated *in vacuo*. The resulting residue was purified by flash chromatography to yielding the corresponding tripeptides **3a-3e**.

Synthesis of Tetrapeptides 3f-3h



3f-3h

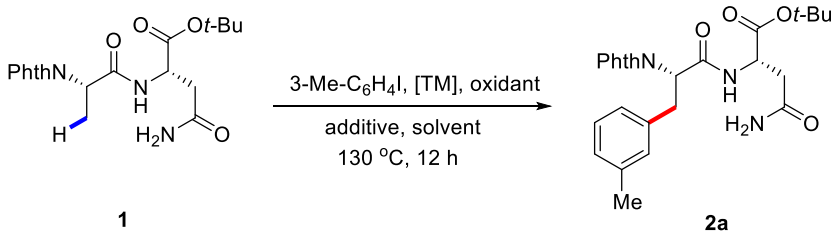
A solution of Phth-Ala-Asn-OH (1.67 g, 5 mmol), (*L*)-amino acid benzyl ester hydrochloride (6.0 mmol), HOBt (5.5 mmol), and NMM (8.5 mmol) in DMF (15 mL) was cooled in an ice bath and subsequently treated with EDCI (6.0 mmol). After 1 h at 0 ^oC, the mixture was warmed to room temperature and stirred for 2 h. Then H_2O (15 mL) was added and the mixture was extracted with EtOAc (2 x 15 mL). The organic phase was washed with H_2O (15 mL) and brine (15 mL), concentrated *in vacuo* to give the corresponding tripeptides. The tripeptides was suspended in a 1/1 mixture of MeOH/EtOAc (20 mL), and treated with Pd/C (10%) and the reaction mixture was stirred for 12 h under hydrogen balloon at room temperature. The reaction mixture was then filtered through a pad of Celite, and the filtrate was concentrated *in vacuo* to give the white solid. The solid was mixed with (*L*)-amino acid methyl ester hydrochloride or benzyl ester hydrochloride (1.2 equiv.), HOBt (1.1 equiv.), and NMM (1.7 equiv.) in DMF. The mixture was cooled in an ice bath and subsequently treated with EDCI (1.2 equiv.). After 1h at 0 ^oC, the mixture was warmed to room temperature for 2 h. Then H_2O was added and the mixture was extracted with EtOAc. The organic phase was washed with water and brine, concentrated *in vacuo*. The resulting residue was purified by flash chromatography to give the

corresponding tetrapeptides **3f-3h**.

Optimization Studies

C(sp^3)–H Arylation of Dipeptide 1

Table S1. Optimization of the C(sp^3)–H arylation of dipeptide **1**.[a]



1 **2a**

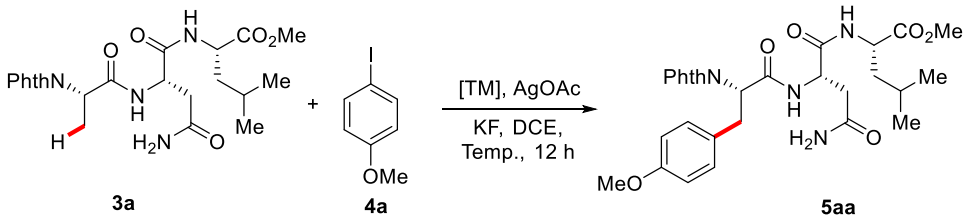
Entry	[TM]	Oxidant	Additive	Solvent	Yield [%][a]
1	$Pd(OAc)_2$	AgOAc	-	*t*AmOH	21
2	$Pd(OAc)_2$	AgOAc	-	HFIP	--
3	$Pd(OAc)_2$	AgOAc	-	MeCN	--
4	$Pd(OAc)_2$	AgOAc	-	DCE	35
5	$Pd(OAc)_2$	AgOAc	-	PhMe	22
6	$Pd(OAc)_2$	AgOAc	NaOAc	DCE	26
7	$Pd(OAc)_2$	AgOAc	Cs_2CO_3	DCE	traces
8	$Pd(OAc)_2$	AgOAc	KF	DCE	41
9	$PdCl_2$	AgOAc	-	DCE	51[b]
10	$PdCl_2$	AgOAc	KF	DCE	67[b]
11	$PdCl_2$	AgOAc	K_3PO_4	DCE	44[b]
12	$PdCl_2$	AgOTf	KF	DCE	--[b]
13	$PdCl_2$	$Cu(OAc)_2$	KF	DCE	10[b]
14	$PdCl_2$	AgOAc	KF	DCE	66[b,c]
15	$PdCl_2$	AgOAc	KF	DCE	36[b,d]
16	$Pd(MeCN)_2Cl_2$	AgOAc	KF	DCE	72[b]
17	$Pd_2(dba)_3$	AgOAc	KF	DCE	36[b]
18	$Pd(PPh_3)_2Cl_2$	AgOAc	KF	DCE	35[b]
19	$Pd(OAc)_2$	AgOAc	KF	DCE	58[b]
20	-	AgOAc	KF	DCE	--[b]
21	$PdCl_2$	-	KF	DCE	12[b]
22	$[RuCl_2(p\text{-cymene})]_2$	AgOAc	KF	DCE	--[b]
23	$[Cp^*RhCl_2]_2$	AgOAc	KF	DCE	--[b]
24	$Co(OAc)_2{\cdot}4H_2O$	AgOAc	KF	DCE	--[b]

[a] Reaction conditions: **1** (0.20 mmol), 3-Me-C_6H_4I (0.40 mmol), oxidant (0.40 mmol), [TM] (10 mol %), solvent (2.0 mL), additive (0.40 mmol), 130 °C, 12 h, yields of the isolated products based

on **1**. [b] oxidant (0.50 mmol), additive (0.50 mmol). [c] 3-Me-C_6H_4I (0.60 mmol). [d] $PdCl_2$ (5.0 mol %).

C(sp^3)–H Arylation of Tri and Tetra peptides 3

Table S2. Optimization of the C(sp^3)–H arylation of tripeptide **3a**.[a]



3a **4a** **5aa**

Entry	[TM]	AgOAc (equiv.)	KF (equiv.)	Temp. (°C)	Yield [%][a]
1	$Pd(MeCN)_2Cl_2$	2.5	2.5	130	40
2	$PdCl_2$	2.5	2.5	130	44
3	$PdBr_2$	2.5	2.5	130	31
4	PdI_2	2.5	2.5	130	30
5	$PdCl_2$	2.5	2.5	120	46
6	$PdCl_2$	2.5	2.5	110	49
7	$PdCl_2$	2.5	2.5	100	32
8	$PdCl_2$	2.5	2.5	110	52[b]
9	$PdCl_2$	2.5	2.0	110	56[b]
10	$PdCl_2$	2.5	2.0	110	61[b,c]
11	$PdCl_2$	2.5	2.0	110	61[b,d]

[a] Reaction conditions: **3a** (0.20 mmol), 4-OMe-C_6H_4I (0.40 mmol), AgOAc (0.50 mmol), [TM] (10 mol %), DCE (3.0 mL), KF (0.50 mmol), 12 h, yields of the isolated products based on **3a**. [b] 4-OMe-C_6H_4I (0.5 mmol). [c] $PdCl_2$ (15 mol %). [d] $PdCl_2$ (20 mol %).

General Procedure A: C(sp^3)–H Arylation of Dipeptides

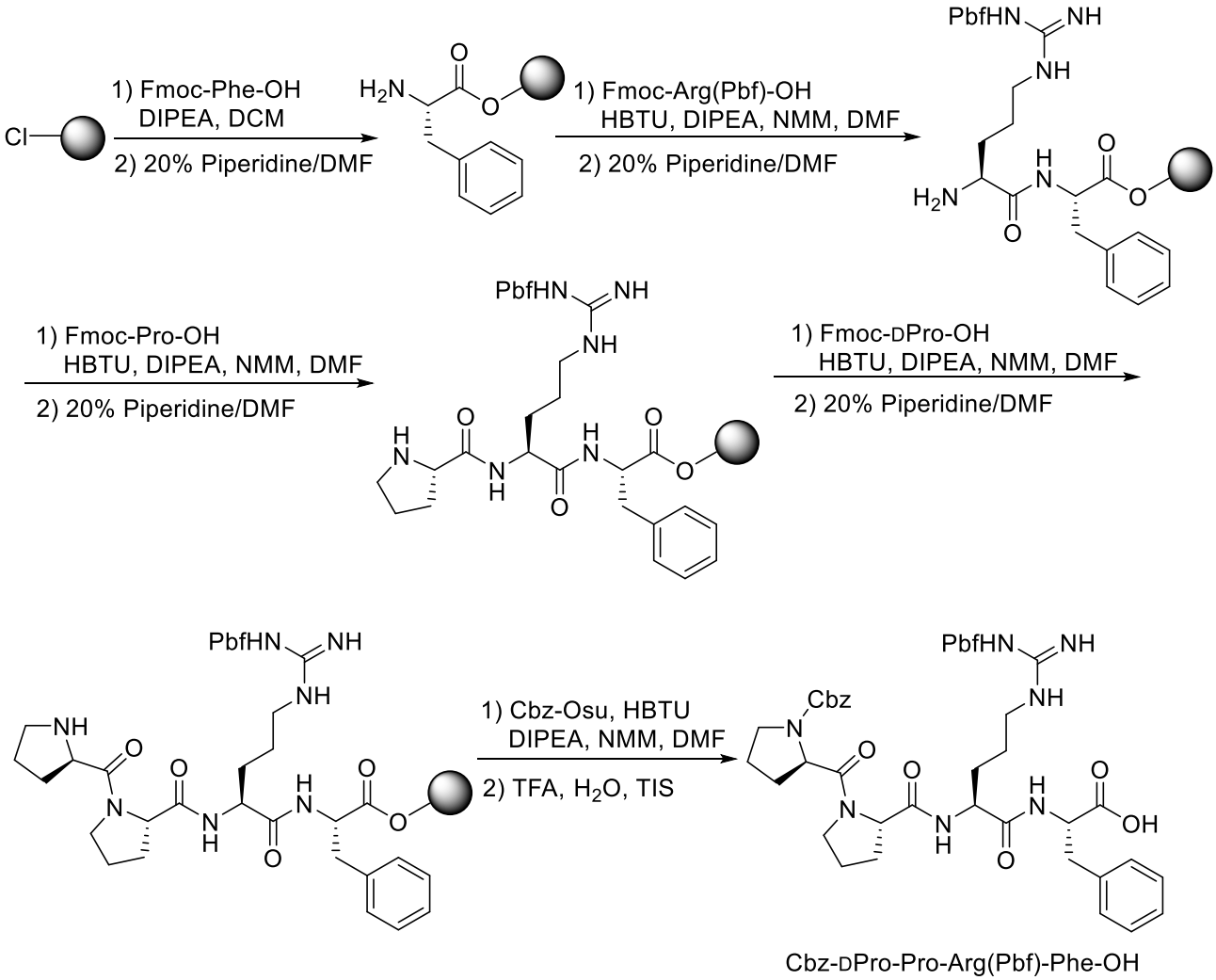
To a 10 mL Schlenk tube dipeptide **1** (77.9 mg, 0.20 mmol), iodoarene (0.40 mmol), $Pd(MeCN)_2Cl_2$ (5.2 mg, 10 mol %), AgOAc (83.5 mg, 0.50 mmol), KF (29.1 mg, 0.50 mmol) and DCE (2.0 mL) were added. The mixture was stirred at 130 °C for 12 h. After cooling to room temperature, the mixture was diluted with CH_2Cl_2 (10 mL) and concentrated *in vacuo*. The resulting residue was purified by column chromatography on silica gel to yield the desired products **2**.

General Procedure B: C(sp^3)–H Arylation of Tripeptides and Tetrapeptides

To a 10 mL Schlenk tube was added tripeptide or tetrapeptide **3** (0.20 mmol), **4** (0.50 mmol), $PdCl_2$ (5.3 mg, 15 mol %), AgOAc (100.1 mg, 0.60 mmol), KF and DCE (3.0 mL) were added. The mixture was stirred at 110 °C for 12 h. After cooling to room temperature, the mixture was diluted with CH_2Cl_2 (10 mL) and concentrated *in vacuo*. The resulting residue was purified by column chromatography on silica gel to yield the desired products **5** or **6**.

Synthesis of AGRP Loop Analogues

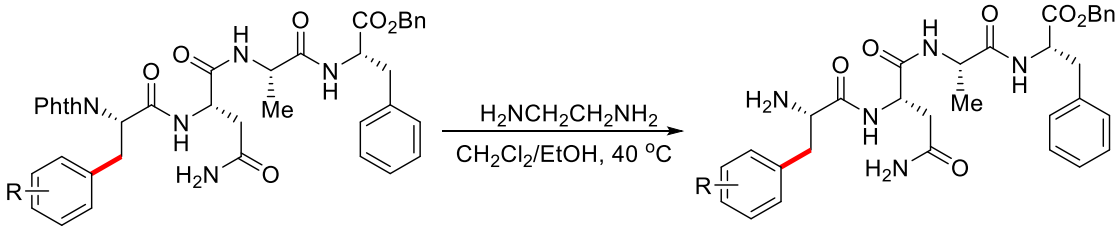
Synthesis of Tetrapeptides Cbz-DPro-Pro-Arg(Pbf)-Phe-OH



2-Chlorotrityl chloride resin (1.00 g, 1.0 mmol) was swelled in CH_2Cl_2 (5 mL) for 30 min and then was added into a peptide synthesis tube. After removing the solvent under vacum, a solution of the Fmoc-Phe-OH (1.16 g, 3.0 mmol) and DIPEA (0.78 g, 6.0 mmol) in CH_2Cl_2 (5

mL) was added. The tube was shaken for 3 h at room temperature, the tube was then drained, and rinsed with DMF (5 x 5 mL) to afford Fmoc-Phe-CTC. The resin was treated with a solution of piperidine/DMF (6 mL, 1/5, v/v) for 30 min followed by washing with DMF (5 x 5 mL). A solution of Fmoc-Arg(Pbf)-OH (0.78 g, 1.2 mmol), HBTU (0.43 g, 1.14 mmol) and NMM (0.24 g, 2.4 mmol) in DMF (5 mL) was added. The tube was shaken for 1 h at room temperature. The resin was then drained and rinsed with DMF (5 x 5 mL). Repeating the deprotection and coupling steps, peptide chain was elongated with Pro, DPro, After the completion of peptide elongation, the solution of Cbz-Osu (0.30 g, 1.2 mmol), NMM (0.24 g, 2.4 mmol) in DMF (5 mL) was added. The tube was shaken for 1 h, after sucking the solvent, the tube was then drained, and rinsed with DMF (5 x 5 mL). The resin was treated with a solution of TFA/H_2O/TIS (10 mL, 9.5/2.5/2.5, v/v/v) for 1 h, ice ether was added to the reaction mixture, the precipitate was centrifuged and dried to give the tetrapeptide as white foam (0.29 g, 80% yield).

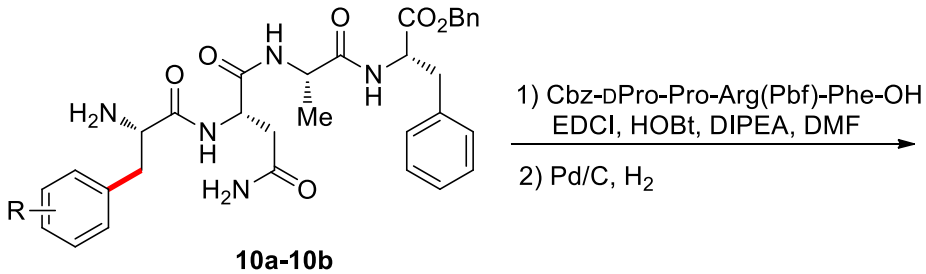
Deprotection of Phthaloyl group from arylated tetrapeptides



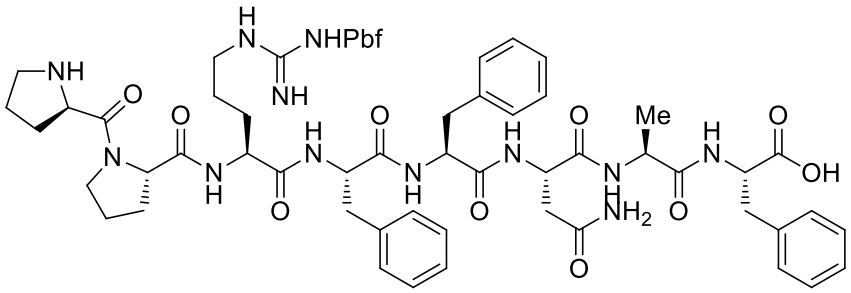
6hg-6hh **10a-10b**

Tetrapeptide **6** (0.15 mmol) was dissolved in a 1/1 mixture of CH_2Cl_2/EtOH (6.0 mL), ethylenediamine (45.1 mg, 0.75 mmol) was added dropwise. The solution was stirred at 40 °C for 4 h. After the solution was cooled to room temperature, then H_2O (15 mL) was added and the mixture was extracted with CH_2Cl_2 (3 x 15 mL). The organic phase was washed with H_2O (15 mL) and brine (15 mL), and concentrated *in vacuo*. The resulting residue was purified by column chromatography on silica gel (CH_2Cl_2/MeOH 20/1) yielding the corresponding tetrapeptides **10**.

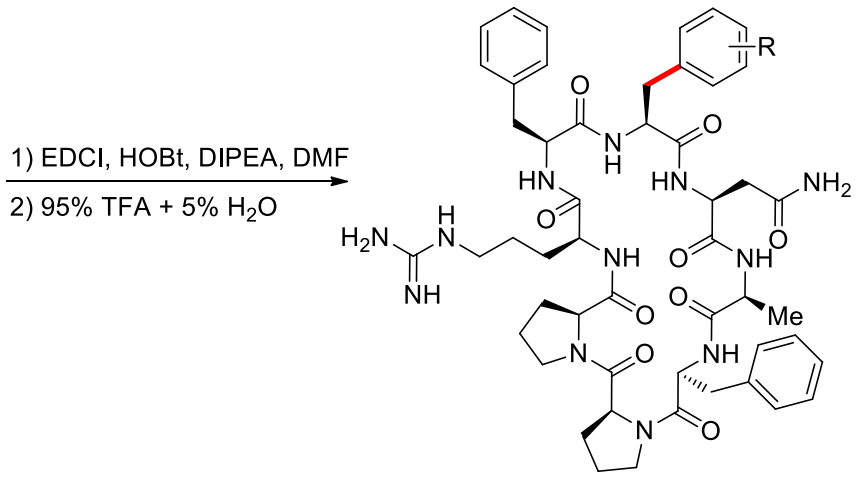
Synthesis of AGRP loop analogues 11a and 11b



10a-10b



DPro-Pro-Arg(Pbf)-Phe-R-Phe-Asn-Ala-Phe



c[Pro[1]-Arg[2]-Phe[3]-R-Phe[4]-Asn[5]-Ala[6]-Phe[7]-DPro[8]]

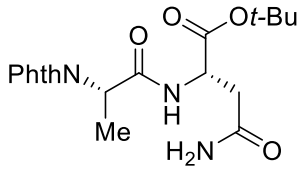
11a-11b

A solution of **10** (1.0 equiv.), Cbz-DPro-Pro-Arg(Pbf)-Phe-OH (1.0 equiv.), HOBt (2.0 equiv.), and DIPEA (2.0 equiv.) in DMF was cooled in an ice bath and subsequently treated with EDCI (1.2 equiv.). After 1 h at 0 °C, the mixture was warmed to room temperature for 15 h. Then, H_3PO_4 (5%) was added and the mixture was extracted with EtOAc. the organic phase was washed with water and brine, concentrated *in vacuo* to give the corresponding octapeptide. The octapeptide suspended in MeOH was treated with Pd/C (10%) and the reaction mixture was stirred for 12 h under hydrogen balloon at room temperature. The reaction mixture was then filtered through a pad of Celite, and the filtrate was concentrated *in vacuo* to give the solid. The solid was mixed with HOBt (2.0 equiv.), and DIPEA (2.0 equiv.) in DMF. The mixture was

cooled in an ice bath and subsequently treated with EDCI (1.2 equiv.). After 1h at 0 °C, the mixture was warmed to room temperature for 15 h. Then, H_3PO_4 (5%) was added and the mixture was extracted with EtOAc. the organic phase was washed with water and brine, concentrated *in vacuo* to give the corresponding cyclic octapeptide. The cyclic octapeptide was treated with a solution of TFA/H_2O (9.5/2.5, v/v) for 2 h, ice ether was added to the reaction mixture, the precipitate was centrifuged and dried to give the crude cyclic peptides **11a** and **11b**, the result residue was purified by RP-HPLC to yield the AGRP active loop analogues **11a** and **11b**.

Characterization Data of Starting Materials

tert-Butyl ((*S*)-2-(1,3-dioxoisoindolin-2-yl)propanoyl)-*L*-asparaginate (1)

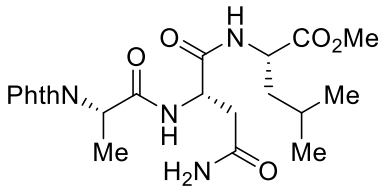


Following the general procedure for synthesis of dipeptide **1**.

White solid (6.22 g, 80% yield). M.p. = 200–201 °C.

^{1}H NMR (400 MHz, DMSO-d_6): δ = 8.35 (d, J = 8.0 Hz, 1H), 7.89–7.84 (m 4H), 7.31 (s, 1H), 6.88 (s, 1H), 4.74 (q, J = 7.2 Hz, 1H), 4.50–4.44 (m, 1H), 2.53 (dd, J = 15.6, 6.8 Hz, 1H), 2.32 (dd, J = 15.6, 6.4 Hz, 1H), 1.58 (d, J = 7.2 Hz, 3H), 1.37 (s, 9H). **^{13}C NMR** (100 MHz, DMSO-d_6): δ = 171.1, 170.2, 168.5, 167.4, 134.4, 131.8, 123.1, 80.5, 49.8, 48.2, 36.7, 27.6, 15.0. **MS** (ESI) *m*/*z*: 412 $[M+Na]^+$. **HR-MS** (ESI): *m*/*z* calcd for $C_{19}H_{23}N_3NaO_6$ $[M+Na]^+$ 412.1479, found 412.1476.

Methyl ((*S*)-2-(1,3-dioxoisoindolin-2-yl)propanoyl)-*L*-asparaginyl-*L*-leucinate (3a)



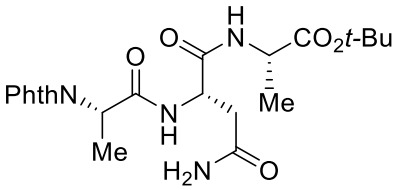
Following the general procedure for synthesis of tripeptide **3a**.

White solid (2.42 g, 75% yield). M.p. = 219–221 °C.

^{1}H NMR (400 MHz, DMSO-d_6): δ = 8.39 (d, J = 7.6 Hz, 1H), 7.84–7.91 (m, 5H), 7.20 (s, 1H), 6.85 (s, 1H), 4.75 (q, J = 7.2 Hz, 1H), 4.56–4.50 (m, 1H), 4.27–4.22 (m, 1H), 3.60 (s, 3H), 2.55 (dd, J = 15.6, 6.0 Hz, 1H), 2.34 (dd, J = 15.6, 7.6 Hz, 1H), 1.68–1.57 (m, 2H), 1.52 (d, J = 7.2 Hz, 3H), 1.48–1.45Ii (m 1H), 0.88 (d, J = 6.4 Hz, 3H), 0.83 (d, J = 6.4 Hz, 3H). **^{13}C NMR** (100 MHz, DMSO-d_6): δ = 172.8,

171.6, 170.8, 168.5, 167.5, 134.4, 131.8, 123.1, 51.8, 50.5, 49.8, 48.1, 36.5, 24.1, 22.8, 21.4, 14.9. **MS** (ESI) *m*/*z*: 483 $[M+Na]^+$. **HR-MS** (ESI): *m*/*z* calcd for $C_{22}H_{28}N_4NaO_7$ $[M+Na]^+$ 483.1850, found 483.1831.

tert-Butyl ((*S*)-2-(1,3-dioxoisoindolin-2-yl)propanoyl)-*L*-asparaginyl-*L*-alaninate (3b)

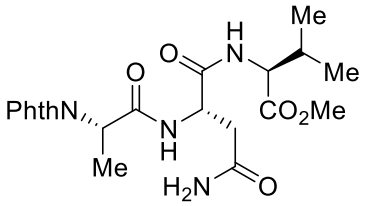


Following the general procedure for synthesis of tripeptide **3b**.

White solid (2.35 g, 73% yield). M.p. = 178–180 °C.

^{1}H NMR (400 MHz, $CDCl_3$): δ = 8.06 (d, *J* = 7.6 Hz, 1H), 7.83–7.81 (m, 2H), 7.72–7.70 (m, 2H), 7.58 (d, *J* = 7.2 Hz, 1H), 6.53 (s, 1H), 5.79 (s, 1H), 4.93 (q, *J* = 7.6 Hz, 1H), 4.77–4.72 (m, 1H), 4.31–4.24 (m, 1H), 2.95–2.86 (m, 1H), 2.53 (dd, *J* = 15.6, 6.0 Hz, 1H), 1.64 (d, *J* = 7.2 Hz, 3H), 1.43–1.38 (m, 12H). **^{13}C NMR** (100 MHz, $CDCl_3$): δ = 174.2, 171.6, 170.3, 169.3, 167.8, 134.3, 132.0, 123.6, 81.7, 50.1, 49.3, 48.8, 36.0, 28.0, 17.7, 15.2. **MS** (ESI) *m*/*z*: 483 $[M+Na]^+$. **HR-MS** (ESI): *m*/*z* calcd for $C_{22}H_{28}N_4NaO_7$ $[M+Na]^+$ 483.1850, found 483.1862.

Methyl ((*S*)-2-(1,3-dioxoisoindolin-2-yl)propanoyl)-*L*-asparaginyl-*L*-valinate (3c)

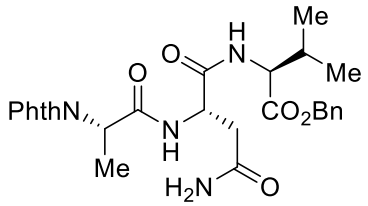


Following the general procedure for synthesis of tripeptide **3c**.

White solid (2.37 g, 76% yield). M.p. = 230–233 °C.

^{1}H NMR (400 MHz, DMSO-d_6): δ = 8.45 (d, *J* = 7.8 Hz, 1H), 7.89–7.84 (m, 5H), 7.26 (s, 1H), 6.90 (s, 1H), 4.74 (q, *J* = 7.2 Hz, 1H), 4.60–4.54 (m, 1H), 4.13 (dd, *J* = 8.0, 6.0 Hz, 1H), 3.62 (s, 3H), 2.56 (dd, *J* = 15.6, 6.4 Hz, 1H), 2.33 (dd, *J* = 15.6, 6.8 Hz, 1H), 2.10–2.02 (m, 1H), 1.53 (d, *J* = 7.6 Hz, 3H), 0.89–0.86 (m, 6H). **^{13}C NMR** (100 MHz, DMSO-d_6): δ = 171.8, 171.7, 171.0, 168.7, 167.5, 134.4, 131.8, 123.1, 57.6, 51.7, 49.7, 48.1, 36.5, 29.9, 18.9, 18.1, 15.0. **MS** (ESI) *m*/*z*: 469 $[M+Na]^+$. **HR-MS** (ESI): *m*/*z* calcd for $C_{21}H_{26}N_4NaO_7$ $[M+Na]^+$ 469.1694, found 469.1684.

Benzyl ((*S*)-2-(1,3-dioxoisoindolin-2-yl)propanoyl)-*L*-asparaginyl-*L*-valinate (3d)

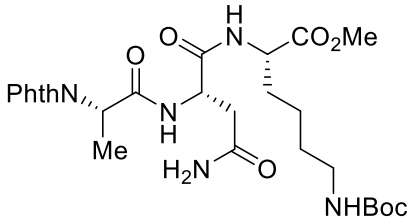


Following the general procedure for synthesis of tripeptide **3d**.

White solid (2.56 g, 70% yield). M.p. = 186–188 °C.

^{1}H NMR (400 MHz, DMSO-d_6): δ = 8.44 (d, J = 7.6 Hz, 1H), 7.90 (d, J = 8.0 Hz, 1H), 7.88–7.83 (m, 4H), 7.38–7.32 (m, 5H), 7.25 (s, 1H), 6.90 (s, 1H), 5.14 (d, J = 12.4 Hz, 1H), 5.10 (d, J = 12.4 Hz, 1H), 4.75 (dd, J = 14.4, 7.2 Hz, 1H), 4.62–4.56 (m, 1H), 4.19 (dd, J = 8.4, 6.4 Hz, 1H), 2.56 (dd, J = 15.6, 6.4 Hz, 1H), 2.35 (dd, J = 15.6, 7.2 Hz, 1H), 2.13–2.05 (m, 1H), 1.53 (d, J = 7.6 Hz, 3H), 0.86 (d, J = 6.8 Hz, 6H). **^{13}C NMR** (100 MHz, DMSO-d_6): δ = 171.7, 171.1, 171.0, 168.6, 167.4, 135.8, 134.4, 131.8, 128.4, 128.1, 128.0, 123.0, 65.9, 57.6, 49.7, 48.1, 36.6, 29.9, 18.9, 18.0, 14.9. **MS** (ESI) m/z: 545 $[M+Na]^+$. **HR-MS** (ESI): m/z calcd for $C_{27}H_{30}N_4NaO_7$ $[M+Na]^+$ 545.2007, found 545.2009.

Methyl N^6-(*tert*-butoxycarbonyl)-N^2-(((*S*)-2-(1,3-dioxoisoindolin-2-yl)propanoyl)-*L*-asparaginyl)-*L*-lysinate (3e)

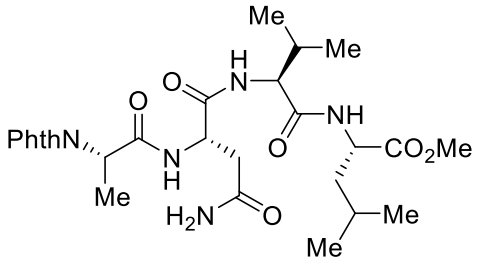


Following the general procedure for synthesis of tripeptide **3e**.

White solid (2.74 g, 68% yield). M.p. = 142–144 °C.

^{1}H NMR (400 MHz, DMSO-d_6): δ = 8.39 (d, J = 7.6 Hz, 1H), 7.94 (d, J = 7.2 Hz, 1H), 7.89–7.83 (m, 4H), 7.20 (s, 1H), 6.85 (s, 1H), 6.75 (t, J = 5.6 Hz, 1H), 4.76 (q, J = 7.2 Hz, 1H), 4.56–4.51 (m, 1H), 4.19–4.13 (m, 1H), 3.60 (s, 3H), 2.91–2.86 (m, 2H), 2.56–2.52 (m, 1H), 2.34 (dd, J = 15.2, 7.2 Hz, 1H), 1.74–1.59 (m, 2H), 1.52 (d, J = 7.2 Hz, 3H), 1.36–1.26 (m, 13H). **^{13}C NMR** (100 MHz, DMSO-d_6): δ = 172.4, 171.6, 170.9, 168.5, 167.5, 155.5, 134.4, 131.8, 123.1, 77.3, 52.2, 51.8, 49.8, 48.0, 36.6, 30.5, 29.1, 28.3, 22.6, 14.9. **MS** (ESI) m/z: 598 $[M+Na]^+$. **HR-MS** (ESI): m/z calcd for $C_{27}H_{37}N_5NaO_9$ $[M+Na]^+$ 598.2483, found 598.2481.

Methyl ((*S*)-2-(1,3-dioxoisoindolin-2-yl)propanoyl)-*L*-asparaginyl-*L*-valyl-*L*-leucinate (3f)

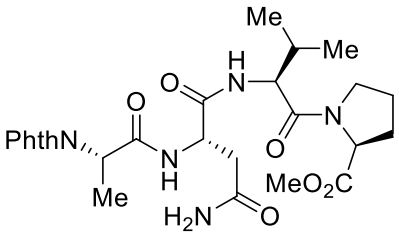


Following the general procedure for synthesis of tetrapeptide **3f**.

White solid (1.12 g, 40% yield over three steps). M.p. = 249–251 °C.

^{1}H NMR (400 MHz, DMSO-d_6): δ = 8.47 (d, J = 7.6 Hz, 1H), 8.28 (d, J = 7.2 Hz, 1H), 7.89–7.83 (m, 4H), 7.52 (d, J = 8.8 Hz, 1H), 7.28 (s, 1H), 6.86 (s, 1H), 4.74 (q, J = 7.2 Hz, 1H), 4.60–4.54 (m, 1H), 4.25–4.16 (m, 2H), 3.59 (s, 3H), 2.57 (dd, J = 15.6, 7.2 Hz, 1H), 2.31 (dd, J = 15.6, 6.4 Hz, 1H), 2.07–1.99 (m, 1H), 1.64–1.43 (m, 6H), 0.89–0.81 (m, 12H). **^{13}C NMR** (100 MHz, DMSO-d_6): δ = 172.8, 171.8, 170.9, 170.5, 168.7, 167.4, 134.4, 131.8, 123.1, 57.2, 51.7, 50.3, 49.9, 48.2, 36.5, 30.6, 24.2, 22.8, 21.3, 19.1, 17.6, 15.0. **MS** (ESI) *m*/*z*: 582 $[M+Na]^+$. **HR-MS** (ESI): *m*/*z* calcd for $C_{27}H_{37}N_5NaO_8$ $[M+Na]^+$ 582.2534, found 582.2525.

Methyl ((*S*)-2-(1,3-dioxoisoindolin-2-yl)propanoyl)-*L*-asparaginyl-*L*-valyl-*L*-prolinate (3g)

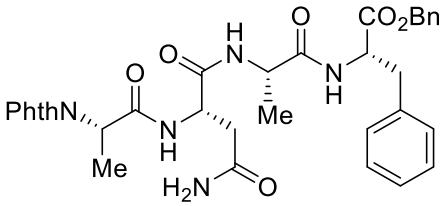


Following the general procedure for synthesis of tetrapeptide **3g**.

White solid (0.54 g, 20% yield over three steps). M.p. = 160–162 °C.

^{1}H NMR (400 MHz, DMSO-d_6): δ = 8.45 (d, J = 7.6 Hz, 1H), 7.89–7.84 (m, 4H), 7.59 (d, J = 8.4 Hz, 1H), 7.24 (s, 1H), 6.85 (s, 1H), 4.74 (q, J = 7.2 Hz, 1H), 4.55–4.49 (m, 1H), 4.32–4.28 (m, 2H), 3.78–3.72 (m, 1H), 3.61 (s, 3H), 3.59–3.54 (m, 1H), 2.57 (dd, J = 15.6, 6.8 Hz, 1H), 2.28 (dd, J = 15.6, 6.0 Hz, 1H), 2.20–2.12 (m, 1H), 2.02–1.95 (m 1H), 1.92–1.88 (m, 2H), 1.85–1.76 (m, 1H), 1.54 (d, J = 7.2 Hz, 3H), 0.91 (d, J = 6.4 Hz, 3H), 0.86 (d, J = 6.4 Hz, 3H). **^{13}C NMR** (100 MHz, DMSO-d_6): δ =172.2, 171.7, 170.4, 168.7, 167.4, 134.4, 131.8, 123.1, 58.4, 55.5, 51.7, 49.7, 48.1, 46.8, 36.3, 30.1, 28.6, 24.6, 18.9, 18.0, 14.9. **MS** (ESI) *m/z*: 566 $[M+Na]^+$. **HR-MS** (ESI) *m/z* calcd for $C_{26}H_{33}N_5NaO_8$ $[M+Na]^+$ 566.2221, found 566.2224.

Benzyl ((*S*)-2-(1,3-dioxoisoindolin-2-yl)propanoyl)-*L*-asparaginyl-*L*-alanyl-*L*-phenylalaninate (3h)



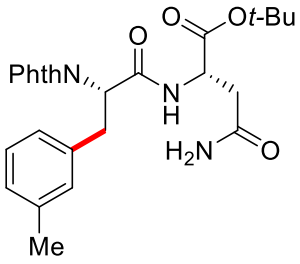
Following the general procedure for synthesis of tetrapeptide **3h**.

White solid (1.38 g, 43% yield over three steps). M.p. = 201–202 °C.

^{1}H NMR (400 MHz, DMSO-d_6): δ = 8.41 (d, J = 7.2 Hz, 2H), 7.92 (d, J = 7.6 Hz, 1H), 7.89–7.83 (m, 4H), 7.36–7.18 (m, 11H), 6.91 (s, 1H), 5.07–4.99 (m, 2H), 4.76 (q, J = 7.2 Hz, 1H), 4.56–4.50 (m, 1H), 4.48–4.42 (m, 1H), 4.27–4.20 (m, 1H), 3.06–2.96 (m, 2H), 2.56 (dd, J = 15.6, 7.6 Hz, 1H), 2.33 (dd, J = 15.6, 6.4 Hz, 1H), 1.52 (d, J = 7.2 Hz, 3H), 1.15 (d, J = 7.2 Hz, 3H). **^{13}C NMR** (100 MHz, DMSO-d_6): δ = 172.3, 171.9, 171.1, 170.3, 168.6, 167.5, 137.1, 135.8, 134.4, 131.8, 129.2, 128.4, 128.3, 128.0, 127.8, 126.5, 123.1, 65.9, 53.9, 49.9, 48.1, 36.8, 36.5, 17.9, 15.1. **MS** (ESI) m/z: 664 $[M+Na]^+$. **HR-MS** (ESI): m/z calcd for $C_{34}H_{35}N_5NaO_8$ $[M+Na]^+$ 664.2378, found 664.2358.

Characterization Data of Products 2a-2o

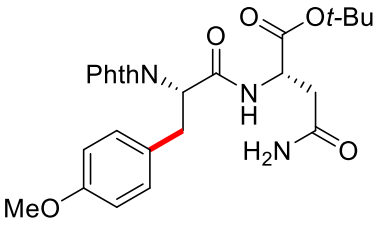
***tert*-Butyl ((*S*)-2-(1,3-dioxoisoindolin-2-yl)-3-(*m*-tolyl)propanoyl)-*L*-asparaginate (2a)**



The general procedure was followed using **1** (77.9 mg, 0.2 mmol) and 3-iodotoluene (87.2 mg, 0.4 mmol). After 12 h, purification by column chromatography on silica gel (*n*-hexane/EtOAc 1:3) yielded **2a** (69.0 mg, 72%) as a white solid. M.p. = 136–137 °C.

^{1}H NMR (400 MHz, DMSO-d_6): δ = 8.53 (d, J = 8.0 Hz, 1H), 7.83–7.78 (m, 4H), 7.33 (s, 1H), 7.02 (t, J = 7.2 Hz, 1H), 6.94 (s, 1H), 6.91–6.88 (m 3H), 4.97 (dd, J = 11.6, 4.8 Hz, 1H), 4.54–4.49 (m, 1H), 3.45 (dd, J = 14.0, 4.8 Hz, 1H), 3.39 (dd, J = 14.0, 11.4 Hz, 1H), 2.57–2.53 (m, 1H), 2.36 (dd, J = 15.2, 6.4 Hz, 1H), 2.10 (s, 3H), 1.39 (s, 9H). **^{13}C NMR** (100 MHz, DMSO-d_6): δ = 171.0, 170.1, 167.5, 167.4, 137.4, 137.2, 134.5, 131.2, 129.3, 128.1, 127.1, 125.6, 123.1, 80.6, 54.5, 49.8, 36.7, 33.7, 27.6, 20.8. **MS** (ESI) m/z: 502 $[M+Na]^+$. **HR-MS** (ESI): m/z calcd for $C_{26}H_{29}N_3NaO_6$ $[M+Na]^+$ 502.1949, found 502.1935.

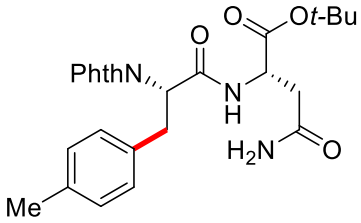
***tert*-Butyl ((*S*)-2-(1,3-dioxoisoindolin-2-yl)-3-(4-methoxyphenyl)propanoy)-*L*-asparaginate (2b)**



The general procedure was followed using **1** (77.9 mg, 0.2 mmol) and 4-iodoanisole (93.6 mg, 0.4 mmol). After 12 h, purification by column chromatography on silica gel (*n*-hexane/EtOAc 1:3) yielded **2b** (64.5 mg, 65%) as a white solid. M.p. = 139–142 °C.

^{1}H NMR (600 MHz, DMSO-d_6): δ = 8.51 (d, J = 7.8 Hz, 1H), 7.81–7.78 (m, 4H), 7.33 (s, 1H), 7.05 (d, J = 9.0 Hz, 2H), 6.89 (s, 1H), 6.71 (d, J = 9.0 Hz, 2H), 4.96 (dd, J = 12.0, 4.8 Hz, 1H), 4.53–4.50 (m, 1H), 3.61 (s, 3H), 3.43 (dd, J = 13.8, 4.8 Hz, 1H), 3.40–3.38 (m 1H), 2.54 (dd, J = 15.6, 6.6 Hz, 1H), 2.38 (dd, J = 15.6, 6.0 Hz, 1H), 1.39 (s, 9H). **^{13}C NMR** (150 MHz, DMSO-d_6): δ = 171.0, 170.1, 167.6, 167.5, 157.8, 134.6, 131.2, 129.6, 129.3, 123.1, 113.7, 80.6, 54.8, 54.7, 49.8, 36.7, 32.9, 27.6. **MS** (ESI) *m*/*z*: 496 $[M+H]^+$. **HR-MS** (ESI): *m*/*z* calcd for $C_{26}H_{30}N_3O_7$ $[M+H]^+$ 496.2078, found 496.2067.

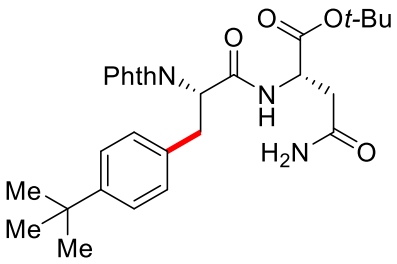
***tert*-Butyl ((*S*)-2-(1,3-dioxoisoindolin-2-yl)-3-(*p*-tolyl)propanoyl)-*L*-asparaginate (2c)**



The general procedure was followed using **1** (77.9 mg, 0.2 mmol) and 1-iodo-4-methylbenzene (87.2 mg, 0.4 mmol). After 12 h, purification by column chromatography on silica gel (*n*-hexane/EtOAc 1:3) yielded **2c** (61.4 mg, 64%) as a white solid. M.p. = 171–173 °C.

^{1}H NMR (600 MHz, DMSO-d_6): δ = 8.53 (d, J = 7.2 Hz, 1H), 7.81–7.79 (m, 4H), 7.33 (s, 1H), 7.02 (d, J = 7.8 Hz, 2H), 6.95 (d, J = 7.8 Hz, 2H), 6.90 (s, 1H), 5.01–4.97 (m, 1H), 4.54–4.50 (m, 1H), 3.47–3.38 (m, 2H), 2.56–2.53 (m, 1H), 2.40–2.37 (m, 1H), 2.14 (s, 3H), 1.39 (s, 9H). **^{13}C NMR** (150 MHz, DMSO-d_6): δ = 171.0, 170.1, 167.6, 167.4, 135.4, 134. 6, 134.4, 131.2, 128.9, 128.5, 123.1, 80.6, 54.6, 49.9, 36.7, 33.4, 27.6, 20.5. **MS** (ESI) *m*/*z*: 480 $[M+H]^+$. **HR-MS** (ESI): *m*/*z* calcd for $C_{26}H_{30}N_3O_6$ $[M+H]^+$ 480.2129, found 480.2104.

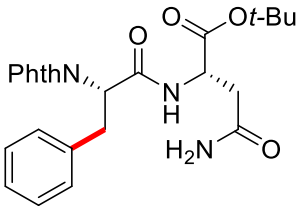
***tert*-Butyl ((S)-3-(4-(*tert*-butyl)phenyl)-2-(1,3-dioxoisoindolin-2-yl)propanoyl)-*L*-asparaginate (2d)**



The general procedure was followed using **1** (77.9 mg, 0.2 mmol) and 1-iodo-4-*tert*-butyl benzene (104.0 mg, 0.4 mmol). After 12 h, purification by column chromatography on silica gel (*n*-hexane/EtOAc 1:3) yielded **2d** (63. 6 mg, 61%) as a white solid. M.p. = 102–104 ℃.

^{1}H NMR (400 MHz, DMSO-d_6): δ = 8.52 (d, J = 8.0 Hz, 1H), 7.83–7.77 (m, 4H), 7.32 (s, 1H), 7.17 (d, J = 8.4 Hz, 2H), 7.07 (d, J = 8.0 Hz, 2H), 6.88 (s, 1H), 4.99 (dd, J = 9.6, 6.4 Hz, 1H), 4.54–4.49 (m, 1H), 3.45–3.43 (m, 2H), 2.55 (dd, J = 15.4, 6.8 Hz, 1H), 2.38 (dd, J = 15.4, 6.4 Hz, 1H), 1.39 (s, 9H), 1.15 (s, 9H). **^{13}C NMR** (100 MHz, DMSO-d_6): δ = 171.0, 170.1, 167.7, 167.5, 148.7, 134.5, 134.4, 131.2, 128.3, 124.9, 123.1, 80.6, 54.5, 49.9, 36.6, 34.0, 33.3, 31.0, 27.6. **MS** (ESI) *m*/*z*: 522 $[M+H]^+$. **HR-MS** (ESI): *m*/*z* calcd for $C_{29}H_{36}N_3O_6$ $[M+H]^+$ 522.2599, found 522.2582.

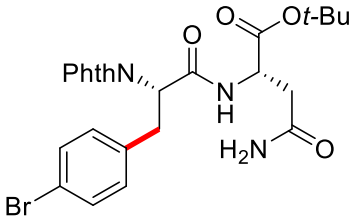
***tert*-Butyl ((*S*)-2-(1,3-dioxoisoindolin-2-yl)-3-phenylpropanoyl)-*L*-asparaginate (2e)**



The general procedure was followed using **1** (77.9 mg, 0.2 mmol) and 1-iodobenzene (81.6 mg, 0.4 mmol). After 12 h, purification by column chromatography on silica gel (*n*-hexane/EtOAc 1:3) yielded **2e** (68.0 mg, 73%) as a white solid. M.p. = 171–173 ℃.

^{1}H NMR (400 MHz, DMSO-d_6): δ = 8.54 (d, J = 8.0 Hz, 1H), 7.83–7.76(m, 4H), 7.33 (s, 1H), 7.17–7.12 (m, 4H), 7.10–7.05 (m, 1H), 6.90 (s, 1H), 5.01 (dd, J = 12.0, 4.8Hz, 1H), 4.55–4.50 (m, 1H), 3.51 (dd, J = 13.6, 4.4 Hz, 1H), 3.44–3.38 (m, 1H), 2.57–2.52 (m, 1H), 2.36 (dd, J = 15.6, 6.4 Hz, 1H), 1.39 (s, 9H). **^{13}C NMR** (100 MHz, DMSO-d_6): δ = 171.0, 170.1, 167.5, 167.4, 137.5, 134.5, 131.1, 128.6, 128.2, 126.5, 123.1, 80.6, 54.4, 49.8, 36.7, 33.8, 27.6. **MS** (ESI) *m*/*z*: 488 $[M+Na]^+$. **HR-MS** (ESI): *m*/*z* calcd for $C_{25}H_{27}N_3NaO_6$ $[M+Na]^+$ 488.1792, found 488.1769.

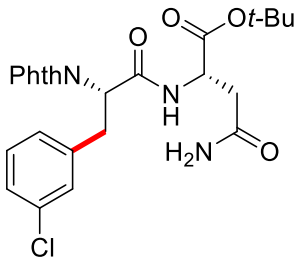
***tert*-Butyl ((*S*)-3-(4-bromophenyl)-2-(1,3-dioxoisoindolin-2-yl)propanoyl)-*L*-asparaginate (2f)**



The general procedure was followed using **1** (77.9 mg, 0.2 mmol) and 1-bromo-4-iodobenzene (113.2 mg, 0.4 mmol). After 12 h, purification by column chromatography on silica gel (*n*-hexane/EtOAc 1:3) yielded **2f** (69.7 mg, 64%) as a pale yellow solid. M.p. = 191–192 °C.

^{1}H NMR (400 MHz, DMSO-d_6): δ = 8.54 (d, J = 8.0 Hz, 1H), 7.83–7.80 (m, 4H), 7.36 (d, J = 8.4 Hz, 2H), 7.33 (s, 1H), 7.12 (d, J = 8.0 Hz, 2H), 6.90 (s, 1H), 5.00 (dd, J = 11.6, 4.8 Hz, 1H), 4.54–4.49 (m, 1H), 3.47 (dd, J = 14.0, 4.8 Hz, 1H), 3.42–3.38 (m, 1H), 2.56–2.52 (m, 1H), 2.36 (dd, J = 15.6, 6.4 Hz, 1H), 1.38 (s, 9H). **^{13}C NMR** (100 MHz, DMSO-d_6): δ = 171.0, 170.1, 167.4, 167.3, 137.1, 134.6, 131.2, 131.1, 131.0, 123.2, 119.6, 80.6, 54.2, 49.8, 36.7, 33.3, 27.6. **MS** (ESI) *m*/*z*: 566 $[M+Na]^+$. **HR-MS** (ESI): *m*/*z* calcd for $C_{25}H_{26}{}^{79}BrN_3NaO_6$ $[M+Na]^+$ 566.0897, found 566.0876.

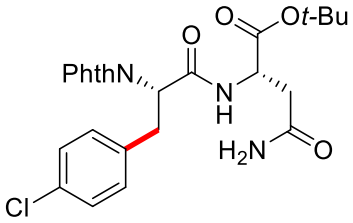
***tert*-Butyl ((*S*)-3-(3-chlorophenyl)-2-(1,3-dioxoisoindolin-2-yl)propanoyl)-*L*-asparaginate (2g)**



The general procedure was followed using **1** (77.9 mg, 0.2 mmol) and 1-chloro-3-iodobenzene (95.4 mg,0.4mmol). After 12 h, purification by column chromatography on silica gel (*n*-hexane/EtOAc 1:3) yielded **2g** (69.9 mg, 70%) as a pale yellow solid. M.p. = 136–138 °C.

^{1}H NMR (400 MHz, DMSO-d_6): δ = 8.53 (d, J = 8.0 Hz, 1H), 7.85–7.78 (m, 4H), 7.32 (s, 1H), 7.27 (s, 1H), 7.19–7.16 (m, 2H), 7.07 (d, J = 6.0 Hz, 1H), 6.88 (s, 1H), 5.03 (dd, J = 11.6, 4.4 Hz, 1H), 4.55–4.50 (m, 1H), 3.51 (dd, J = 14.0, 4.8 Hz, 1H), 3.44–3.38 (m, 1H), 2.56–2.52 (m, 1H), 2.36 (dd, J = 15.6, 6.0 Hz, 1H), 1.39 (s, 9H). **^{13}C NMR** (100 MHz, DMSO-d_6): δ = 170.9, 170.1, 167.4, 167.3, 140.2, 134.6, 132.8, 131.1, 130.0, 128.6, 127.4, 126.5, 123.1, 80.6, 54.2, 49.8, 36.7, 33.5, 27.6. **MS** (ESI) *m/z*: 500 $[M+H]^+$. **HR-MS** (ESI): *m/z* calcd for $C_{25}H_{27}{}^{35}ClN_3O_6$ $[M+H]^+$ 500.1583, found 500.1564.

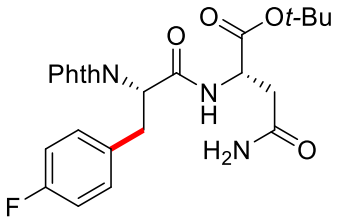
***tert*-Butyl ((*S*)-3-(4-chlorophenyl)-2-(1,3-dioxoisoindolin-2-yl)propanoyl)-*L*-asparaginate (2h)**



The general procedure was followed using **1** (77.9 mg, 0.2 mmol) and 1-chloro-4-iodobenzene (95.4 mg, 0.4 mmol). After 12 h, purification by column chromatography on silica gel (*n*-hexane/EtOAc 1:3) yielded **2h** (60.0 mg, 60%) as a pale yellow solid. M.p. = 176–178 °C.

^{1}H NMR (400 MHz, DMSO-d_6): δ = 8.53 (d, J = 7.6 Hz, 1H), 7.83–7.79 (m, 4H), 7.32 (s, 1H), 7.23–7.16 (m, 4H), 6.89 (s, 1H), 5.01 (dd, J = 11.6, 4.8 Hz, 1H), 4.54–4.49 (m, 1H), 3.49 (dd, J = 14.0, 4.8 Hz, 1H), 3.43–3.37 (m, 1H), 2.56–2.52 (m, 1H), 2.36 (dd, J = 15.6, 6.4 Hz, 1H), 1.39 (s, 9H). **^{13}C NMR** (100 MHz, DMSO-d_6): δ = 171.0, 170.1, 167.4, 167.3, 136.6, 134.6, 131.1, 130.6, 128.2, 123.2, 80.6, 54.2, 49.8, 36.7, 33.2, 27.6. **MS** (ESI) *m/z*: 522 $[M+Na]^+$. **HR-MS** (ESI): *m/z* calcd for $C_{25}H_{26}{}^{35}ClN_3NaO_6$ $[M+Na]^+$ 522.1402, found 522.1397.

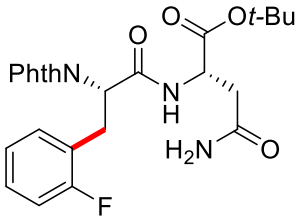
***tert*-Butyl ((*S*)-2-(1,3-dioxoisoindolin-2-yl)-3-(4-fluorophenyl)propanoyl)-*L*-asparaginate (2i)**



The general procedure was followed using **1** (77.9 mg, 0.2 mmol) and 1-fluoro-4-iodobenzene (88.8 mg, 0.4 mmol). After 12 h, purification by column chromatography on silica gel (*n*-hexane/EtOAc 1:3) yielded **2i** (59.0 mg, 61%) as a white solid. M.p. = 147–150 °C.

^{1}H NMR (400 MHz, DMSO-d_6): δ = 8.53 (d, J = 8.0Hz, 1H), 7.88–7.76 (m, 4H), 7.32 (s, 1H), 7.19–7.16 (m, 2H), 7.00–6.96 (m, 2H), 6.89 (s, 1H), 4.99 (dd, J = 12.0, 5.2 Hz, 1H), 4.55–4.50 (m, 1H), 3.49 (dd, J = 14.0, 4.8 Hz, 1H), 3.42–3.36 (m, 1H), 2.56–2.53 (m, 1H), 2.36 (dd, J = 15.6, 6.4 Hz, 1H), 1.39 (s, 9H). **^{13}C NMR** (100 MHz, DMSO-d_6): δ = 171.0, 170.1, 167.4, 160.9 (d, $^{1}J_{C\text{-}F}$ = 240.0 Hz), 134.6, 133.7 (d, $^{4}J_{C\text{-}F}$ = 3.0 Hz), 131.1, 130.6 (d, $^{3}J_{C\text{-}F}$ = 8.0 Hz), 123.1, 115.0 (d, $^{2}J_{C\text{-}F}$ = 21.0 Hz), 80.6, 54.4, 49.8, 36.7, 33.0, 27.6. **^{19}F NMR** (376 MHz, DMSO-d_6): δ = -116.26 – -116.28 (m). **MS** (ESI) *m/z*: 484 $[M+H]^+$. **HR-MS** (ESI): *m/z* calcd for $C_{25}H_{27}FN_3O_6$ $[M+H]^+$ 484.1878, found 484.1854.

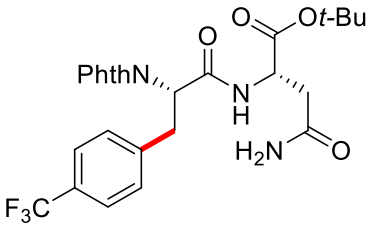
***tert*-butyl ((*S*)-2-(1,3-dioxoisoindolin-2-yl)-3-(2-fluorophenyl)propanoyl)-*L*-asparaginate (2j)**



The general procedure was followed using **1** (77.9 mg, 0.2 mmol) and 1-fluoro-2-iodobenzene (88.8 mg, 0.4 mmol). After 12 h, purification by column chromatography on silica gel (*n*-hexane/EtOAc 1:3) yielded **2j** (44.5 mg, 46%) as a white solid. M.p. = 198–200 °C.

^{1}H NMR (400 MHz, DMSO-d_6): δ = 8.54 (d, J = 7.6 Hz, 1H), 7.81–7.80 (m, 4H), 7.30 (s, 1H), 7.18–7.13 (m, 2H), 7.04–7.01 (m, 1H), 6.99–6.94 (m, 1H), 6.88 (s, 1H), 4.94 (dd, J = 12.0, 4.4 Hz, 1H), 4.57–4.52 (m, 1H), 3.52 (dd, J = 14.4, 4.4 Hz, 1H), 3.40–3.37 (m, 1H), 2.55–2.51 (m, 1H), 2.30 (dd, J = 15.6, 6.4 Hz, 1H), 1.39 (s, 9H). **^{13}C NMR** (100 MHz, DMSO-d_6): δ = 171.0, 170.2, 167.2, 167.1, 160.8 (d, $^{1}J_{C\text{-}F}$ = 242.0 Hz), 134.6, 131.3 (d, $^{4}J_{C\text{-}F}$ = 4.0 Hz), 131.3, 128.9 (d, $^{3}J_{C\text{-}F}$ = 8.0 Hz), 124.3 (d, $^{4}J_{C\text{-}F}$ = 4.0 Hz), 124.2 (d, $^{2}J_{C\text{-}F}$ = 15.0 Hz), 123.1, 115.1 (d, $J_{C\text{-}F}$ = 21.0 Hz), 80.7, 52.5, 49.9, 36.7, 27.7, 27.6. **^{19}F NMR** (376 MHz, DMSO-d_6): δ = -118.49 – -118.52 (m). **MS** (ESI) *m*/*z*: 506 $[M+Na]^+$. **HR-MS** (ESI): *m*/*z* calcd for $C_{25}H_{26}FN_3NaO_6$ $[M+Na]^+$ 506.1698, found 506.1701.

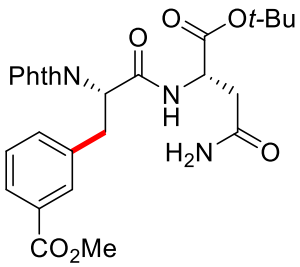
***tert*-Butyl ((*S*)-2-(1,3-dioxoisoindolin-2-yl)-3-(4-(trifluoromethyl)phenyl)propanoyl)-*L*-asparaginate (2k)**



The general procedure was followed using **1** (77.9 mg, 0.2 mmol) and 4-iodobenzotrifluoride (108.8 mg, 0.4 mmol). After 12 h, purification by column chromatography on silica gel (*n*-hexane/EtOAc 1:3) yielded **2k** (60.8 mg, 57%) as a white solid. M.p. = 124–126 °C.

^{1}H NMR (400 MHz, DMSO-d_6): δ = 8.57 (d, J = 8.0 Hz, 1H), 7.84–7.78 (m, 4H), 7.54 (d, J = 8.0 Hz, 2H), 7.40 (d, J = 8.0 Hz, 2H), 7.33 (s, 1H), 6.90 (s, 1H), 5.08 (dd, J = 11.6, 4.8 Hz, 1H), 4.55–4.50 (m, 1H), 3.61 (dd, J = 14.0, 4.8 Hz, 1H), 3.54–3.48 (m, 1H), 2.57–2.53 (m, 1H), 2.37 (dd, J = 15.6, 6.4 Hz, 1H), 1.39 (s, 9H). **^{13}C NMR** (100 MHz, DMSO-d_6): δ = 171.0, 170.1, 167.4, 167.3, 142.7, 134.7, 131.1, 129.6, 127.2 (q, $^{2}J_{C\text{-}F}$ = 40.0 Hz), 125.1 (q, $^{3}J_{C\text{-}F}$ = 3.0 Hz), 124.2 (q, $^{1}J_{C\text{-}F}$ = 270.0 Hz), 123.2, 80.6, 54.1, 49.9, 36.7, 33.8, 27.6. **^{19}F NMR** (376 MHz, DMSO-d_6): δ = -60.89 (s). **MS** (ESI) *m*/*z*: 534 $[M+H]^+$. **HR-MS** (ESI): *m*/*z* calcd for $C_{26}H_{27}F_3N_3O_6$ $[M+H]^+$ 534.1846, found 534.1817.

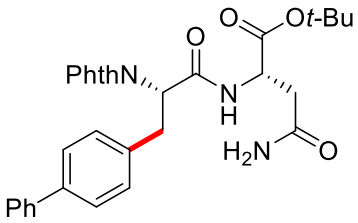
Methyl 3-((*S*)-3-(((*S*)-4-amino-1-(*tert*-butoxy)-1,4-dioxobutan-2-yl)amino)-2-(1,3-dioxoisoindolin-2-yl)-3-oxopropyl)benzoate (2l)



The general procedure was followed using **1** (77.9 mg, 0.2 mmol) and methyl 3-iodobenzoate (104.8 mg, 0.4 mmol). After 12 h, purification by column chromatography on silica gel (*n*-hexane/EtOAc 1:3) yielded 2**l** (74.3 mg, 71%) as a white solid. M.p. = 126–128 °C.

^{1}H NMR (400 MHz, DMSO-d_6): δ = 8.58 (d, J = 8.0 Hz, 1H), 7.86–7.74 (m, 5H), 7.69 (d, J = 8.0 Hz, 1H), 7.43 (d, J = 7.6 Hz, 1H), 7.33–7.32 (m, 2H), 6.89 (s, 1H), 5.03–5.01 (m, 1H), 4.55–4.50 (m, 1H), 3.75 (s, 3H), 3.58–3.46 (m, 2H), 2.57–2.53 (m, 1H), 2.38 (dd, J = 15.6, 6.4 Hz, 1H), 1.39 (s, 9H). **^{13}C NMR** (100 MHz, DMSO-d_6): δ = 170.9, 170.1, 167.5, 167.3, 165.9, 138.4, 134.6, 133.7, 131.1, 129.6, 129.4, 128.7, 127.4, 123.1, 80.6, 54.4, 52.0, 49.8, 36.7, 33.6, 27.6. **MS** (ESI) *m*/z: 546 $[M+Na]^+$. **HR-MS** (ESI): *m*/*z* calcd for $C_{27}H_{29}N_3NaO_8$ $[M+Na]^+$ 546.1847, found 546.1846.

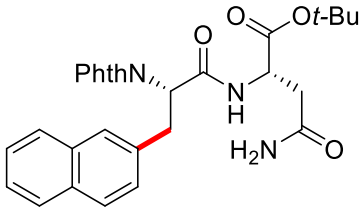
***tert*-Butyl ((*S*)-3-([1,1'-biphenyl]-4-yl)-2-(1,3-dioxoisoindolin-2-yl)propanoyl)-*L*-asparaginate (2m)**



The general procedure was followed using **1** (77.9 mg, 0.2 mmol) and 4-iodobiphenyl (112.0 mg, 0.4 mmol). After 12 h, purification by column chromatography on silica gel (*n*-hexane/EtOAc 1:3) yielded **2m** (68.2 mg, 63%) as a pale yellow solid. M.p. = 154–156 °C.

^{1}H NMR (400 MHz, DMSO-d_6): δ = 8.59 (d, J = 7.6 Hz, 1H), 7.83–7.78 (m, 4H), 7.56 (d, J = 7.6 Hz, 2H), 7.49 (d, J = 8.0 Hz, 2H), 7.41–7.35 (m, 3H), 7.31–7.24 (m, 3H), 6.93 (s, 1H), 5.07 (dd, J = 11.6, 5.6 Hz, 1H), 4.56–4.51 (m, 1H), 3.56–3.46 (m, 2H), 2.59–2.53 (m, 1H), 2.39 (dd, J = 15.6, 6.4 Hz, 1H), 1.40 (s, 9H). **^{13}C NMR** (100 MHz, DMSO-d_6): δ = 171.0, 170.2, 167.5, 167.5, 139.5, 138.1, 136.9, 134.6, 131.2, 129.3, 128.9, 127.3, 126.5, 126.4, 123.2, 80.6, 54.5, 49.9, 36.7, 33.5, 27.6. **MS** (ESI) *m*/*z*: 564 $[M+Na]^+$. **HR-MS** (ESI): *m*/*z* calcd for $C_{31}H_{31}N_3NaO_6$ $[M+Na]^+$ 564.2105, found 564.2099.

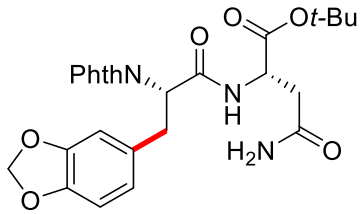
***tert*-Butyl ((*S*)-2-(1,3-dioxoisoindolin-2-yl)-3-(naphthalen-2-yl)propanoyl)-*L*-asparaginate (2n)**



The general procedure was followed using **1** (77.9 mg, 0.2 mmol) and 2-iodonaphthalene (101.6 mg, 0.4 mmol). After 12 h, purification by column chromatography on silica gel (*n*-hexane/EtOAc 1:3) yielded **2n** (66.0 mg, 64%) as a pale yellow solid. M.p. = 193–196 °C.

^{1}H NMR (400 MHz, DMSO-d_6): δ = 8.61 (d, J = 8.0 Hz, 1H), 7.78–7.72 (m, 6H), 7.69–7.67 (m, 1H), 7.61 (s, 1H), 7.40–7.36 (m, 4H), 6.93 (s, 1H), 5.14 (dd, J = 12.0, 4.8 Hz, 1H), 4.58–4.52 (m, 1H), 3.68 (dd, J = 14.0, 4.8 Hz, 1H), 3.59 (dd, J = 14.0, 12.0 Hz, 1H), 2.56 (dd, J = 15.6, 6.8 Hz, 1H), 2.39 (dd, J = 15.6, 6.4 Hz, 1H), 1.40 (s, 9H). **^{13}C NMR** (100 MHz, DMSO-d_6): δ = 171.0, 170.2, 167.5, 167.5, 135.3, 134.6, 132.9, 131.7, 131.1, 127.8, 127.4, 127.2, 127.2, 127.0, 126.1, 125.5, 123.1, 80.6, 54.4, 49.9, 36.7, 34.1, 27.6. **MS** (ESI) *m*/*z*: 516 $[M+H]^+$. **HR-MS** (ESI): *m*/*z* calcd for $C_{29}H_{30}N_3O_6$ $[M+H]^+$ 516.2129, found 516.2105.

***tert*-Butyl ((S)-3-(benzo[d][1,3]dioxol-5-yl)-2-(1,3-dioxoisoindolin-2-yl)propanoyl)-*L*-asparaginate (2o)**

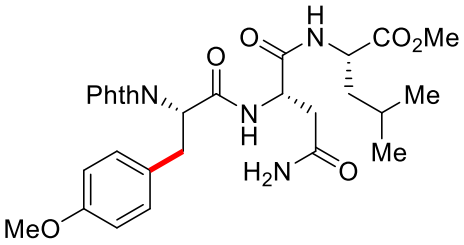


The general procedure was followed using **1** (77.9 mg, 0.2 mmol) and (mg, 0.4 mmol). After 12 h, purification by column chromatography on silica gel (*n*-hexane/EtOAc 1:3) yielded **2o** (69.2 mg, 68%) as a white solid. M.p. = 115–116 °C.

^{1}H NMR (400 MHz, DMSO-d_6): δ = 8.50 (d, J = 7.6 Hz, 1H), 7.85–7.79 (m, 4H), 7.33 (s, 1H), 6.90 (s, 1H), 6.80 (s, 1H), 6.65 (d, J = 8.0 Hz, 1H), 6.51 (d, J = 8.0 Hz, 1H), 5.88 (d, J = 8.0 Hz, 2H), 4.97 (dd, J = 11.6, 4.8 Hz, 1H), 4.54–4.49 (m, 1H), 3.41 (dd, J = 14.0, 5.2 Hz, 1H), 3.37–3.30 (m, 1H), 2.54 (dd, J = 15.6, 6.4 Hz, 1H), 2.37 (dd, J = 15.6, 6.4 Hz, 1H), 1.39 (s, 9H). **^{13}C NMR** (100 MHz, DMSO-d_6): δ = 171.0, 170.1, 167.5, 167.5, 147.1, 145.7, 134.6, 131.2, 131.2, 123.1, 121.7, 108.9, 108.0, 100.7, 80.6, 54.6, 49.8, 36.7, 33.5, 27.6. **MS** (ESI) *m*/*z*: 532 $[M+Na]^+$. **HR-MS** (ESI): *m*/*z* calcd for $C_{26}H_{27}N_3NaO_8$ $[M+Na]^+$ 532.1690, found 532.1689.

Characterization Data of Products 5aa-5ej and 6fa-6hk

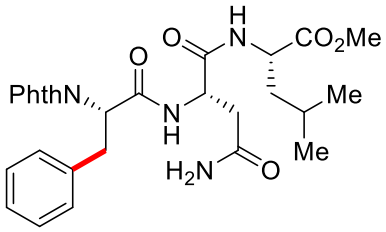
Methyl ((*S*)-2-(1,3-dioxoisoindolin-2-yl)-3-(4-methoxyphenyl)propanoyl)-*L*-asparaginyl-*L*-leucinate (5aa)



The general procedure was followed using **3a** (92.1 mg, 0.2 mmol) and **4a** (117.0 mg, 0.5 mmol). After 12 h, purification by column chromatography on silica gel (*n*-hexane/EtOAc 1:6) yielded **5aa** (69.1 mg, 61%) as a white solid. M.p. = 81–83 °C.

^{1}H NMR (400 MHz, DMSO-d_6): δ = 8.50 (d, J = 7.6 Hz, 1H), 7.98 (d, J = 7.6 Hz, 1H), 7.84–7.77 (m, 4H), 7.22 (s, 1H), 7.01 (d, J = 8.4 Hz, 2H), 6.87 (s, 1H), 6.71 (d, J = 8.4 Hz, 2H), 4.94 (dd, J = 12.0, 4.8 Hz, 1H), 4.60–4.55 (m , 1H), 4.29–4.23 (m, 1H), 3.61 (s, 3H), 3.61 (s, 3H), 3.42 (dd, J = 14.0, 4.4 Hz, 1H), 3.26 (dd, J = 14.0, 12.0 Hz, 1H), 2.57 (dd, J = 15.6, 6.0 Hz, 1H), 2.36 (dd, J = 15.6, 7.6 Hz, 1H), 1.70–1.58 (m, 2H), 1.52–1.46 (m, 1H), 0.90 (d, J = 6.4 Hz, 3H), 0.84 (d, J = 6.4 Hz, 3H). **^{13}C NMR** (100 MHz, DMSO-d_6): δ = 172.8, 171.5, 170.9, 167.7 167.5 157.8, 134.5, 131.2, 129.7, 129.2, 123.1, 113.7, 54.8, 54.5, 51.8, 50.5, 49.8, 36.6, 33.1, 24.1, 22.8, 21.4. **MS** (ESI) *m*/*z*: 589 $[M+Na]^+$. **HR-MS** (ESI): *m*/*z* calcd for $C_{29}H_{34}N_4NaO_8$ $[M+Na]^+$ 589.2269, found 589.2247.

Methyl ((*S*)-2-(1,3-dioxoisoindolin-2-yl)-3-phenylpropanoyl)-*L*-asparaginyl-*L*-leucinate (5ab)

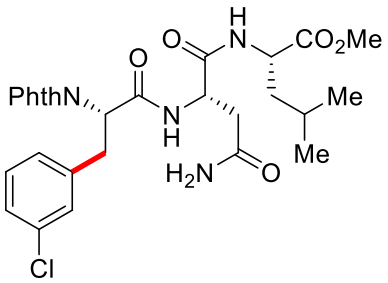


The general procedure was followed using **3a** (92.1 mg, 0.2 mmol) and **4b** (102.0 mg, 0.5 mmol). After 12 h, purification by column chromatography on silica gel (*n*-hexane/EtOAc 1:6) yielded **5ab** (64.4 mg, 60%) as a white solid. M.p. = 104–107 °C.

^{1}H NMR (400 MHz, DMSO-d_6): δ = 8.54 (d, J = 7.6 Hz, 1H), 8.01 (d, J = 7.6 Hz, 1H), 7.83–7.76 (m , 4H), 7.23 (s, 1H), 7.16–7.06 (m, 5H), 6.89 (s, 1H), 5.00 (dd, J = 12.0, 4.8 Hz, 1H), 4.61–4.55 (m, 1H), 4.28–4.23 (m, 1H), 3.61 (s, 3H), 3.50 (dd, J = 14.0, 4.8 Hz, 1H), 3.33–3.27 (m, 1H), 2.58 (dd, J = 15.6, 5.6 Hz, 1H), 2.36 (dd, J = 15.6, 7.6 Hz, 1H), 1.70–1.59 (m, 2H), 1.53–1.46 (m, 1H), 0.90 (d, J = 6.4 Hz, 3H), 0.84 (d, J = 6.0 Hz, 3H). **^{13}C NMR** (100 MHz, DMSO-d_6): δ = 172.8, 171.5, 170.9, 167.6, 167.5, 137.5, 134.5, 131.2, 128.7, 128.3, 126.5, 123.1, 54.3, 51.9, 50.5, 49.8, 36.6, 34.0, 24.1, 22.8, 21.4.

MS (ESI) *m*/*z*: 559 $[M+Na]^+$. **HR-MS** (ESI): *m*/*z* calcd for $C_{28}H_{32}N_4NaO_7$ $[M+Na]^+$ 559.2163, found 559.2140.

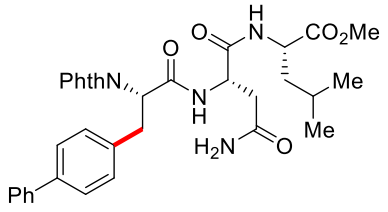
Methyl ((*S*)-3-(3-chlorophenyl)-2-(1,3-dioxoisoindolin-2-yl)propanoyl)-*L*-asparaginyl-*L*-leucinate (5ac)



The general procedure was followed using **3a** (92.1 mg, 0.2 mmol) and **4c** (119.2 mg, 0.5 mmol). After 12 h, purification by column chromatography on silica gel (*n*-hexane/EtOAc 1:6) yielded **5ac** (58.2 mg, 51%) as a pale yellow solid. M.p. = 168–170 °C.

^{1}H NMR (400 MHz, DMSO-d_6): δ = 8.52 (d, *J* = 7.6 Hz, 1H), 8.01 (d, *J* = 7.2 Hz, 1H), 7.86–7.78 (m, 4H), 7.22–7.16 (m, 4H), 7.04 (d, *J* = 3.6 Hz, 1H), 6.87 (s, 1H), 5.01 (dd, *J* = 12, 4.8 Hz, 1H), 4.61–4.55 (m, 1H), 4.28–4.23 (m, 1H), 3.61 (s, 3H), 3.50 (dd, *J* = 14.4, 4.8 Hz, 1H), 3.31–3.27 (m, 1H), 2.57 (dd, *J* = 15.6, 6.0 Hz, 1H), 2.35 (dd, *J* = 15.6, 7.2 Hz, 1H), 1.70–1.58 (m, 2H), 1.53–1.46 (m 1H), 0.90 (d, *J* = 6.0 Hz, 3H), 0.84 (d, *J* = 6.4 Hz, 3H).**^{13}C NMR** (100 MHz, DMSO-d_6): δ = 172.8, 171.4, 170.8, 167.4, 167.3, 140.2, 134.6, 132.8, 131.2, 130.1, 128.6, 127.5, 126.5, 123.1, 54.0, 51.8, 50.5, 49.8, 36.7, 33.7, 24.1, 22.8, 21.4. **MS** (ESI) *m*/*z*: 593 $[M+Na]^+$. **HR-MS** (ESI): *m*/*z* calcd for $C_{28}H_{31}{}^{35}ClN_4NaO_7$ $[M+Na]^+$ 593.1773, found 593.1751.

Methyl ((*S*)-3-([1,1'-biphenyl]-4-yl)-2-(1,3-dioxoisoindolin-2-yl)propanoyl)-*L*-asparaginyl-*L*-leucinate (5ad)

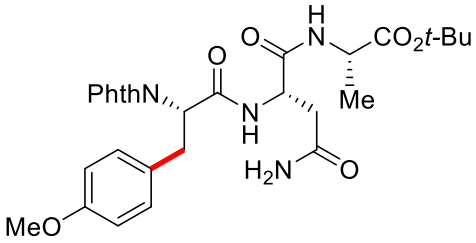


The general procedure was followed using **3a** (92.1 mg, 0.2 mmol) and **4d** (140.1 mg, 0.5 mmol). After 12 h, purification by column chromatography on silica gel (*n*-hexane/EtOAc 1:6) yielded **5ad** (73.5 mg, 60%) as a white solid. M.p. = 109–112 °C.

^{1}H NMR (400 MHz, DMSO-d_6): δ = 8.56 (d, *J* = 8.0 Hz, 1H), 8.02 (d, *J* = 7.6 Hz, 1H), 7.84–7.77 (m, 4H), 7.55 (d, *J* = 8.0 Hz, 2H), 7.48 (d, *J* = 8.0 Hz, 2H), 7.39 (t, *J* = 7.6 Hz, 2H), 7.30 (t, *J* = 7.6 Hz, 1H), 7.24–7.20 (m, 3H), 6.89 (s, 1H), 5.05 (dd, *J* = 11.6, 4.8 Hz, 1H), 4.63–4.58 (m, 1H), 4.30–4.24 (m, 1H), 3.61 (s, 3H), 3.54 (dd, *J* = 13.6, 4.4 Hz, 1H), 3.42–3.36 (m, 1H), 2.59 (dd, *J* = 15.6, 6.0 Hz, 1H), 2.38

(dd, *J* = 15.6, 7.6 Hz, 1H), 1.70–1.60 (m, 2H), 1.54–1.47 (m 1H), 0.91 (d, *J* = 6.4 Hz, 3H), 0.82 (d, *J* = 6.4 Hz, 3H). **^{13}C NMR** (100 MHz, DMSO-d_6): δ = 172.8, 171.5, 170.9, 167.6, 167.5, 139.5, 138.1, 136.9, 134.6, 131.2, 129.3, 128.8, 127.3, 126.4, 126.3, 123.1, 54.3, 51.8, 50.5, 49.8, 36.7, 33.6, 24.1, 22.8, 21.4. **MS** (ESI) *m/z*: 635 $[M+Na]^+$. **HR-MS** (ESI): *m/z* calcd for $C_{34}H_{36}N_4NaO_7$ $[M+Na]^+$ 635.2476, found 635.2494.

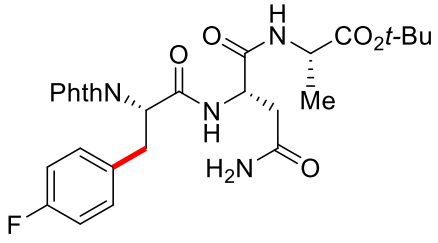
***tert*-Butyl ((*S*)-2-(1,3-dioxoisoindolin-2-yl)-3-(4-methoxyphenyl)propanoyl)-*L*-asparaginyl-*L*-alaninate (5ba)**



The general procedure was followed using **3b** (92.1 mg, 0.2 mmol) and **4a**(117.0 mg, 0.5 mmol). After 12 h, purification by column chromatography on silica gel (*n*-hexane/EtOAc 1:6) yielded **5ba** (70.3 mg, 62%) as a white solid. M.p. = 192–193 °C.

^{1}H NMR (400 MHz, DMSO-d_6): δ = 8.46 (d, *J* = 8.0 Hz, 1H), 8.04 (d, *J* = 7.2 Hz, 1H), 7.84–7.77 (m, 4H), 7.20 (s, 1H), 7.02 (d, *J* = 8.0 Hz, 2H), 6.88 (s, 1H), 6.70 (d, *J* = 8.0 Hz, 2H), 4.95 (dd, *J* = 12.0, 4.8 Hz, 1H), 4.64–4.59 (m, 1H), 4.13–4.06 (m, 1H), 3.61 (s, 3H), 3.43 (dd, *J* = 14.0, 4.4 Hz, 1H), 3.30–3.24 (m, 1H), 2.57–2.53 (m, 1H), 2.38 (dd, *J* = 15.6, 8.0 Hz, 1H), 1.38 (s, 9H), 1.27 (d, *J* = 7.2 Hz, 3H). **^{13}C NMR** (100 MHz, DMSO-d_6): δ = 171.6, 171.4, 170.7, 167.6, 167.5, 157.8, 134.5, 131.2, 129.7, 129.3, 123.1, 113.7, 80.4, 54.8, 54.5, 49.6, 48.5, 37.0, 33.1, 27.6, 16.9. **MS** (ESI) *m/z*: 589 $[M+Na]^+$. **HR-MS** (ESI): *m/z* calcd for $C_{29}H_{34}N_4NaO_8$ $[M+Na]^+$ 589.2269, found 589.2240.

***tert*-Butyl ((*S*)-2-(1,3-dioxoisoindolin-2-yl)-3-(4-fluorophenyl)propanoyl)-*L*-asparaginyl-*L*-alaninate (5be)**

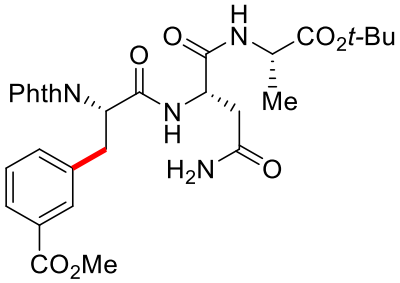


The general procedure was followed using **3b** (92.1 mg, 0.2 mmol) and **4e** (111.0 mg, 0.5 mmol). After 12 h, purification by column chromatography on silica gel (*n*-hexane/EtOAc 1:6) yielded **5be** (64.3 mg, 58%) as a white solid. M.p. = 195–198 °C.

^{1}H NMR (400 MHz, DMSO-d_6): δ = 8.48 (d, *J* = 8.0 Hz, 1H), 8.05 (d, *J* = 6.8 Hz, 1H), 7.85–7.76 (m, 4H), 7.19–7.13 (m, 3H), 6.97 (t, *J* = 8.4 Hz, 2H), 6.88 (s, 1H), 4.98 (dd, *J* = 11.6, 4.8 Hz, 1H), 4.65–

4.59 (m, 1H), 4.13–4.06 (m, 1H), 3.49 (dd, *J* = 14.4, 4.8 Hz, 1H), 3.30–3.26 (m, 1H), 2.57–2.53 (m, 1H), 2.37 (dd, *J* = 15.6, 7.6 Hz, 1H), 1.38 (s, 9H), 1.27 (d, *J* = 7.2 Hz, 3H). **^{13}C NMR** (100 MHz, DMSO-d_6): δ = 171.6, 171.4, 170.6, 167.4, 167.4, 160.9 (d, $^{1}J_{C\text{-}F}$ = 240 Hz), 134.5, 133.7 (d, $^{4}J_{C\text{-}F}$ = 4.0 Hz), 131.2, 130.6 (d, $^{3}J_{C\text{-}F}$ = 8.0 Hz), 123.1, 115.0 (d, $^{2}J_{C\text{-}F}$ = 20.0 Hz), 80.4, 54.3, 49.6, 48.5, 37.0, 33.2, 27.6, 16.9. **^{19}F NMR** (376 MHz, DMSO-d_6): δ = -116.38 – -116.40 (m). **MS** (ESI) *m/z*: 577 $[M+Na]^+$. **HR-MS** (ESI): *m/z* calcd for $C_{28}H_{31}FN_4NaO_7$ $[M+Na]^+$ 577.2069, found 577.2079.

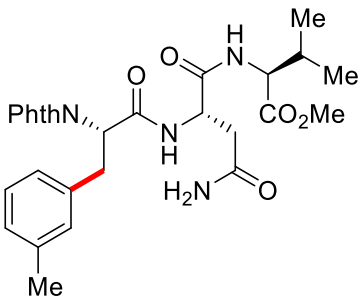
Methyl 3-((*S*)-3-(((*S*)-4-amino-1-(((*S*)-1-(*tert*-butoxy)-1-oxopropan-2-yl)amino)-1,4-dioxobutan-2-yl)amino)-2-(1,3-dioxoisoindolin-2-yl)-3-oxopropyl)benzoate (5bf)



The general procedure was followed using **3b** (92.1 mg, 0.2 mmol) and **4f** (131.0 mg, 0.5 mmol). After 12h, purification by column chromatography on silica gel (*n*-hexane/EtOAc 1:6) yielded **5bf** (72.5 mg, 61%) as a white solid. M.p. = 197–198 °C.

^{1}H NMR (400 MHz, DMSO-d_6): δ = 8.51 (d, *J* = 8.0 Hz, 1H), 8.06 (d, *J* = 6.8 Hz, 1H), 7.83–7.77 (m, 4H), 7.75 (s, 1H), 7.69 (d, *J* = 8.0 Hz, 1H), 7.40 (d, *J* = 8.0 Hz, 1H), 7.32–7.29 (m, 1H), 7.20 (s, 1H), 6.88 (s, 1H), 5.01 (dd, *J* = 12.0, 4.8 Hz, 1H), 4.65–4.60 (m, 1H), 4.14–4.06 (m, 1H), 3.74 (s, 3H), 3.56 (dd, *J* = 14.0, 4.4 Hz, 1H), 3.42–3.35 (m, 1H), 2.54 (dd, *J* = 15.6, 5.6 Hz, 1H), 2.36 (dd, *J* = 15.6, 7.6 Hz, 1H), 1.38 (s, 9H), 1.27 (d, *J* = 7.2 Hz, 3H). **^{13}C NMR** (100 MHz, DMSO-d_6): δ = 171.6, 171.4, 170.6, 167.5, 167.3, 165.9, 138.4, 134.5, 133.8, 131.2, 129.6, 129.5, 128.8, 127.4, 123.1, 80.4, 54.3, 52.0, 49.7, 48.5, 37.0, 33.8, 27.6, 16.9. **MS** (ESI) *m/z*: 617 $[M+Na]^+$. **HR-MS** (ESI): *m/z* calcd for $C_{30}H_{34}N_4NaO_9$ $[M+Na]^+$ 617.2218, found 617.2227.

Methyl ((*S*)-2-(1,3-dioxoisoindolin-2-yl)-3-(*m*-tolyl)propanoyl)-*L*-asparaginyl-*L*-valinate (5cg)

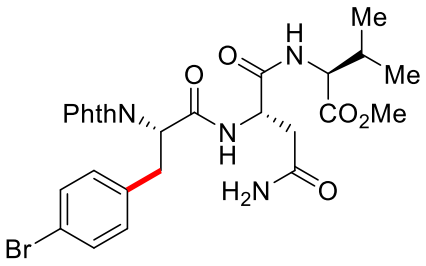


The general procedure was followed using **3c** (89.3 mg, 0.2 mmol) and **4g** (109.0 mg, 0.5 mmol). After

12 h, purification by column chromatography on silica gel (*n*-hexane/EtOAc 1:6) yielded **5cg** (55.8 mg, 52%) as a white solid. M.p. = 174–176 °C.

^{1}H NMR (400 MHz, DMSO-d_6): δ = 8.56 (d, J = 7.6 Hz, 1H), 7.92 (d, J = 8.0 Hz, 1H), 7.85–7.77 (m, 4H), 7.28 (s, 1H), 7.01 (dd, J = 7.2, 7.2 Hz, 1H), 6.91–6.86 (m, 4H), 4.96 (dd, J = 11.6, 4.4 Hz, 1H), 4.65–4.60 (m, 1H), 4.15 (dd, J = 8.0, 6.0 Hz, 1H), 3.62 (s, 3H), 3.45 (dd, J = 14.0, 4.4 Hz, 1H), 3.32–3.25 (m, 1H), 2.59 (dd, J = 15.6, 6.4 Hz, 1H), 2.37 (dd, J = 15.6, 7.2 Hz, 1H), 2.09 (s, 3H), 2.06–2.03 (m, 1H), 0.89 (t, J = 6.4 Hz, 6H). **^{13}C NMR** (100 MHz, DMSO-d_6): δ = 171.8, 171.6, 171., 167.7, 167.5, 137.4, 137.2, 134.5, 131.3, 129.4, 128.1, 127.1, 125.7, 123.1, 57.6, 54.4, 51.7, 49.7, 36.6, 33.8, 29.9, 20.8, 18.9, 18.1. **MS** (ESI) *m*/*z*: 559 $[M+Na]^+$. **HR-MS** (ESI): *m*/*z* calcd for $C_{28}H_{32}N_4NaO_7$ $[M+Na]^+$ 559.2163, found 559.2181.

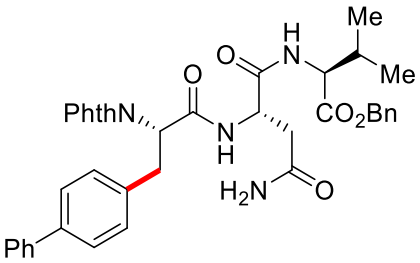
Methyl ((*S*)-3-(4-bromophenyl)-2-(1,3-dioxoisoindolin-2-yl)propanoyl)-*L*-asparaginyl-*L*-valinate (5ch)



The general procedure was followed using **3c** (89.3 mg, 0.2 mmol) and **4h** (141.5 mg, 0.5 mmol). After 12 h, purification by column chromatography on silica gel (*n*-hexane/EtOAc 1:6) yielded **5ch** (74.6 mg, 62%) as a pale yellow solid. M.p. = 99–101 °C.

^{1}H NMR (400 MHz, DMSO-d_6): δ = 8.56 (d, J = 7.6 Hz, 1H), 7.93 (d, J = 8.4 Hz, 1H), 7.83–7.79 (m, 4H), 7.35 (d, J = 8.4 Hz, 2H), 7.26 (s, 1H), 7.09 (d, J = 8.0 Hz, 2H), 6.91 (s, 1H), 4.99 (dd, J = 11.2, 4.0 Hz, 1H), 4.65–4.60 (m, 1H), 4.15–4.12 (m, 1H), 3.62 (s, 3H), 3.48 (dd, J = 14.0, 4.8 Hz, 1H), 3.30–3.27 (m, 1H), 2.57 (dd, J = 15.6, 6.4 Hz, 1H), 2.36 (dd, J = 15.6, 7.2Hz, 1H), 2.11–2.03 (m, 1H), 0..90–0.87 (m, 6H). **^{13}C NMR** (100 MHz, DMSO-d_6): δ = 171.8, 171.6, 170.9, 167.4, 167.4, 137.0, 134.6, 131.2, 131.0, 123.2, 119.6, 57.6, 54.1, 51.7, 49.7, 36.7, 33.4, 29.8, 18.9, 18.1. **MS** (ESI) *m*/*z*: 623$[M+Na]^+$. **HR-MS** (ESI): *m*/*z* calcd for $C_{27}H_{29}{}^{79}BrN_4NaO_7$ $[M+Na]^+$ 623.1112, found 623.1119.

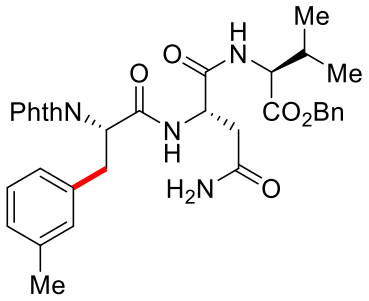
Benzyl ((*S*)-3-([1,1'-biphenyl]-4-yl)-2-(1,3-dioxoisoindolin-2-yl)propanoyl)-*L*-asparaginyl-*L*-valinate (5dd)



The general procedure was followed using **3d** (104.5 mg, 0.2 mmol) and **4d** (140.1 mg, 0.5 mmol). After 12 h, purification by column chromatography on silica gel (*n*-hexane/EtOAc 1:6) yielded **5dd** (67.5 mg, 50%) as a pale yellow solid. M.p. = 96–98 °C.

^{1}H NMR (400 MHz, DMSO-d_6): δ = 8.60 (d, J = 7.6 Hz, 1H), 8.03 (d, J = 8.0 Hz, 1H), 7.82–7.77 (m, 4H), 7.56–7.54 (m, 2H), 7.48 (d, J = 8.4 Hz, 2H), 7.41–7.35 (m, 6H), 7.34–7.28 (m, 3H), 7.22 (d, J = 8.0 Hz, 2H), 6.93 (s, 1H), 5.16–5.09 (m, 2H), 5.05 (dd, J = 11.6, 4.8 Hz, 1H), 4.69–4.64 (m, 1H), 4.21 (dd, J = 8.0, 6.0 Hz, 1H), 3.55 (dd, J = 14.0, 4.8 Hz, 1H), 3.41 (dd, J = 14.0, 11.6 Hz, 1H), 2.59 (dd, J = 15.6, 6.4 Hz, 1H), 2.38 (dd, J = 15.6, 7.2 Hz, 1H), 2.15–2.07 (m, 1H), 0.89–0.87 (m, 6H). **^{13}C NMR** (100 MHz, DMSO-d_6): δ = 171.6, 171.1, 171.0, 167.7, 167.5, 139.5, 138.1, 136.8, 135.8, 134.6, 131.2, 129.3, 128.8, 128.4, 128.1, 128.0, 127.3, 126.4, 126.4, 123.1, 65.9, 57.7, 54.3, 49.7, 36.7, 33.6, 29.9, 18.9, 18.1. **MS** (ESI) *m*/*z*: 697 $[M+Na]^+$. **HR-MS** (ESI): *m*/*z* calcd for $C_{39}H_{38}N_4NaO_7$ $[M+Na]^+$ 697.2633, found 697.2616.

Benzyl ((*S*)-2-(1,3-dioxoisoindolin-2-yl)-3-(*m*-tolyl)propanoyl)-*L*-asparaginyl-*L*-valinate (5dg)

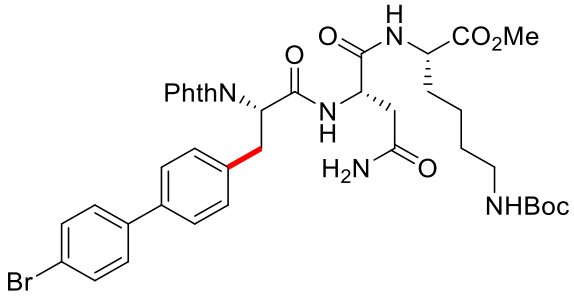


The general procedure was followed using **3d** (104.5 mg, 0.2 mmol) and **4g** (109.0 mg, 0.5 mmol). After 12 h, purification by column chromatography on silica gel (*n*-hexane/EtOAc 1:6) yielded **5dg** (64.9 mg, 53%) as a white solid. M.p. = 101–103 °C.

^{1}H NMR (400 MHz, DMSO-d_6): δ = 8.57 (d, J = 8.0 Hz, 1H), 8.00 (d, J = 8.0 Hz, 1H), 7.84–7.76 (m, 4H), 7.37–7.31 (m, 5H), 7.27 (s, 1H), 7.01 (dd, J = 7.2, 7.2 Hz, 1H), 6.92–6.86 (m, 4H), 5.16–5.09 (m, 2H), 4.96 (dd, J = 12.0, 4.8 Hz, 1H), 4.67–4.61 (m, 1H), 4.20 (dd, J = 8.0, 8.0 Hz, 1H), 3.45 (dd, J = 14.0, 4.4 Hz, 1H), 3.31–3.25 (m, 1H), 2.58 (dd, J = 15.6, 6.0 Hz, 1H), 2.37 (dd, J = 15.6, 7.2 Hz, 1H), 2.15–2.08 (m, 4H), 0.88 (d, J = 6.4 Hz, 6H). **^{13}C NMR** (100 MHz, DMSO-d_6): δ = 171.6, 171.1, 171.0,

167.7, 167.5, 137.4, 137.2, 135.8, 134.5, 131.3, 129.4, 128.4, 128.1, 128.1, 128.0, 127.1, 125.7, 123.1, 65.9, 57.6, 54.4, 49.7, 36.7, 33.8, 29.9, 20.8, 18.9, 18.1. **MS** (ESI) *m*/*z*: 635 $[M+Na]^+$. **HR-MS** (ESI): *m*/*z* calcd for $C_{34}H_{36}N_4NaO_7$ $[M+Na]^+$ 635.2476, found 635.2498.

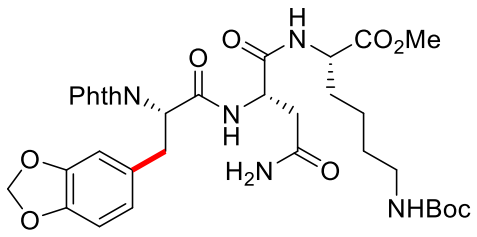
Methyl N^2-(((*S*)-3-(4'-bromo-[1,1'-biphenyl]-4-yl)-2-(1,3-dioxoisoindolin-2-yl)propanoyl)-*L*-asparaginyl)-N^6-(*tert*-butoxycarbonyl)-*L*-lysinate (5ei)



The general procedure was followed using **3e** (115.1mg, 0.2 mmol) and **4i** (179.5 mg, 0.5 mmol). After 12 h, purification by column chromatography on silica gel (*n*-hexane/EtOAc 1:6) yielded **5ei** (82.3 mg, 51%) as yellow solid. M.p. = 121–123 °C.

^{1}H NMR (400 MHz, DMSO-d_6): δ = 8.54 (d, *J* = 7.6 Hz, 1H), 8.06 (d, *J* = 7.6 Hz, 1H), 7.90–7.74 (m, 4H), 7.58–7.47 (m, 6H), 7.22 (d, *J* = 8.0 Hz, 3H), 6.89 (s, 1H), 6.77 (t, *J* = 5.6 Hz, 1H), 5.05 (dd, *J* = 11.6, 4.8 Hz, 1H), 4.63–4.58 (m, 1H), 4.21–4.16 (m, 1H), 3.61 (s, 3H), 3.55 (dd, *J* = 14.0, 4.4 Hz, 1H), 3.42–3.35 (m, 1H), 2.93–2.88 (m, 2H), 2.57 (dd, *J* = 15.6, 5.6 Hz, 1H), 2.37 (dd, *J* = 15.6, 7.6 Hz, 1H), 1.74–1.63 (m, 2H), 1.39–1.26 (m, 13H). **^{13}C NMR** (100 MHz, DMSO-d_6): δ = 172.4, 171.4, 171.0, 167.6, 167.5, 155.5, 138.7, 137.4, 136.8, 134.6, 131.7, 131.2, 129.4, 128.5, 126.4, 123.2, 120.7, 77.3, 54.2, 52.2, 51.8, 49.8, 36.8, 33.6, 30.5, 29.1, 28.3, 22.7. **MS** (ESI) *m*/*z*: 828 $[M+Na]^+$. **HR-MS (ESI):** *m*/*z*: calcd for $C_{39}H_{44}{}^{79}BrN_5NaO_9$ $[M+Na]^+$ 828.2215, found 828.2203.

Methyl N^2-(((*S*)-3-(benzo[d][1,3]dioxol-5-yl)-2-(1,3-dioxoisoindolin-2-yl)propanoyl)-*L*-asparaginyl)-N^6-(*tert*-butoxycarbonyl)-*L*-lysinate (5ej)

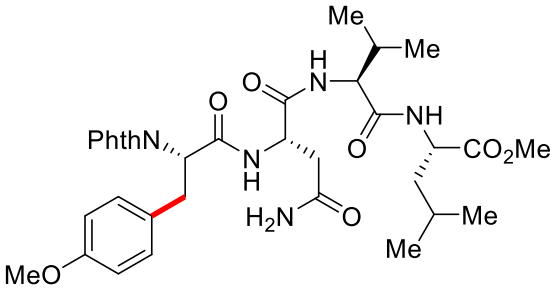


The general procedure was followed using **3e** (115.1 mg, 0.2 mmol) and **4j** (124.0 mg, 0.5 mmol). After 12 h, purification by column chromatography on silica gel (*n*-hexane/EtOAc 1:6) yielded **5ej** (72.3 mg, 52%) as a pale yellow solid. M.p. = 70–73 °C.

^{1}H NMR (400 MHz, DMSO-d_6): δ = 8.49 (d, *J* = 7.6 Hz, 1H), 8.03 (d, *J* = 7.2 Hz, 1H), 7.84–7.79 (m,

4H), 7.22 (s, 1H), 6.88 (s, 1H), 6.77–6.76 (m, 2H), 6.63 (d, *J* = 8.0 Hz, 1H), 6.47 (dd, *J* = 8.0, 1.6 Hz, 1H), 5.88 (d, *J* = 9.6 Hz, 2H), 4.95 (dd, *J* = 12.0, 4.4 Hz, 1H), 4.60–4.55 (m, 1H), 4.20–4.15 (m, 1H), 3.61 (s, 3H), 3.40 (dd, *J* = 14.4, 4.8 Hz, 1H), 3.22 (dd, *J* = 14.0, 11.6 Hz, 1H), 2.92–2.87 (m, 2H), 2.55 (dd, *J* = 15.6, 6.0 Hz, 1H), 2.36 (dd, *J* = 15.6, 7.6 Hz, 1H), 1.71–1.61 (m, 2H), 1.38–1.25 (m, 13H). **^{13}C NMR** (100 MHz, DMSO-d_6): δ = 172.5, 171.4, 171.0, 167.6, 167.5, 155.6, 147.1, 145.7, 134.6, 131.3, 131.2, 123.2, 121.8, 109.0, 108.0, 100.7, 77.4, 54.4, 52.2, 51.8, 49.8, 36.7, 33.7, 30.5, 29.1, 28.3, 22.6. **MS** (ESI) *m*/*z*: 718 $[M+Na]^+$. **HR-MS** (ESI): *m*/*z* calcd for $C_{34}H_{41}N_5NaO_{11}$ $[M+Na]^+$ 718.2695, found 718.2690.

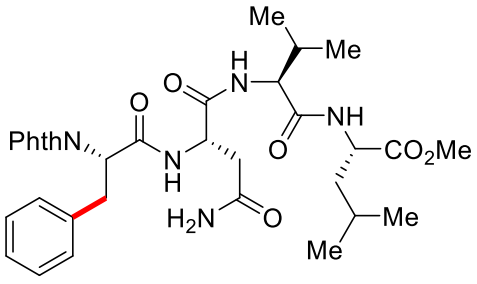
Methyl ((*S*)-2-(1,3-dioxoisoindolin-2-yl)-3-(4-methoxyphenyl)propanoyl)-*L*-asparaginyl-*L*-valyl-*L*-leucinate (6fa)



The general procedure was followed using **3f** (111.9 mg, 0.2 mmol) and **4a** (117.0 mg, 0.5 mmol). After 12 h, purification by column on silica gel (CH_2Cl_2/MeOH 30:1) yielded **6fa** (66.6 mg, 50%) as a white solid. M.p. = 202–205 °C.

^{1}H NMR (400 MHz, DMSO-d_6): δ = 8.60 (d, *J* = 7.6 Hz, 1H), 8.30 (d, *J* = 7.2 Hz, 1H), 7.86–7.75 (m, 4H), 7.60 (d, *J* = 8.8 Hz, 1H), 7.30 (s, 1H), 7.02 (d, *J* = 8.0 Hz, 2H), 6.88 (s, 1H), 6.70 (s, *J* = 8.4 Hz, 2H), 4.94 (dd, *J* = 12.0, 4.8 Hz, 1H), 4.65–4.60 (m, 1H), 4.27–4.17 (m, 2H), 3.61 (s, 3H), 3.60 (s, 3H), 3.42 (dd, *J* = 14.0, 4.8 Hz, 1H), 3.34–3.28 (m, 1H), 2.60 (dd, *J* = 15.6, 7.2 Hz, 1H), 2.35 (dd, *J* = 15.6, 6.4 Hz, 1H), 2.09–2.01 (m, 1H), 1.67–1.56 (m, 2H), 1.51–1.45 (m, 1H), 0.89–0.82 (m, 12H). **^{13}C NMR** (100 MHz, DMSO-d_6): δ = 172.7, 171.7, 170.9, 170.5, 167.8, 167.5, 157.8, 134.5, 131.2, 129.7, 129.2, 123.1, 113.7, 57.2, 54.8, 54.7, 51.7, 50.3, 49.9, 36.6, 33.1, 30.6, 24.2, 22.8, 21.2, 19.1, 17.6. **MS** (ESI) *m*/*z*: 666 $[M+H]^+$. **HR-MS** (ESI): *m*/*z* calcd for $C_{33}H_{41}N_5NaO_8$ $[M+H]^+$ 666.3134, found 666.3125.

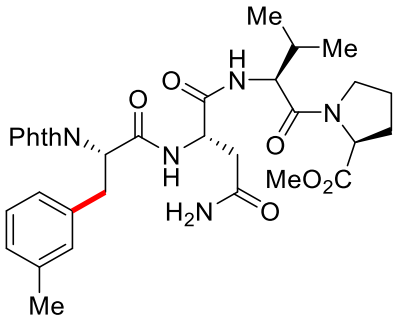
Methyl ((*S*)-2-(1,3-dioxoisoindolin-2-yl)-3-phenylpropanoyl)-*L*-asparaginyl-*L*-valyl-*L*-leucinate (6fb)



The general procedure was followed using **3f** (111.9 mg, 0.2 mmol) and **4b** (102.0 mg, 0.5 mmol). After 12 h, purification by column on silica gel (CH_2Cl_2/MeOH 30:1) yielded **6fb** (66.1 mg, 52%) as a white solid. M.p. = 206–208 °C.

^{1}H NMR (400 MHz, DMSO-d_6): δ = 8.62 (d, J = 8.0 Hz, 1H), 8.31 (d, J = 7.6 Hz, 1H), 7.82–7.75 (m, 4H), 7.62 (d, J = 8.8 Hz, 1H), 7.30 (s, 1H), 7.16–7.06 (m, 5H), 6.89 (s, 1H), 4.99 (dd, J = 12.0, 4.4 Hz, 1H), 4.65–4.60 (m, 1H), 4.26–4.17 (m, 2H), 3.59 (s, 3H), 3.50 (dd, J = 14.0, 4.8 Hz, 1H), 3.38–3.31 (m, 1H), 2.60 (dd, J = 15.6, 6.8 Hz, 1H), 2.34 (dd, J = 15.6, 6.8 Hz, 1H), 2.07–2.02 (m, 1H), 1.65–1.56 (m, 2H), 1.50–1.43 (m, 1H), 0.89–0.81 (m, 12H). **^{13}C NMR** (100 MHz, DMSO-d_6): δ = 172.8, 171.7, 171.0, 170.5, 167.7, 167.4, 137.5, 134.5, 131.2, 128.7, 128.3, 126.5, 123.1, 57.3, 54.4, 51.8, 50.3, 49.9, 36.6, 34.0, 30.6, 24.2, 22.8, 21.3, 19.1, 17.7. **MS** (ESI) *m*/*z*: 658 $[M+Na]^+$. **HR-MS** (ESI): *m*/*z* calcd for $C_{33}H_{41}N_5NaO_8$ $[M+Na]^+$ 658.2847, found 658.2822.

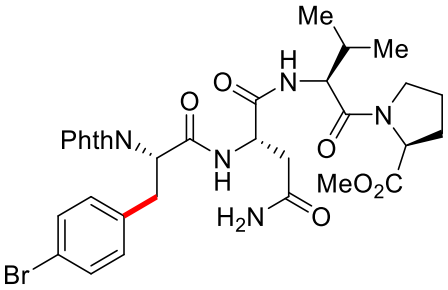
Methyl ((*S*)-2-(1,3-dioxoisoindolin-2-yl)-3-(*m*-tolyl)propanoyl)-*L*-asparaginyl-*L*-valyl-*L*-prolinate (6gg)



The general procedure was followed using **3g** (108.7 mg, 0.2 mmol) and **4g** (109.0 mg, 0.5 mmol). After 12 h, purification by column on silica gel (CH_2Cl_2/MeOH 30:1) yielded **6gg** (73.4 mg, 58%) as a white solid. M.p. = 114–117 °C.

^{1}H NMR (400 MHz, DMSO-d_6): δ = 8.58 (d, J = 8.0 Hz, 1H), 7.83–7.78 (m, 4H), 7.68 (d, J = 8.4 Hz, 1H), 7.27 (s, 1H), 7.01 (t, J = 7.6 Hz, 1H), 6.90–6.86 (m, 4H), 4.96 (dd, J = 11.6, 4.4 Hz, 1H), 4.60–4.55 (m, 1H), 4.34–4.29 (m, 2H), 3.79–3.73 (m, 1H), 3.61 (s, 3H), 3.60–3.55 (m, 1H), 3.45 (dd, J = 14.0, 4.4 Hz, 1H), 3.32–3.26 (m, 1H), 2.59 (dd, J = 15.6, 6.8 Hz, 1H), 2.32 (dd, J = 15.6, 6.4 Hz, 1H), 2.21–2.12 (m, 1H), 2.09 (s, 3H), 2.06–1.99 (m, 1H), 1.97–1.86 (m, 2H), 1.85–1.77 (m, 1H), 0.93 (d, J = 6.8 Hz, 3H), 0.89 (d, J = 6.8 Hz, 3H). **^{13}C NMR** (100 MHz, DMSO-d_6): δ = 172.7, 172.1, 170.9, 170.2, 168.2, 167.9, 137.9, 137.7, 135.0, 131.7, 129.9, 128.6, 127.6, 126.2, 123.5, 58.9, 56.1, 54.9, 52.2, 50.2, 47.3, 36.9, 34.3, 30.6, 29.1, 25.1, 21.3, 19.3, 18.5. **MS** (ESI) *m/z*: 656 $[M+Na]^+$. **HR-MS** (ESI): *m/z* calcd for $C_{33}H_{39}N_5NaO_8$ $[M+Na]^+$ 656.2691, found 656.2686.

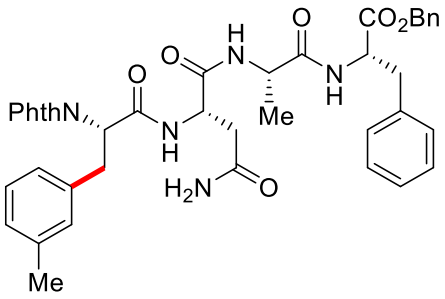
Methyl ((*S*)-3-(4-bromophenyl)-2-(1,3-dioxoisoindolin-2-yl)propanoyl)-*L*-asparaginyl-*L*-valyl-*L*-prolinate (6gh)



The general procedure was followed using **3g** (108.7 mg, 0.2 mmol) and **4h** (141.5 mg, 0.5 mmol). After 12 h, purification by column on silica gel (CH_2Cl_2/MeOH 30:1) yielded **6gh** (69.8 mg, 50%) as a white solid. M.p. = 133–136 °C.

^{1}H NMR (400 MHz, DMSO-d_6): δ = 8.58 (d, J = 7.6 Hz, 1H), 7.85–7.78 (m, 4H), 7.69 (d, J = 8.4 Hz, 1H), 7.35 (d, J = 8.0 Hz, 2H), 7.26 (s, 1H), 7.09 (d, J = 8.0 Hz, 2H), 6.87 (s, 1H), 4.98 (dd, J = 11.6, 4.4 Hz, 1H), 4.60–4.55 (m, 1H), 4.33-4.28 (m, 2H), 3.77–3.73 (m, 1H), 3.61 (s, 3H), 3.59–3.57 (m, 1H), 3.48 (dd, J = 14.0, 4.4 Hz, 1H), 3.30–3.27 (m, 1H), 2.58 (dd, J = 15.6, 6.4 Hz, 1H), 2.30 (dd, J = 15.6, 7.6 Hz, 1H), 2.21–2.10 (m, 1H), 2.05–1.98 (m, 1H), 1.96–1.86 (m, 2H), 1.84–1.76 (m, 1H), 0.92 (d, J = 6.8 Hz, 3H), 0.88 (d, J = 6.8 Hz, 3H). **^{13}C NMR** (100 MHz, DMSO-d_6): δ = 172.2, 171.6, 170.4, 169.8, 167.5, 167.4, 137.0, 134.6, 131.2, 131.0, 123.2, 119.6, 58.5, 55.6, 54.1, 51.7, 49.7, 46.8, 36.5, 33.4, 30.1, 28.7, 24.6, 18.9, 18.1. **MS** (ESI) *m/z*: 698 $[M+H]^+$. **HR-MS** (ESI): *m/z* calcd for $C_{32}H_{37}{}^{79}BrN_5O_8$ $[M+H]^+$ 698.1820, found 698.1821.

Benzyl ((*S*)-2-(1,3-dioxoisoindolin-2-yl)-3-(*m*-tolyl)propanoyl)-*L*-asparaginyl-*L*-alanyl-*L*-phenylalaninate (6hg)

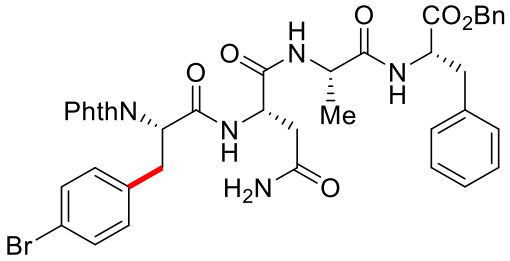


The general procedure was followed using **3h** (128.3 mg, 0.2 mmol) and **4g** (109.0 mg, 0.5 mmol). After 12 h, purification by column on silica gel (CH_2Cl_2/MeOH 30:1) yielded **6hg** (52.7 mg, 36%) as a pale yellow solid. M.p. = 198–201 °C.

^{1}H NMR (400 MHz, DMSO-d_6): δ = 8.55 (d, J = 7.6 Hz, 1H), 8.43 (d, J = 7.2 Hz, 1H), 8.00 (d, J = 7.6 Hz, 1H), 7.83–7.75 (m, 4H), 7.36–7.30 (m, 4H), 7.28–7.19 (m, 7H), 7.01 (t, J = 7.6 Hz, 1H), 6.94–6.87 (m, 4H), 5.08–4.96 (m, 3H), 4.61–4.55 (m, 1H), 4.49–4.43 (m, 1H), 4.28–4.21 (m, 1H), 3.45 (dd, J = 14.0, 4.4 Hz, 1H), 3.30–3.24 (m, 1H), 3.07–2.97 (m, 2H), 2.59 (dd, J = 15.2, 7.2 Hz, 1H), 2.35 (dd, J =

15.2, 6.0 Hz, 1H), 2.08 (s, 3H), 1.17 (d, *J* = 6.8 Hz, 3H). **^{13}C NMR** (100 MHz, DMSO-d_6): δ = 172.3, 171.9, 171.2, 170.3, 167.7, 167.5, 137.5, 137.2, 137.1, 135.8, 134.5, 131.3, 129.5, 129.2, 128.4, 128.3, 128.1, 128.0, 127.8, 127.1, 126.6, 125.8, 123.1, 65.9, 54.4, 53.9, 49.9, 48.1, 36.9, 36.5, 33.9, 20.8, 17.9. **MS** (ESI) *m/z*: 754 $[M+Na]^+$. **HR-MS** (ESI): *m/z* calcd for $C_{41}H_{41}N_5NaO_8$ $[M+Na]^+$ 754.2847, found 754.2857.

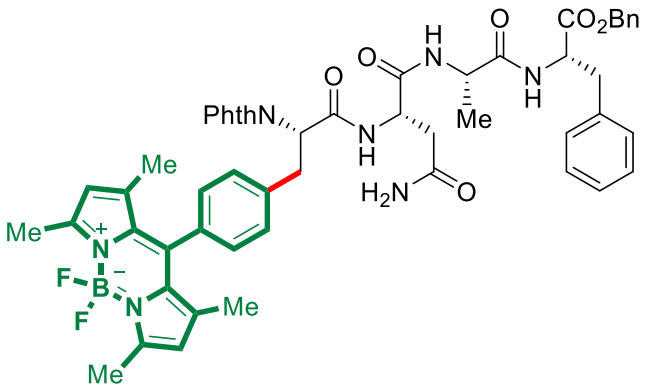
Benzyl ((*S*)-3-(4-bromophenyl)-2-(1,3-dioxoisoindolin-2-yl)propanoyl)-*L*-asparaginyl-*L*-alanyl-*L*-phenylalaninate (6hh)



The general procedure was followed using **3h** (128.3 mg, 0.2 mmol) and **4h** (141.5 mg, 0.5 mmol). After 12 h, purification by column on silica gel (CH_2Cl_2/MeOH 30:1) yielded **6hh** (55.7 mg, 35%) as a pale yellow solid. M.p. = 213–216 °C

^{1}H NMR (400 MHz, DMSO-d_6): δ = 8.55 (d, *J* = 6.4 Hz, 1H), 8.41 (d, *J* = 7.6 Hz, 1H), 7.99 (d, *J* = 7.2 Hz, 1H), 7.88–7.72 (m, 4H), 7.35–7.30 (m, 6H), 7.28–7.20 (m, 7H), 7.10 (d, *J* = 7.6 Hz, 2H), 6.91 (s, 1H), 5.08–5.00 (m, 3H), 4.61–4.55 (m, 1H), 4.50–4.44 (m, 1H), 4.27–4.23 (m, 1H), 3.47 (dd, *J* = 14.0, 4.4 Hz, 1H), 3.29 (d, *J* = 14.8 Hz, 1H), 3.07–2.98 (m, 2H), 2.59 (dd, *J* = 15.2, 6.4 Hz, 1H), 2.35 (dd, *J* = 15.6, 6.4 Hz, 1H), 1.17 (d, *J* = 7.2 Hz, 3H). **^{13}C NMR** (100 MHz, DMSO-d_6): δ = 172.2, 171.8, 171.1, 170.2, 167.4, 167.3, 137.1, 135.7, 134.5, 131.2, 131.1, 131.0, 129.1, 128.3, 128.2, 127.9, 127.7, 126.5, 123.1, 119.6, 65.9, 54.1, 53.9, 49.9, 48.1, 36.9, 36.5, 33.5. 17.8. **MS** (ESI) *m/z*: 794 $[M-H]^+$. **HR-MS** (ESI): *m/z* calcd for $C_{40}H_{39}{}^{79}BrN_5O_8$ $[M+H]^+$ 796.1977, found 796.1993.

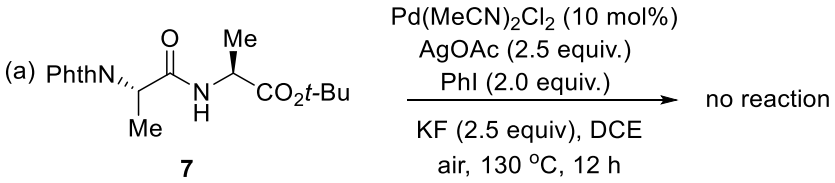
Benzyl ((*S*)-3-(4-(5,5-difluoro-1,3,7,9-tetramethyl-5*H*-4λ^4,5λ^4-dipyrrolo[1,2-c:2',1'-f][1,3,2]diazaborinin-10-yl)phenyl)-2-(1,3-dioxoisoindolin-2-yl)propanoyl)-*L*-asparaginyl-*L*-alanyl-*L*-phenylalaninate (6hk)



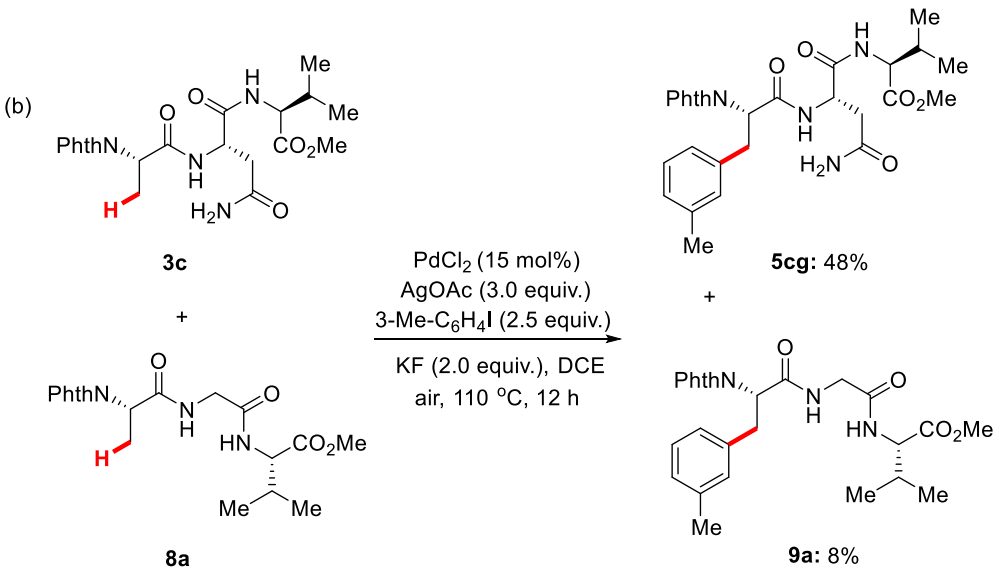
The general procedure was followed using **3h** (128.3 mg, 0.2 mmol) and **4k** (225.0 mg, 0.5 mmol). After 12 h, purification by column on silica gel (CH_2Cl_2/MeOH 30:1) yielded **6hk** (48.2 mg, 25%) as a pale orange solid. M.p. = 195–196 °C.

^{1}H NMR (400 MHz, DMSO-d_6): δ = 8.55 (d, J = 8.0 Hz, 1H), 8.42 (d, J = 7.2 Hz, 1H), 8.00 (d, J = 7.6 Hz, 1H), 7.81–7.76 (m, 4H), 7.36–7.29 (m, 6H), 7.27–7.20 (m, 7H), 7.12 (d, J = 7.6 Hz, 2H), 6.92 (s, 1H), 6.08 (s, 2H), 5.15 (dd, J = 12.4, 4.8 Hz, 1H), 5.08–5.00 (m, 2H), 4.63–4.58 (m, 1H), 4.50–4.44 (m , 1H), 4.30–4.22 (m, 1H), 3.61 (dd, J = 14.0, 4.8 Hz, 1H), 3.44–3.37 (m, 1H), 3.07–2.98 (m, 2H), 2.60 (dd, J = 15.6, 7.2 Hz, 1H), 2.40 (s, 6H), 2.37–2.33 (m, 1H), 1.18 (d, J = 7.2 Hz, 3H), 1.02 (s, 6H). **^{13}C NMR** (100 MHz, DMSO-d_6): δ = 172.2, 171.8, 171.1, 170.2, 167.5, 167.3, 154.7, 142.5, 141.8, 138.7, 137.1, 135.7, 134.4, 132.2, 131.2, 130.6, 129.8, 129.1, 128.3, 128.2, 127.9, 127.7, 127.6, 126.5, 123.1, 121.2, 65.9, 53.9, 53.9, 49.9, 48.1, 36.9, 36.5, 33.9, 17.9, 14.1, 13.7. **^{19}F NMR** (376 MHz, DMSO-d_6): δ = -143.72 (dd, $J_{B\text{-}F}$ = 62.8, 27.4 Hz). **MS** (ESI) *m/z*: 962 $[M\text{-}H]^+$. **HR-MS** (ESI): *m/z* calcd for $C_{53}H_{52}BF_2N_7NaO_8$ $[M+Na]^+$ 986.3839, found 986.3837.

Control and Competition Experiment

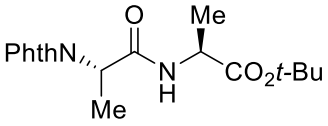


To a 10 mL Schlenk tube dipeptide **7** (69.3 mg, 0.20 mmol), iodobenzene (81.6 mg, 0.40 mmol), $Pd(MeCN)_2Cl_2$ (5.2 mg, 10 mol %), AgOAc (83.5 mg, 0.50 mmol) and KF (29.1 mg, 0.50 mmol), DCE (2.0 mL) were added. The mixture was stirred at 130 °C for 12 h and monitored by LC-MS.



To a 10 mL Schlenk tube tripeptide **3c** (89.3 mg, 0.20 mmol) and **8a** (77.9 mg, 0.20 mmol), **4g** (109.0 mg, 0.50 mmol), $PdCl_2$ (5.3 mg, 15 mol %), AgOAc (100.1 mg, 0.60 mmol) and KF (23.2 mg, 0.40 mmol), DCE (3.0 mL) were added. The mixture was stirred at 110 °C for 12 h and monitored by TLC. At room temperature, the reaction was diluted with CH_2Cl_2 (10 mL) and concentrated *in vacuo*. The resulting residue was purified by column chromatography on silica gel to yield the desired products **5cg** and **9a**.

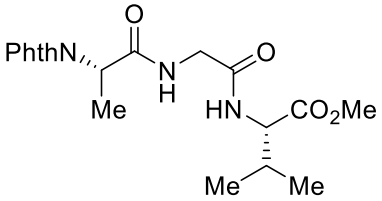
***tert*-Butyl ((*S*)-2-(1,3-dioxoisoindolin-2-yl)propanoyl)-*L*-alaninate (7)**



White solid. M.p. = 116–118 °C

^{1}H NMR (400 MHz, $CDCl_3$): δ = 7.88–7.84 (m, 2H), 7.75–7.71 (m, 2H), 6.57 (d, J = 6.8 Hz, 1H), 4.94 (q, J = 7.6 Hz, 1H), 4.49–4.42 (m, 1H), 1.72 (d, J = 7.2 Hz, 3H), 1.44 (s, 9H), 1.37 (d, J = 6.8 Hz, 3H). **^{13}C NMR** (100 MHz, $CDCl_3$): δ = 172.2, 168.4, 167.9, 134.4, 132.0, 123.7, 82.4, 49.4, 49.2, 28.1, 18.7, 15.4. **MS** (ESI) *m/z*: 369 $[M+Na]^+$. **HR-MS** (ESI): *m/z* calcd for $C_{18}H_{22}N_2NaO_5$ $[M+Na]^+$ 369.1421, found 369.1409.

Methyl ((*S*)-2-(1,3-dioxoisoindolin-2-yl)propanoyl)glycyl-*L*-valinate (8a)

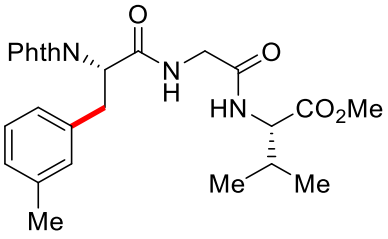


White foam. M.p. = 129–131 °C

^{1}H NMR (400 MHz, $CDCl_3$): δ = 7.83–7.79 (m, 2H), 7.72–7.68 (m, 2H), 7.27–7.25 (m, 1H), 6.97 (d, J = 8.4 Hz, 1H), 4.84 (q, J =7.2 Hz, 1H), 4.38–4.34 (m, 1H), 4.04 (dd, J = 16.8, 6.0 Hz, 1H), 3.77 (dd, J = 16.8, 4.8

Hz, 1H), 3.66 (s, 3H), 2.19–2.11 (m, 1H), 1.62 (d, *J* = 7.6 Hz, 3H), 0.92–0.89 (m, 6H). **^{13}C NMR** (100 MHz, $CDCl_3$): δ = 172.3, 169.8, 169.1, 167.9, 134.4, 132.0, 123.6, 57.7, 52.2, 48.8, 43.4, 30.9, 19.1, 18.0, 15.4. **MS** (ESI) *m/z*: 390 $[M+H]^+$. **HR-MS** (ESI): *m/z* calcd for $C_{19}H_{24}N_3O_6$ $[M+H]^+$ 390.1660, found 390.1660.

Benzyl ((*S*)-2-(1,3-dioxoisoindolin-2-yl)propanoyl)-*L*-valyl-*L*-valinate (9a)

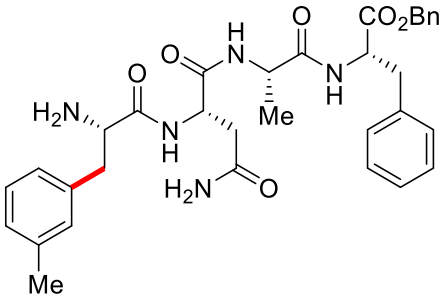


White solid. M.p. = 152–153 °C.

^{1}H NMR (400 MHz, $CDCl_3$): δ = 7.78–7.74 (m, 2H), 7.71–7.68 (m, 2H), 7.05–6.98 (m, 2H), 6.91–6.90 (m, 3H), 6.72 (d, *J* = 8.4 Hz, 1H), 5.08 (dd, *J* = 11.2, 5.2 Hz, 1H), 4.46 (dd, *J* = 8.4, 5.2 Hz, 1H), 4.14 (dd, *J* = 16.4, 3.2 Hz, 1H), 3.82 (dd, *J* = 16.4, 4.4 Hz, 1H), 3.69 (s, 3H), 3.54 (dd, *J* = 14.4, 5.6 Hz, 1H), 3.41 (dd, *J* = 14.4, 11.2 Hz, 1H), 2.25–2.19 (m, 1H), 2.13 (s, 3H), 0.96–0.94 (m, 6H). **^{13}C NMR** (100 MHz, $CDCl_3$): δ = 172.3, 169.1, 168.9, 168.0, 138.2, 136.6, 134.4, 131.6, 129.8, 128.5, 127.7, 126.0, 123.6, 57.6, 55.4, 52.2, 43.5, 34.7, 31.0, 21.2, 19.1, 18.0. **MS** (ESI) *m/z*: 480 $[M+H]^+$. **HR-MS** (ESI): *m/z* calcd for $C_{26}H_{30}N_3O_6$ $[M+H]^+$ 480.2129, found 480.2119.

Characterization Data of AGRP Loop Analogues

Benzyl ((*S*)-2-amino-3-(*m*-tolyl)propanoyl)-*L*-asparaginyl-*L*-alanyl-*L*-phenylalaninate (10a)



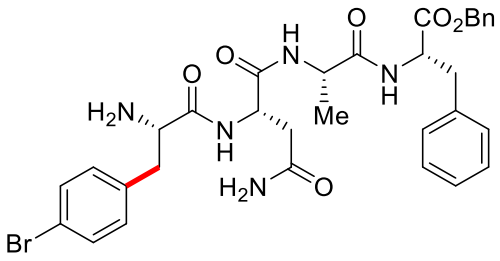
Following the general procedure for synthesis of tetrapeptide **10a**.

White solid (62.3 mg, 69% yield). M.p. = 194–195 °C.

^{1}H NMR (400 MHz, DMSO-d_6): δ = 8.44 (d, *J* = 7.6 Hz, 1H), 8.25 (d, *J* = 8.0 Hz, 1H), 8.04 (d, *J* = 7.6 Hz, 1H), 7.45 (s, 1H), 7.37–7.32 (m, 3H), 7.30–7.22 (m, 7H), 7.17 (t, *J* = 7.6 Hz, 1H), 7.05–7.01 (m, 3H), 6.97 (s, 1H), 5.08 (d, *J* = 12.4 Hz, 1H), 5.03 (d, *J* = 12.4 Hz, 1H), 4.57–4.52 (m, 1H), 4.51–4.45 (m, 1H), 4.30–4.22 (m, 1H), 3.44 (dd, *J* = 8.8, 4.4 Hz, 1H), 3.35 (s, 1H), 3.09–3.00 (m, 2H), 2.96 (dd, *J* = 13.6, 4.4 Hz, 1H), 2.56–2.53 (m, 1H), 2.50–2.48 (m, 1H), 2.28 (s, 3H), 2.08 (br s, 2H), 1.15 (d, *J* =

6.8 Hz, 3H). **^{13}C NMR** (100 MHz, DMSO-d_6): δ = 174.1, 172.2, 171.8, 171.1, 170.4, 138.5, 137.2, 137.1, 135.7, 130.0, 129.1, 128.3, 128.3, 128.1, 128.0, 127.8, 126.8, 126.5, 126.4, 65.9, 56.0, 53.9, 49.2, 48.0, 40.6, 37.4, 36.5, 21.0, 17.9. **MS** (ESI) *m/z*: 602 $[M+H]^+$. **HR-MS** (ESI): *m/z* calcd for $C_{33}H_{40}N_5O_6$ $[M+H]^+$ 602.2973, found 602.2966.

Benzyl ((*S*)-2-amino-3-(4-bromophenyl)propanoyl)-*L*-asparaginyl-*L*-alanyl-*L*-phenylalaninate (10b)

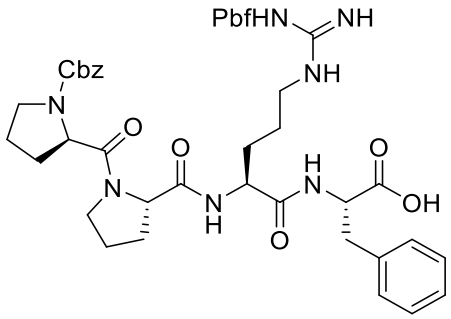


Following the general procedure for synthesis of tetrapeptide **10b**.

Pale yellow solid (66.9 mg, 67% yield). M.p. = 175–177 °C.

1H NMR (400 MHz, DMSO-d_6): δ = 8.42 (d, *J* = 7.2 Hz, 1H), 8.22 (d, *J* = 8.0 Hz, 1H), 8.02 (d, *J* = 7.6 Hz, 1H), 7.45–7.42 (m, 3H), 7.37–7.31 (m, 3H), 7.29–7.17 (m, 9H), 6.97 (s, 1H), 5.06 (d, *J* = 12.8 Hz, 1H), 5.02 (d, *J* = 12.8 Hz, 1H), 4.55–4.50 (m, 1H), 4.50–4.44 (m, 1H), 4.28–4.21 (m, 1H), 3.41 (dd, *J* = 8.4, 4.8 Hz, 1H), 3.37–3.29 (m, 1H), 3.07–2.97 (m, 2H), 2.92 (dd, *J* = 13.6, 4.8 Hz, 1H), 2.58 (dd, *J* = 13.6, 8.4 Hz, 1H), 2.48–2.47 (m, 1H), 1.95 (br s, 2H), 1.13 (d, *J* = 7.2 Hz, 3H). **^{13}C NMR** (100 MHz, DMSO-d_6): δ = 174.0, 172.2, 171.8, 171.1, 170.4, 138.1, 137.1, 135.7, 131.6, 130.9, 129.1, 128.3, 128.3, 128.0, 127.8, 126.5, 119.3, 65.9, 55.8, 53.9, 49.2, 48.0, 40.0, 37.4, 36.5, 17.9. **MS** (ESI) *m/z*: 666 $[M+H]^+$. **HR-MS** (ESI): *m/z* calcd for $C_{32}H_{37}{}^{79}BrN_5O_6$ $[M+H]^+$ 666.1922, found 666.1912.

***N*^{2}-((benzyloxy)carbonyl)-*D*-prolyl-*L*-prolyl-*N*$^{\omega}$-((2,2,4,6,7-pentamethyl-2,3-dihydrobenzofuran-5-yl)sulfonyl)-*L*-arginyl-*L*-phenylalanine**

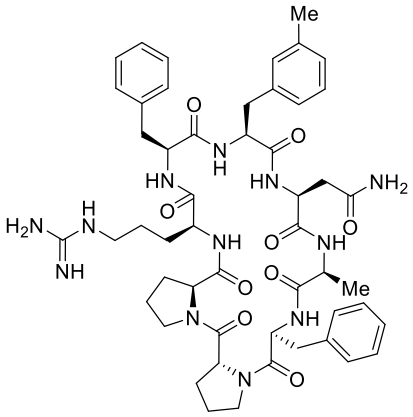


White foam (0.29 g, 80% yield). M.p. = 127-129 °C.

^{1}H NMR (400 MHz, $CDCl_3$): δ = 7.62–7.56 (m, 2H), 7.32–7.25 (m, 7H), 7.19–7.10 (m, 5H), 6.42 (br s, 1H), 5.09 (d, *J* = 12.4 Hz, 1H), 4.80 (d, *J* = 12.4 Hz, 1H), 4.51–4.37 (m, 3H), 4.01–3.95 (m, 1H), 3.54–

3.50 (m, 3H), 3.29–3.12 (m, 3H), 2.99–2.93 (m, 2H), 2.90 (s, 2H), 2.87 (s, 1H), 2.53 (s, 3H), 2.47 (s, 3H), 2.19–2.08 (m, 3H), 2.05–1.84 (m, 8H), 1.74–1.49 (m, 3H), 1.43 (s, 6H). **^{13}C NMR** (100 MHz, $CDCl_3$): δ = 173.3, 172.9, 172.9, 172.4, 162.8, 155.5, 136.9, 136.0, 129.2, 128.7, 128.5, 128.4, 127.9, 126.8, 124.8, 117.6, 86.5, 67.7, 61.4, 58.4, 55.0, 53.3, 48.0, 47.2, 43.3, 37.0, 36.7, 31.6, 29.4, 28.7, 28.2, 25.5, 25.0, 24.8, 19.4, 18.0, 12.6. **MS** (ESI) *m/z*: 902 $[M+H]^+$. **HR-MS** (ESI) *m/z*: calcd for $C_{46}H_{60}N_7O_{10}S$ $[M+H]^+$ 902.4117, found 902.4137.

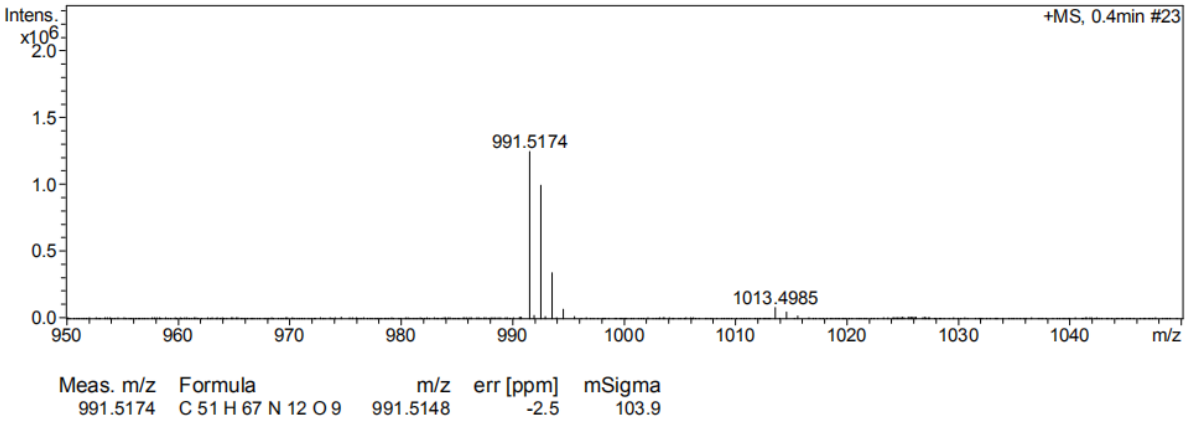
c(Pro-Arg-Phe-*m*-Me-Phe-Asn-Ala-Phe-ᴅPro) (11a)

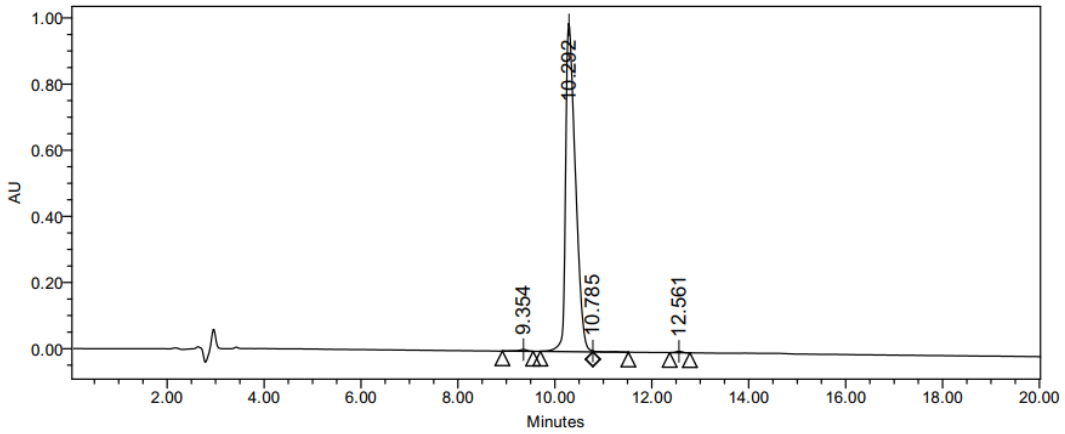


Crude compound **11a** was prepared in 25% yield (37.2 mg, 0.038mmol) from compound **6hg** after 5steps and purified by RP-HPLC to yield the **11a** as white powder in 14% yield (20.8 mg, 0.021mmol).

MS (ESI) *m/z*: 991 $[M+H]^+$.

HR-MS (ESI) *m/z*: calcd for $C_{51}H_{67}N_{12}O_9$ $[M+H]^+$ 991.5148, found 991.5174.



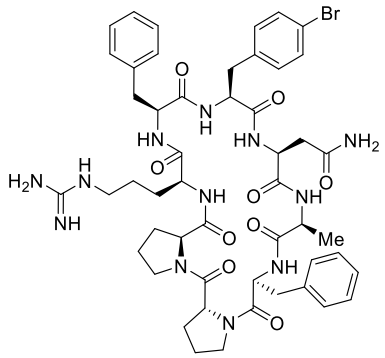


Peak Results

	Name	RT	Area	Height	% Area	Amount	Units
1		9.354	66612	5198	0.47		
2		10.292	13915977	996095	99.04		
3		10.785	29331	2485	0.21		
4		12.561	39550	4378	0.28		

t_R = 10.292, 30% to 50% B for 20 min, λ = 220 nm, flow: 1 mL/min

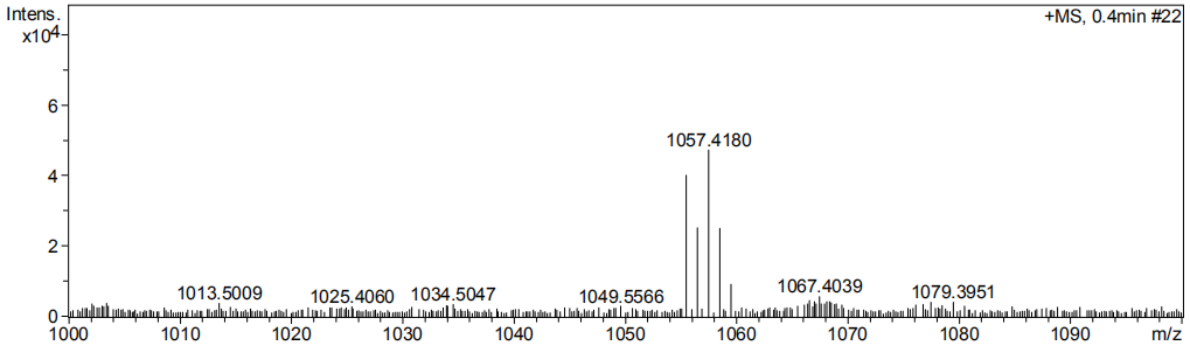
c(Pro-Arg-Phe-*p*-Br-Phe-Asn-Ala-Phe-ᴅPro) (10b):



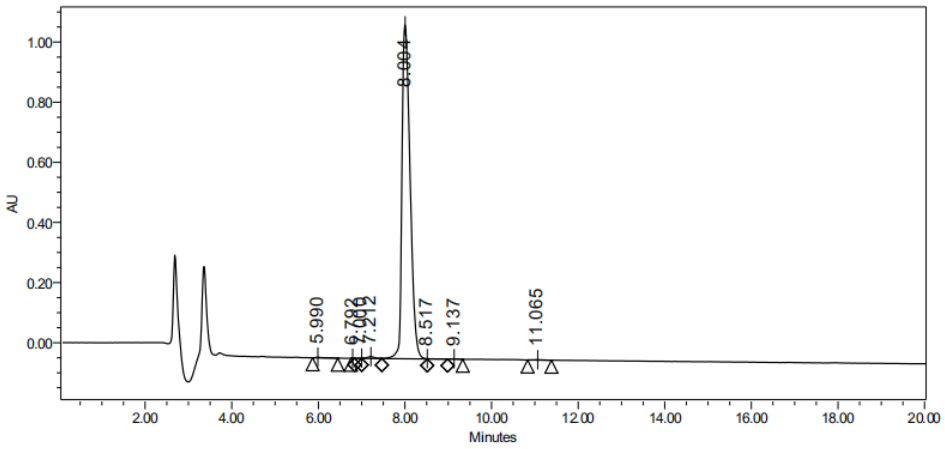
Crude compound **11b** was prepared in 31% yield (49.1 mg, 0.047mmol) from compound **6hh** after 5steps and purified by RP-HPLC to yield the **11b** as white powder in 15% yield (23.8 mg, 0.023mmol).

MS (ESI) *m/z*: 1055 $[M+H]^+$.

HR-MS (ESI) *m/z*: calcd for $C_{50}H_{64}{}^{79}BrN_{12}O_9$ $[M+H]^+$ 1055.4097, found 1055.4170.



Meas. m/z	Formula	m/z	err [ppm]	mSigma
1055.4170	C 50 H 64 Br N 12 O 9	1055.4097	-6.9	18.4



Peak Results

	Name	RT	Area	Height	% Area	Amount	Units
1		5.990	23530	1807	0.16		
2		6.792	897	271	0.01		
3		7.000	6261	1176	0.04		
4		7.212	82550	6272	0.57		
5		8.004	14450913	111211	98.94		
6		8.517	14102	979	0.10		
7		9.137	10818	1142	0.07		
8		11.065	17223	1005	0.12		

t_R = 8.004, 36% to 56% B for 20 min, λ = 220 nm, flow: 1 mL/min

Computational Studies

All calculation were performed using Gaussian 16, Revision A.03 package.[3] All structures were optimized at the PBE0[4] level of theory in combination with D3 dispersion corrections with Becke-Johnson damping scheme (D3BJ).[5] In order to identify each stationary point as either an intermediate (no imaginary frequencies) or a transition state (only one imaginary frequency), analytical frequencies were carried out at the same level of theory. These also provided thermal and non-thermal corrections to the Gibbs free energy at 403.15 K. Atoms were described with the def2-SVP basis set,[6] while palladium was described also with a SSD pseudopotential.[7] The electronic energy was then refined through PW6B95[8] single-point calculations on the optimized geometries in combination with a standalone version of Grimme's most recent dispersion correction D4,[9] with a def2-TZVP basis set combined with SSD pseudopotential for palladium.[7] Solvent effects were included implicitly through the use

of the SMD model[10] for 1,2-dichloroethane (DCE), which corresponds the solvent used in the experimental work. Energies reported are based on gas-phase Gibbs free energies with def2-SVP basis set for which the electronic energies were corrected to PW6B95-D4 with def2-TZVP basis set and solvent effects.

Table S3. Calculated electronic energies at the PW6B95-D4/def2-TZVP+SMD(DCE) level of theory and Gibbs free Energies with dispersion corrections for all structures in the present work (all in Hartree).[a]

Structure	Electronic Energy	Total Gibbs Free Energy
I-1^{i}	-1712.113158	-1711.760215
TS(1-2)^{i}	-1712.076364	-1711.729020
I-2^{i}	-1712.109569	-1711.758358
I-3^{i}	-1765.381015	-1764.986158
TS(3-4)^{i}	-1765.373537	-1764.978680
I-4^{i}	-1765.397155	-1764.997647
TS(4-5)^{i}	-1765.378988	-1764.981488
I-5^{i}	-1765.440795	-1765.037451
I-1^{t}	-1712.098791	-1711.749972
TS(1-2)^{t}	-1712.064435	-1711.716072
I-2^{t}	-1712.098791	-1711.745730
I-3^{t}	-1765.368435	-1764.969599
TS(3-4)^{t}	-1765.350381	-1764.955803
I-4^{t}	-1765.371385	-1764.972105
TS(4-5)^{t}	-1765.347449	-1764.948849
I-5^{t}	-1765.430079	-1765.030063
Acetic acid	-229.460566	-229.437215
3-Me-C_6H_4I	-282.750672	-282.685354

[a] Superscripts i and t correspond to structures for the pathway where the internal and terminal amide is deprotonated, respectively.

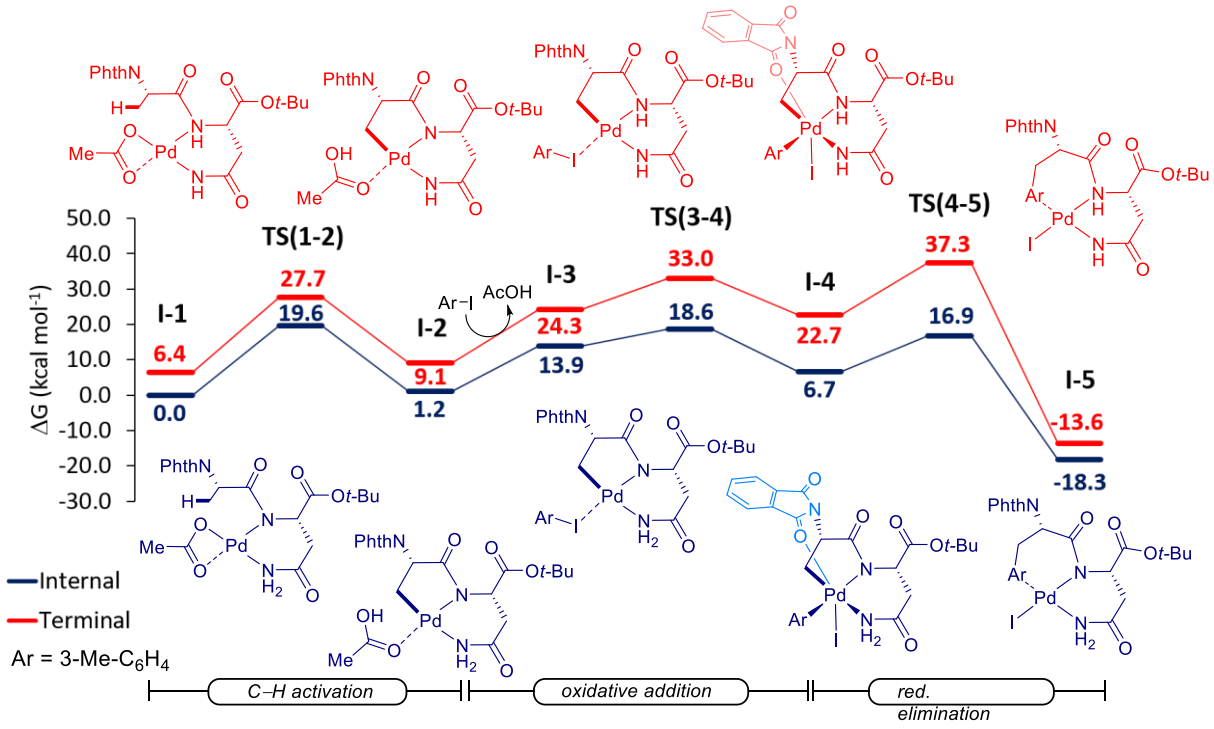


Figure S1. Computed relative Gibbs free energies ($\Delta G_{403.15}$) in kcal mol^{-1} for palladium-catalyzed C(sp^3)–H arylation at the PW6B95-D4/def-TZVP+SMD(DCE)//PBE0-D3BJ/def2-SVP level of theory. The blue energy profile correspond the pathway where the internal amide is deprotonated, while the red correspond the pathway where the terminal amide is deprotonated.

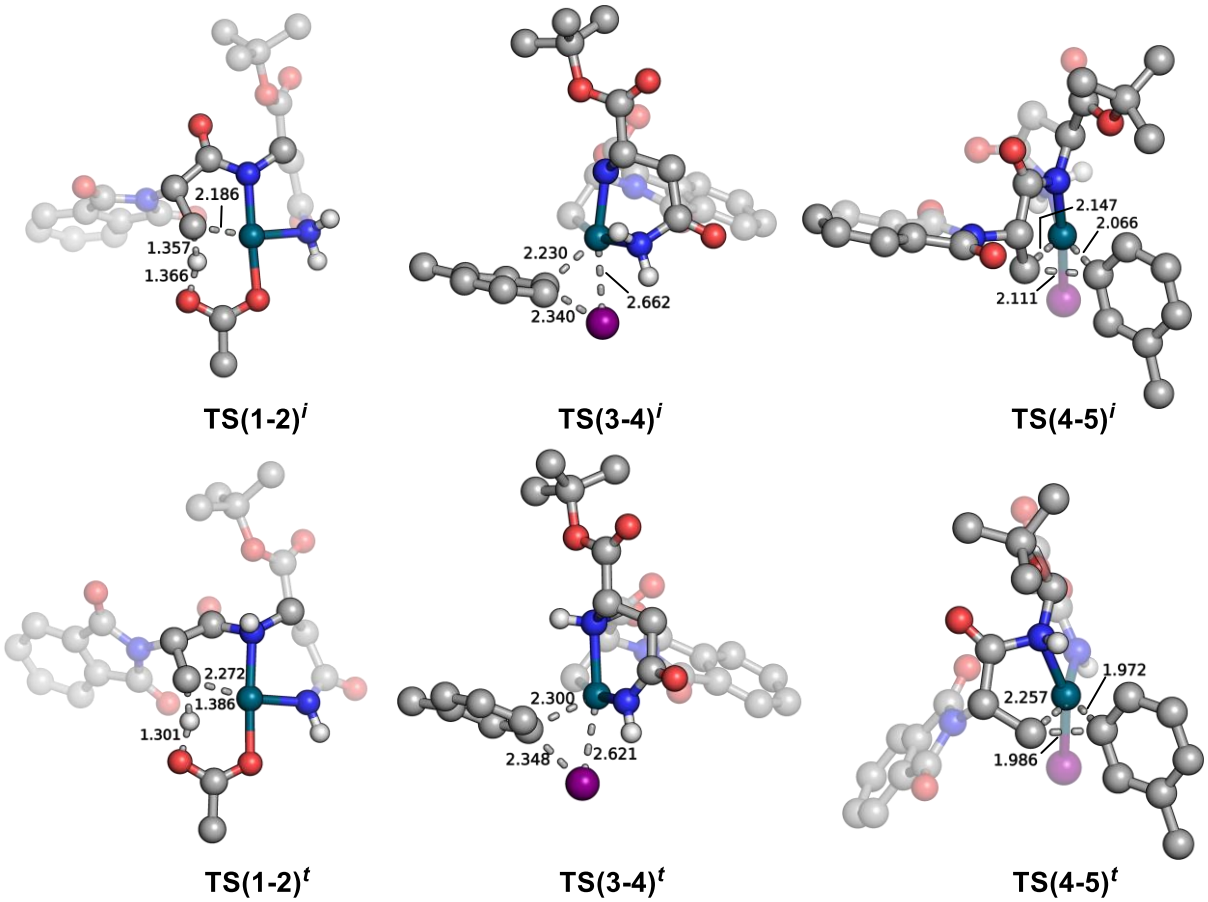


Figure S2. 3D structures of the optimized transition states with key distances given in Å. Superscripts *i* and *t* correspond to structures for the pathway where the internal and terminal amide is deprotonated, respectively.

Cartesian coordinates of the optimized structures

I-1^{i}

Lowest frequency = 19.3482 cm^{-1}

Charge = 0, Multiplicity = 1

```
   58

 C     0.220540     0.559440    -0.225531
 N    -1.055432     0.285775     0.093121
Pd    -1.964899    -1.471450    -0.000489
 O     0.877367     1.432542     0.340594
 C     0.910855    -0.164184    -1.393146
```

H	1.045241	0.631520	-2.144679
C	2.556958	-1.136664	0.215446
C	3.400405	0.086227	-1.552536
C	4.035481	-1.087928	0.359976
C	4.546132	-0.347843	-0.705426
C	4.860943	-1.625573	1.333754
C	5.904460	-0.115805	-0.841214
C	6.235465	-1.397482	1.205223
H	4.448150	-2.199457	2.165741
C	6.748024	-0.655645	0.136448
H	6.292024	0.468974	-1.677776
H	6.921561	-1.802595	1.952469
H	7.826123	-0.493759	0.067131
O	3.396377	0.758806	-2.547535
O	1.753471	-1.655530	0.967116
N	2.258193	-0.466589	-0.950873
C	0.261751	-1.356440	-2.069663
H	0.179880	-2.219024	-1.391042
H	-0.741139	-1.101585	-2.438177
H	0.875872	-1.659590	-2.930649
C	-1.575907	1.053113	1.206631
H	-2.676086	0.952477	1.190636
C	-1.327416	2.559292	1.099772
O	-1.131430	3.254681	2.063040
O	-1.479466	2.968543	-0.149118
C	-1.180664	4.335335	-0.549284
C	-2.197479	5.282964	0.072995
H	-2.106928	5.286703	1.166554
H	-2.029517	6.304348	-0.300095
H	-3.220010	4.981535	-0.200554
C	-1.335084	4.285680	-2.061296
H	-2.347530	3.954126	-2.334254
H	-1.160743	5.280820	-2.495193
H	-0.611141	3.581474	-2.496574
C	0.250812	4.687165	-0.165076
H	0.359483	4.774711	0.922923

H	0.938432	3.904456	-0.515590
H	0.527875	5.645249	-0.629536
O	-3.129916	-3.159766	-0.377976
C	-3.553725	-2.618900	-1.443598
O	-3.115414	-1.463566	-1.733602
C	-4.550824	-3.299454	-2.317143
H	-4.602289	-4.368759	-2.080183
H	-5.538507	-2.845135	-2.144750
H	-4.291695	-3.142777	-3.372622
C	-1.051201	0.528335	2.551165
H	0.046029	0.638592	2.535324
H	-1.449638	1.121210	3.381784
C	-1.424278	-0.905552	2.778210
O	-2.087763	-1.321475	3.687933
N	-0.957894	-1.824517	1.769022
H	0.038940	-1.699397	1.509042
H	-1.130394	-2.780503	2.085845

TS(1-2)^{i}

Lowest frequency = -1073.4821 cm^{-1}

Charge = 0, Multiplicity = 1

58

C	0.892395	-0.748068	-0.274134
N	1.366601	0.514281	-0.222406
Pd	0.000067	1.906123	-0.576453
O	1.311084	-1.693719	0.375144
C	-0.247100	-0.909033	-1.286440
H	0.047679	-1.716519	-1.976352
C	-1.932760	-0.917136	0.583926
C	-2.173379	-2.486921	-1.108788
C	-3.129345	-1.748924	0.889074
C	-3.273379	-2.693257	-0.125589
C	-4.008660	-1.691287	1.957849

C	-4.304865	-3.618014	-0.114346
C	-5.054143	-2.620598	1.978658
H	-3.880699	-0.947908	2.747296
C	-5.199869	-3.567715	0.959801
H	-4.405858	-4.353336	-0.915119
H	-5.769500	-2.609570	2.804267
H	-6.026778	-4.280104	1.006686
O	-1.937134	-3.084815	-2.126027
O	-1.469730	-0.001514	1.220779
N	-1.425957	-1.411597	-0.615194
C	-0.517729	0.379492	-2.053467
H	-1.509658	1.180008	-1.589191
H	0.358516	0.679561	-2.646657
H	-1.311131	0.204751	-2.800763
C	2.389334	0.801580	0.754333
H	2.955704	1.680915	0.389190
C	3.474952	-0.273138	0.863265
O	3.961426	-0.599712	1.915378
O	3.868578	-0.655993	-0.339977
C	4.819547	-1.743643	-0.525162
C	6.191437	-1.305467	-0.029751
H	6.175439	-1.130002	1.053445
H	6.932644	-2.088280	-0.249636
H	6.507403	-0.381916	-0.538529
C	4.819716	-1.937774	-2.033308
H	5.106480	-1.005940	-2.542550
H	5.532033	-2.726239	-2.315782
H	3.817669	-2.229218	-2.379862
C	4.324045	-2.999874	0.179015
H	4.371893	-2.889397	1.269239
H	3.279806	-3.200410	-0.097997
H	4.949919	-3.853774	-0.120324
O	-1.423744	3.371291	-0.772864
C	-2.556896	2.939114	-1.140401
O	-2.744799	1.757884	-1.513309
C	-3.717847	3.887462	-1.093557

H	-3.375757	4.928736	-1.104323
H	-4.401273	3.687520	-1.928199
H	-4.268976	3.706373	-0.157784
C	1.795035	1.102371	2.125056
H	1.243376	0.221585	2.487247
H	2.588817	1.288264	2.866202
C	0.835262	2.259830	2.158487
O	0.104668	2.526204	3.067517
N	0.806132	3.080160	0.965457
H	0.201290	3.890910	1.110436
H	1.733142	3.371414	0.650645

I-2*i*

Lowest frequency = 19.9970 cm^{-1}

Charge = 0, Multiplicity = 1

58

C	0.777663	-0.489307	-0.316812
N	1.224875	0.777980	-0.251872
Pd	-0.183687	2.119621	-0.618104
O	1.154006	-1.433155	0.363930
C	-0.306361	-0.651361	-1.394620
H	0.150751	-1.238250	-2.208403
C	-2.161102	-1.213083	0.189961
C	-1.347451	-2.904776	-1.152305
C	-2.822957	-2.478998	0.600576
C	-2.336116	-3.500775	-0.211438
C	-3.765257	-2.718467	1.587230
C	-2.771990	-4.807583	-0.070882
C	-4.209044	-4.036452	1.740690
H	-4.135061	-1.907248	2.217483
C	-3.721141	-5.062779	0.925465
H	-2.381645	-5.600162	-0.712323
H	-4.947289	-4.270931	2.510991

H	-4.087149	-6.081475	1.072951
O	-0.692196	-3.438771	-2.004711
O	-2.323262	-0.108847	0.676602
N	-1.331350	-1.526213	-0.863348
C	-0.814215	0.703699	-1.889723
H	-2.718578	1.447261	0.120789
H	-0.376918	0.951654	-2.868826
H	-1.910310	0.715069	-1.991382
C	2.248002	1.094170	0.716980
H	2.817593	1.955773	0.315486
C	3.325344	0.018495	0.873067
O	3.795865	-0.285773	1.939664
O	3.729302	-0.405042	-0.313798
C	4.662607	-1.512466	-0.457988
C	6.036595	-1.083147	0.039886
H	6.011172	-0.876480	1.117432
H	6.767295	-1.883703	-0.149547
H	6.372829	-0.179332	-0.490955
C	4.674397	-1.749470	-1.960100
H	4.979106	-0.836337	-2.492305
H	5.377746	-2.555886	-2.213199
H	3.671215	-2.036140	-2.307374
C	4.139732	-2.741255	0.274548
H	4.175033	-2.600016	1.361756
H	3.096479	-2.933857	-0.011599
H	4.757692	-3.611670	0.007731
O	-1.781032	3.429327	-0.963066
C	-2.955545	3.222008	-0.658021
O	-3.400667	2.148122	-0.081132
C	-4.015217	4.235695	-0.942826
H	-3.573978	5.130407	-1.393570
H	-4.759988	3.797185	-1.623138
H	-4.539396	4.490683	-0.010671
C	1.661270	1.459672	2.077167
H	1.165310	0.583148	2.517366
H	2.466163	1.736231	2.778404

C	0.649157	2.579121	2.060019
O	-0.201387	2.733597	2.896818
N	0.721172	3.466782	0.953583
H	0.177055	4.312321	1.113078
H	1.656330	3.666047	0.604376

I-3*i*

Lowest frequency = 15.4913 cm^{-1}

Charge = 0, Multiplicity = 1

65

C	0.826165	1.592175	-0.172753
N	-0.250941	0.888728	0.210994
Pd	-0.133886	-1.075886	-0.066940
O	1.150416	2.704134	0.215755
C	1.623848	0.798900	-1.221482
H	1.850110	1.482427	-2.056548
C	3.215749	-0.062711	0.566543
C	4.101459	0.699491	-1.431472
C	4.699365	-0.176944	0.640607
C	5.233138	0.280256	-0.560860
C	5.508858	-0.634457	1.667539
C	6.599376	0.298995	-0.788739
C	6.890657	-0.620982	1.448742
H	5.077379	-0.985976	2.606892
C	7.426758	-0.162308	0.241023
H	7.004316	0.662762	-1.735207
H	7.564762	-0.972025	2.233452
H	8.510420	-0.163392	0.102902
O	4.130388	1.156530	-2.542796
O	2.419551	-0.363806	1.429768
N	2.932261	0.453825	-0.689956
C	0.807350	-0.401803	-1.700325
H	0.074133	-0.085180	-2.456487

H	1.440647	-1.202909	-2.114269
C	-1.197125	1.409671	1.156602
H	-2.182408	0.971134	0.904708
C	-1.428464	2.916061	1.027625
O	-1.507318	3.662170	1.967877
O	-1.656225	3.232900	-0.242996
C	-1.803100	4.615672	-0.672952
C	-3.117719	5.169483	-0.139353
H	-3.104225	5.207760	0.957405
H	-3.278166	6.186892	-0.526354
H	-3.961570	4.541863	-0.465247
C	-1.833197	4.498229	-2.189168
H	-2.665518	3.856742	-2.515045
H	-1.959697	5.490654	-2.645231
H	-0.892717	4.060845	-2.554288
C	-0.602343	5.439717	-0.226609
H	-0.605365	5.590408	0.859626
H	0.328477	4.921539	-0.495988
H	-0.632041	6.421086	-0.723243
C	-0.876925	1.015059	2.606947
H	0.180445	1.245561	2.806864
H	-1.506650	1.596924	3.289810
C	-1.194295	-0.443635	2.817362
O	-2.211717	-0.842990	3.334869
N	-0.273527	-1.339598	2.265667
H	-0.419486	-2.295835	2.578758
C	-2.805193	-2.254282	-0.399757
C	-3.488222	-2.472173	0.789598
C	-3.075092	-1.169544	-1.231143
C	-4.467867	-1.547814	1.154114
H	-3.250416	-3.313329	1.441430
C	-4.039756	-0.231770	-0.847416
H	-2.506833	-1.017419	-2.150360
C	-4.733366	-0.443391	0.351864
H	-5.000291	-1.682098	2.097346
H	-5.483951	0.284814	0.669383

I	-1.129305	-3.498731	-0.883259
C	-4.246942	1.009331	-1.663408
H	-4.148232	0.808766	-2.739948
H	-5.236411	1.451686	-1.481631
H	-3.484781	1.761089	-1.395662
H	0.705988	-1.040885	2.253395

TS(3-4)^{i}

Lowest frequency = -125.6799 cm^{-1}

Charge = 0, Multiplicity = 1

65

C	-0.722234	1.614179	0.309226
N	0.445805	1.296719	-0.286992
Pd	0.843235	-0.674256	-0.313430
O	-1.418544	2.582475	0.050179
C	-1.110476	0.576639	1.371600
H	-1.263826	1.108078	2.326085
C	-2.777705	-0.477410	-0.188825
C	-3.480865	0.058686	1.956437
C	-4.216665	-0.842161	-0.068419
C	-4.639919	-0.519205	1.219367
C	-5.078987	-1.398316	-0.999107
C	-5.944345	-0.740529	1.630390
C	-6.398448	-1.626301	-0.593809
H	-4.732754	-1.641657	-2.005708
C	-6.823763	-1.303070	0.698941
H	-6.264044	-0.480670	2.641552
H	-7.111385	-2.062085	-1.297600
H	-7.861601	-1.492247	0.982904
O	-3.426761	0.468903	3.086562
O	-2.051252	-0.587993	-1.146444
N	-2.411491	0.032059	1.054287
C	-0.013859	-0.468376	1.506013

H	0.780248	-0.101306	2.169188
H	-0.396776	-1.435665	1.863527
C	0.893151	2.124936	-1.378648
H	1.989071	1.987691	-1.463103
C	0.755562	3.627858	-1.121191
O	0.450443	4.411434	-1.983588
O	1.131161	3.924583	0.112453
C	0.981568	5.265764	0.657564
C	1.949350	6.209656	-0.043974
H	1.692265	6.309678	-1.106146
H	1.904710	7.203677	0.425676
H	2.981166	5.835899	0.041803
C	1.362219	5.079773	2.118132
H	2.382673	4.677828	2.202292
H	1.317711	6.041404	2.649416
H	0.670564	4.376867	2.604664
C	-0.466005	5.722942	0.533356
H	-0.733427	5.914382	-0.513020
H	-1.140297	4.946791	0.921490
H	-0.605603	6.648359	1.111852
C	0.216986	1.746750	-2.691851
H	-0.865330	1.922985	-2.611147
H	0.570525	2.397850	-3.508073
C	0.394990	0.313585	-3.122913
O	-0.306147	-0.242185	-3.922127
N	1.466948	-0.399959	-2.506851
H	1.616998	-1.282553	-2.994302
C	2.528550	-1.981858	0.336925
C	3.605111	-1.827300	-0.543188
C	2.731819	-1.971596	1.720078
C	4.865374	-1.551733	-0.016022
H	3.474640	-1.940411	-1.619645
C	3.995257	-1.690910	2.245183
H	1.900754	-2.168748	2.398459
C	5.059604	-1.472246	1.359381
H	5.709223	-1.415070	-0.696904

H	6.055848	-1.261417	1.755931
I	0.779594	-3.332753	-0.433126
C	4.198441	-1.604899	3.729537
H	4.226248	-0.552854	4.057760
H	3.386345	-2.101455	4.278482
H	5.150629	-2.066067	4.030256
H	2.329857	0.133758	-2.416689

I-4*i*

Lowest frequency = 19.3021 cm^{-1}

Charge = 0, Multiplicity = 1

65

C	-0.196324	1.690405	-0.633014
N	-0.869665	0.880917	0.206143
Pd	-0.121021	-0.994778	0.246118
O	-0.132524	2.906740	-0.565394
C	0.609646	0.887158	-1.675978
H	0.510977	1.375679	-2.658906
C	2.526175	0.569393	-0.135552
C	2.958171	1.747636	-2.071984
C	3.935679	1.008508	-0.079145
C	4.200932	1.722632	-1.249523
C	4.900056	0.810413	0.894959
C	5.450384	2.266815	-1.492422
C	6.164501	1.360651	0.656923
H	4.671270	0.251787	1.804693
C	6.434124	2.074641	-0.514667
H	5.651208	2.823772	-2.409656
H	6.955723	1.231785	1.398691
H	7.432299	2.491130	-0.667659
O	2.747330	2.249312	-3.139826
O	1.904499	-0.069998	0.701576
N	2.010424	1.015397	-1.324731
C	0.153200	-0.555496	-1.711166

H	-0.814808	-0.649276	-2.214137
H	0.891444	-1.252060	-2.129996
C	-1.480816	1.434504	1.385530
H	-2.312382	0.766319	1.670153
C	-2.204664	2.762401	1.137166
O	-2.165087	3.679321	1.915999
O	-2.943797	2.681488	0.045209
C	-3.675056	3.828150	-0.478077
C	-4.803624	4.185963	0.479605
H	-4.403833	4.525533	1.443625
H	-5.414287	4.992748	0.047679
H	-5.455800	3.315362	0.647532
C	-4.221910	3.304119	-1.796372
H	-4.846887	2.414811	-1.628389
H	-4.830959	4.075307	-2.289452
H	-3.396444	3.025829	-2.467327
C	-2.722222	4.992563	-0.712307
H	-2.361822	5.408397	0.236578
H	-1.851185	4.656641	-1.291922
H	-3.245669	5.782673	-1.270930
C	-0.507330	1.559036	2.552704
H	0.277066	2.290511	2.309487
H	-1.029348	1.974613	3.430002
C	0.200656	0.294350	2.984416
O	1.211733	0.299575	3.631524
N	-0.355751	-0.936964	2.539294
H	0.137220	-1.735900	2.940478
C	-1.856962	-1.869334	-0.206999
C	-2.974717	-1.602935	0.580145
C	-1.964792	-2.756862	-1.276659
C	-4.188039	-2.231829	0.296526
H	-2.947789	-0.896910	1.410710
C	-3.178115	-3.393938	-1.568888
H	-1.093638	-2.993300	-1.890161
C	-4.291034	-3.118912	-0.768942
H	-5.061380	-2.013537	0.916160

H	-5.245863	-3.605292	-0.984134
I	1.092963	-3.354831	0.314275
C	-3.250626	-4.375164	-2.702426
H	-2.787243	-3.969960	-3.614657
H	-2.710623	-5.302158	-2.449876
H	-4.289790	-4.644973	-2.936660
H	-1.363610	-1.029863	2.649310

TS(4-5)*i*

Lowest frequency = -293.0432 cm^{-1}

Charge = 0, Multiplicity = 1

65

C	-1.166001	0.628270	-0.279260
N	0.040513	1.008889	-0.726284
Pd	1.597753	-0.231599	-0.555631
O	-2.232283	1.126226	-0.605947
C	-1.082735	-0.467722	0.783927
H	-1.151179	0.034359	1.762941
C	-2.615337	-1.969176	-0.476822
C	-3.248449	-1.328961	1.669980
C	-3.966937	-2.528830	-0.204975
C	-4.345121	-2.148159	1.082743
C	-4.794802	-3.297382	-1.007275
C	-5.567389	-2.520604	1.618696
C	-6.030719	-3.678362	-0.474621
H	-4.486880	-3.585469	-2.014385
C	-6.410417	-3.296692	0.816431
H	-5.853096	-2.213481	2.626726
H	-6.713786	-4.282831	-1.075788
H	-7.383521	-3.609811	1.201687
O	-3.188843	-0.779773	2.738541
O	-1.936353	-2.043773	-1.469325
N	-2.241151	-1.311281	0.698365

C	0.194689	-1.274655	0.690753
H	0.407931	-1.864595	1.582774
H	0.180904	-1.944063	-0.187411
C	0.125012	2.061165	-1.704082
H	1.139471	2.497017	-1.628355
C	-0.787805	3.249703	-1.393951
O	-1.378186	3.859968	-2.244994
O	-0.719676	3.547068	-0.104460
C	-1.574393	4.560199	0.504552
C	-1.181481	5.934083	-0.020331
H	-1.382681	6.012653	-1.096240
H	-1.759581	6.709448	0.503889
H	-0.112295	6.123709	0.159417
C	-1.252623	4.426957	1.984836
H	-0.181158	4.602529	2.164118
H	-1.827608	5.161811	2.566081
H	-1.509064	3.419983	2.345495
C	-3.036477	4.231044	0.237164
H	-3.285709	4.363657	-0.822875
H	-3.245945	3.187428	0.510179
H	-3.673749	4.897025	0.837512
C	-0.110623	1.523979	-3.110358
H	-1.167020	1.248354	-3.235081
H	0.105866	2.292946	-3.870758
C	0.704619	0.293430	-3.411127
O	0.385583	-0.569392	-4.175441
N	1.942126	0.168232	-2.680905
H	2.501120	-0.608830	-3.045080
C	1.668615	0.004409	1.496092
C	1.287493	1.286605	1.908302
C	2.491133	-0.778325	2.318733
C	1.773348	1.778234	3.123020
H	0.640975	1.911395	1.292858
C	2.980745	-0.285079	3.527234
H	2.759744	-1.791461	2.014941
C	2.609617	1.009643	3.920802

H	1.483987	2.783824	3.438108
H	2.977339	1.410261	4.869466
I	3.664844	-1.906765	-0.728009
C	3.883890	-1.120691	4.386526
H	4.875641	-0.651312	4.484748
H	3.475339	-1.233843	5.402851
H	4.029581	-2.122947	3.961397
H	2.502544	1.022352	-2.672870

I-5*i*

Lowest frequency = 17.3620 cm^{-1}

Charge = 0, Multiplicity = 1

65

C	0.999665	0.896825	0.159463
N	-0.312701	0.928172	0.424590
Pd	-1.520406	-0.673502	0.132803
O	1.855381	1.459780	0.840424
C	1.487662	0.236301	-1.143484
H	1.953035	1.081259	-1.676623
C	2.632995	-1.531968	0.217659
C	3.833562	-0.533810	-1.492091
C	4.002072	-2.111463	0.216367
C	4.726308	-1.511605	-0.813310
C	4.567918	-3.070684	1.039992
C	6.047227	-1.846282	-1.060880
C	5.901780	-3.416612	0.797274
H	3.990352	-3.532009	1.843421
C	6.628520	-2.814881	-0.234820
H	6.605178	-1.367526	-1.867998
H	6.386137	-4.168708	1.424085
H	7.668623	-3.106960	-0.396371
O	4.060819	0.208386	-2.409915
O	1.718523	-1.778859	0.974346

N	2.596650	-0.633500	-0.834965
C	0.488674	-0.431627	-2.100446
H	0.977407	-0.496103	-3.087783
H	0.282722	-1.463076	-1.777775
C	-0.703183	1.735103	1.554556
H	-1.790111	1.918346	1.469207
C	-0.075999	3.133315	1.573440
O	0.161510	3.712135	2.601914
O	0.062838	3.631399	0.352471
C	0.770119	4.887119	0.134597
C	-0.057276	6.039008	0.688558
H	-0.155271	5.957390	1.778208
H	0.429602	6.995826	0.447957
H	-1.061711	6.041844	0.238368
C	0.870351	4.972878	-1.380400
H	-0.128580	4.943452	-1.839251
H	1.358351	5.912752	-1.674890
H	1.467486	4.137282	-1.774118
C	2.162413	4.818064	0.750052
H	2.116469	4.839887	1.845234
H	2.659892	3.885863	0.446173
H	2.756820	5.675471	0.401061
C	-0.427322	1.044332	2.899399
H	0.658036	0.857363	2.948328
H	-0.711885	1.698350	3.730632
C	-1.189487	-0.237123	3.030193
O	-2.034536	-0.463831	3.851828
N	-0.880044	-1.230560	2.041714
H	-1.331663	-2.118688	2.277246
C	-0.800038	0.338868	-2.208887
C	-0.789537	1.725422	-2.391423
C	-2.045634	-0.323355	-2.059570
C	-1.978106	2.437524	-2.362923
H	0.154621	2.257699	-2.508039
C	-3.270044	0.409222	-2.060262
H	-2.087062	-1.407147	-2.212455

C	-3.204066	1.794564	-2.170324
H	-1.955328	3.523523	-2.478808
H	-4.127320	2.378312	-2.151689
I	-2.903396	-2.948809	0.083087
C	-4.587942	-0.296298	-2.037821
H	-4.738919	-0.841314	-2.983930
H	-4.632922	-1.044966	-1.233535
H	-5.416795	0.413887	-1.917474
H	0.124074	-1.361932	1.840927

I-1^t

Lowest frequency = 9.7320 cm^{-1}

Charge = 0, Multiplicity = 1

58

C	0.190865	-0.492072	0.136133
N	1.478215	0.054729	-0.184947
Pd	1.241379	2.133325	-0.103807
O	-0.136636	-0.737729	1.260899
C	-0.716748	-0.834171	-1.047180
H	-0.542878	-1.917206	-1.159450
C	-2.666451	0.459150	-0.166311
C	-2.855187	-1.855351	-0.307622
C	-3.996857	0.065606	0.374422
C	-4.110112	-1.322634	0.288759
C	-5.011688	0.844199	0.906574
C	-5.243319	-1.986312	0.730592
C	-6.160398	0.183102	1.354066
H	-4.907510	1.928875	0.974732
C	-6.274480	-1.208164	1.267184
H	-5.317927	-3.073418	0.662586
H	-6.982507	0.760879	1.782550
H	-7.183944	-1.693355	1.628749
O	-2.527574	-2.996040	-0.518108

O	-2.153457	1.546421	-0.233440
N	-2.076810	-0.732824	-0.598468
C	-0.476332	-0.166267	-2.391174
H	-0.596284	0.923242	-2.347457
H	0.529744	-0.395670	-2.776631
H	-1.188015	-0.582416	-3.117613
C	2.637226	-0.444301	0.589309
H	3.513329	0.070162	0.161322
C	2.874836	-1.937999	0.358767
O	3.753783	-2.530224	0.921971
O	2.020700	-2.455739	-0.524165
C	2.024719	-3.892873	-0.840935
C	3.356745	-4.262649	-1.477149
H	4.185602	-4.134903	-0.770605
H	3.326211	-5.314271	-1.797273
H	3.543279	-3.642285	-2.366922
C	0.888779	-4.049908	-1.839133
H	1.024633	-3.370885	-2.694392
H	0.877985	-5.079979	-2.222662
H	-0.090554	-3.858569	-1.375318
C	1.735626	-4.683164	0.426768
H	2.556284	-4.599247	1.149537
H	0.806001	-4.323586	0.892641
H	1.599654	-5.743654	0.169201
O	0.854109	4.134244	-0.341896
C	0.396209	3.936888	-1.509528
O	0.450354	2.761131	-1.974557
C	-0.220756	5.050010	-2.284153
H	0.153595	6.018921	-1.932214
H	-0.025741	4.917620	-3.356098
H	-1.310134	5.014118	-2.127975
C	2.605229	-0.157665	2.083517
H	1.773312	-0.696662	2.555641
H	3.532264	-0.563616	2.508114
C	2.515842	1.289800	2.533752
O	2.893098	1.577156	3.660604

N	2.000547	2.192645	1.681296
H	1.950489	3.122679	2.095447
H	1.658525	-0.106706	-1.176376

TS(1-2)^{t}

Lowest frequency = -1147.4672 cm^{-1}

Charge = 0, Multiplicity = 1

58

C	0.542211	-0.549949	-0.075510
N	1.620108	0.336640	-0.404561
Pd	0.532553	2.100498	-0.503267
O	0.491399	-1.156819	0.953943
C	-0.517582	-0.580708	-1.171686
H	-0.236152	-1.409928	-1.848704
C	-2.436687	-0.316090	0.422250
C	-2.294114	-2.275296	-0.828143
C	-3.577701	-1.196032	0.797145
C	-3.492590	-2.369429	0.047637
C	-4.591890	-0.997036	1.719682
C	-4.418489	-3.390585	0.190529
C	-5.533232	-2.020851	1.868955
H	-4.643676	-0.075919	2.303506
C	-5.448215	-3.197369	1.117175
H	-4.338478	-4.305926	-0.399184
H	-6.348609	-1.903057	2.586306
H	-6.198752	-3.978132	1.259902
O	-1.829880	-3.087366	-1.587756
O	-2.114703	0.752140	0.871226
N	-1.760021	-1.004040	-0.593527
C	-0.594019	0.745669	-1.937368
H	-1.272677	1.861636	-1.474570
H	0.215089	0.819839	-2.682403
H	-1.502123	0.702228	-2.562476

C	2.802580	0.291754	0.472252
H	3.581419	0.863785	-0.059967
C	3.331319	-1.140116	0.585790
O	4.032769	-1.516108	1.482363
O	2.949568	-1.854315	-0.472640
C	3.184360	-3.295857	-0.571849
C	4.677586	-3.547926	-0.715451
H	5.215890	-3.230565	0.186701
H	4.857319	-4.621491	-0.873097
H	5.079079	-3.002685	-1.582884
C	2.432648	-3.678632	-1.836885
H	2.798148	-3.097039	-2.696335
H	2.582614	-4.745500	-2.055085
H	1.351751	-3.505267	-1.721517
C	2.587876	-3.996783	0.640772
H	3.136979	-3.749449	1.557413
H	1.535500	-3.705461	0.771051
H	2.630989	-5.084731	0.485672
O	-0.479289	3.851177	-0.496089
C	-1.670727	3.810784	-0.917573
O	-2.185722	2.786823	-1.428185
C	-2.501158	5.048239	-0.763628
H	-1.865543	5.939025	-0.701389
H	-3.219355	5.128229	-1.588828
H	-3.069158	4.958316	0.175303
C	2.572747	0.947864	1.820499
H	1.688813	0.505520	2.305184
H	3.432365	0.721748	2.462947
C	2.428169	2.464571	1.779768
O	2.889287	3.141828	2.685416
N	1.799826	2.988540	0.703623
H	1.643047	3.989983	0.805217
H	1.902708	0.177745	-1.373610

I-2^t

Lowest frequency = 22.1736 cm^{-1}

Charge = 0, Multiplicity = 1

58

C	0.190865	-0.492072	0.136133
N	1.478215	0.054729	-0.184947
Pd	1.241379	2.133325	-0.103807
O	-0.136636	-0.737729	1.260899
C	-0.716748	-0.834171	-1.047180
H	-0.542878	-1.917206	-1.159450
C	-2.666451	0.459150	-0.166311
C	-2.855187	-1.855351	-0.307622
C	-3.996857	0.065606	0.374422
C	-4.110112	-1.322634	0.288759
C	-5.011688	0.844199	0.906574
C	-5.243319	-1.986312	0.730592
C	-6.160398	0.183102	1.354066
H	-4.907510	1.928875	0.974732
C	-6.274480	-1.208164	1.267184
H	-5.317927	-3.073418	0.662586
H	-6.982507	0.760879	1.782550
H	-7.183944	-1.693355	1.628749
O	-2.527574	-2.996040	-0.518108
O	-2.153457	1.546421	-0.233440
N	-2.076810	-0.732824	-0.598468
C	-0.476332	-0.166267	-2.391174
H	-0.596284	0.923242	-2.347457
H	0.529744	-0.395670	-2.776631
H	-1.188015	-0.582416	-3.117613
C	2.637226	-0.444301	0.589309
H	3.513329	0.070162	0.161322
C	2.874836	-1.937999	0.358767
O	3.753783	-2.530224	0.921971
O	2.020700	-2.455739	-0.524165
C	2.024719	-3.892873	-0.840935

C	3.356745	-4.262649	-1.477149
H	4.185602	-4.134903	-0.770605
H	3.326211	-5.314271	-1.797273
H	3.543279	-3.642285	-2.366922
C	0.888779	-4.049908	-1.839133
H	1.024633	-3.370885	-2.694392
H	0.877985	-5.079979	-2.222662
H	-0.090554	-3.858569	-1.375318
C	1.735626	-4.683164	0.426768
H	2.556284	-4.599247	1.149537
H	0.806001	-4.323586	0.892641
H	1.599654	-5.743654	0.169201
O	0.854109	4.134244	-0.341896
C	0.396209	3.936888	-1.509528
O	0.450354	2.761131	-1.974557
C	-0.220756	5.050010	-2.284153
H	0.153595	6.018921	-1.932214
H	-0.025741	4.917620	-3.356098
H	-1.310134	5.014118	-2.127975
C	2.605229	-0.157665	2.083517
H	1.773312	-0.696662	2.555641
H	3.532264	-0.563616	2.508114
C	2.515842	1.289800	2.533752
O	2.893098	1.577156	3.660604
N	2.000547	2.192645	1.681296
H	1.950489	3.122679	2.095447
H	1.658525	-0.106706	-1.176376

I-3^t

Lowest frequency = 16.7289 cm^{-1}

Charge = 0, Multiplicity = 1

65

C	0.844718	0.987725	-0.432698

N	-0.466135	0.776556	-0.156641
Pd	0.171050	-1.776743	0.108433
O	1.535506	1.741292	0.224260
C	1.485119	0.093263	-1.533052
H	1.601345	0.696083	-2.451337
C	3.075511	-0.830400	0.097735
C	3.972673	0.525114	-1.535497
C	4.516506	-0.680394	0.393392
C	5.063250	0.139947	-0.595745
C	5.285988	-1.194056	1.424453
C	6.406063	0.476563	-0.592004
C	6.643789	-0.856728	1.435374
H	4.842757	-1.829197	2.193770
C	7.193628	-0.036885	0.445076
H	6.824066	1.121323	-1.367543
H	7.286448	-1.237054	2.232436
H	8.257180	0.209013	0.485578
O	4.000521	1.240598	-2.498297
O	2.234372	-1.429147	0.754504
N	2.831212	-0.151688	-1.068512
C	0.752602	-1.222331	-1.769646
H	-0.124443	-1.058457	-2.419349
H	1.410540	-1.937327	-2.288010
C	-1.050634	1.281437	1.071976
H	-2.134097	1.094115	1.004433
C	-0.920905	2.801711	1.167611
O	-0.822460	3.400395	2.204198
O	-1.014987	3.351979	-0.042793
C	-0.791332	4.774250	-0.252617
C	-1.908480	5.571556	0.407163
H	-1.885897	5.444744	1.496679
H	-1.792292	6.639898	0.171351
H	-2.888990	5.242582	0.029768
C	-0.845916	4.910610	-1.766568
H	-1.824495	4.588142	-2.152714
H	-0.686967	5.957980	-2.060571

H	-0.065111	4.293934	-2.235206
C	0.586707	5.162458	0.268300
H	0.626526	5.110073	1.362975
H	1.348675	4.481657	-0.138013
H	0.821669	6.189643	-0.047641
C	-0.506863	0.568191	2.313938
H	0.586875	0.490943	2.230830
H	-0.738421	1.204797	3.176733
C	-1.161973	-0.789054	2.591476
O	-2.168090	-0.812693	3.308932
N	-0.596174	-1.875565	2.036912
H	-1.120605	-2.700111	2.329673
H	-1.071662	0.326494	-0.831110
C	-3.237823	-1.289941	-0.369550
C	-3.812632	-1.181132	0.889367
C	-3.364956	-0.295007	-1.340116
C	-4.539732	-0.023499	1.171798
H	-3.654707	-1.924231	1.670543
C	-4.064368	0.879625	-1.038182
H	-2.909984	-0.417364	-2.327088
C	-4.660305	0.989662	0.226470
H	-4.969356	0.093113	2.168271
H	-5.208946	1.900773	0.478748
I	-1.995043	-2.963806	-0.795944
C	-4.103319	2.017128	-2.014375
H	-4.005400	1.669614	-3.052559
H	-5.035533	2.592900	-1.927480
H	-3.265323	2.704419	-1.809271

TS(3-4)^{t}

Lowest frequency = -171.6716 cm^{-1}

Charge = 0, Multiplicity = 1

65

C	0.794930	1.456168	-0.169618
N	-0.564149	1.270240	0.217058
Pd	-0.616740	-0.861794	0.360002
O	1.541456	2.186032	0.415737
C	1.210433	0.518765	-1.319321
H	1.361156	1.135288	-2.224842
C	2.808459	-0.659057	0.179232
C	3.659942	0.246962	-1.782349
C	4.265624	-0.945310	0.137766
C	4.778611	-0.399090	-1.040024
C	5.075402	-1.608536	1.045148
C	6.123454	-0.497130	-1.356929
C	6.434994	-1.713359	0.732035
H	4.660946	-2.026330	1.964785
C	6.949746	-1.167459	-0.448082
H	6.514481	-0.063845	-2.279636
H	7.108270	-2.228220	1.421079
H	8.016689	-1.265443	-0.660957
O	3.671198	0.845094	-2.825497
O	1.996281	-0.921883	1.036026
N	2.521476	0.017923	-0.999741
C	0.169849	-0.583579	-1.518587
H	-0.615411	-0.238545	-2.209053
H	0.631479	-1.485985	-1.944576
C	-1.050770	2.012134	1.386904
H	-2.139679	1.831447	1.408216
C	-0.884752	3.519603	1.185866
O	-0.802058	4.309350	2.084406
O	-0.920030	3.809656	-0.115373
C	-0.693096	5.162504	-0.615262
C	-1.824580	6.071165	-0.156543
H	-1.821080	6.180975	0.935067
H	-1.706589	7.065459	-0.611969
H	-2.796860	5.663441	-0.472015
C	-0.719055	4.975009	-2.123831
H	-1.683466	4.554558	-2.445480

H	-0.575164	5.940398	-2.629418
H	0.085258	4.295296	-2.442891
C	0.671988	5.654312	-0.153972
H	0.692700	5.809607	0.931633
H	1.450291	4.923233	-0.417274
H	0.904005	6.607107	-0.652084
C	-0.457226	1.517933	2.695144
H	0.639724	1.472038	2.610628
H	-0.678554	2.266389	3.465430
C	-0.971842	0.177616	3.228188
O	-1.132499	0.062180	4.437961
N	-1.197482	-0.803024	2.334429
H	-1.457024	-1.656391	2.828036
H	-1.182713	1.388117	-0.586987
C	-2.575665	-1.733636	-0.471881
C	-3.567382	-1.298512	0.407729
C	-2.757835	-1.686110	-1.856958
C	-4.720624	-0.730962	-0.134942
H	-3.415481	-1.346374	1.485252
C	-3.917564	-1.120344	-2.392442
H	-1.996628	-2.088772	-2.527331
C	-4.894366	-0.633077	-1.512303
H	-5.492706	-0.358452	0.542989
H	-5.807654	-0.187235	-1.914906
I	-1.106180	-3.432851	0.210547
C	-4.124039	-1.064300	-3.878790
H	-3.204402	-1.314278	-4.425775
H	-4.904099	-1.776221	-4.193624
H	-4.451408	-0.063336	-4.198752

I-4^t

Lowest frequency = 19.8036 cm^{-1}

Charge = 0, Multiplicity = 1

65

C	-0.230533	1.669904	-0.473013
N	-1.193482	0.780580	0.116749
Pd	-0.062079	-1.021415	0.286718
O	-0.029182	2.767002	-0.045338
C	0.621309	0.996453	-1.567655
H	0.482989	1.553739	-2.511354
C	2.494288	0.815178	0.021969
C	2.938240	1.951266	-1.944997
C	3.901766	1.261530	0.076322
C	4.172811	1.949431	-1.110210
C	4.863026	1.088174	1.058249
C	5.421495	2.493672	-1.357305
C	6.127249	1.636430	0.814345
H	4.635028	0.544653	1.977211
C	6.400590	2.326533	-0.370428
H	5.626342	3.029939	-2.285906
H	6.915473	1.523862	1.561884
H	7.398362	2.742323	-0.527591
O	2.724276	2.441966	-3.018504
O	1.839136	0.221872	0.862505
N	1.996894	1.221428	-1.194568
C	0.293253	-0.484999	-1.682488
H	-0.620285	-0.628970	-2.276210
H	1.113830	-1.045297	-2.149525
C	-1.841740	1.237739	1.353933
H	-2.639089	0.499419	1.543022
C	-2.573714	2.562227	1.135355
O	-2.790042	3.356881	2.006302
O	-2.990556	2.640007	-0.127973
C	-3.688307	3.815361	-0.645240
C	-5.030923	3.957515	0.056951
H	-4.895919	4.173023	1.124230
H	-5.599378	4.781099	-0.399518
H	-5.620263	3.034461	-0.050440
C	-3.873462	3.479447	-2.116177

H	-4.452070	2.551098	-2.232140
H	-4.412375	4.290685	-2.625739
H	-2.898550	3.350226	-2.609616
C	-2.809312	5.046540	-0.474897
H	-2.683472	5.302076	0.584312
H	-1.815908	4.872077	-0.913404
H	-3.273048	5.899567	-0.991582
C	-0.898534	1.249191	2.544347
H	0.027559	1.787743	2.290236
H	-1.376512	1.827997	3.344123
C	-0.540364	-0.114787	3.147436
O	-0.375779	-0.184288	4.357741
N	-0.450097	-1.162092	2.302208
H	-0.168751	-2.005330	2.800164
H	-1.887181	0.487715	-0.577555
C	-1.637714	-2.119232	-0.271446
C	-2.739089	-2.126283	0.584897
C	-1.674221	-2.811454	-1.480705
C	-3.898514	-2.793147	0.182475
H	-2.673802	-1.660334	1.567382
C	-2.833013	-3.493436	-1.876596
H	-0.796407	-2.854335	-2.126806
C	-3.950000	-3.462414	-1.035496
H	-4.766217	-2.796854	0.847216
H	-4.863486	-3.984088	-1.332993
I	1.398318	-3.166116	0.263432
C	-2.844567	-4.272905	-3.159707
H	-2.252945	-3.775398	-3.942002
H	-2.407767	-5.274078	-3.009150
H	-3.867517	-4.412324	-3.537300

TS(4-5)^{t}

Lowest frequency = -248.9903 cm^{-1}

Charge = 0, Multiplicity = 1

65

C	1.203159	-1.276309	-0.658055
N	1.700515	-0.225373	0.199661
Pd	-0.091071	0.829982	0.663679
O	1.634934	-2.387601	-0.642161
C	0.082642	-0.777176	-1.577049
H	0.384186	-1.038200	-2.607835
C	-1.542421	-2.094831	-0.137514
C	-2.110179	-1.616164	-2.344216
C	-2.912999	-2.604836	-0.388775
C	-3.251330	-2.326804	-1.712916
C	-3.791114	-3.247224	0.467839
C	-4.483884	-2.683458	-2.235864
C	-5.038463	-3.609460	-0.050927
H	-3.514667	-3.447036	1.504775
C	-5.378410	-3.333841	-1.379520
H	-4.740077	-2.457994	-3.272861
H	-5.763388	-4.113011	0.592533
H	-6.362237	-3.628822	-1.751373
O	-1.983445	-1.183605	-3.460482
O	-0.873897	-2.152530	0.861470
N	-1.130663	-1.516166	-1.343021
C	-0.123890	0.755547	-1.552184
H	0.582474	1.175439	-2.278459
H	-1.133351	0.996169	-1.900497
C	2.545821	-0.635416	1.326127
H	2.855635	0.308298	1.809063
C	3.837089	-1.291728	0.839430
O	4.464486	-2.091129	1.474421
O	4.177493	-0.776399	-0.343352
C	5.340332	-1.247954	-1.094303
C	6.609447	-0.917441	-0.322619
H	6.652191	-1.474824	0.621430
H	7.487938	-1.183516	-0.928564
H	6.658200	0.160176	-0.105042

C	5.258622	-0.446951	-2.383567
H	5.294247	0.632462	-2.173781
H	6.102118	-0.699714	-3.041371
H	4.324447	-0.670661	-2.920115
C	5.196396	-2.738178	-1.368698
H	5.271814	-3.322462	-0.443465
H	4.223953	-2.949275	-1.837019
H	5.992181	-3.060770	-2.055888
C	1.790730	-1.472078	2.337366
H	1.361830	-2.359546	1.849973
H	2.508726	-1.841622	3.079766
C	0.676724	-0.782076	3.108629
O	0.407815	-1.175856	4.230706
N	0.021912	0.273745	2.550052
H	-0.762702	0.538014	3.144145
H	2.219856	0.426731	-0.395145
C	0.327844	2.438973	-0.599594
C	1.660229	2.858927	-0.464371
C	-0.648507	3.369414	-0.954895
C	1.977037	4.203592	-0.639896
H	2.472565	2.182777	-0.189313
C	-0.336104	4.723363	-1.125355
H	-1.684640	3.046643	-1.075289
C	0.991248	5.131078	-0.966261
H	3.012889	4.527249	-0.512778
H	1.254965	6.183151	-1.098861
I	-2.657172	1.282007	1.040997
C	-1.426427	5.702209	-1.447509
H	-2.045850	5.349551	-2.285942
H	-2.097347	5.831450	-0.583117
H	-1.019587	6.688269	-1.710514

I-5^t

Lowest frequency = 17.6556 cm^{-1}

Charge = 0, Multiplicity = 1

65

C	0.943349	0.199435	0.355119
N	-0.201307	1.039848	0.433604
Pd	-1.920188	-0.230472	0.275731
O	1.598854	-0.086010	1.317011
C	1.378044	-0.222836	-1.058363
H	1.867993	0.687652	-1.447864
C	2.263511	-2.481485	-0.433932
C	3.781329	-0.794154	-0.946857
C	3.639160	-3.007338	-0.221811
C	4.548863	-1.996912	-0.533180
C	4.059853	-4.253463	0.213640
C	5.916540	-2.191768	-0.422021
C	5.438465	-4.459930	0.328695
H	3.336633	-5.033414	0.459880
C	6.351107	-3.446886	0.015862
H	6.618613	-1.391651	-0.664581
H	5.811518	-5.427502	0.672019
H	7.421035	-3.641045	0.119597
O	4.178954	0.306023	-1.243616
O	1.202439	-3.013508	-0.246704
N	2.438551	-1.177428	-0.927402
C	0.307752	-0.682192	-2.058539
H	0.836210	-0.903638	-3.000602
H	-0.140903	-1.620746	-1.705726
C	-0.272022	1.970517	1.573183
H	-1.191414	2.556756	1.403322
C	0.878714	2.981053	1.527839
O	1.177296	3.661237	2.469938
O	1.443488	3.015243	0.321470
C	2.599783	3.873182	0.033160
C	2.215914	5.331498	0.238335
H	2.002204	5.545100	1.292393
H	3.045103	5.974146	-0.091643

H	1.330197	5.583382	-0.364777
C	2.892284	3.592086	-1.431630
H	2.016782	3.832855	-2.053492
H	3.729838	4.219373	-1.768256
H	3.179809	2.540955	-1.580500
C	3.767156	3.440297	0.907527
H	3.557347	3.618601	1.969558
H	3.982029	2.373069	0.751344
H	4.663045	4.012849	0.626325
C	-0.354771	1.329118	2.946609
H	0.610400	0.869522	3.198260
H	-0.517133	2.130992	3.677314
C	-1.403553	0.270357	3.213517
O	-1.722479	0.048961	4.371879
N	-1.885128	-0.492128	2.205924
H	-2.559966	-1.169869	2.555589
H	-0.278366	1.577167	-0.435256
C	-0.753671	0.355449	-2.306591
C	-0.396436	1.679311	-2.599933
C	-2.118404	0.025998	-2.207770
C	-1.381596	2.651991	-2.748349
H	0.654532	1.954026	-2.714086
C	-3.127113	1.002301	-2.395442
H	-2.406185	-1.028357	-2.129696
C	-2.730582	2.321503	-2.633137
H	-1.093110	3.682916	-2.968791
H	-3.492315	3.093263	-2.766670
I	-3.933142	-1.903806	0.217081
C	-4.579033	0.643756	-2.368957
H	-4.754686	-0.354595	-2.791060
H	-4.951077	0.608006	-1.332312
H	-5.174010	1.380665	-2.925777

Acetic Acid

Lowest frequency = 80.2401 cm^{-1}

Charge = 0, Multiplicity = 1

8

H	-1.005284	-2.950461	0.315291
O	-2.795484	-2.563472	-1.007446
C	-2.583401	-3.597742	-0.433210
O	-1.503717	-3.781668	0.343622
C	-3.449335	-4.820550	-0.477546
H	-4.318006	-4.633574	-1.117599
H	-2.870886	-5.673324	-0.861945
H	-3.776103	-5.083335	0.539183

3-Me-C_6H_4I

Lowest frequency = 8.0434 cm^{-1}

Charge = 0, Multiplicity = 1

15

C	-3.223192	-1.328619	-0.380663
C	-3.773597	-1.228319	0.893400
C	-3.355231	-0.297636	-1.309593
C	-4.467606	-0.065705	1.228868
H	-3.666624	-2.039616	1.615272
C	-4.050509	0.868511	-0.973476
H	-2.916149	-0.396267	-2.304795
C	-4.604765	0.968499	0.309046
H	-4.906001	0.027287	2.225460
H	-5.152396	1.872730	0.588198
I	-2.165894	-3.078182	-0.922116
C	-4.196313	1.989103	-1.961583
H	-3.748521	1.733855	-2.931733
H	-5.256717	2.233110	-2.130730
H	-3.707150	2.905389	-1.594592

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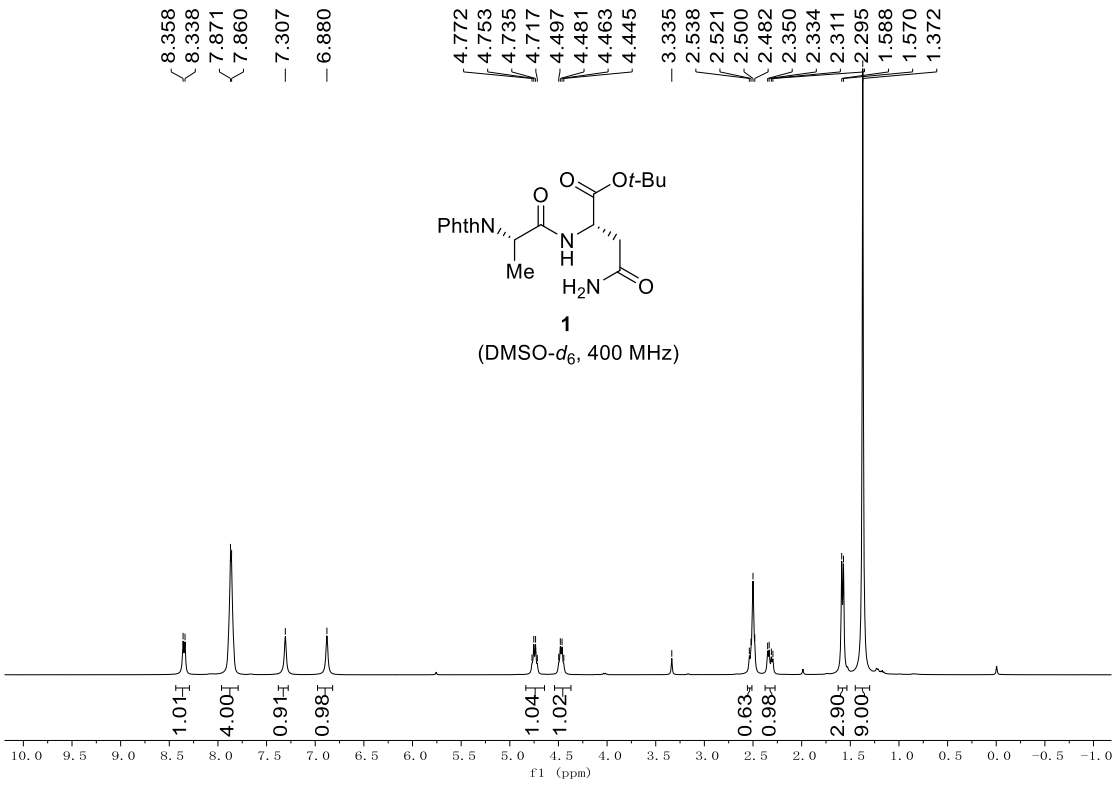
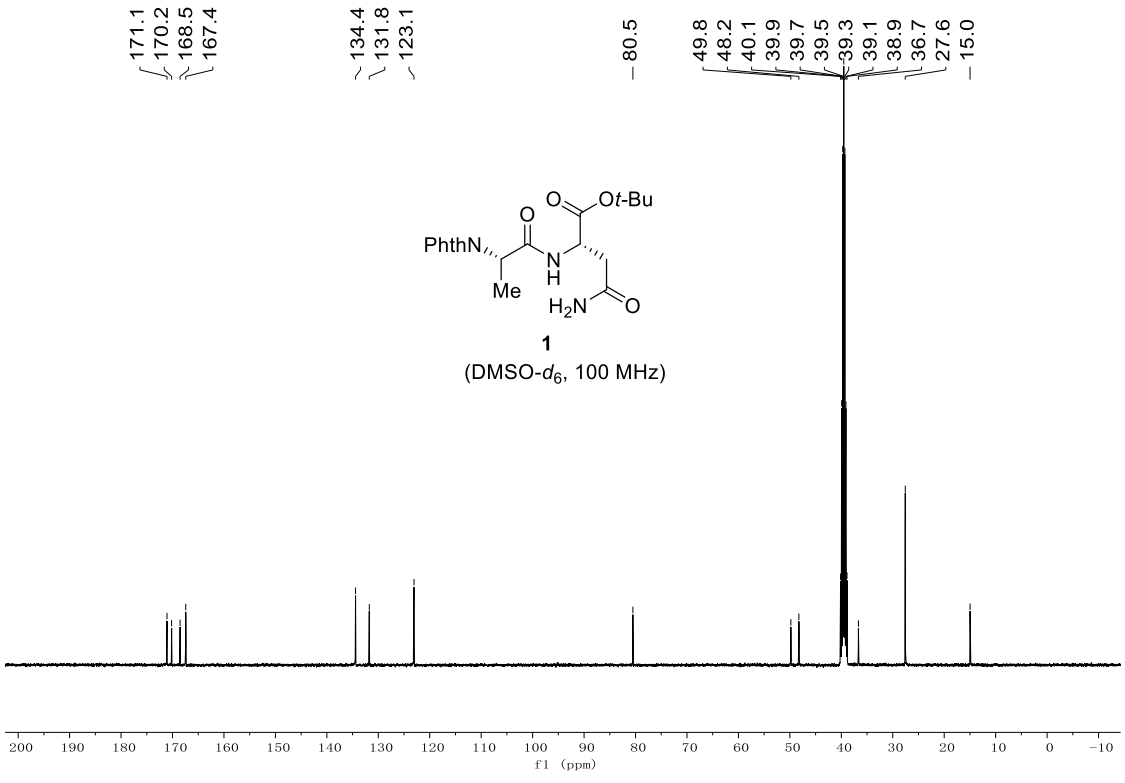
^{1}H, ^{13}C and ^{19}F NMR Spectra



1

(DMSO-d_6, 400 MHz)



1

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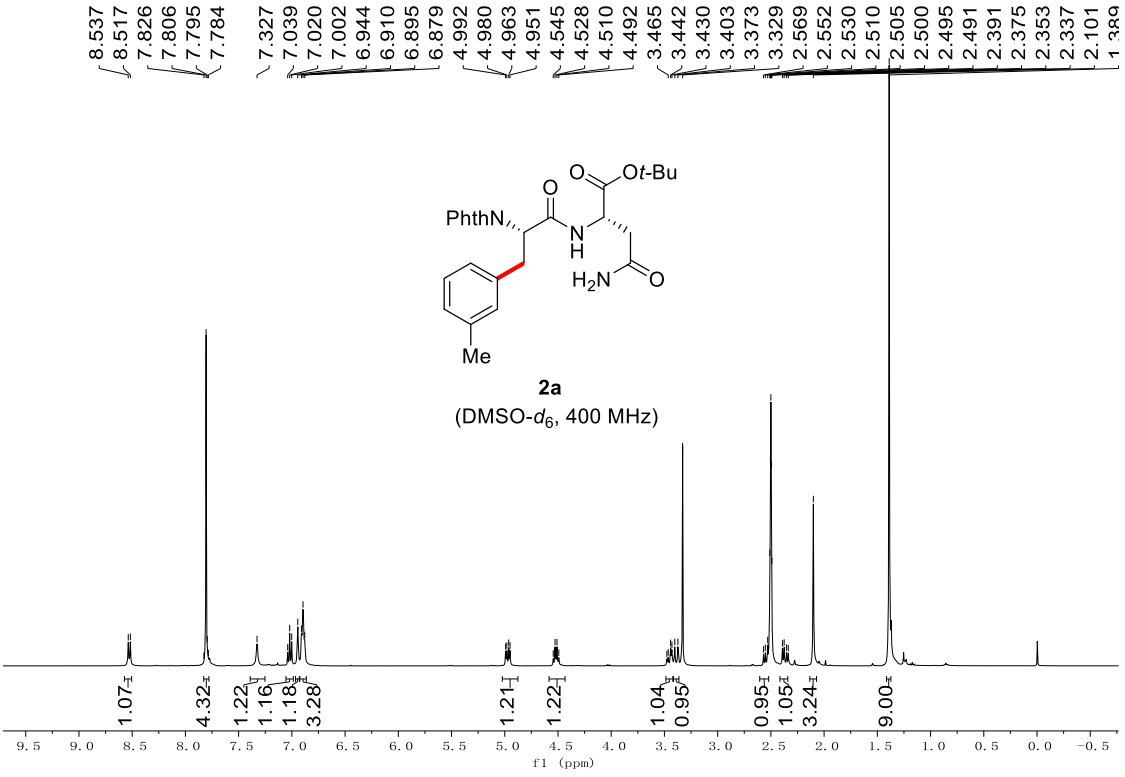
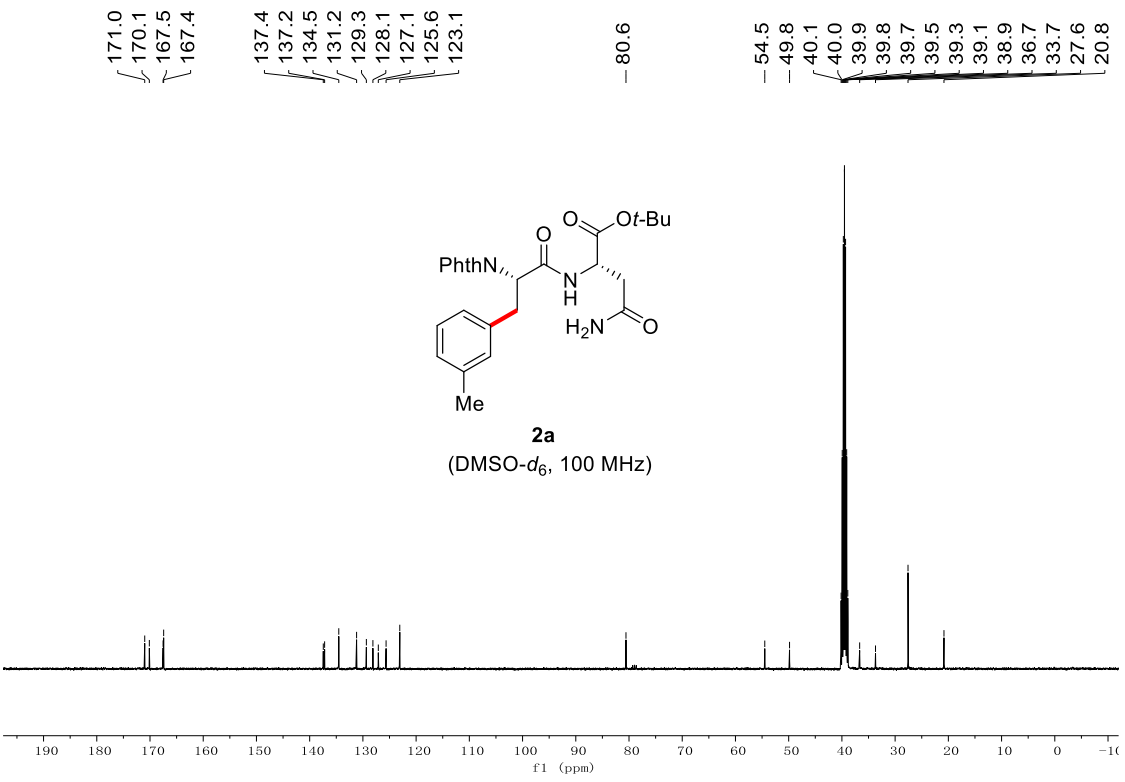


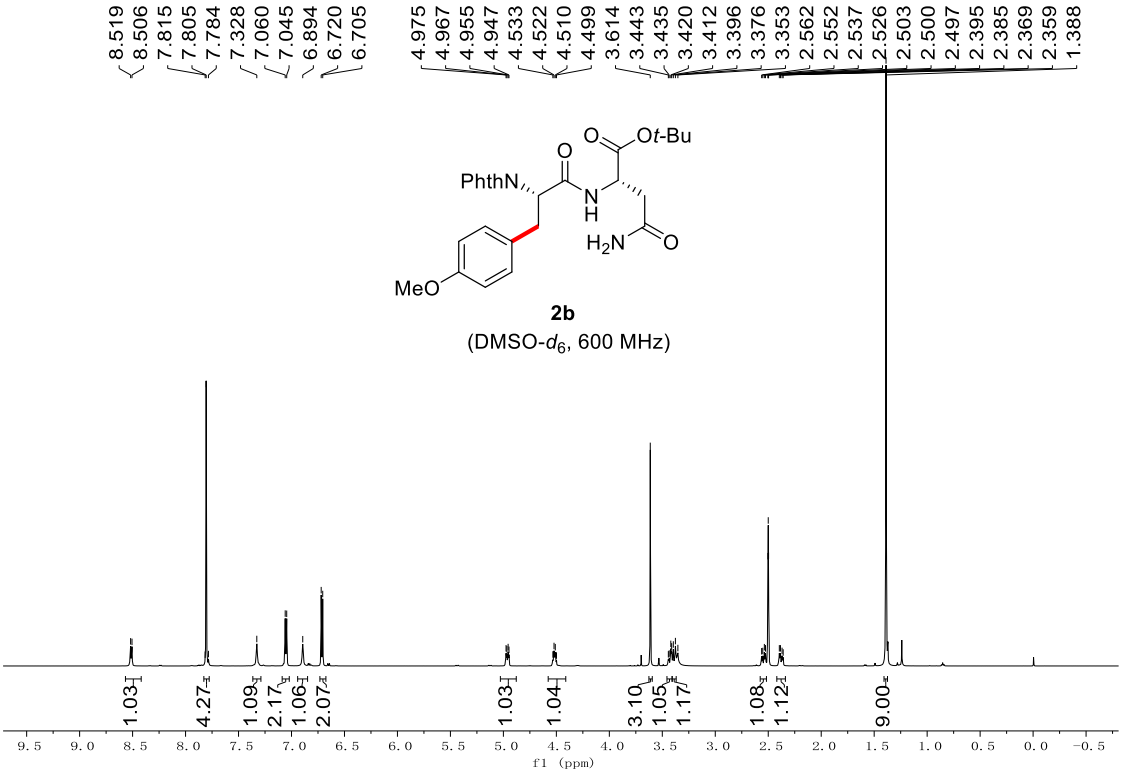
2a

(DMSO-d_6, 400 MHz)



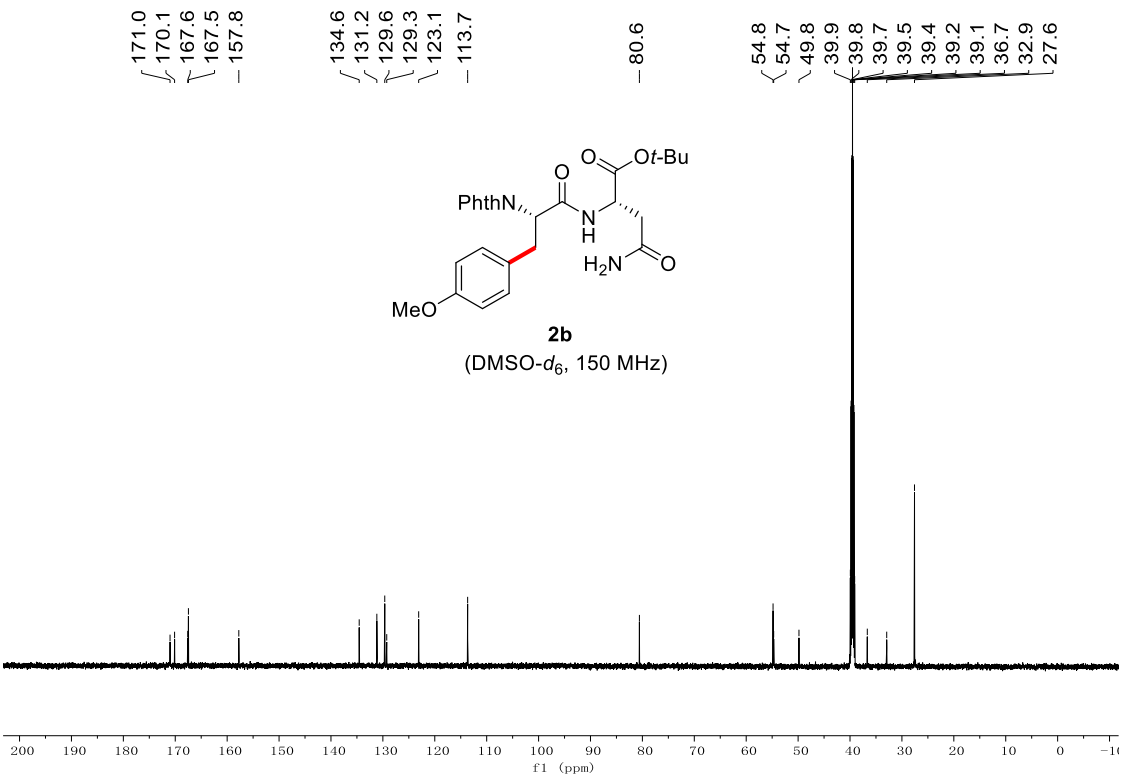
2a

(DMSO-d_6, 100 MHz)



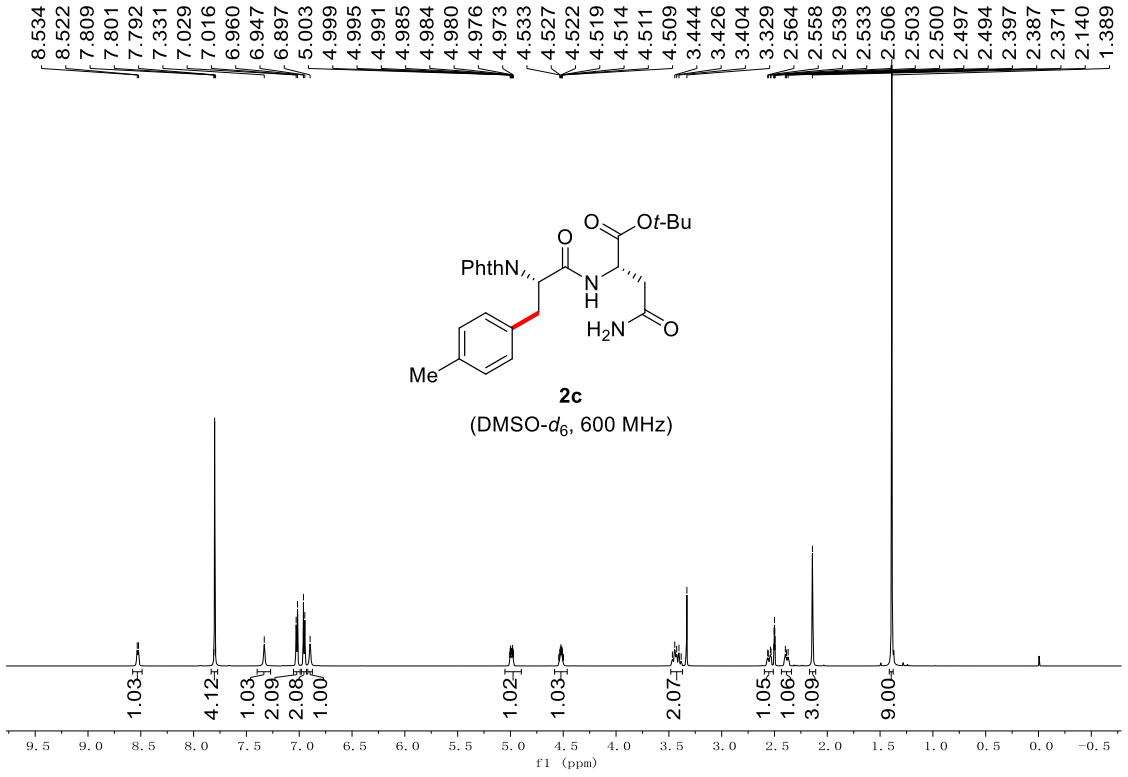
2b

(DMSO-d_6, 600 MHz)



2b

(DMSO-d_6, 150 MHz)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8.522
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7.801
7.792
7.331
7.029
7.016
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6.947
6.897
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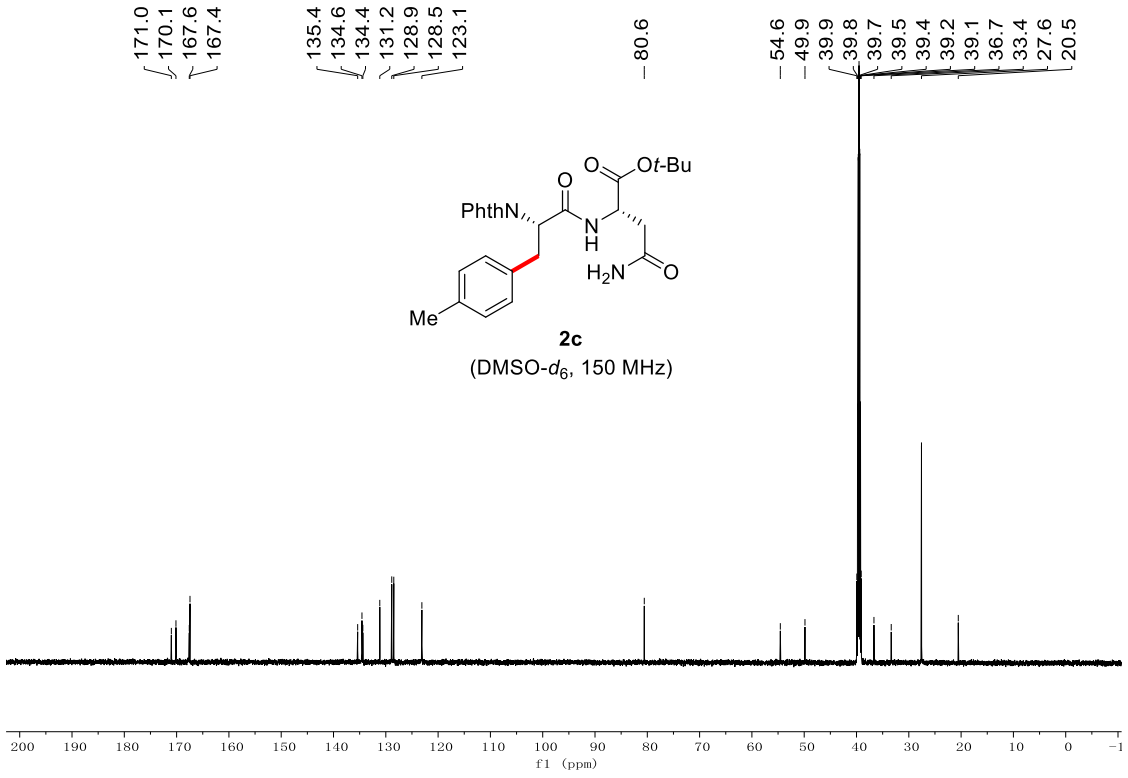
4.999
4.995
4.991
4.985
4.984
4.980
4.976
4.973
4.533
4.527
4.522
4.519
4.514
4.511
4.509
3.444
3.426
3.404
3.329
2.564
2.558
2.539
2.533
2.506
2.503
2.500
2.497
2.494
2.397
2.387
2.371
2.140
1.389
O
Ot-Bu
PhthN
O
N
H
H2N
O
Me
2c
(DMSO-d6, 600 MHz)
1.03
4.12
1.03
2.09
2.08
1.00
1.02
1.03
2.07
1.05
1.06
3.09
9.00
f1 (ppm)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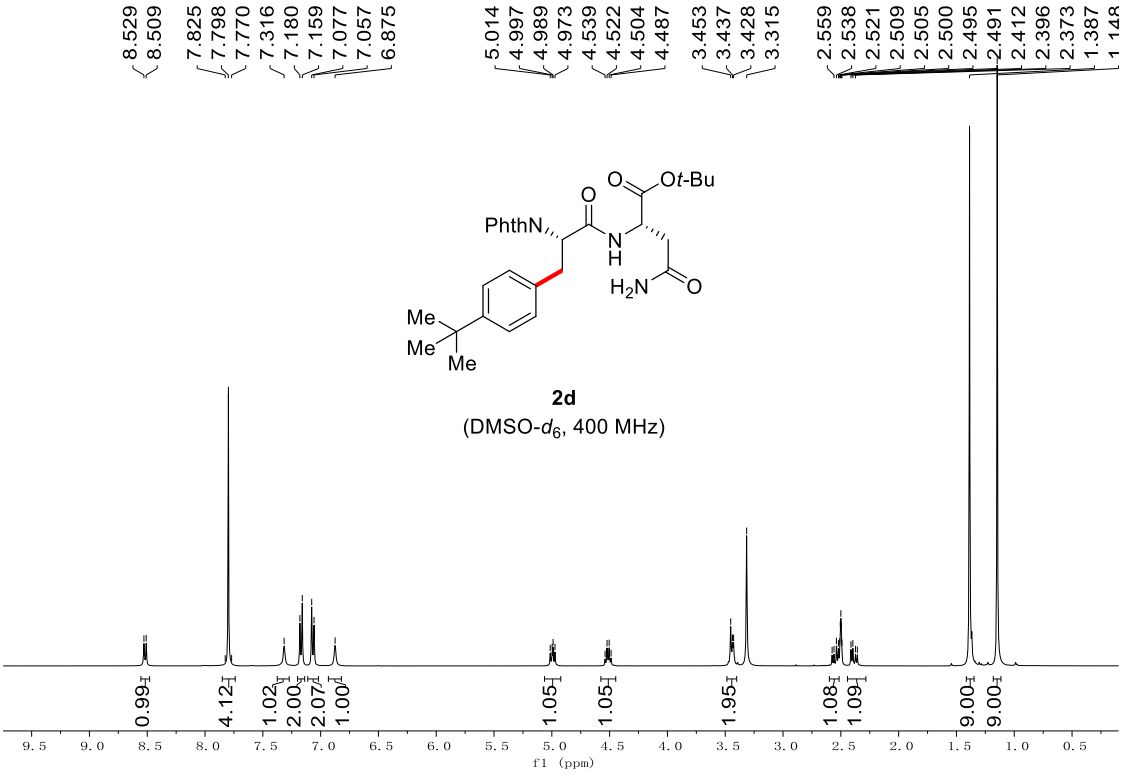
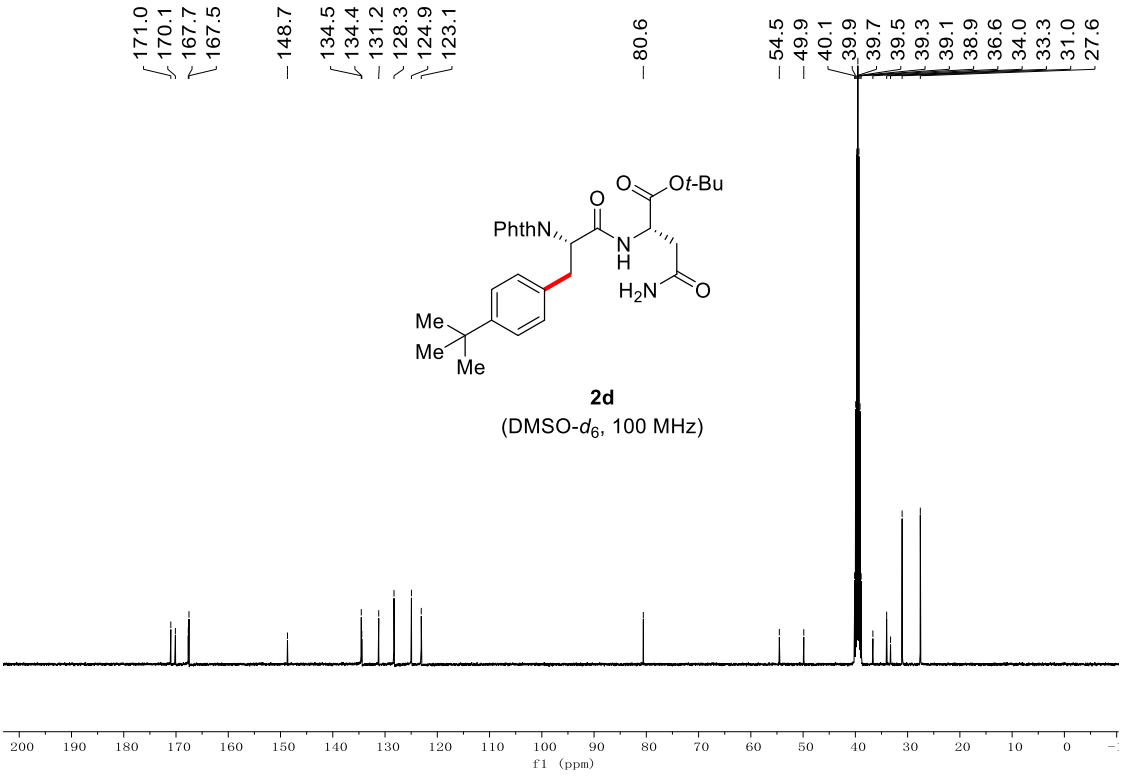
170.1
167.6
167.4
135.4
134.6
134.4
131.2
128.9
128.5
123.1
80.6
54.6
49.9
39.9
39.8
39.7
39.5
39.4
39.2
39.1
36.7
33.4
27.6
20.5
O
Ot-Bu
PhthN
O
N
H
H2N
O
Me
2c
(DMSO-d6, 150 MHz)
f1 (ppm)



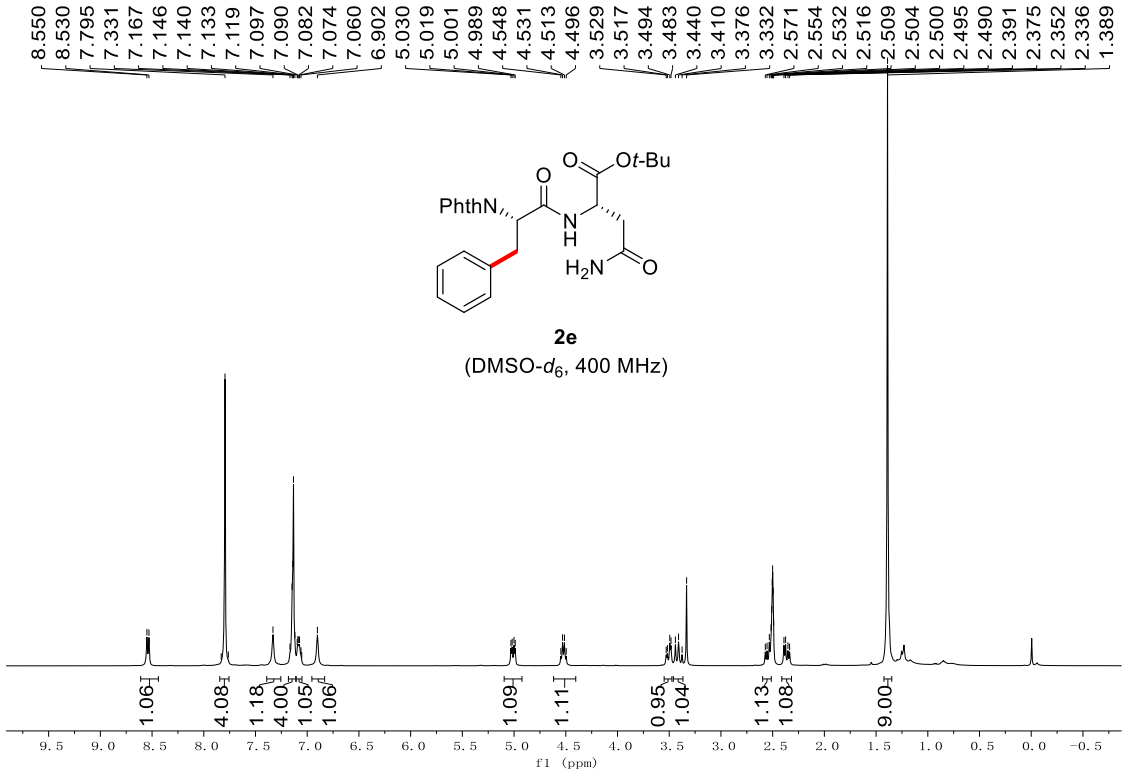
2d

(DMSO-d_6, 400 MHz)



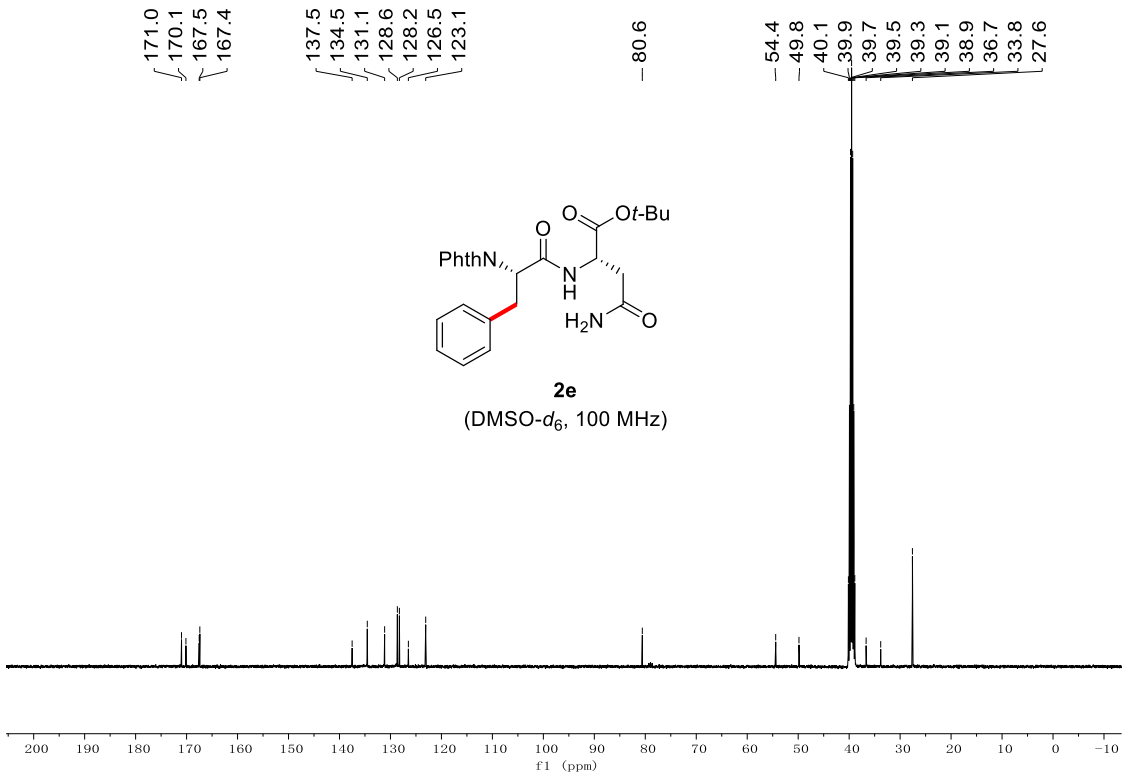
2d

(DMSO-d_6, 100 MHz)



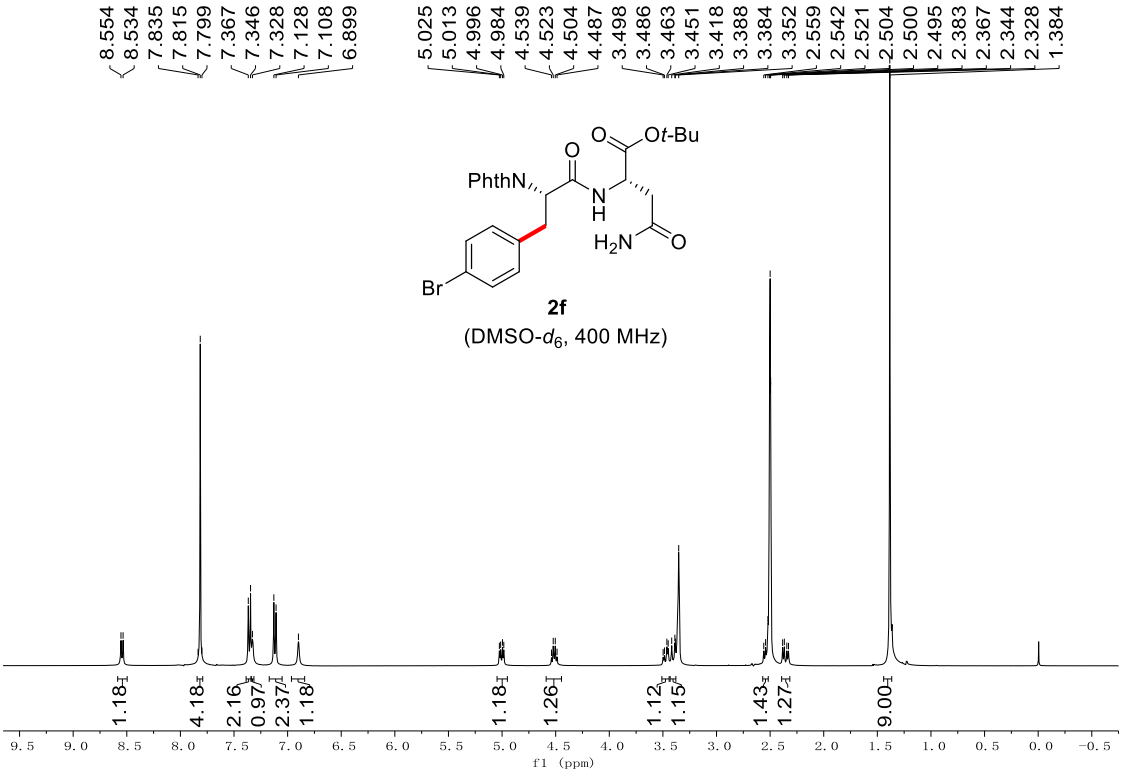
2e

(DMSO-d_6, 400 MHz)



2e

(DMSO-d_6, 100 MHz)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7.108
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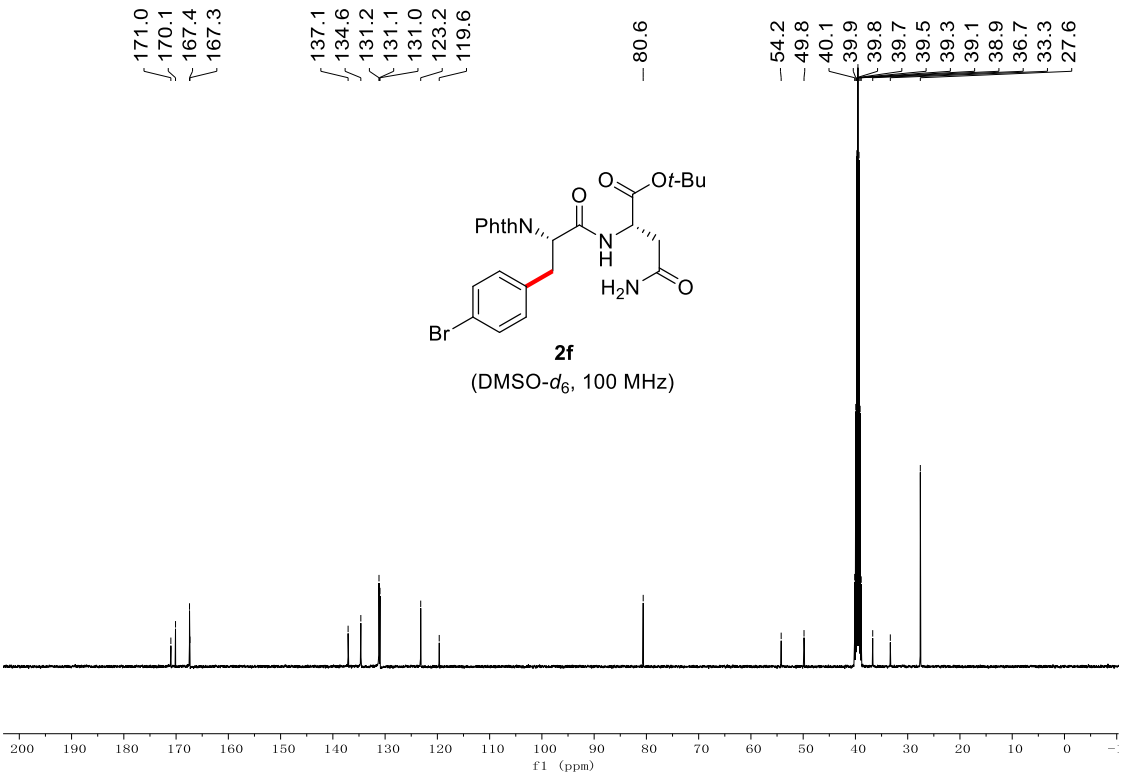
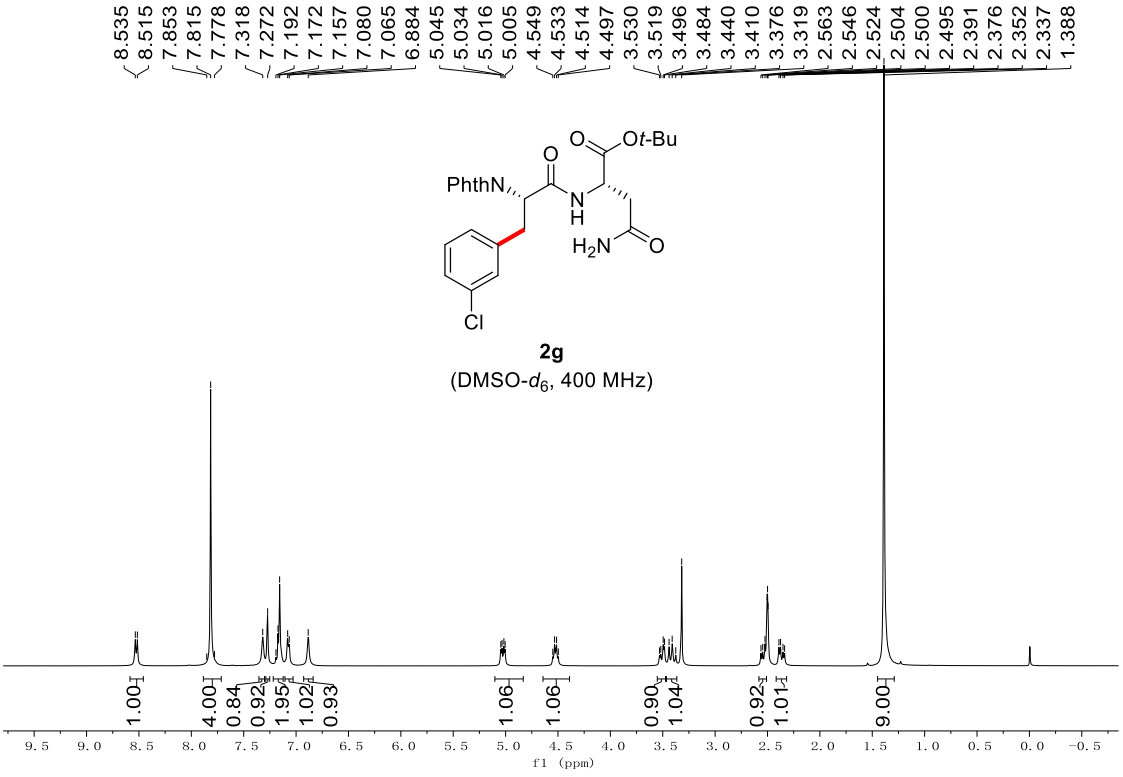
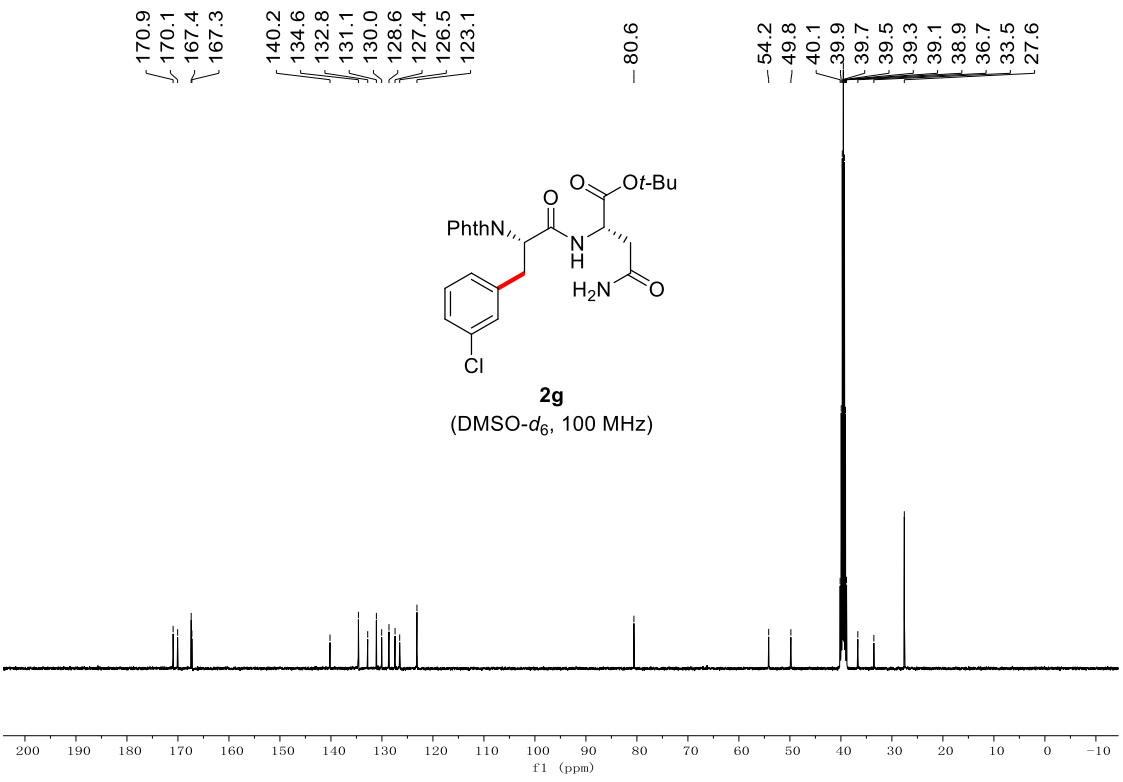
5.025
5.013
4.996
4.984
4.539
4.523
4.504
4.487
3.498
3.486
3.463
3.451
3.418
3.388
3.384
3.352
2.559
2.542
2.521
2.504
2.500
2.495
2.383
2.367
2.344
2.328
1.384
PhthN
O
Ot-Bu
N
H
H2N
O
Br
2f
(DMSO-d6, 400 MHz)
1.18
4.18
2.16
0.97
2.37
1.18
1.18
1.26
1.12
1.15
1.43
1.27
9.00
f1 (ppm)


171.0
170.1
167.4
167.3
137.1
134.6
131.2
131.1
131.0
123.2
119.6
80.6
54.2
49.8
40.1
39.9
39.8
39.7
39.5
39.3
39.1
38.9
36.7
33.3
27.6
PhthN
O
Ot-Bu
N
H
H2N
O
Br
2f
(DMSO-d6, 100 MHz)
f1 (ppm)



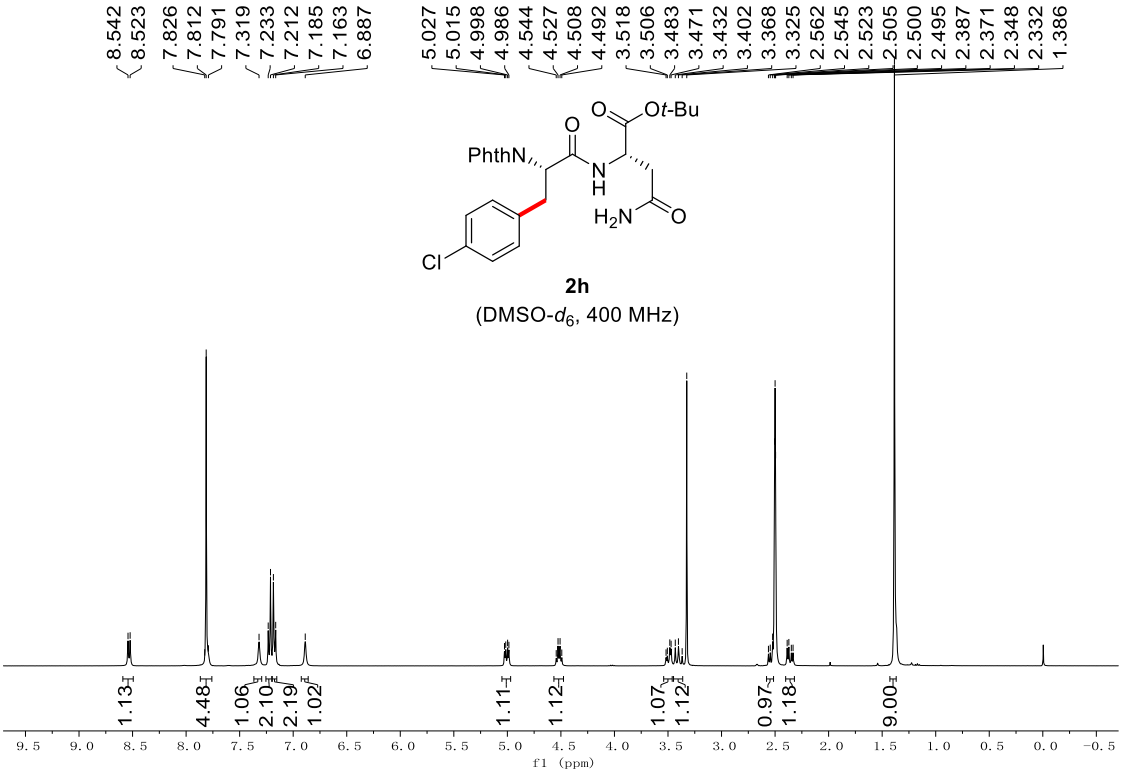
2g

(DMSO-d_6, 400 MHz)



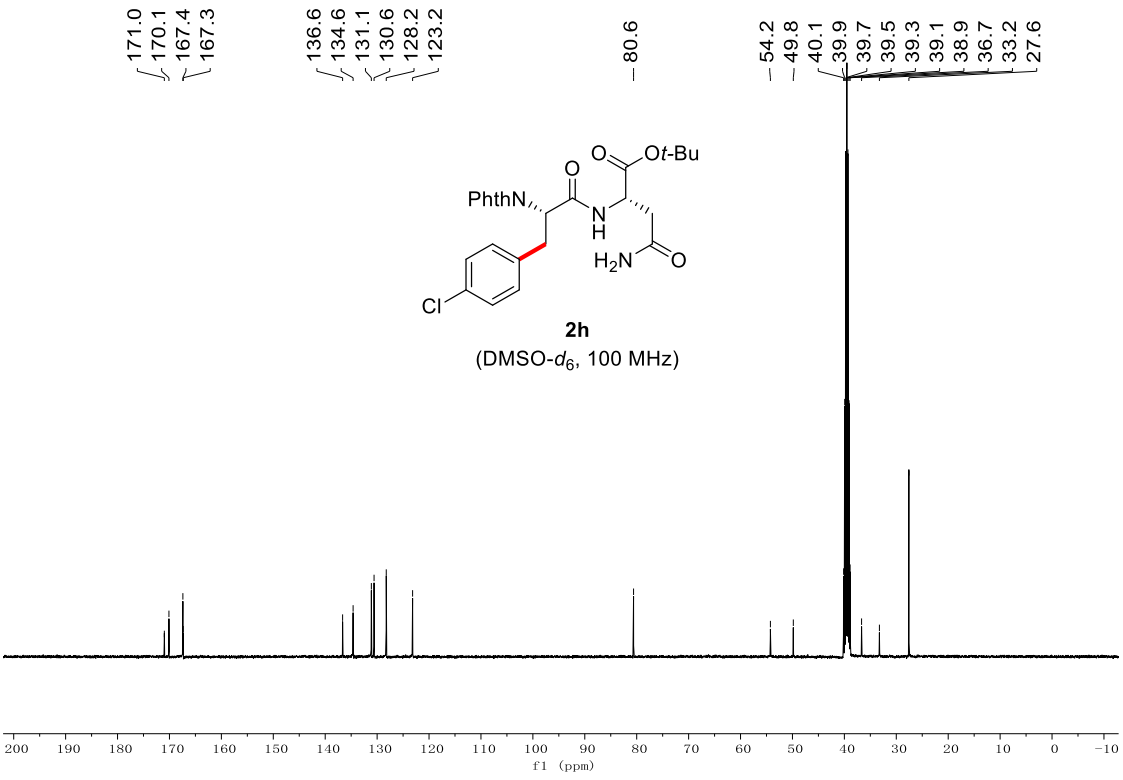
2g

(DMSO-d_6, 100 MHz)



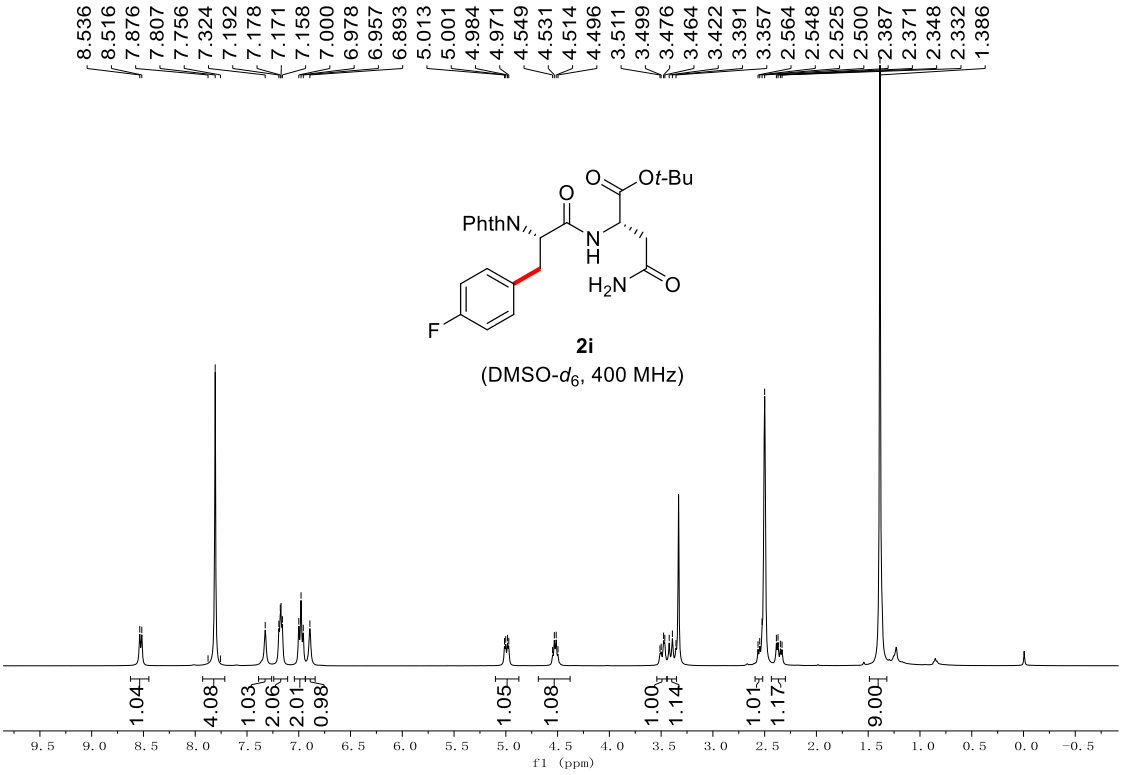
2h

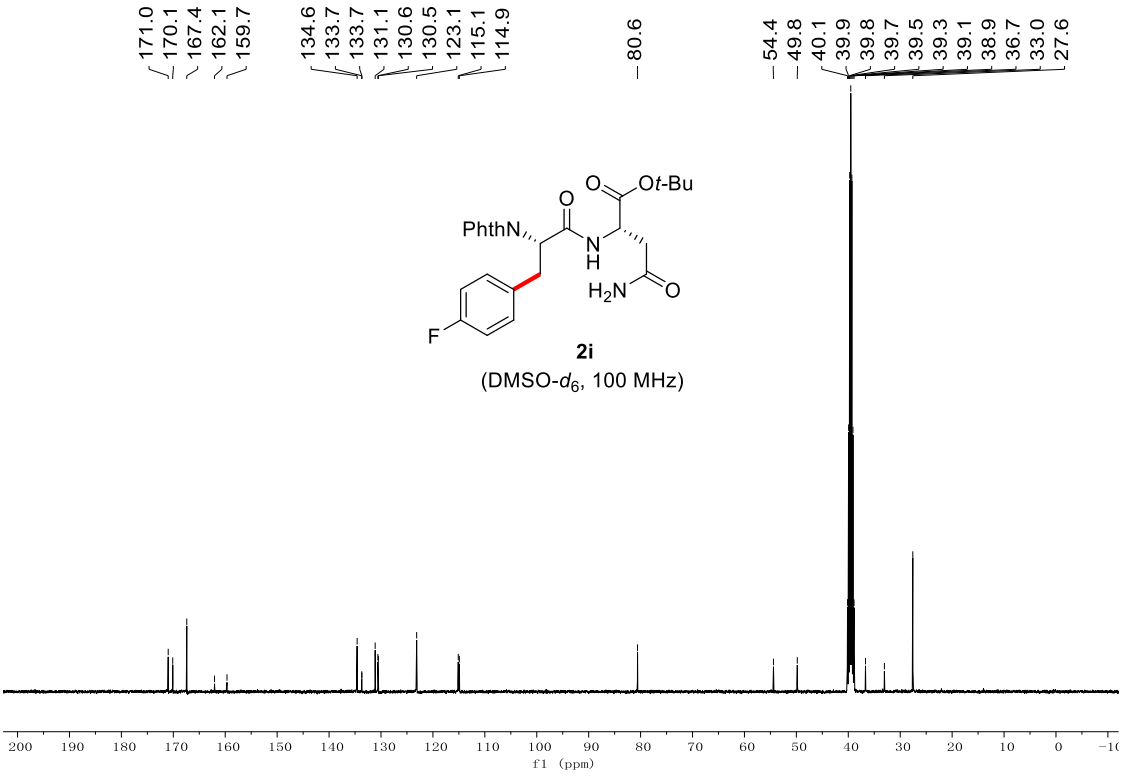
(DMSO-d_6, 400 MHz)

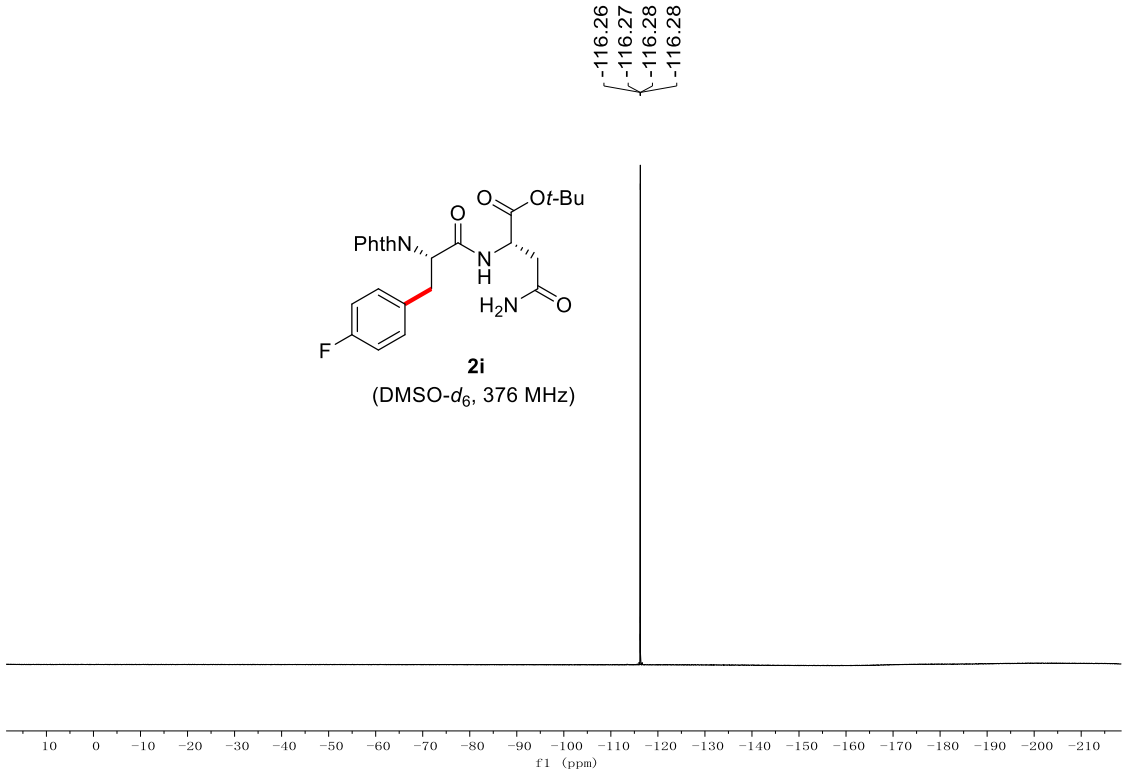


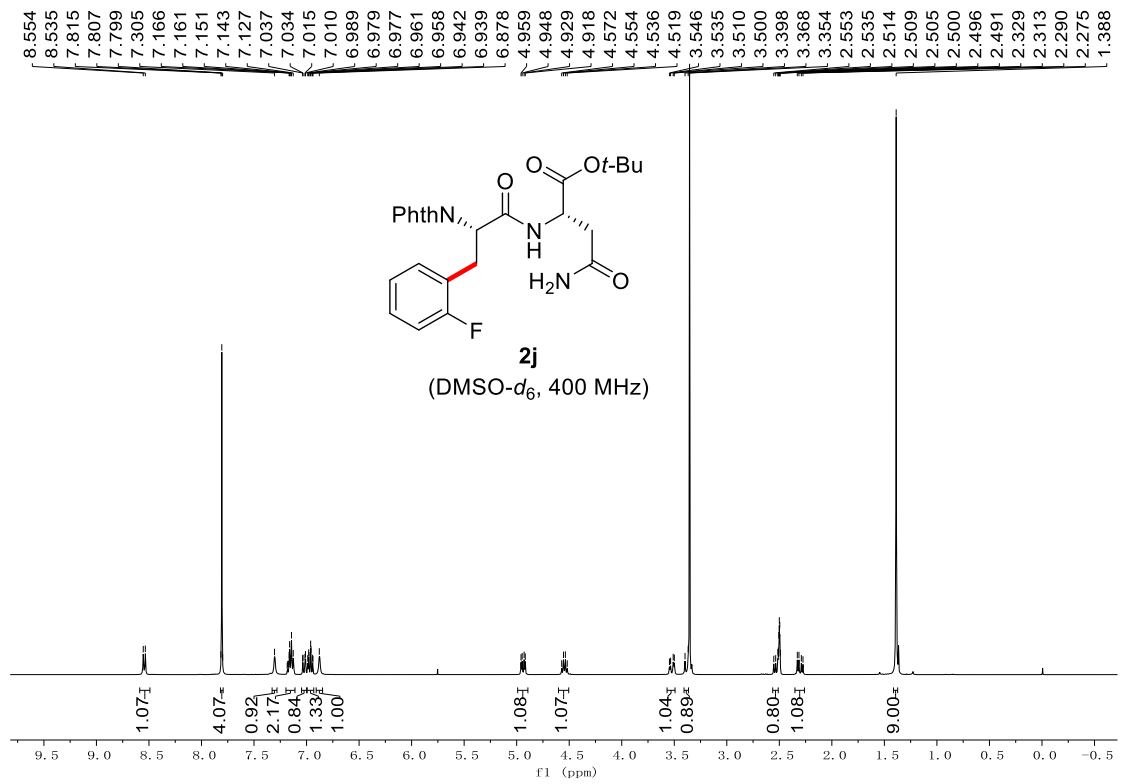
2h

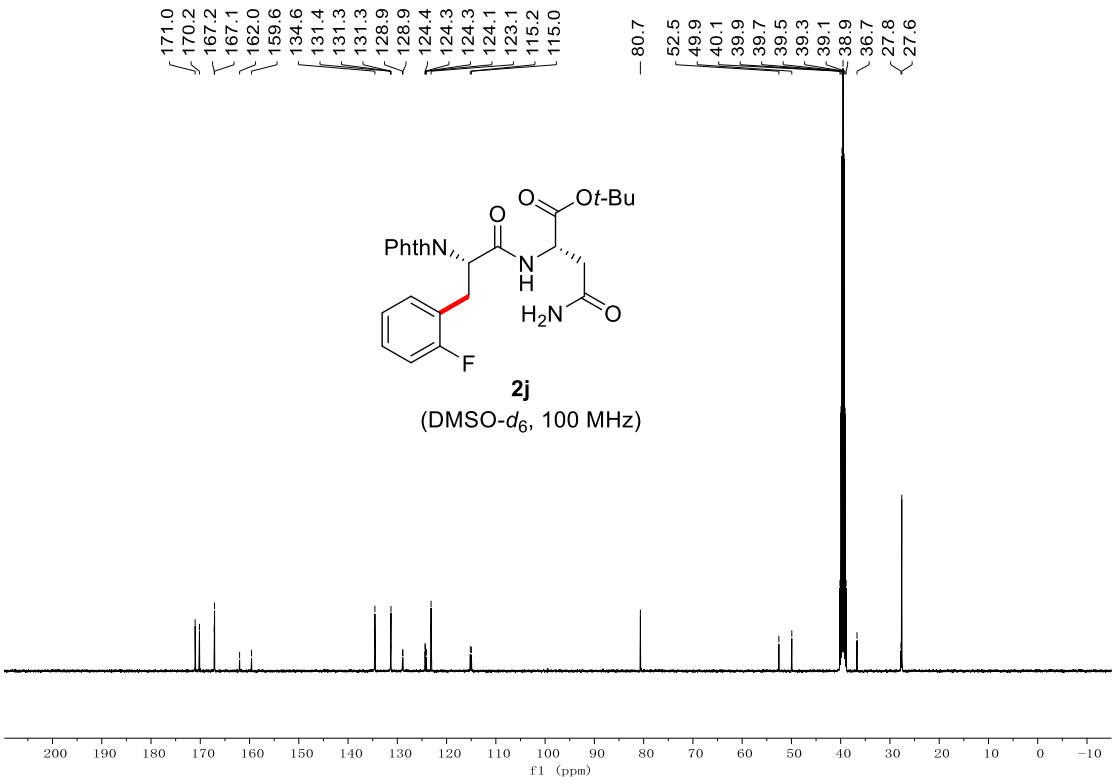
(DMSO-d_6, 100 MHz)

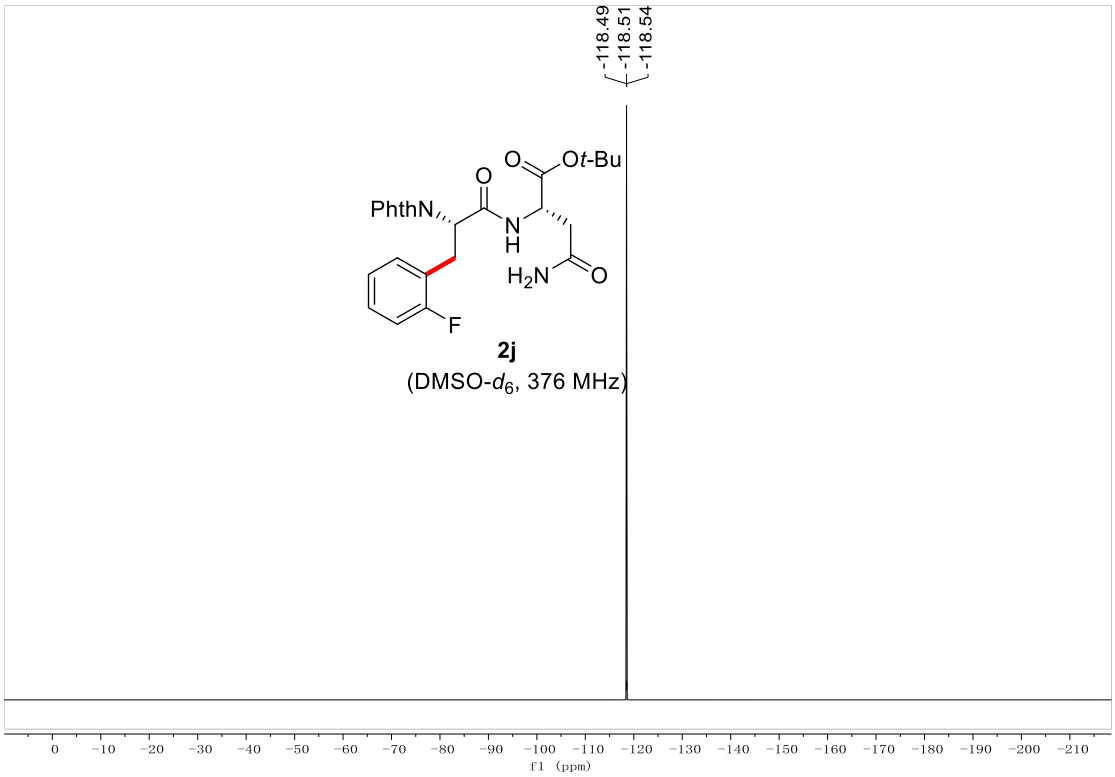

8.536
8.516
7.876
7.807
7.756
7.324
7.192
7.178
7.171
7.158
7.000
6.978
6.957
6.893
5.013
5.001
4.984
4.971
4.549
4.531
4.514
4.496
3.511
3.499
3.476
3.464
3.422
3.391
3.357
2.564
2.548
2.525
2.500
2.387
2.371
2.348
2.332
1.386
O
Ot-Bu
O
PhthN
N
H
H2N
O
F
2i
(DMSO-d6, 400 MHz)
1.04
4.08
1.03
2.06
2.01
0.98
1.05
1.08
1.00
1.14
1.01
1.17
9.00
f1 (ppm)

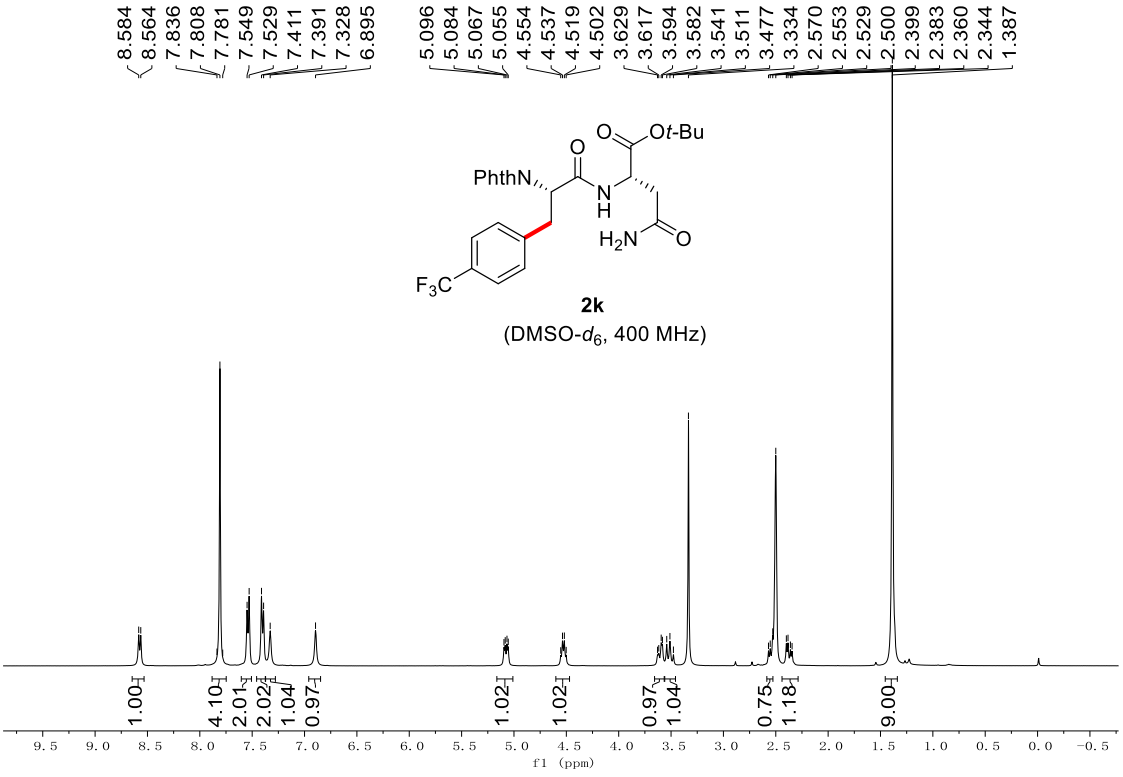

171.0
170.1
167.4
162.1
159.7
134.6
133.7
133.7
131.1
130.6
130.5
123.1
115.1
114.9
80.6
54.4
49.8
40.1
39.9
39.8
39.7
39.5
39.3
39.1
38.9
36.7
33.0
27.6
O
Ot-Bu
O
PhthN
N
H
H2N
O
F
2i
(DMSO-d6, 100 MHz)
f1 (ppm)

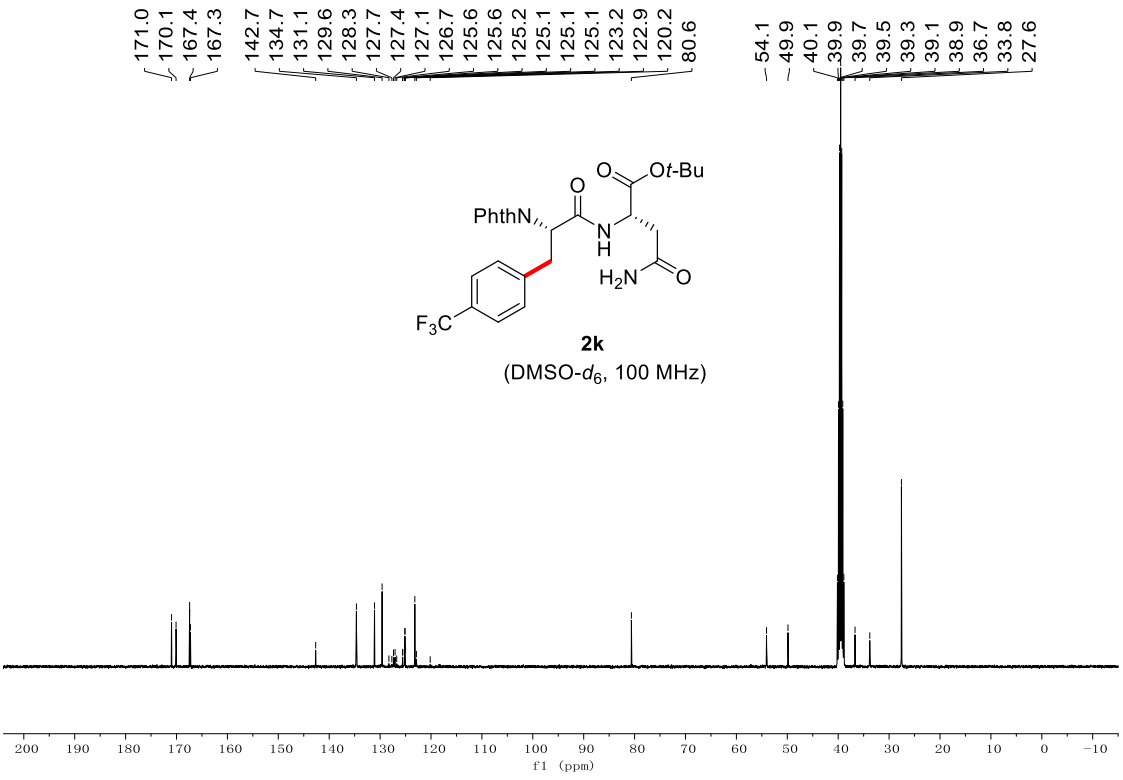

-116.26
-116.27
-116.28
-116.28
O
Ot-Bu
O
PhthN
N
H
H2N
O
F
2i
(DMSO-d6, 376 MHz)
10 0 −10 −20 −30 −40 −50 −60 −70 −80 −90 −100 −110 −120 −130 −140 −150 −160 −170 −180 −190 −200 −210
f1 (ppm)

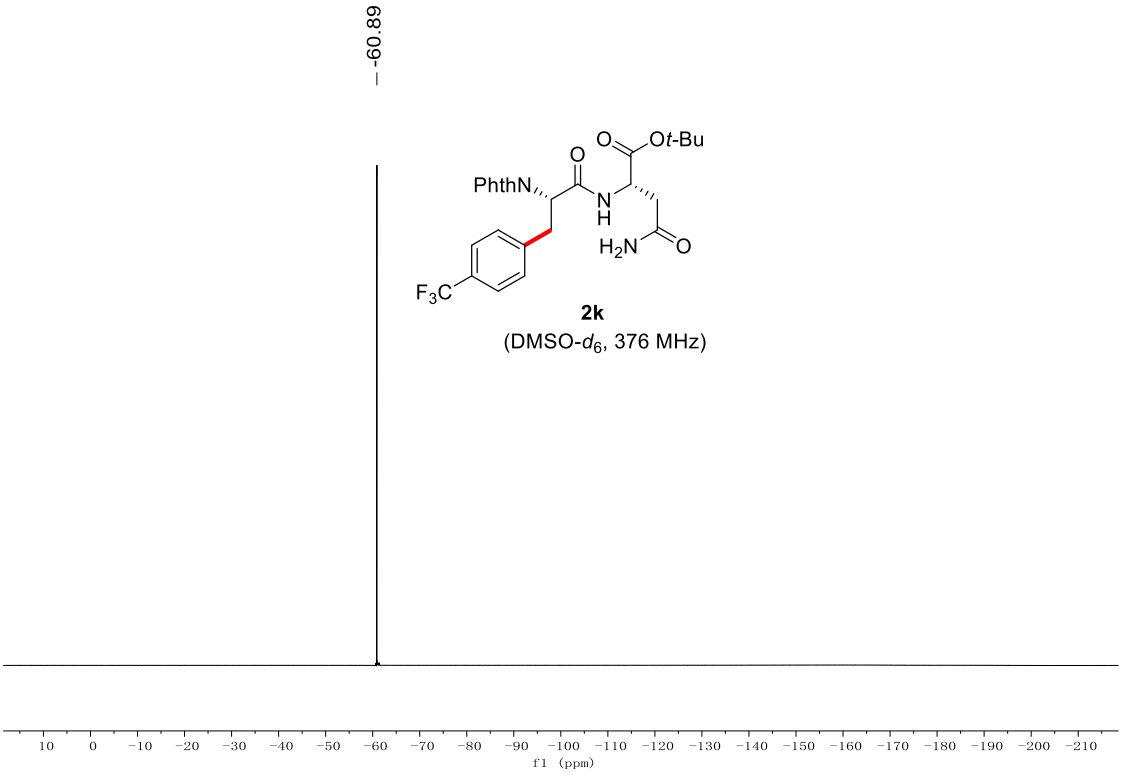

8.554
8.535
7.815
7.807
7.799
7.305
7.166
7.161
7.151
7.143
7.127
7.037
7.034
7.015
7.010
6.989
6.979
6.977
6.961
6.958
6.942
6.939
6.878
4.959
4.948
4.929
4.918
4.572
4.554
4.536
4.519
3.546
3.535
3.510
3.500
3.398
3.368
3.354
2.553
2.535
2.514
2.509
2.505
2.500
2.496
2.491
2.329
2.313
2.290
2.275
1.388
O
Ot-Bu
O
PhthN
N
H
H2N
O
F
2j
(DMSO-d6, 400 MHz)
1.07
4.07
0.92
2.17
0.84
1.33
1.00
1.08
1.07
1.04
0.89
0.80
1.08
9.00
9.5 9.0 8.5 8.0 7.5 7.0 6.5 6.0 5.5 5.0 4.5 4.0 3.5 3.0 2.5 2.0 1.5 1.0 0.5 0.0 −0.5
f1 (ppm)

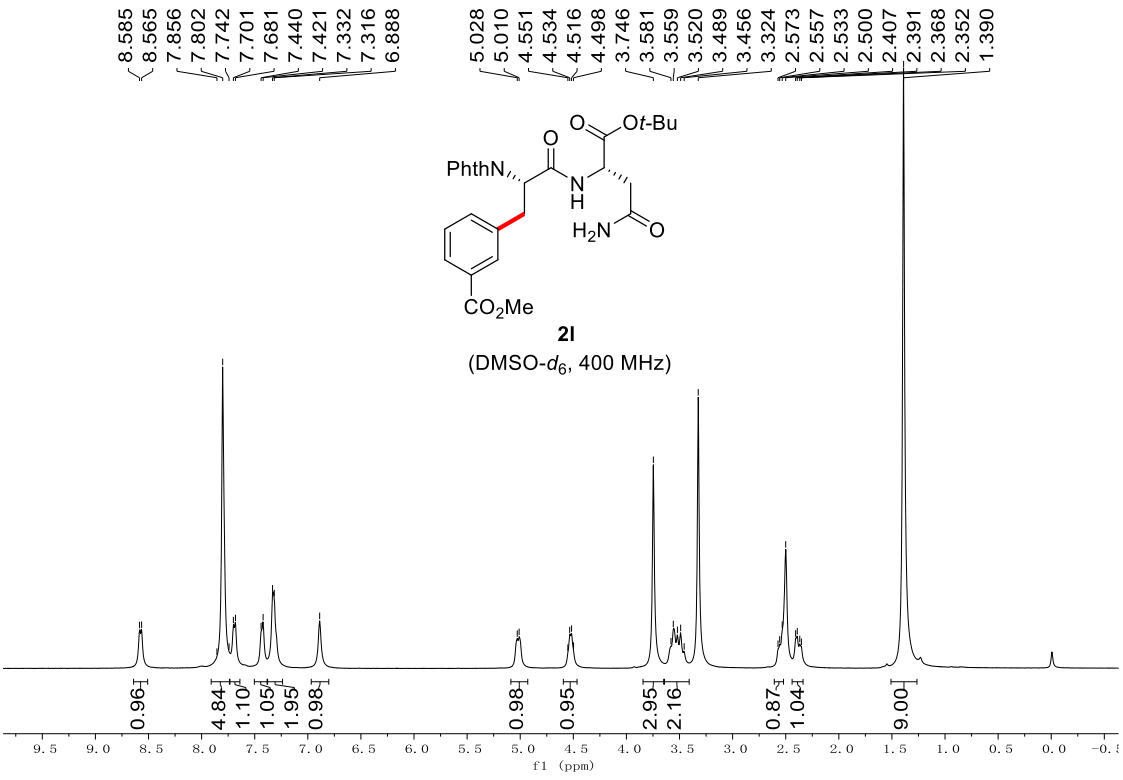

171.0
170.2
167.2
167.1
162.0
159.6
134.6
131.4
131.3
131.3
128.9
128.9
124.4
124.3
124.3
124.1
123.1
115.2
115.0
80.7
52.5
49.9
40.1
39.9
39.7
39.5
39.3
39.1
38.9
36.7
27.8
27.6
PhthN
O
Ot-Bu
N
H
H2N
F
2j
(DMSO-d6, 100 MHz)
f1 (ppm)

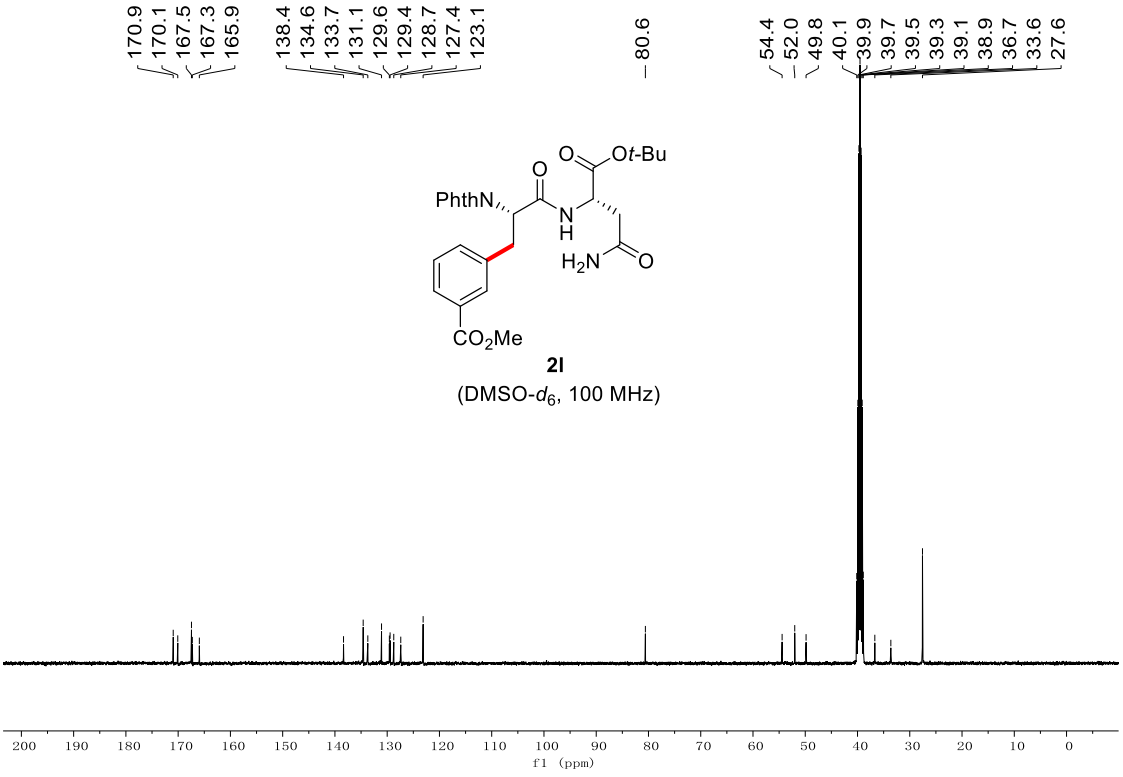

-118.49
-118.51
-118.54
PhthN
O
Ot-Bu
N
H
H2N
F
2j
(DMSO-d6, 376 MHz)
f1 (ppm)


8.584
8.564
7.836
7.808
7.781
7.549
7.529
7.411
7.391
7.328
6.895
5.096
5.084
5.067
5.055
4.554
4.537
4.519
4.502
3.629
3.617
3.594
3.582
3.541
3.511
3.477
3.334
2.570
2.553
2.529
2.500
2.399
2.383
2.360
2.344
1.387
O
Ot-Bu
PhthN
N
H
O
H2N
O
F3C
2k
(DMSO-d6, 400 MHz)
1.00
4.10
2.01
2.02
1.04
0.97
1.02
1.02
0.97
1.04
0.75
1.18
9.00
f1 (ppm)


171.0
170.1
167.4
167.3
142.7
134.7
131.1
129.6
128.3
127.7
127.4
127.1
126.7
125.6
125.6
125.2
125.1
125.1
125.1
123.2
122.9
120.2
80.6
54.1
49.9
40.1
39.9
39.7
39.5
39.3
39.1
38.9
36.7
33.8
27.6
O
Ot-Bu
PhthN
N
H
O
H2N
O
F3C
2k
(DMSO-d6, 100 MHz)
f1 (ppm)

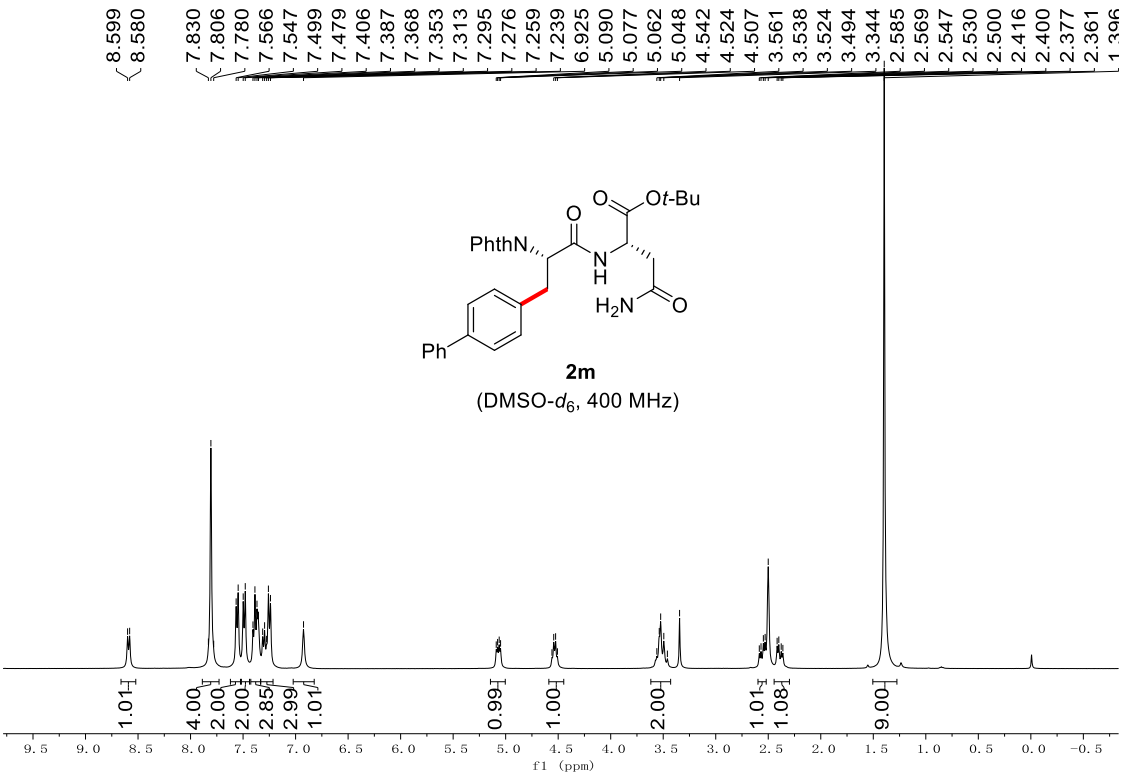

-60.89
PhthN
O
Ot-Bu
N
H
H2N
O
F3C
2k
(DMSO-d6, 376 MHz)
f1 (ppm)


8.585
8.565
7.856
7.802
7.742
7.701
7.681
7.440
7.421
7.332
7.316
6.888
5.028
5.010
4.551
4.534
4.516
4.498
3.746
3.581
3.559
3.520
3.489
3.456
3.324
2.573
2.557
2.533
2.500
2.407
2.391
2.368
2.352
1.390
PhthN
O
Ot-Bu
N
H
H2N
O
CO2Me
2l
(DMSO-d6, 400 MHz)
0.96
4.84
1.10
1.05
1.95
0.98
0.98
0.95
2.95
2.16
0.87
1.04
9.00
f1 (ppm)



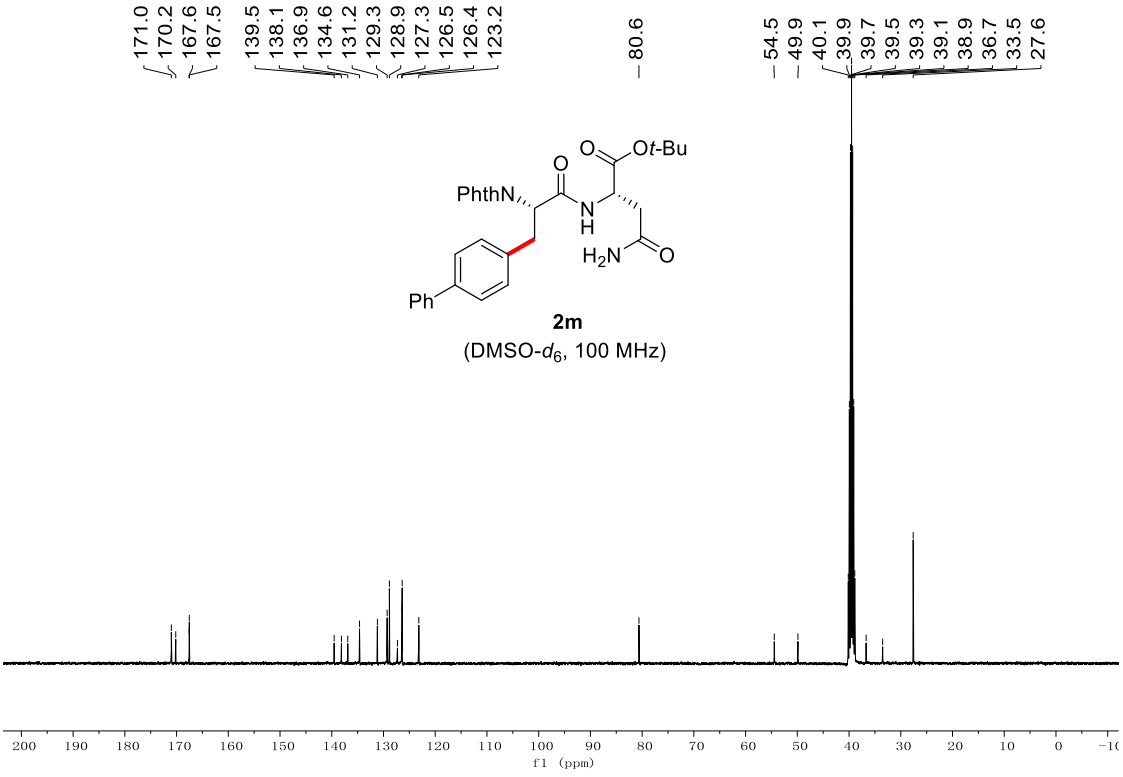
2l

(DMSO-d_6, 100 MHz)



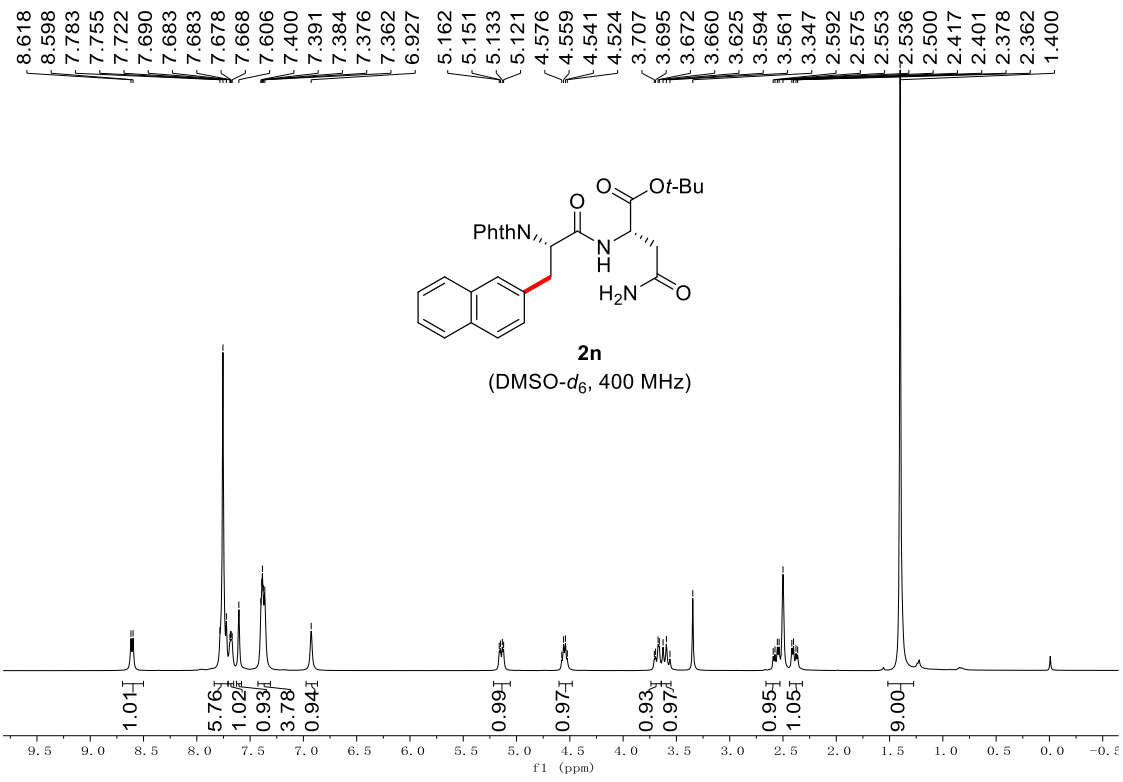
2m

(DMSO-d_6, 400 MHz)



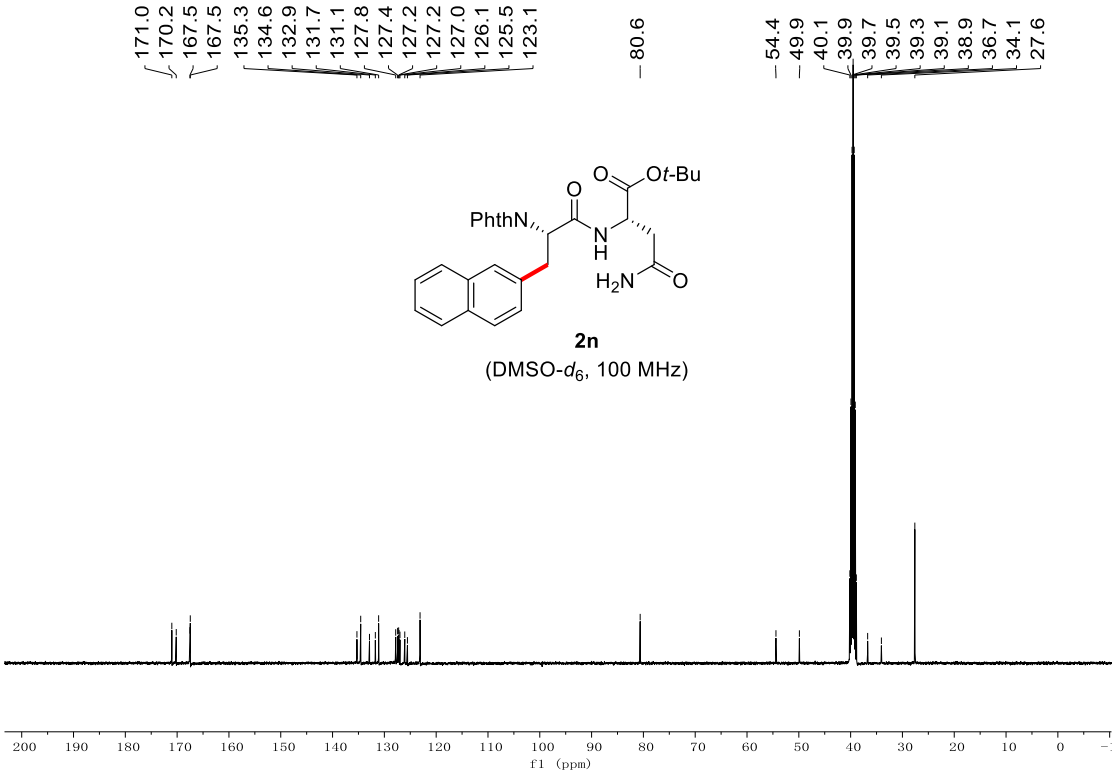
2m

(DMSO-d_6, 100 MHz)



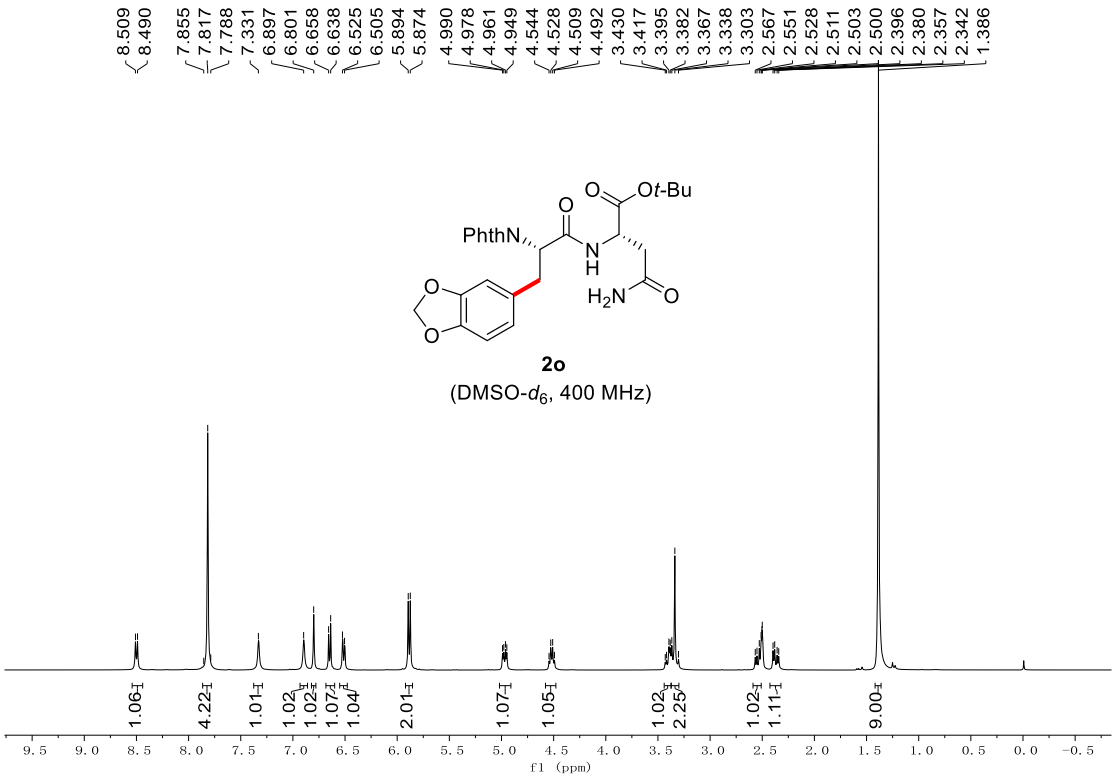
2n

(DMSO-d_6, 400 MHz)



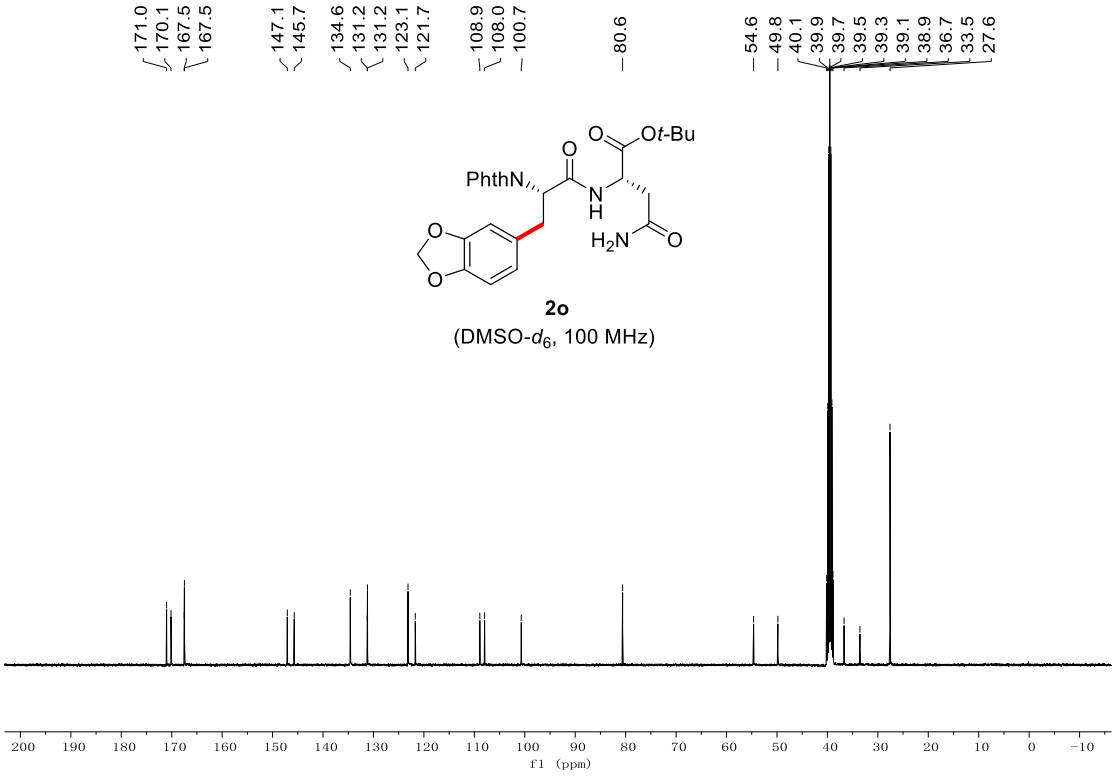
2n

(DMSO-d_6, 100 MHz)



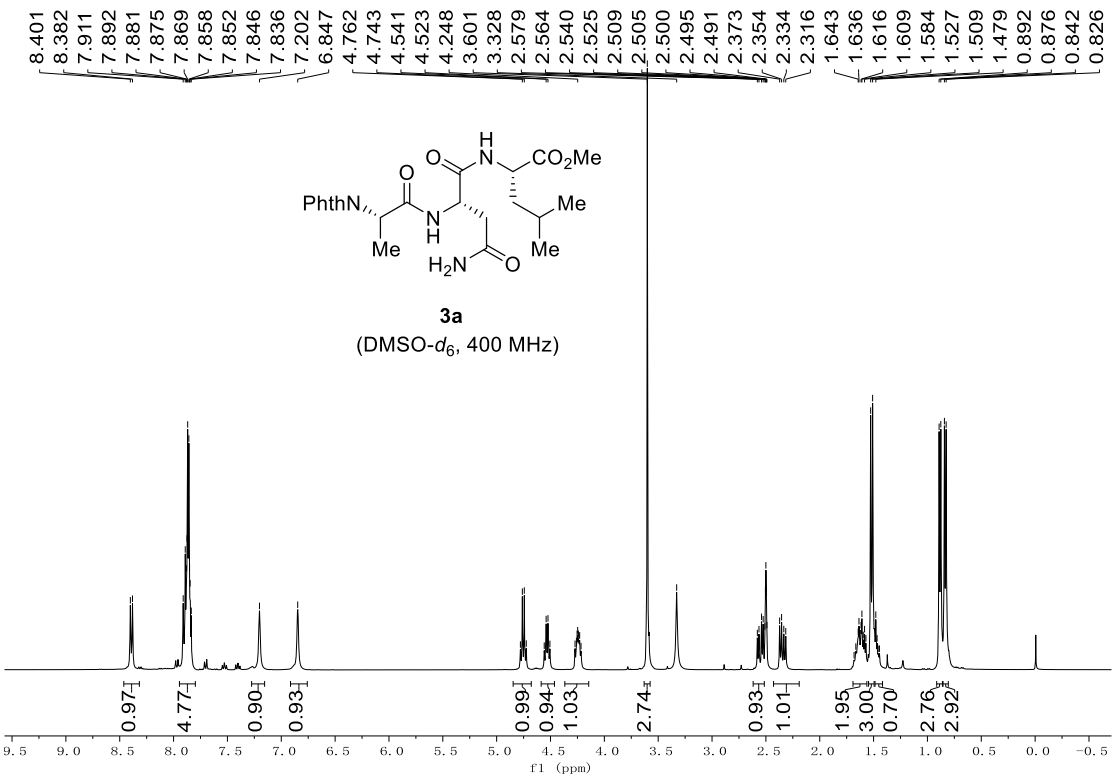
2o

(DMSO-d_6, 400 MHz)



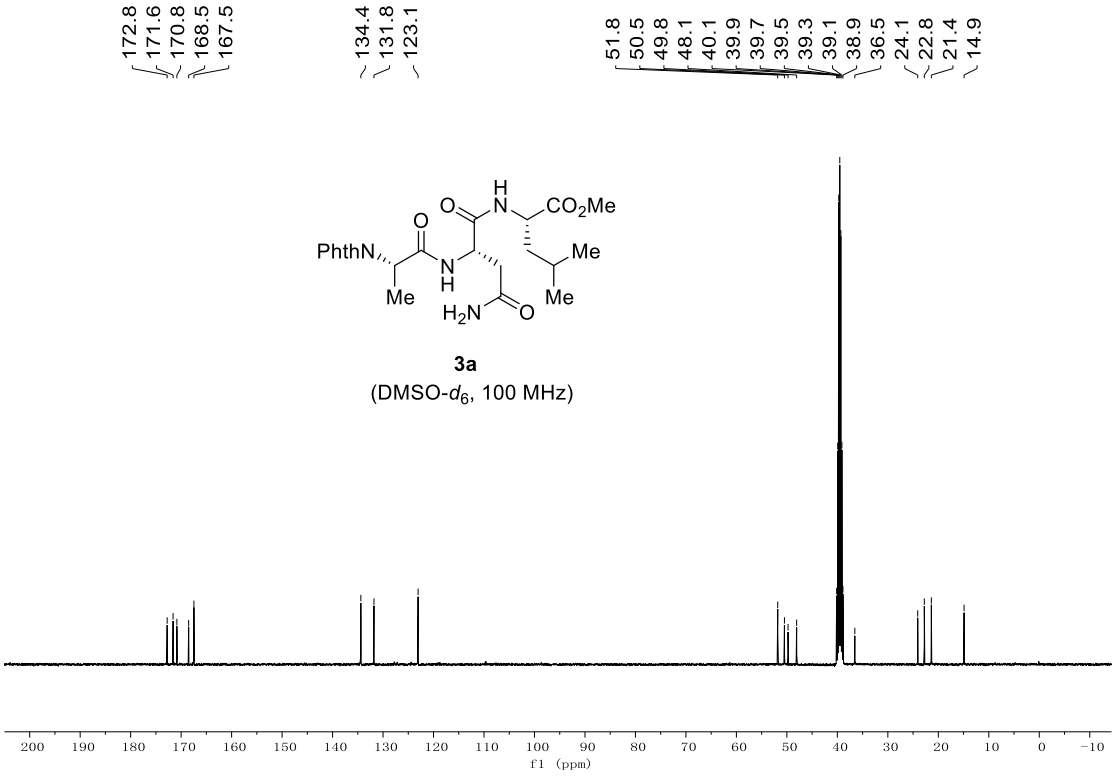
2o

(DMSO-d_6, 100 MHz)

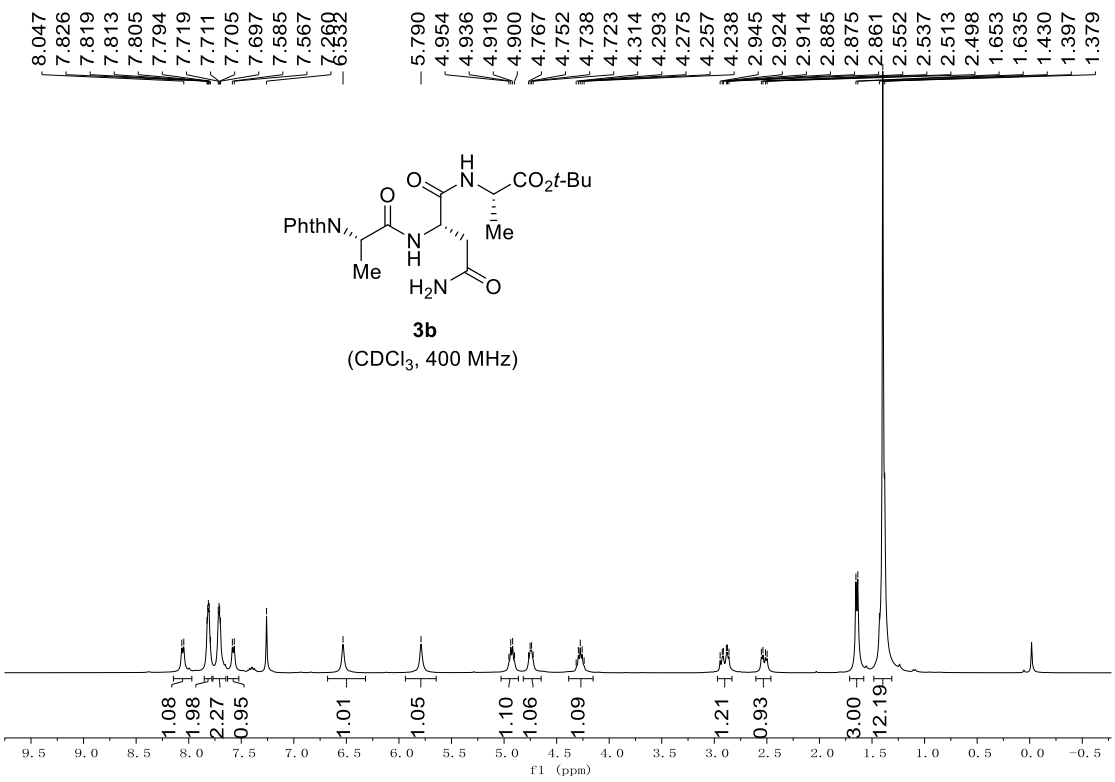


3a

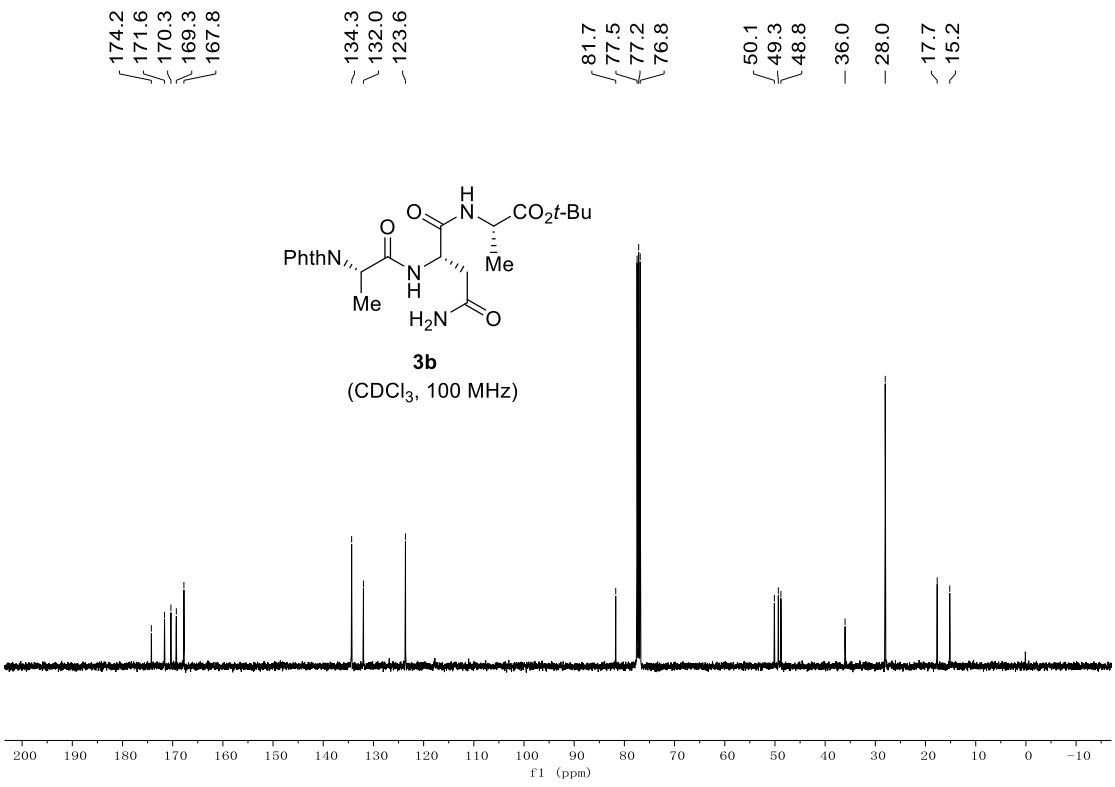
(DMSO-d_6, 400 MHz)



3a
(DMSO-d_6, 100 MHz)

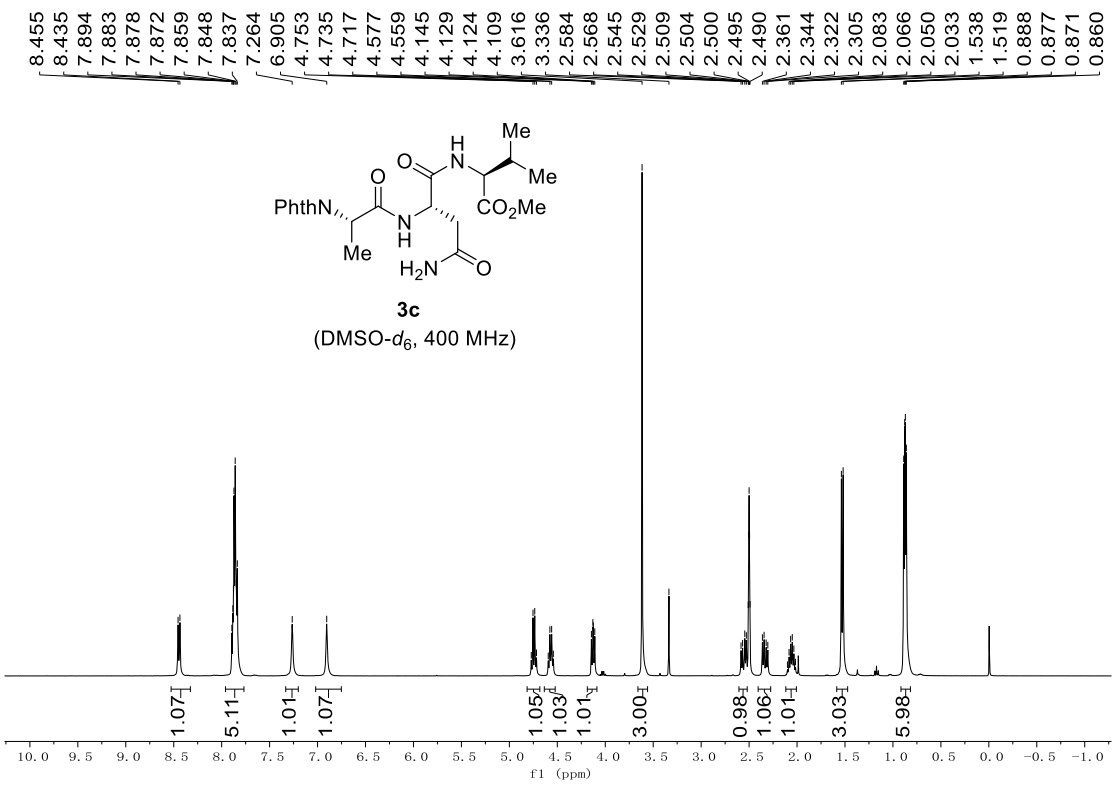


3b
($CDCl_3$, 400 MHz)



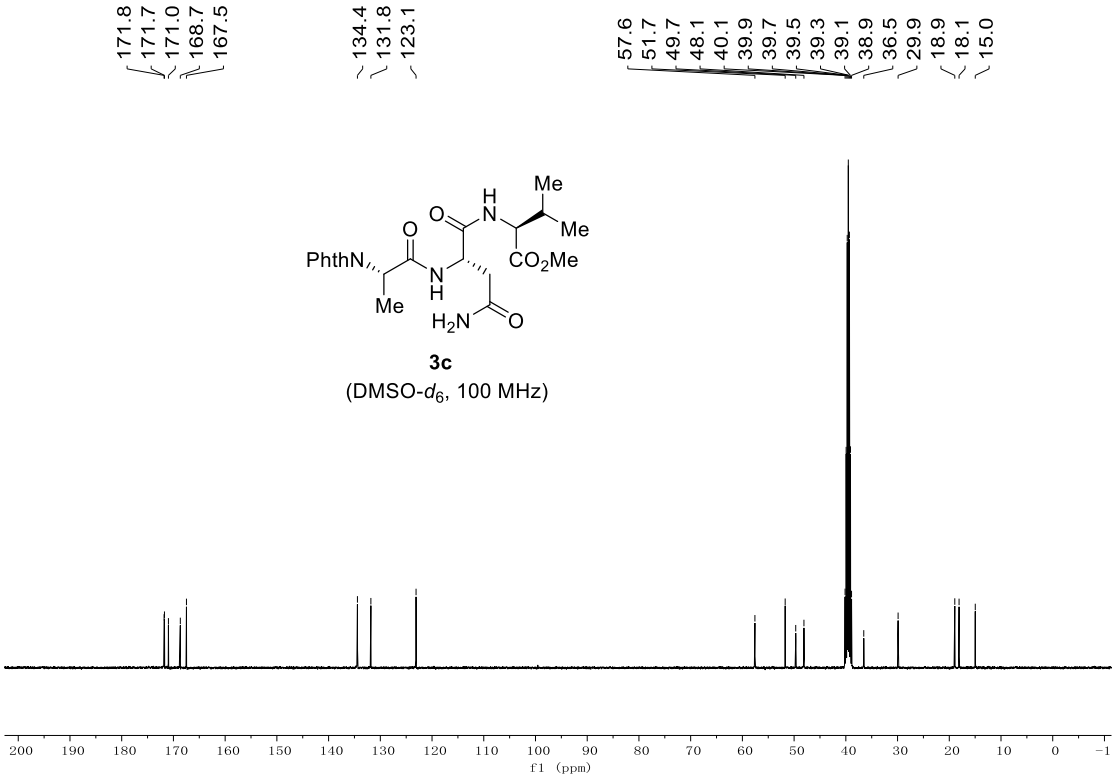
3b

($CDCl_3$, 100 MHz)



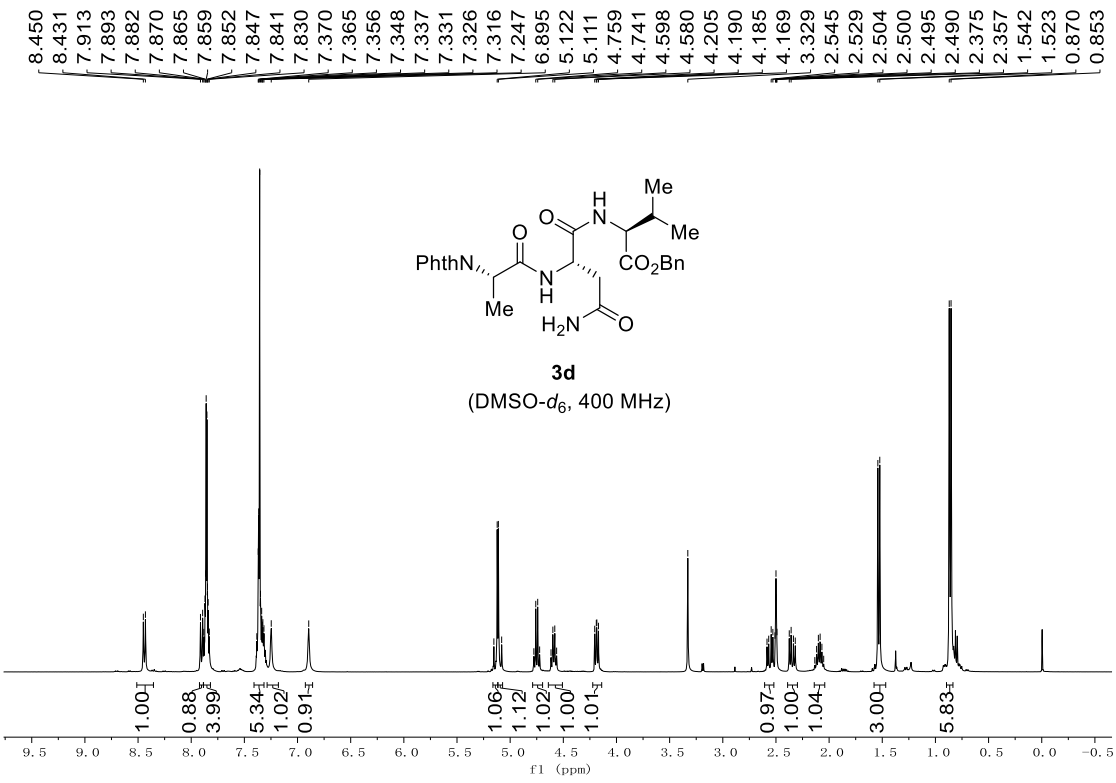
3c

(DMSO-d_6, 400 MHz)



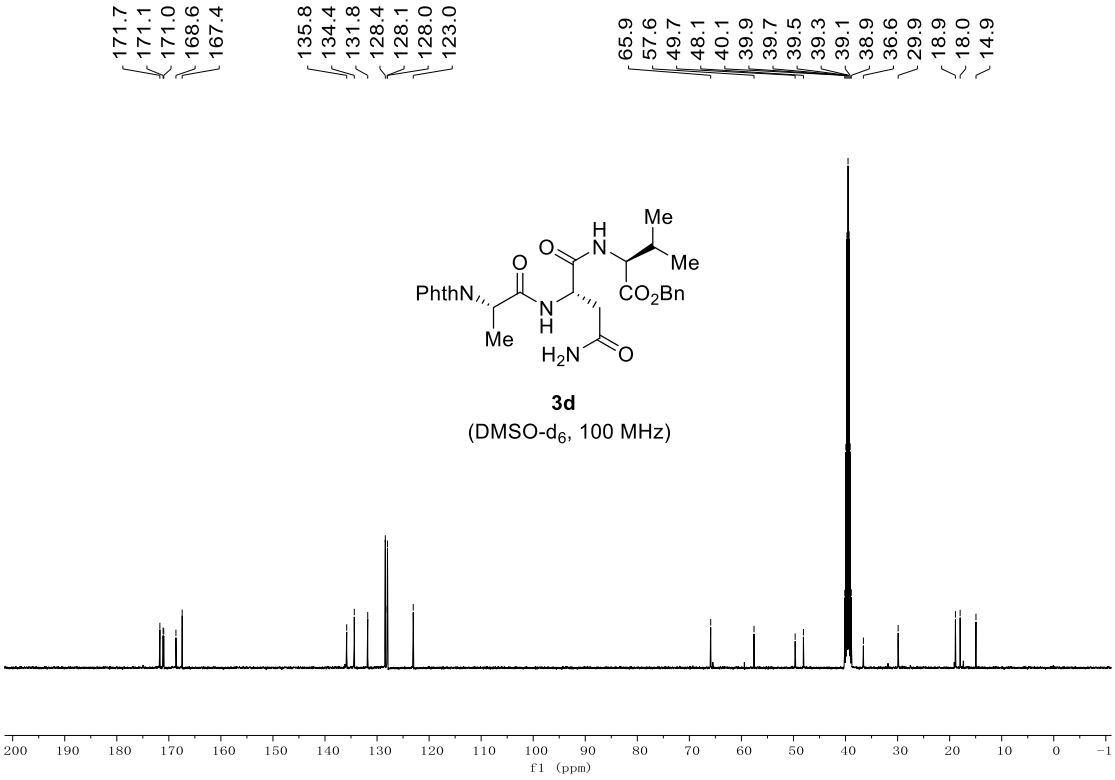
3c

(DMSO-d_6, 100 MHz)



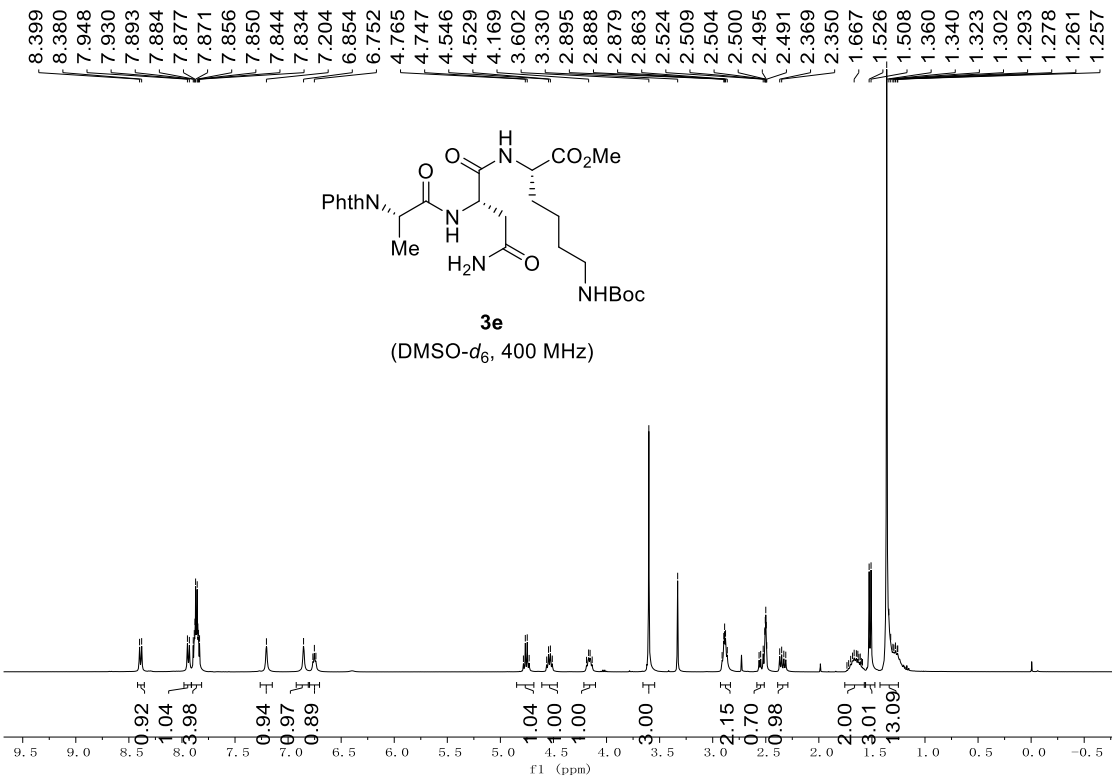
3d

(DMSO-d_6, 400 MHz)



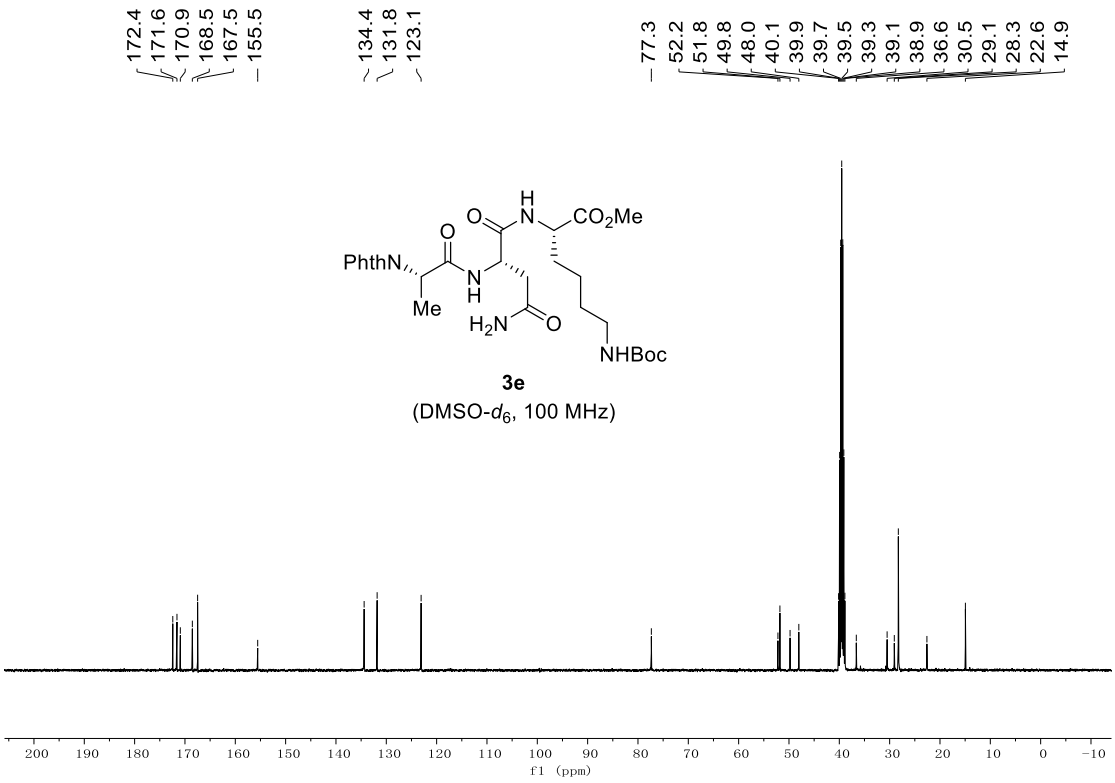
3d

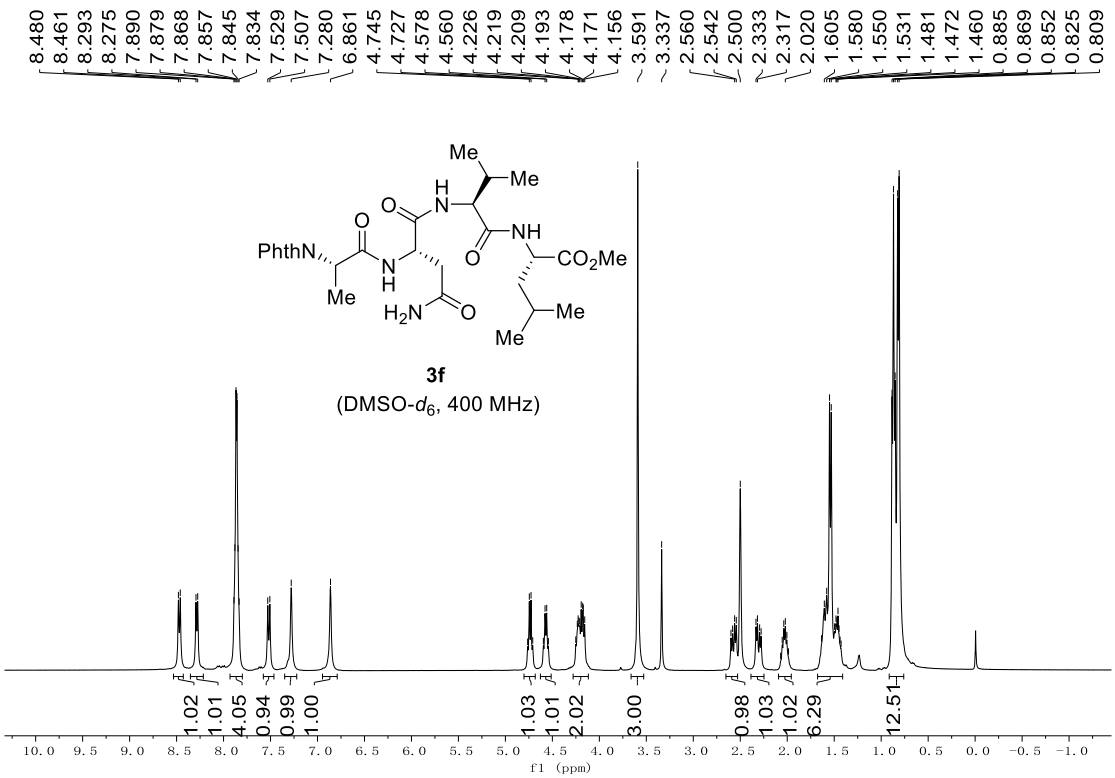
(DMSO-d_6, 100 MHz)

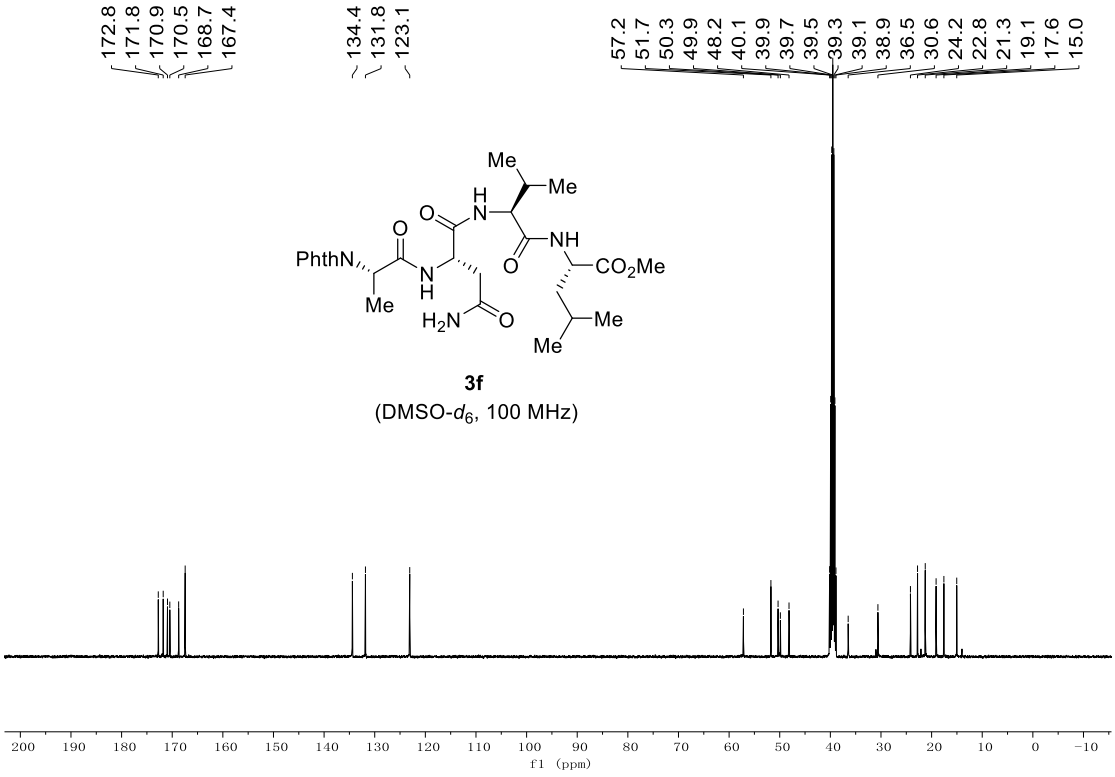


3e

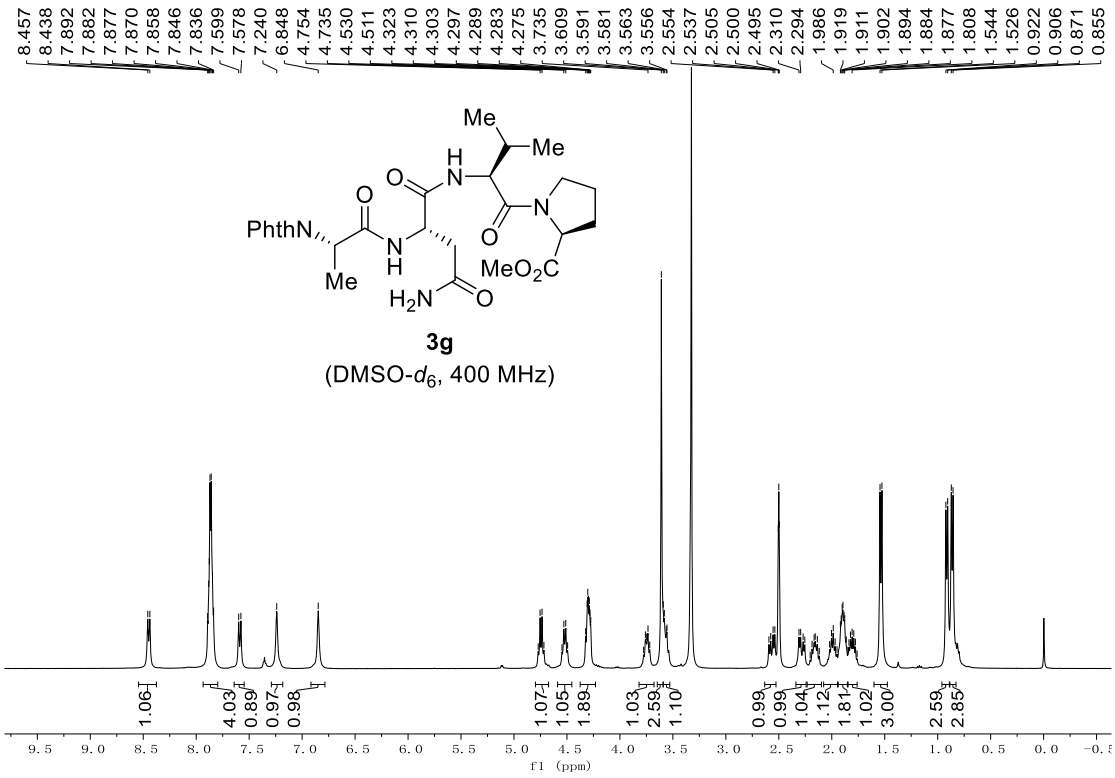
(DMSO-d_6, 400 MHz)


172.4
171.6
170.9
168.5
167.5
155.5
134.4
131.8
123.1
77.3
52.2
51.8
49.8
48.0
40.1
39.9
39.7
39.5
39.3
39.1
38.9
36.6
30.5
29.1
28.3
22.6
14.9
PhthN
Me
CO2Me
NHBoc
H2N
3e
(DMSO-d6, 100 MHz)
f1 (ppm)

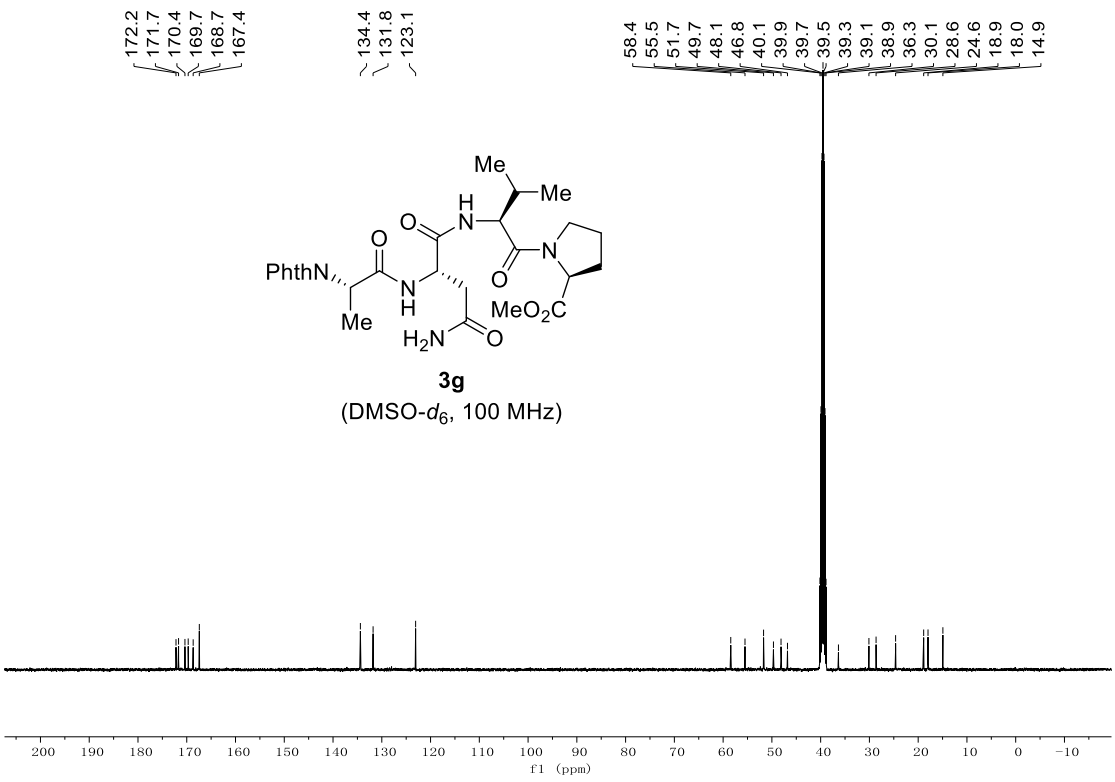

8.480
8.461
8.293
8.275
7.890
7.879
7.868
7.857
7.845
7.834
7.529
7.507
7.280
6.861
4.745
4.727
4.578
4.560
4.226
4.219
4.209
4.193
4.178
4.171
4.156
3.591
3.337
2.560
2.542
2.500
2.333
2.317
2.020
1.605
1.580
1.550
1.531
1.481
1.472
1.460
0.885
0.869
0.852
0.825
0.809
PhthN
Me
CO2Me
H2N
3f
(DMSO-d6, 400 MHz)
1.02
1.01
4.05
0.94
0.99
1.00
1.03
1.01
2.02
3.00
0.98
1.03
1.02
6.29
12.51
f1 (ppm)



3f
(DMSO-d_6, 100 MHz)

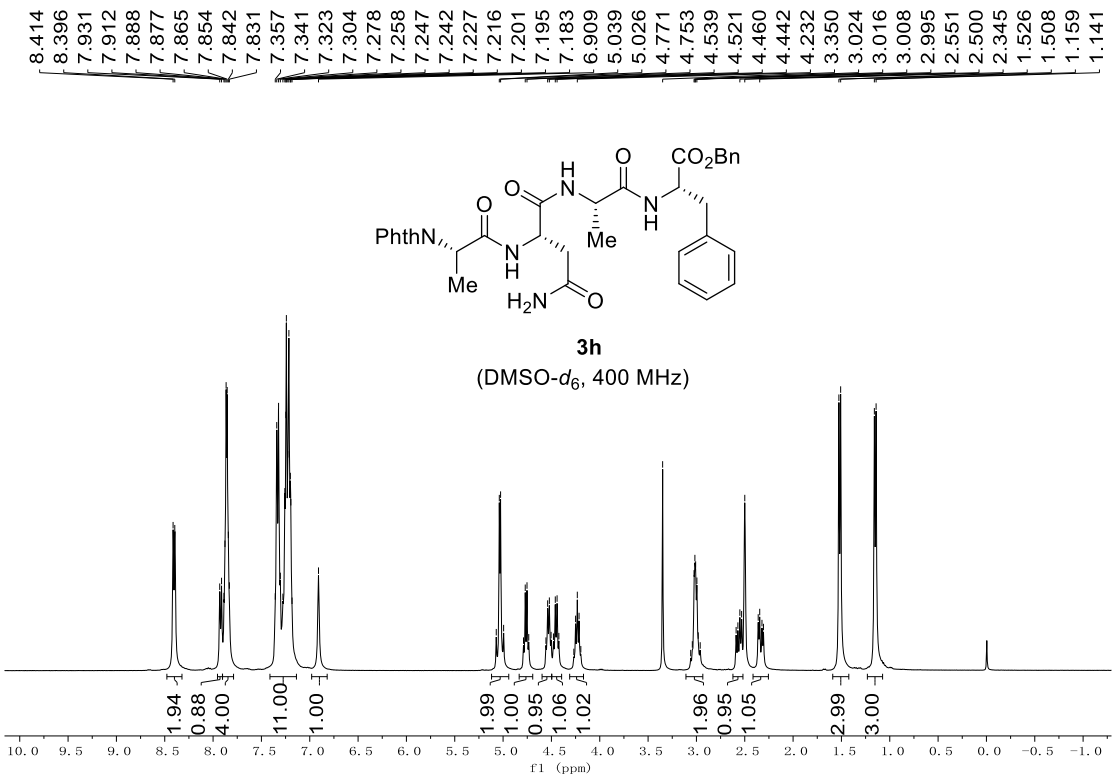


3g
(DMSO-d_6, 400 MHz)



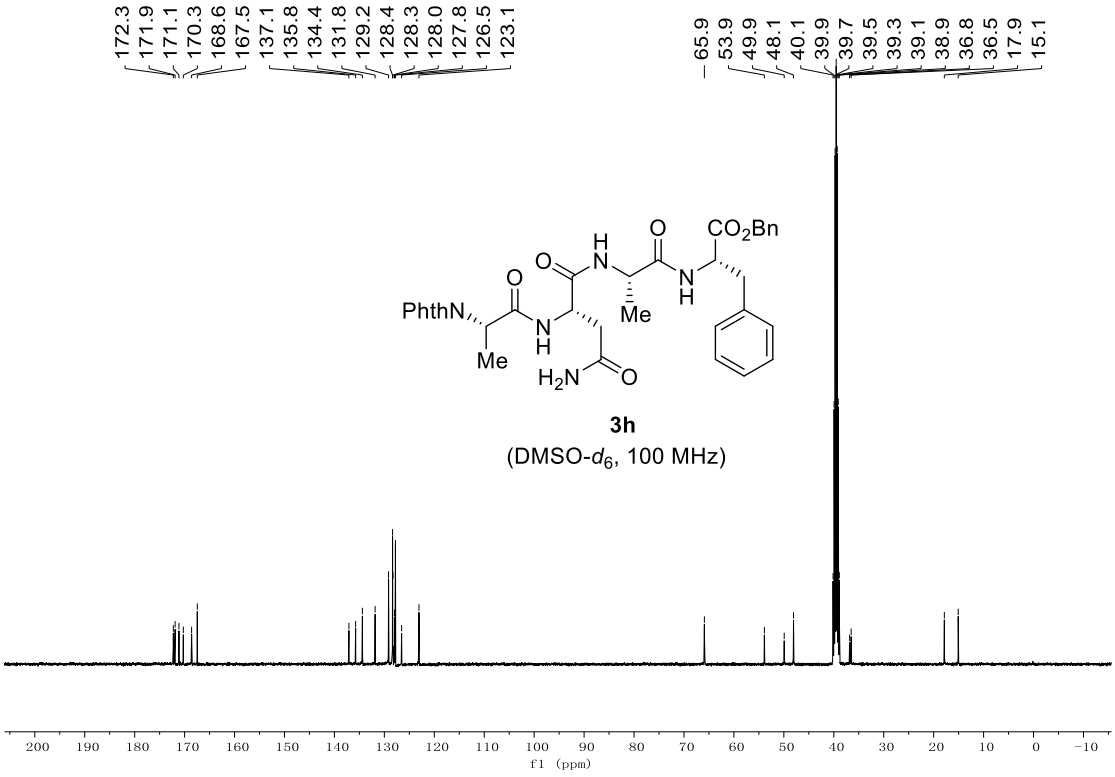
3g

(DMSO-d_6, 100 MHz)



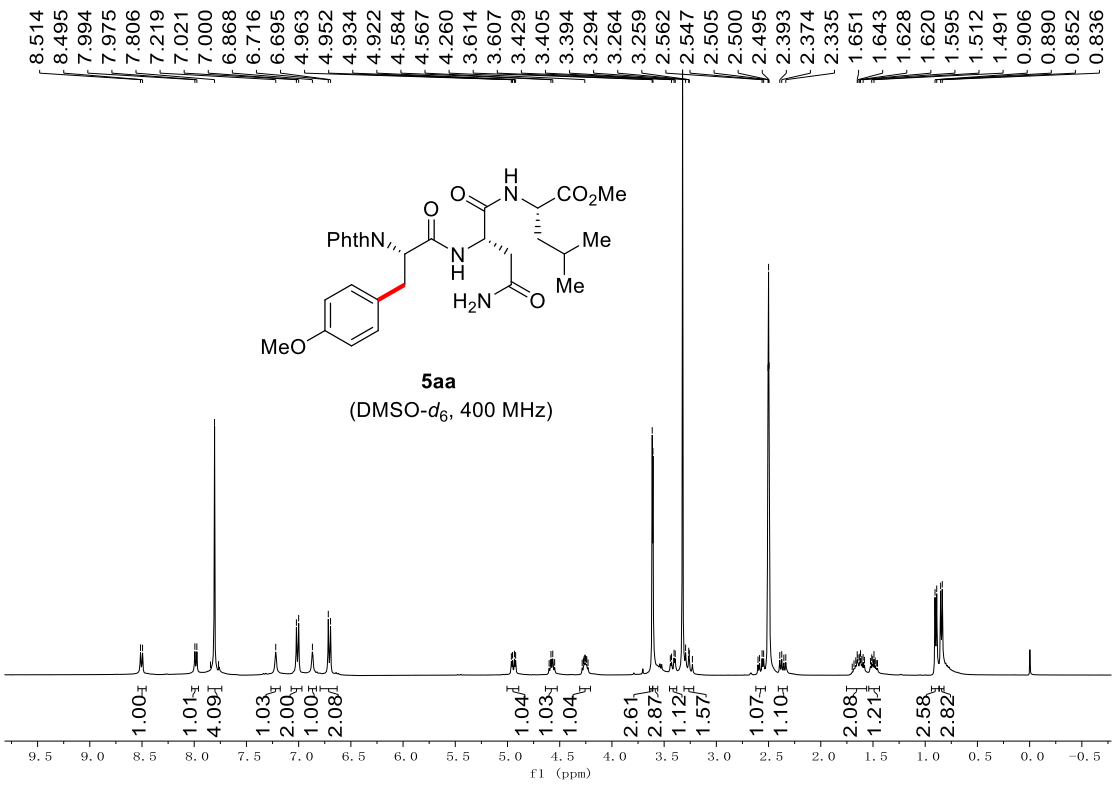
3h

(DMSO-d_6, 400 MHz)



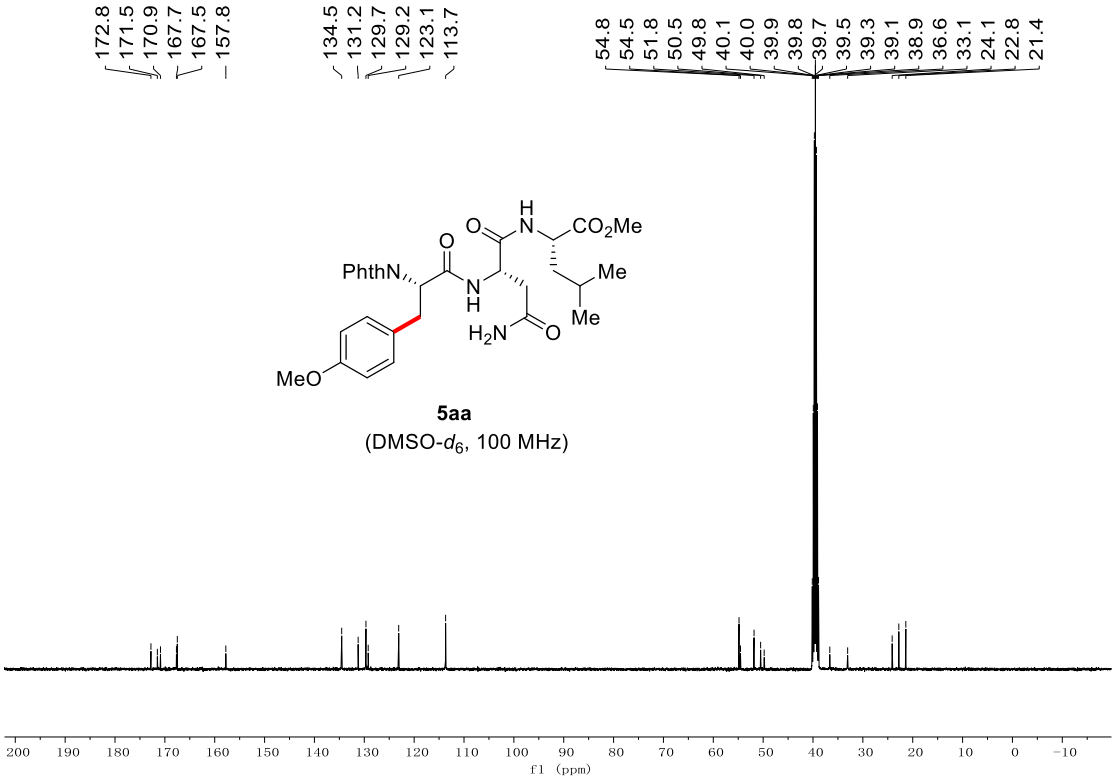
3h

(DMSO-d_6, 100 MHz)

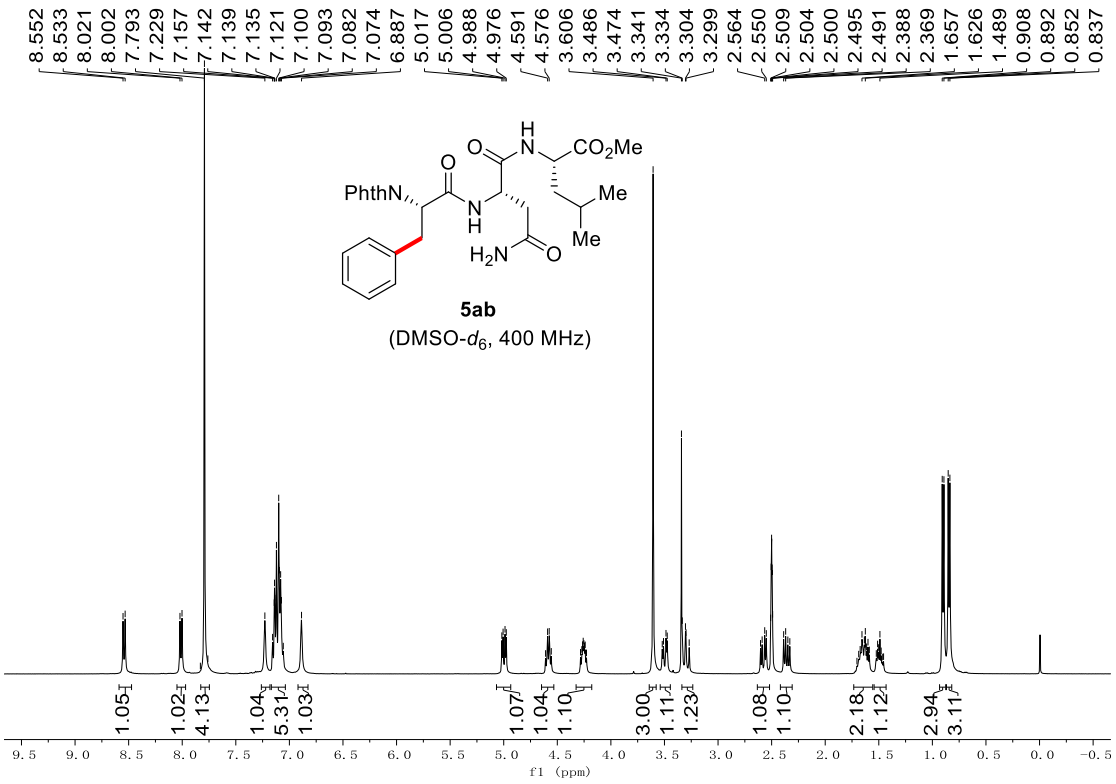


5aa

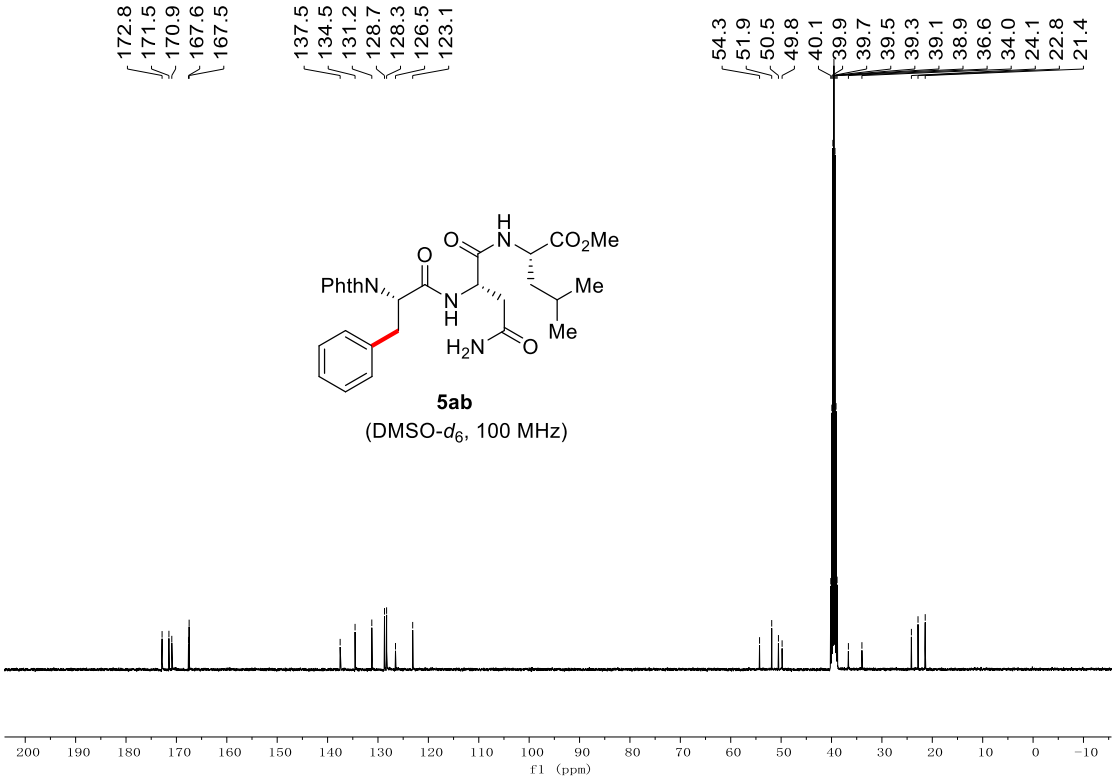
(DMSO-d_6, 400 MHz)



5aa
(DMSO-d_6, 100 MHz)

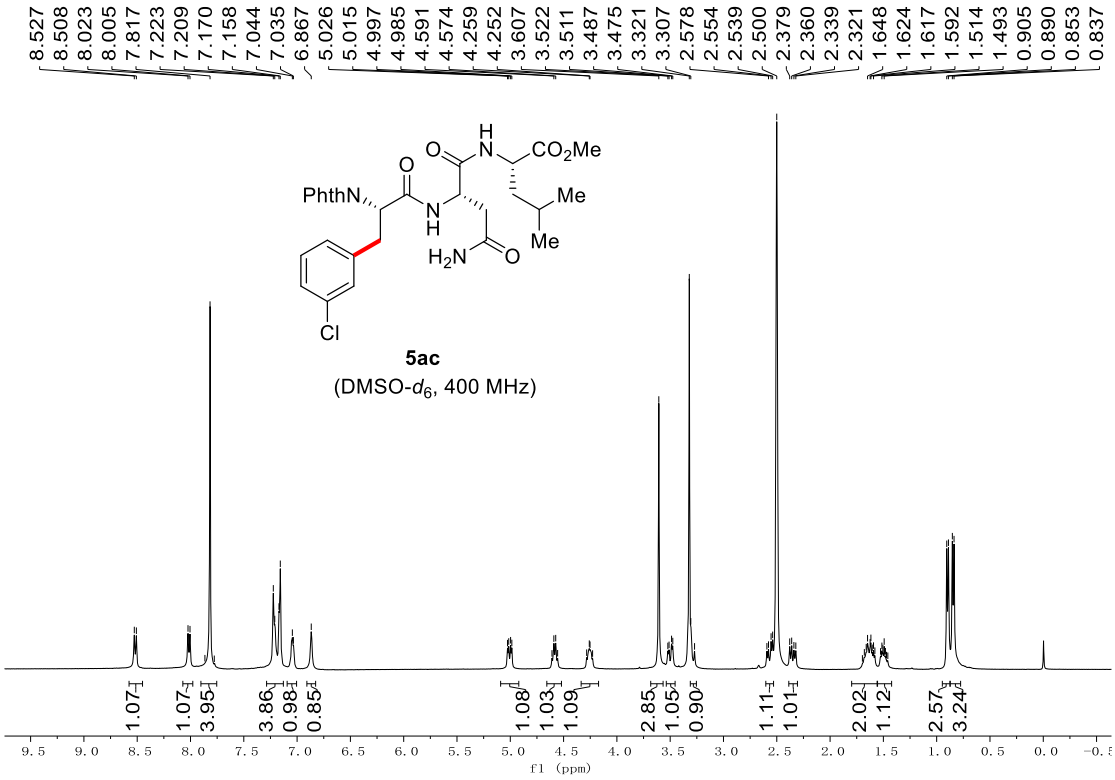


5ab
(DMSO-d_6, 400 MHz)



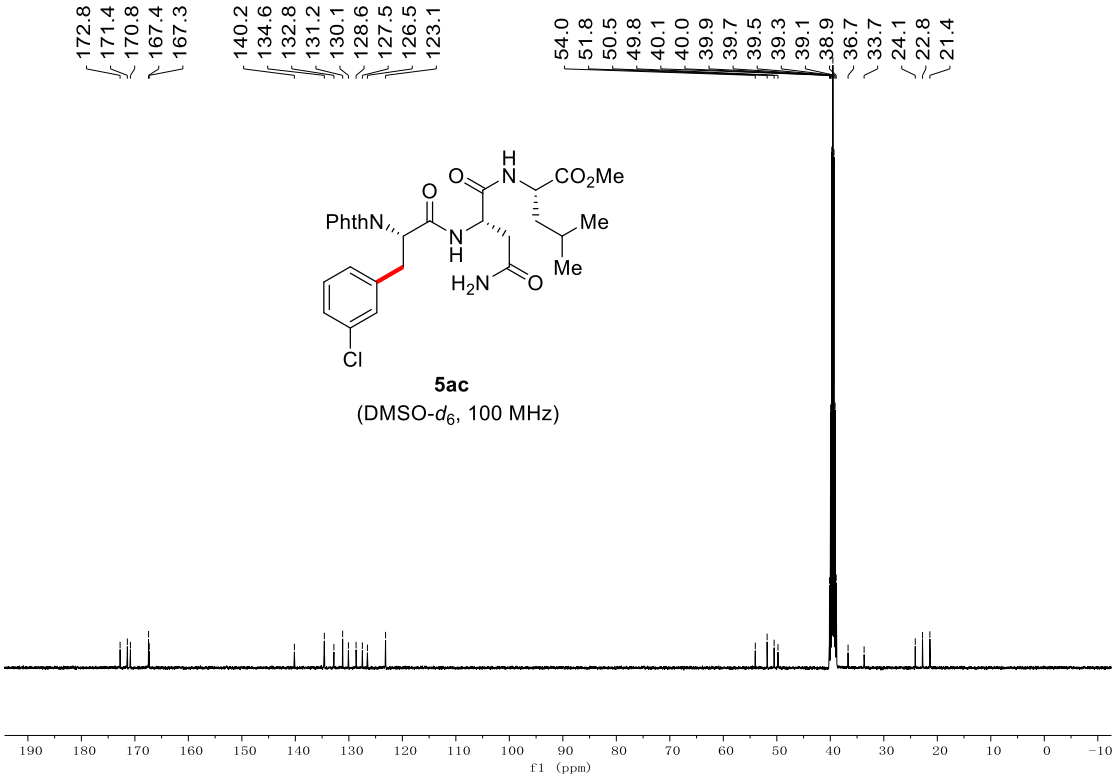
5ab

(DMSO-d_6, 100 MHz)



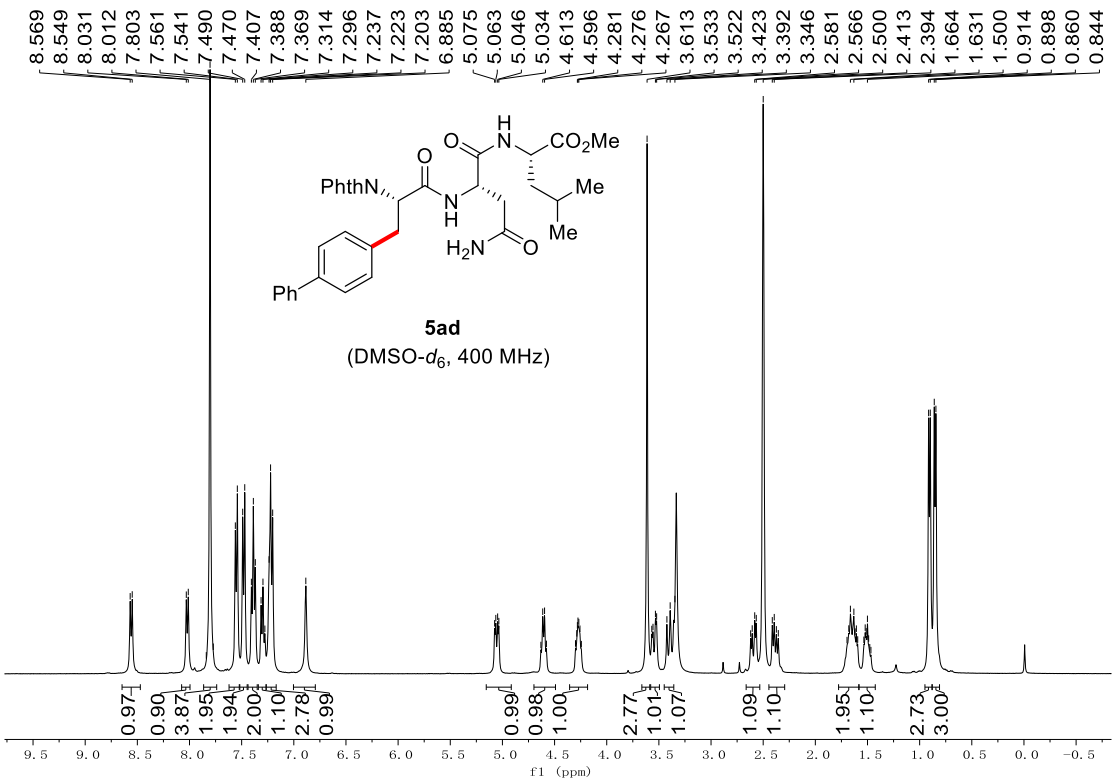
5ac

(DMSO-d_6, 400 MHz)



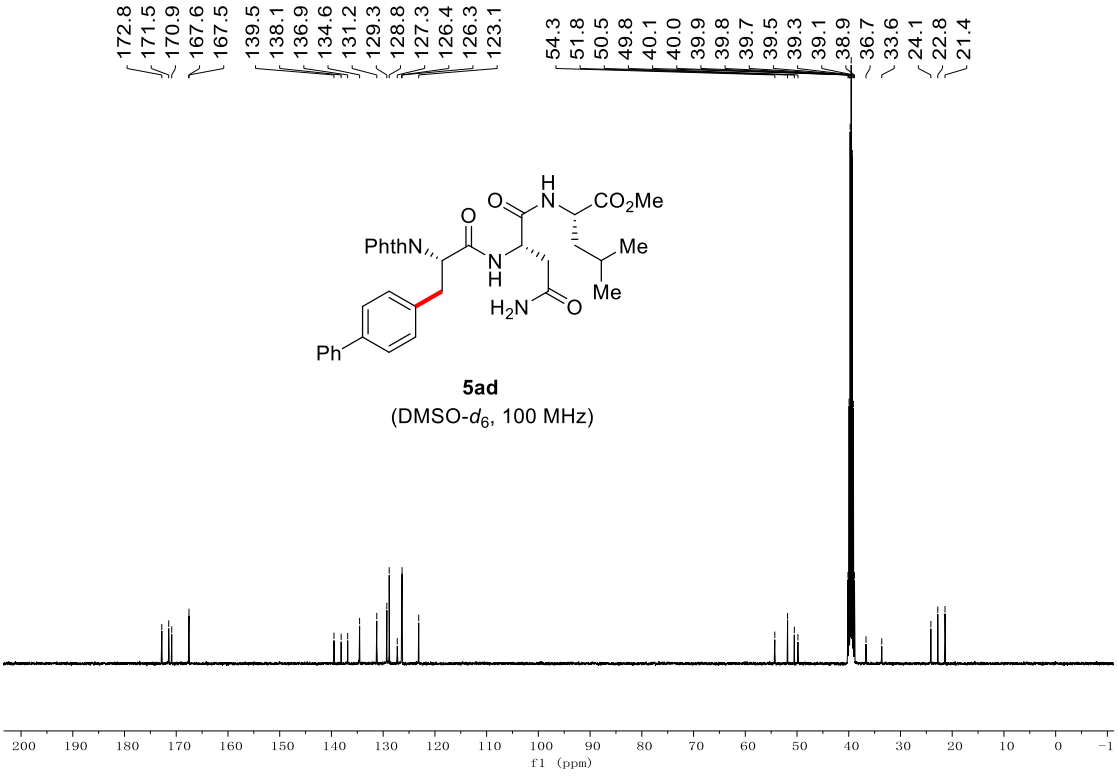
5ac

(DMSO-d_6, 100 MHz)



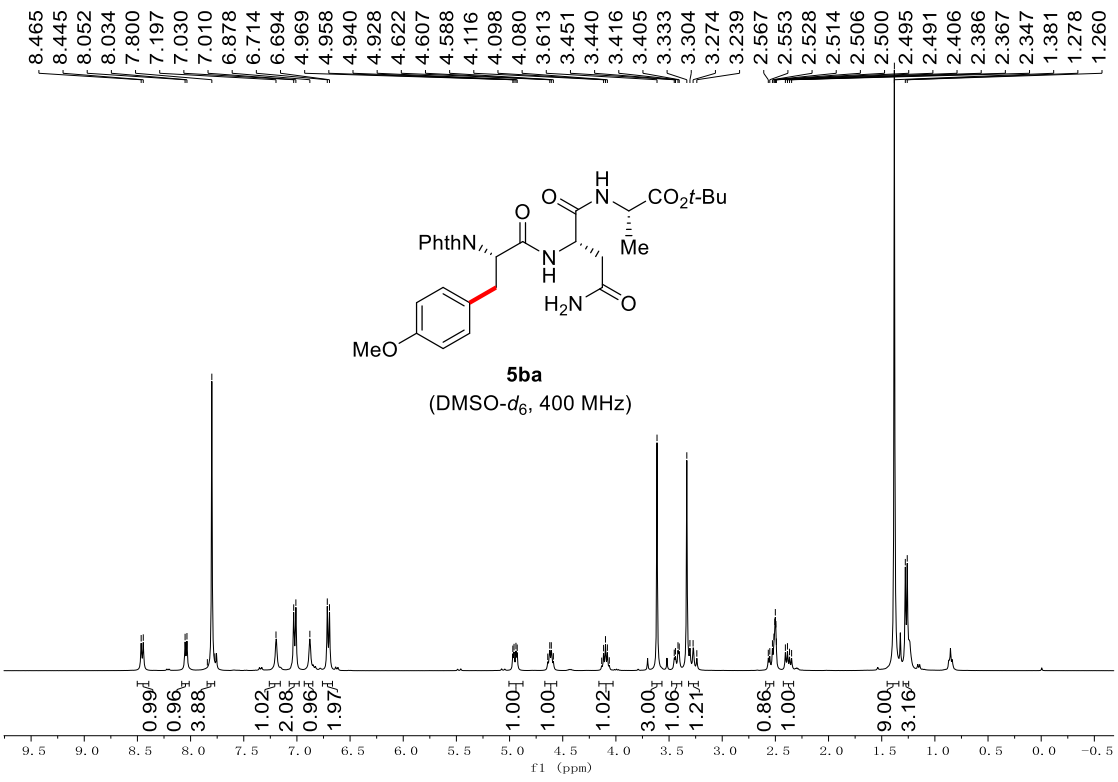
5ad

(DMSO-d_6, 400 MHz)



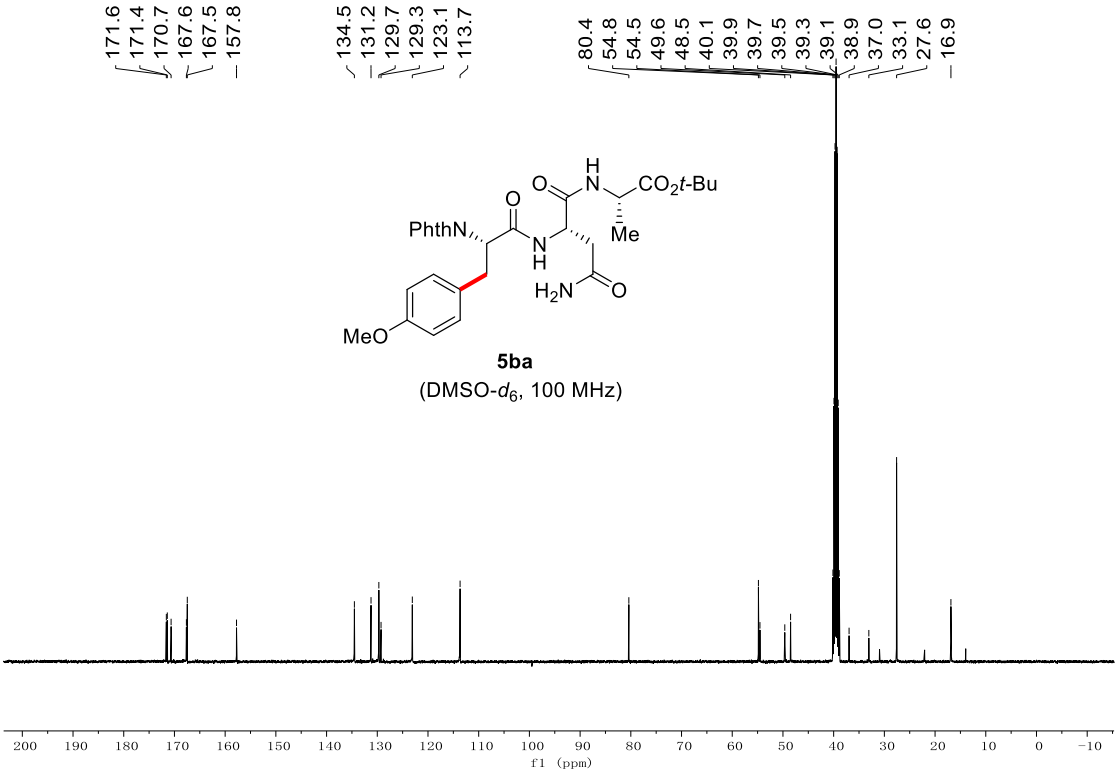
5ad

(DMSO-d_6, 100 MHz)



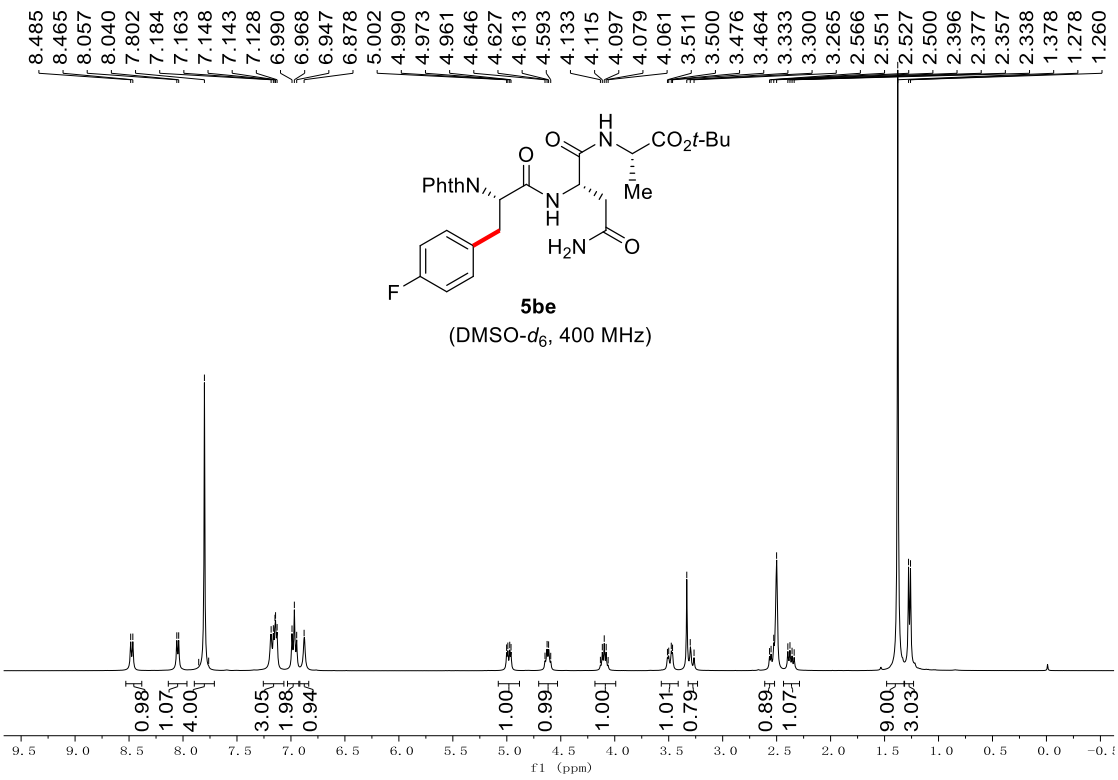
5ba

(DMSO-d_6, 400 MHz)



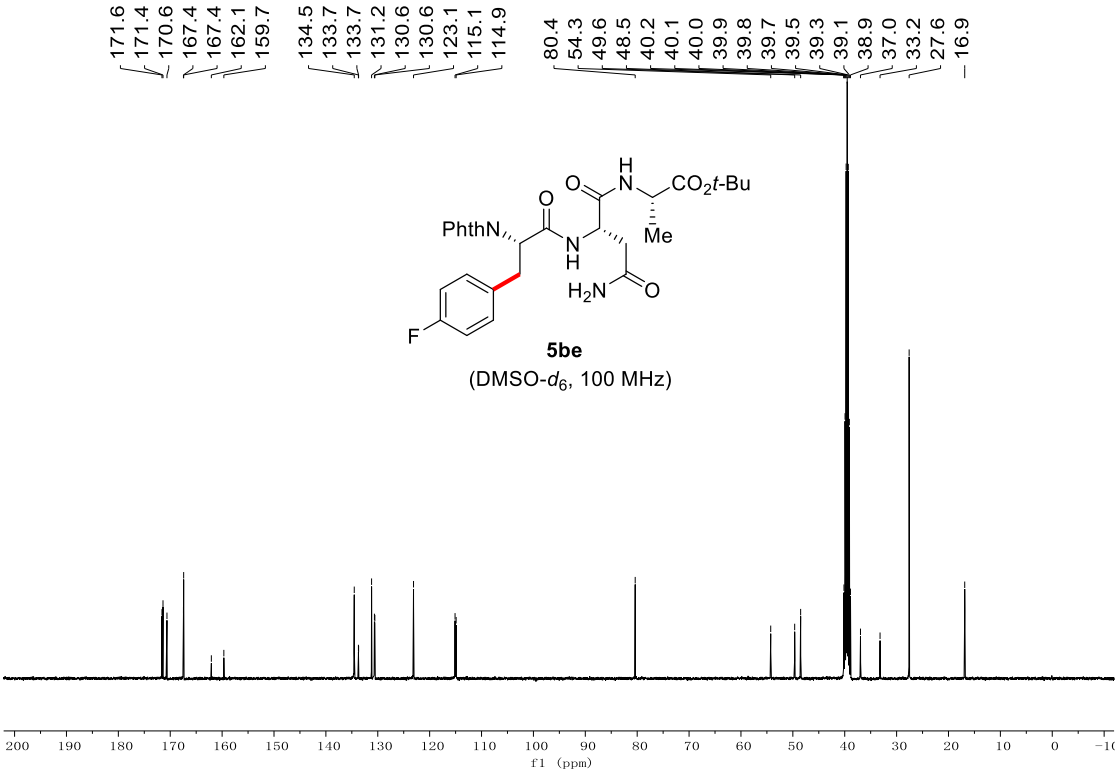
5ba

(DMSO-d_6, 100 MHz)



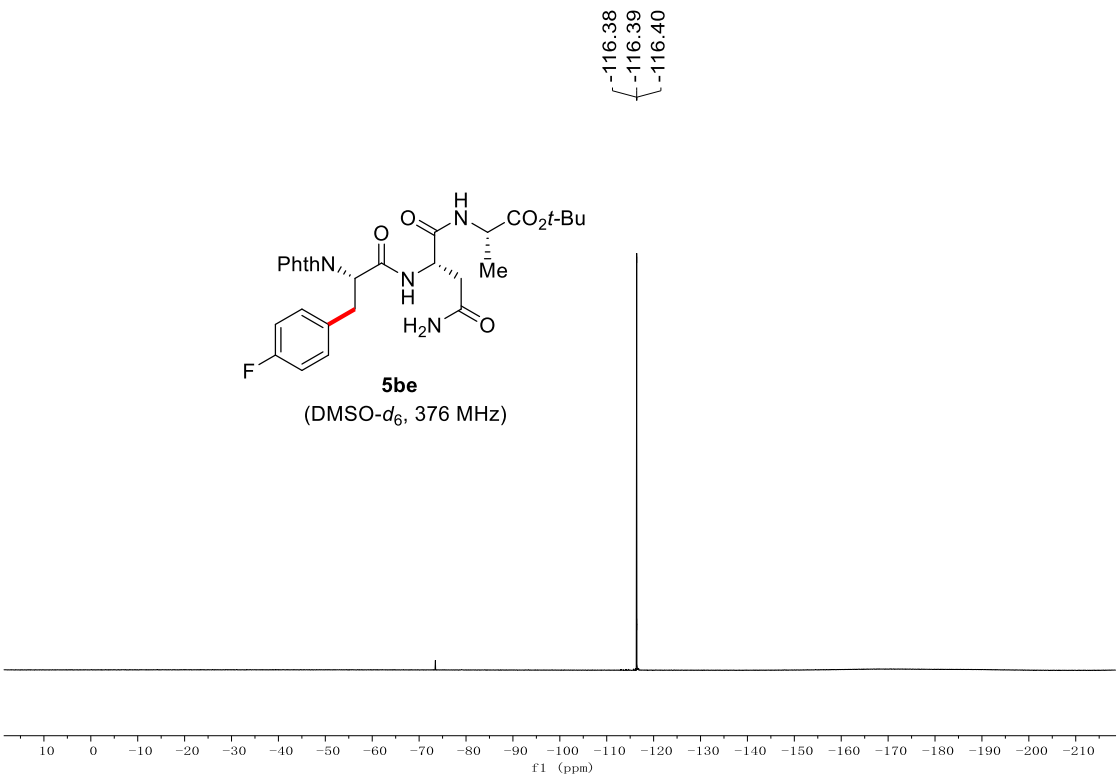
5be

(DMSO-d_6, 400 MHz)



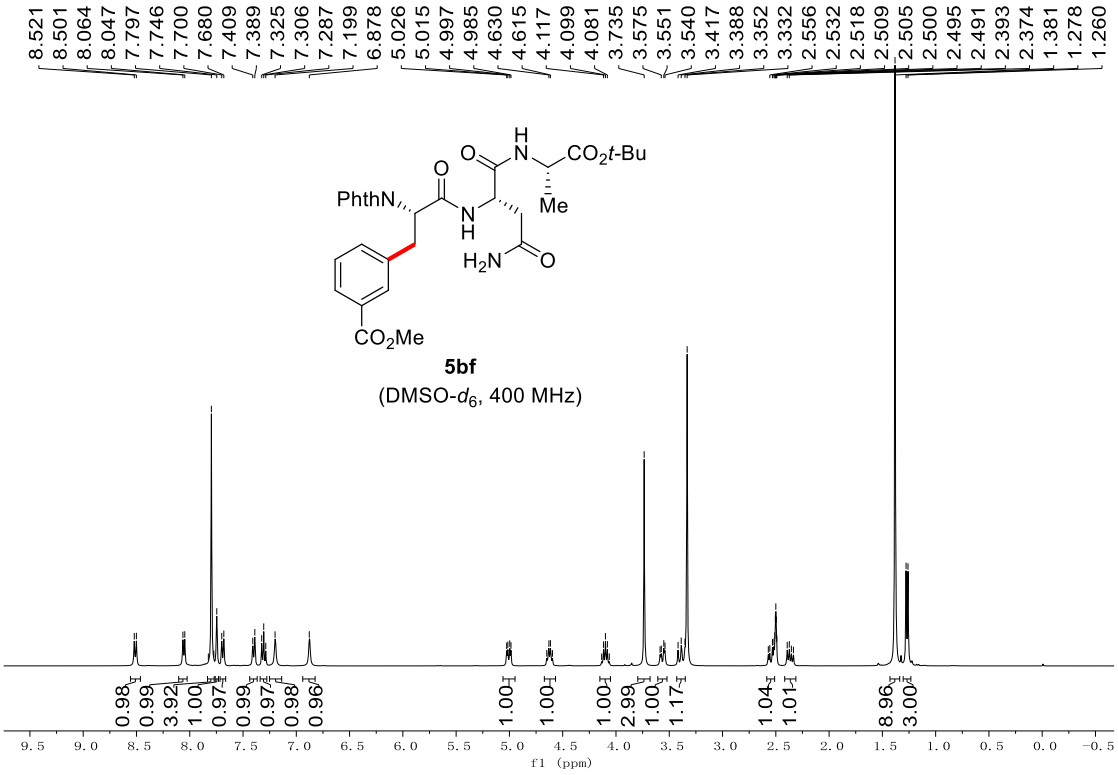
5be

(DMSO-d_6, 100 MHz)



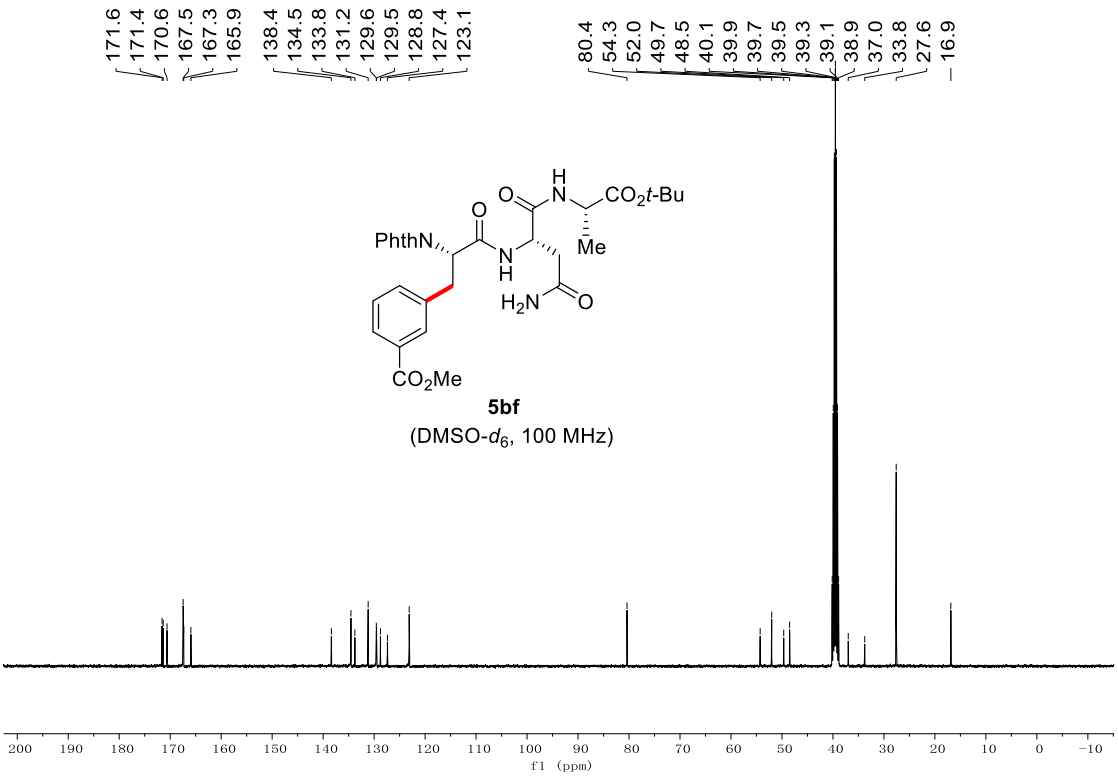
5be

(DMSO-d_6, 376 MHz)



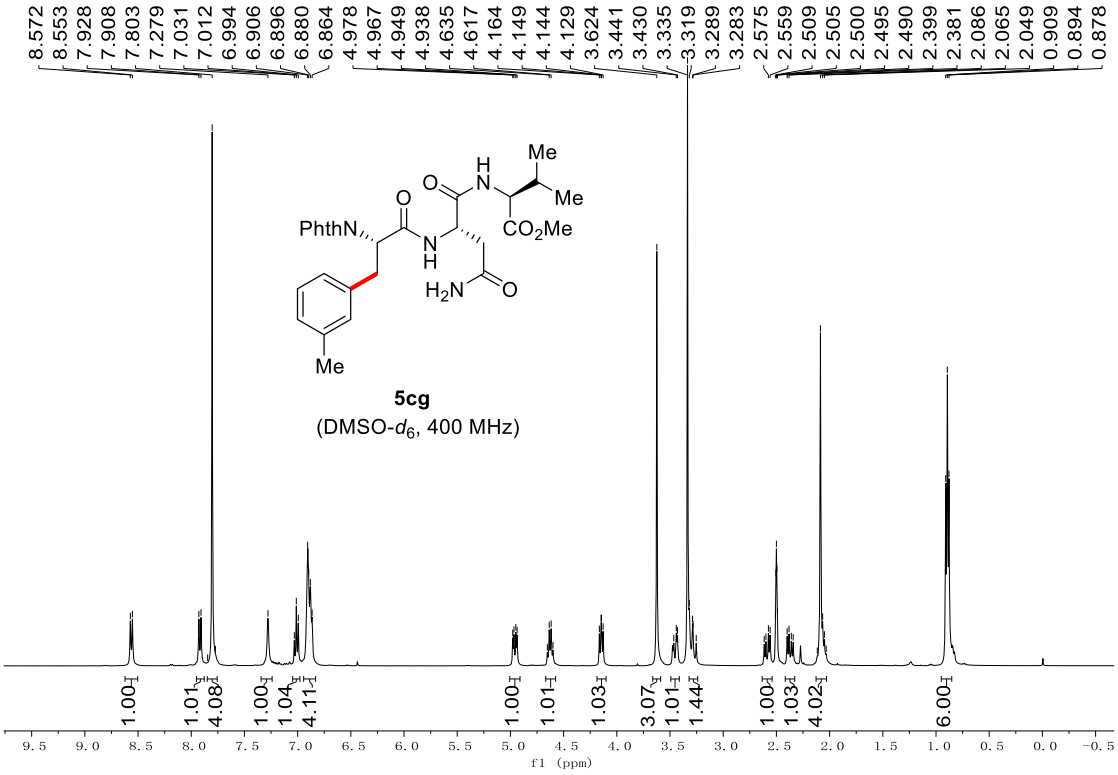
5bf

(DMSO-d_6, 400 MHz)



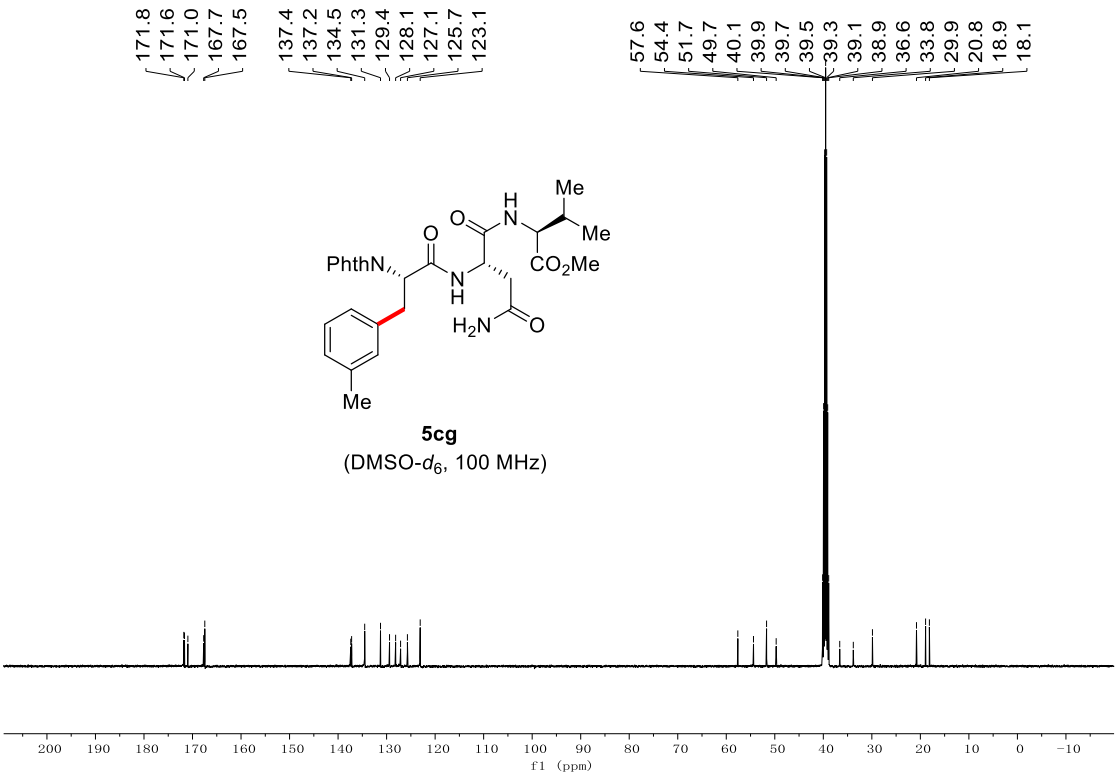
5bf

(DMSO-d_6, 100 MHz)



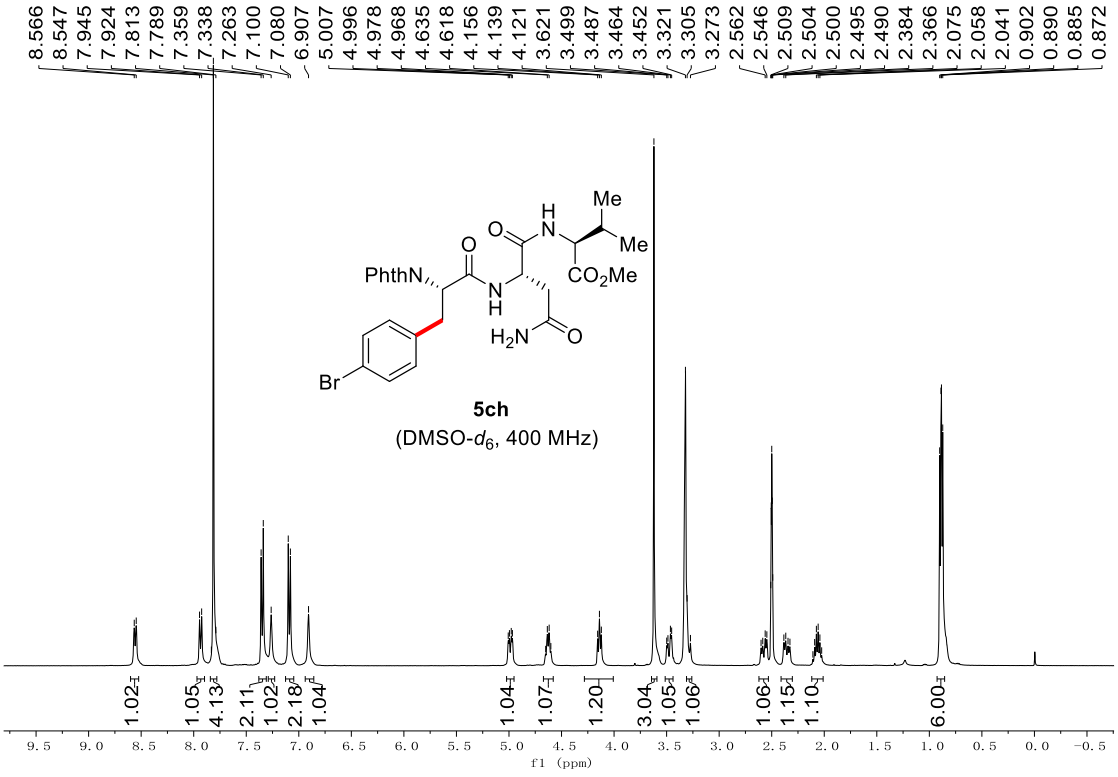
5cg

(DMSO-d_6, 400 MHz)



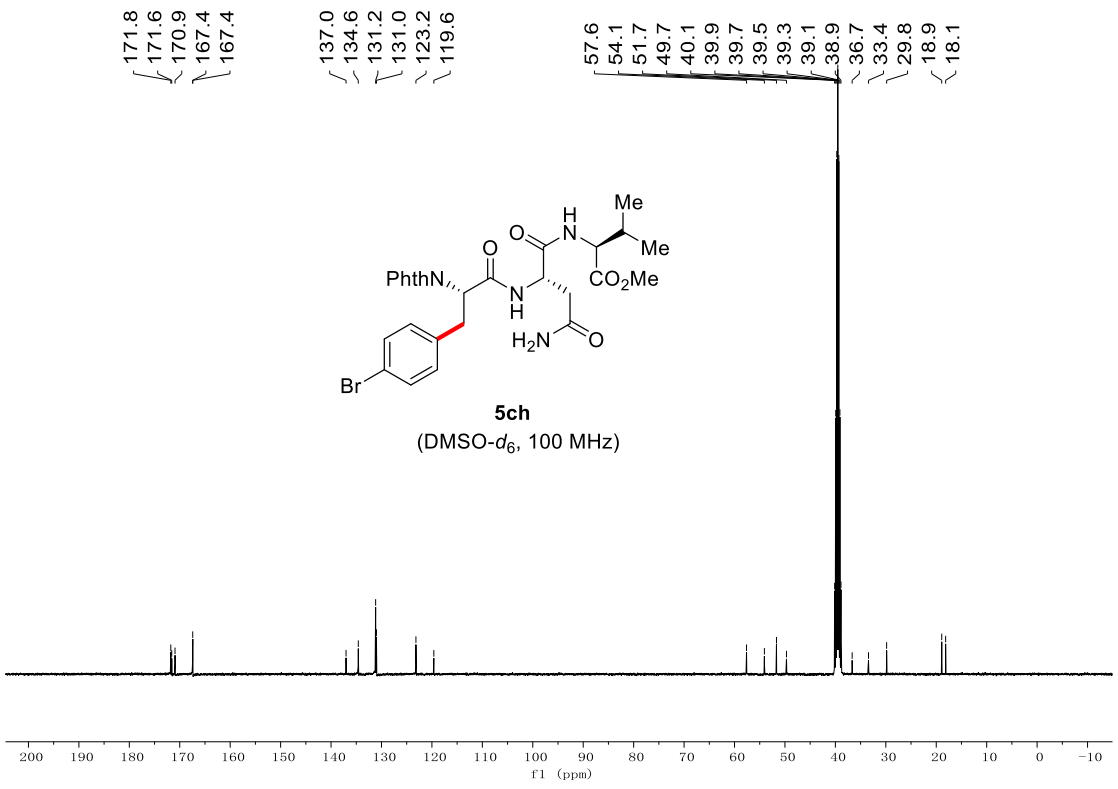
5cg

(DMSO-d_6, 100 MHz)



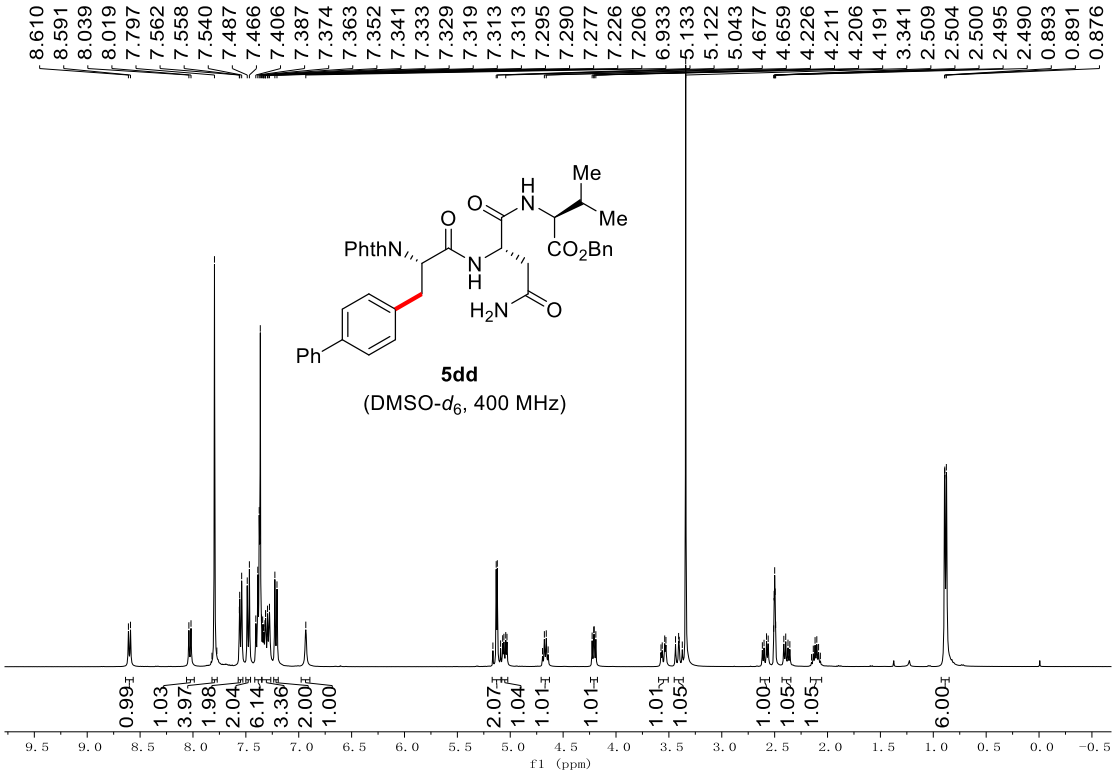
5ch

(DMSO-d_6, 400 MHz)



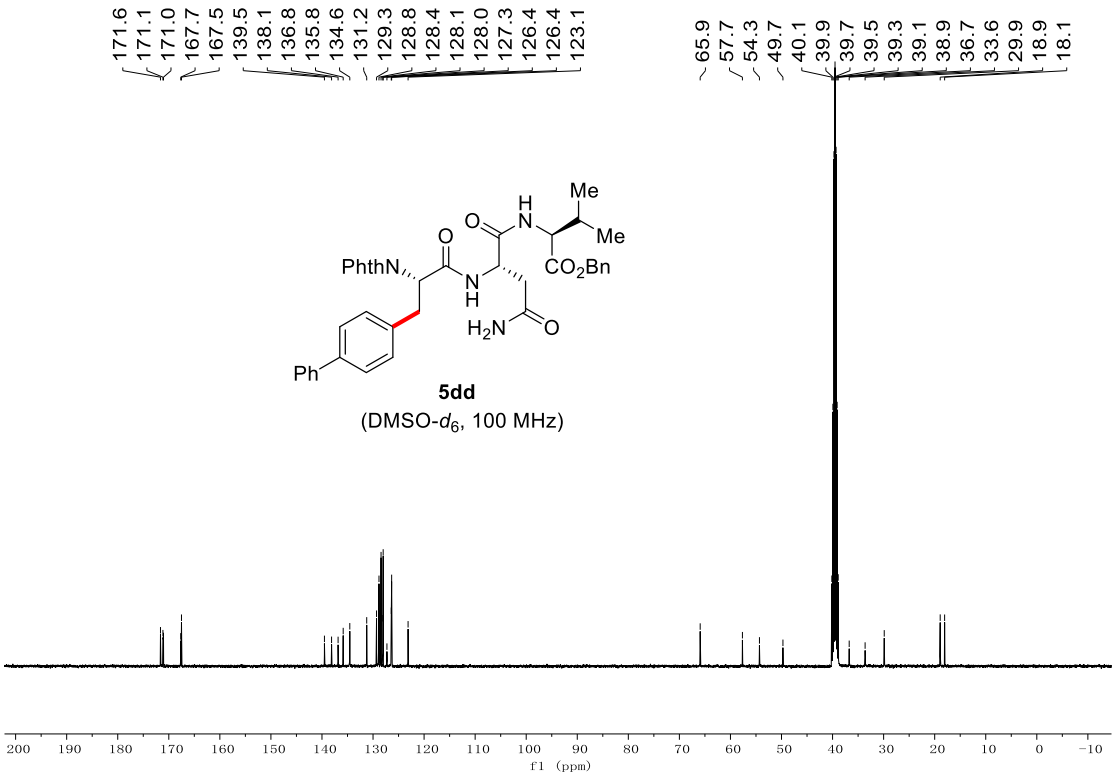
5ch

(DMSO-d_6, 100 MHz)



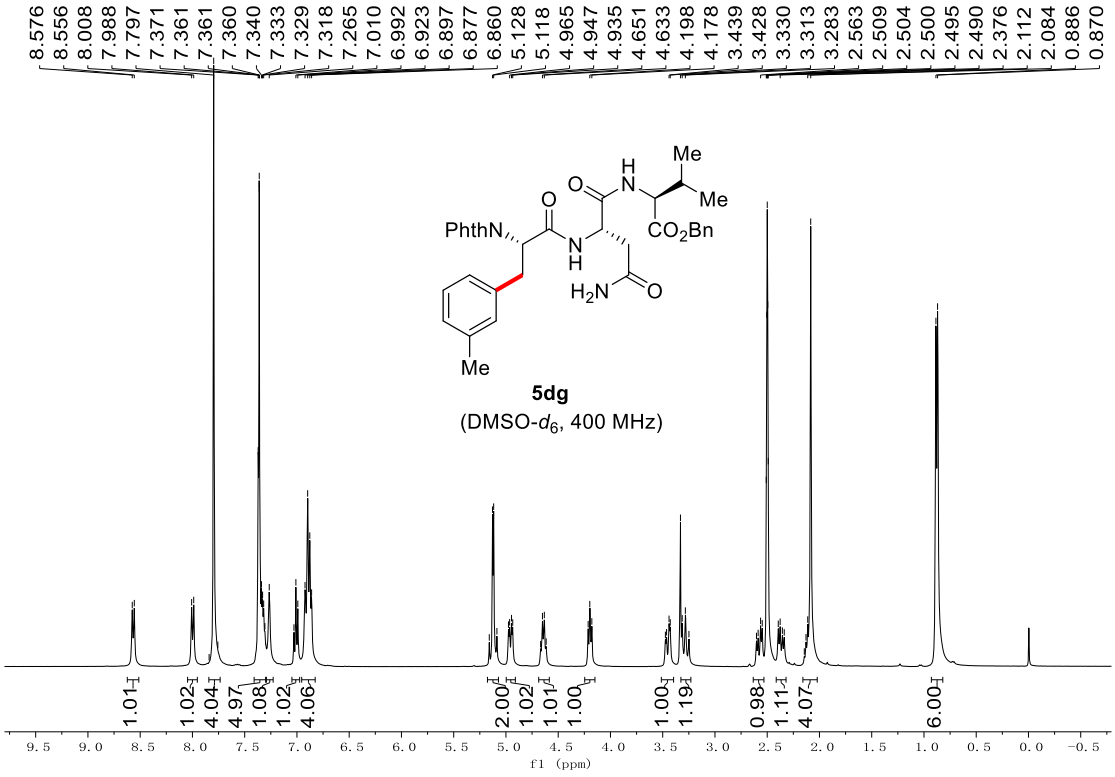
5dd

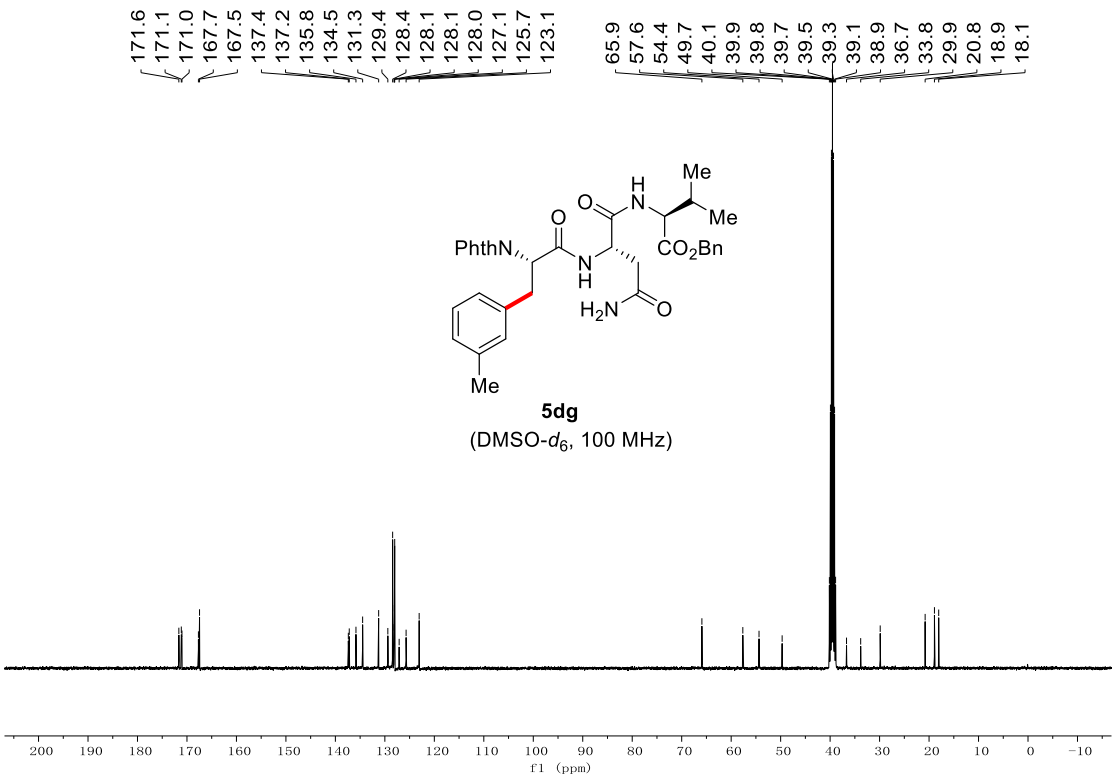
(DMSO-d_6, 400 MHz)

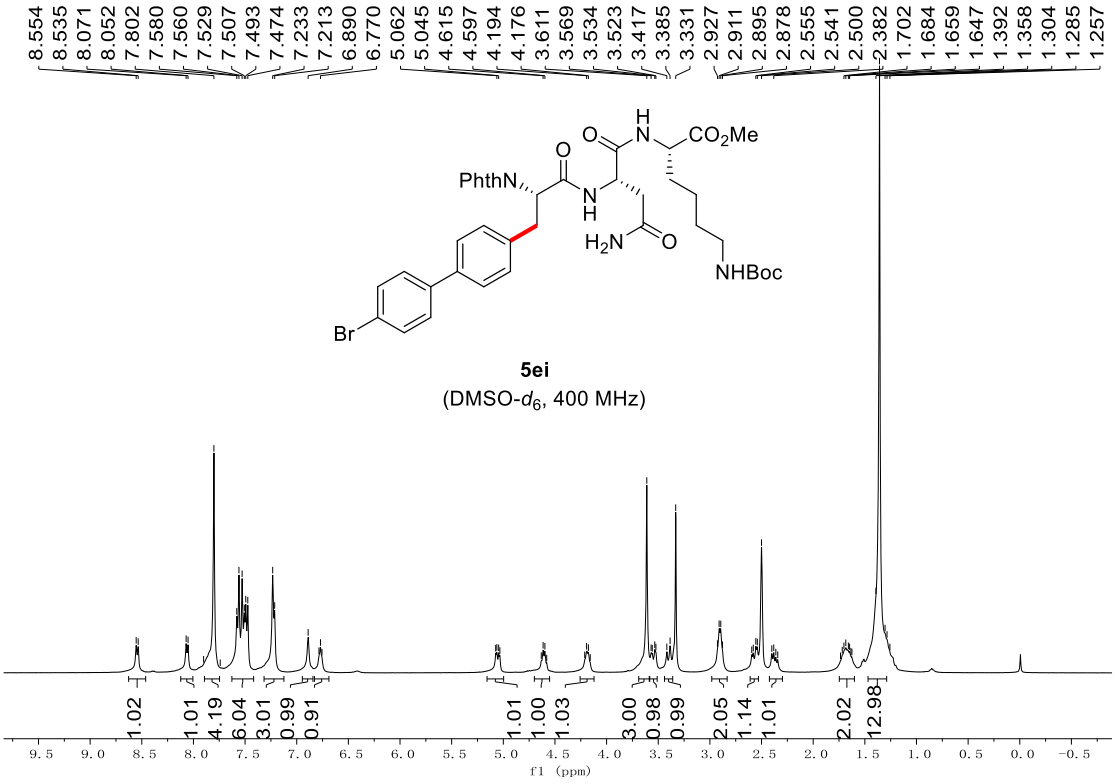


5dd

(DMSO-d_6, 100 MHz)

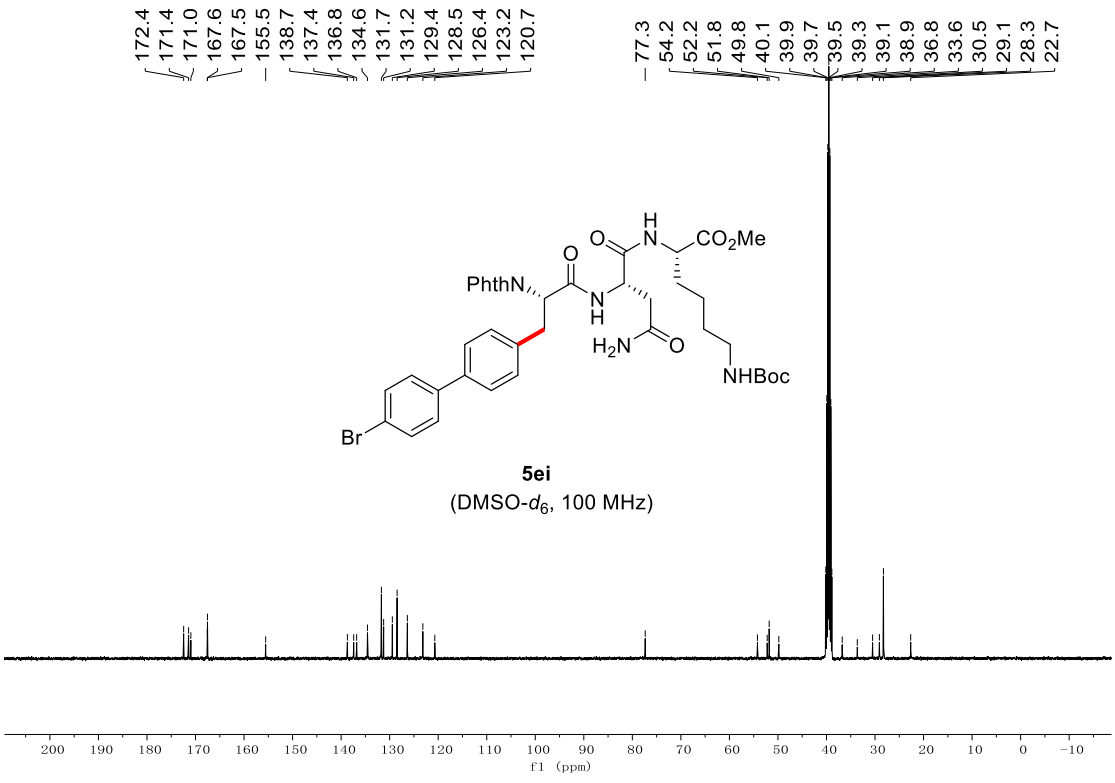

8.576 8.556 8.008 7.988 7.797 7.371 7.361 7.361 7.360 7.340 7.333 7.329 7.318 7.265 7.010 6.992 6.923 6.897 6.877 6.860 5.128 5.118 4.965 4.947 4.935 4.651 4.633 4.198 4.178 3.439 3.428 3.330 3.313 3.283 2.563 2.509 2.504 2.500 2.495 2.490 2.376 2.112 2.084 0.886 0.870
Me
H
N
O
Me
O
PhthN
N
CO2Bn
H
H2N
O
Me
5dg
(DMSO-d6, 400 MHz)
1.01 1.02 4.04 4.97 1.08 1.02 4.06 2.00 1.02 1.01 1.00 1.00 1.19 0.98 1.11 4.07 6.00
f1 (ppm)


171.6 171.1 171.0 167.7 167.5 137.4 137.2 135.8 134.5 131.3 129.4 128.4 128.1 128.1 128.0 127.1 125.7 123.1
65.9 57.6 54.4 49.7 40.1 39.9 39.8 39.7 39.5 39.3 39.1 38.9 36.7 33.8 29.9 20.8 18.9 18.1
Me
H
N
O
Me
O
PhthN
N
CO2Bn
H
H2N
O
Me
5dg
(DMSO-d6, 100 MHz)
f1 (ppm)



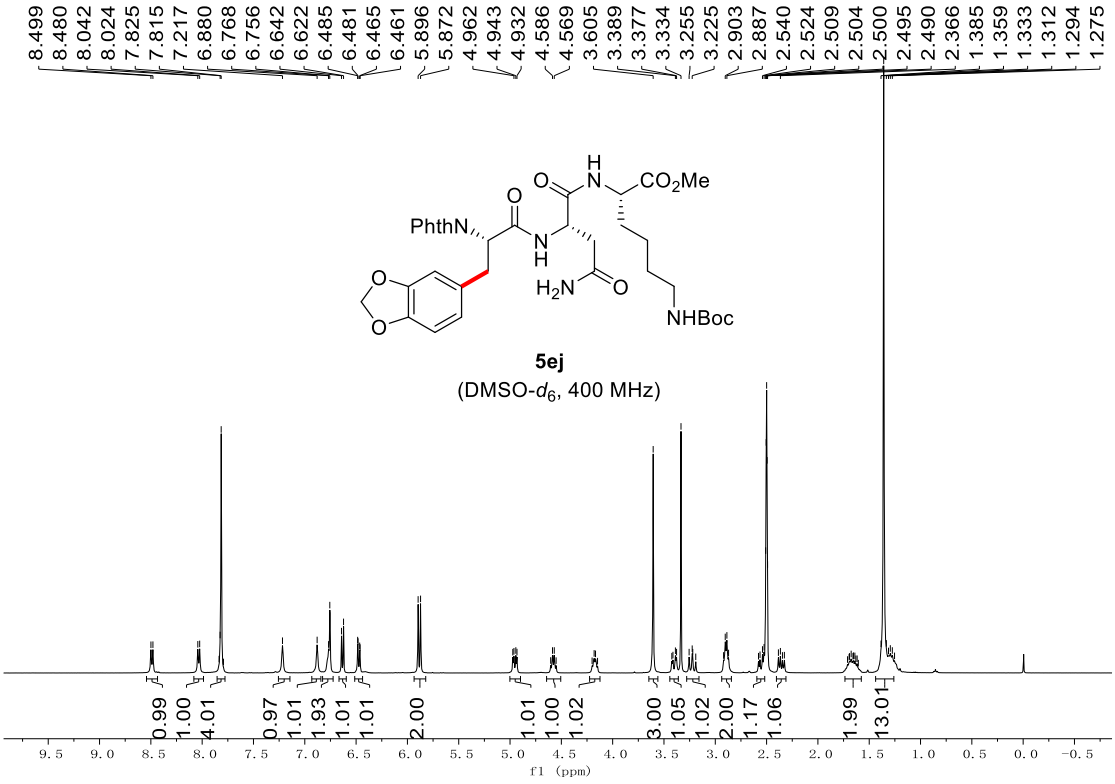
5ei

(DMSO-d_6, 400 MHz)



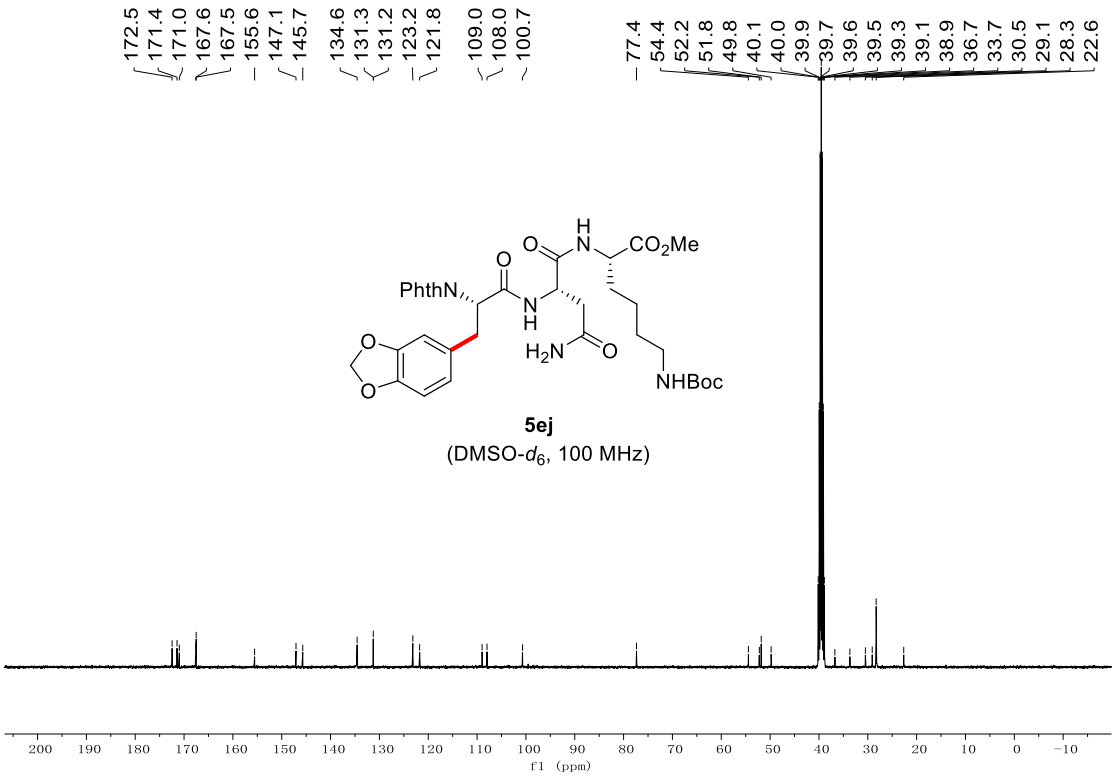
5ei

(DMSO-d_6, 100 MHz)



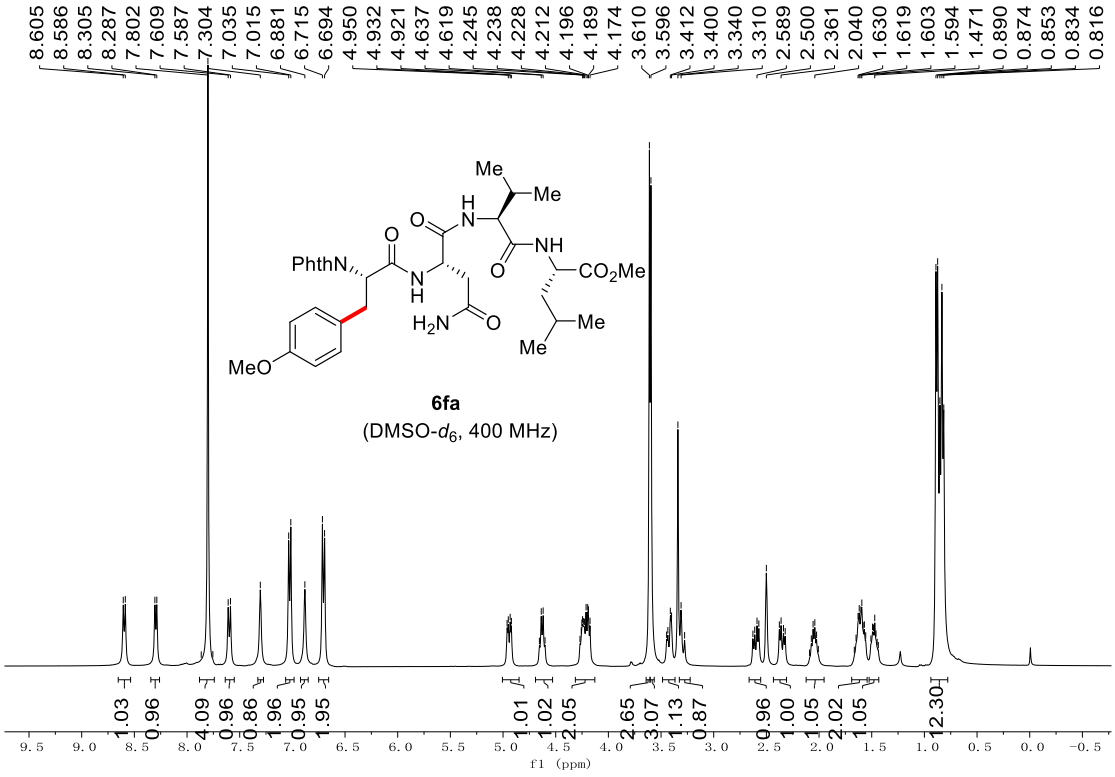
5ej

(DMSO-d_6, 400 MHz)

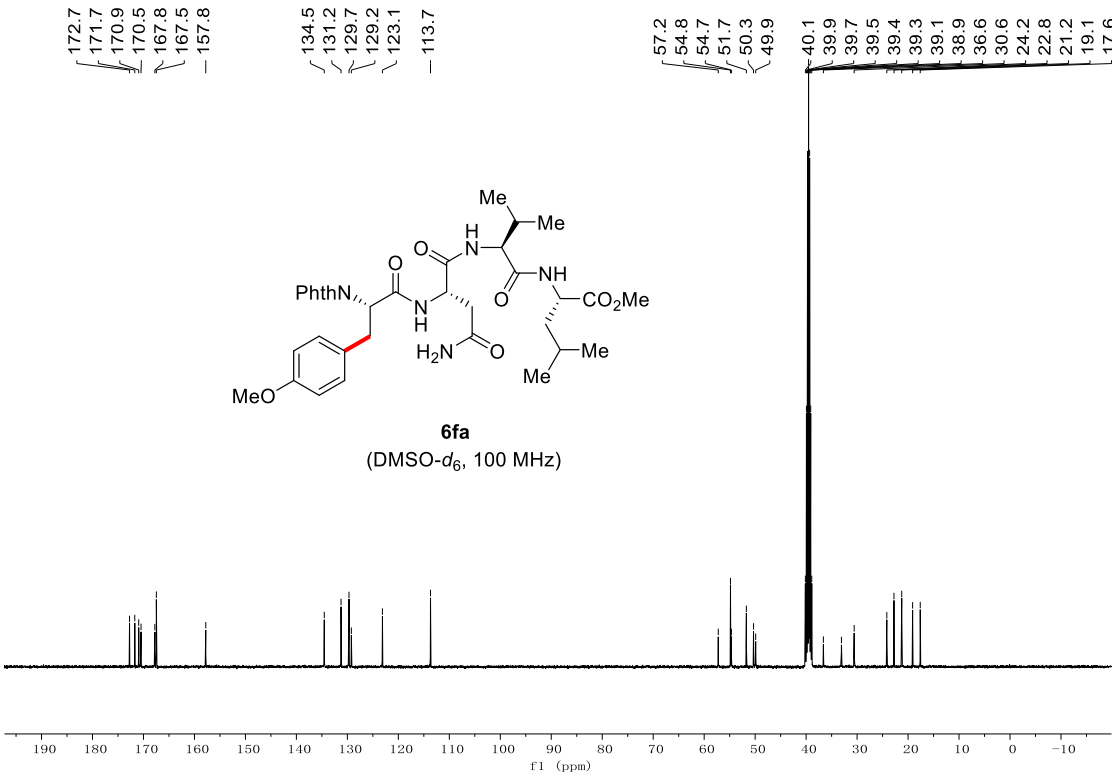


5ej

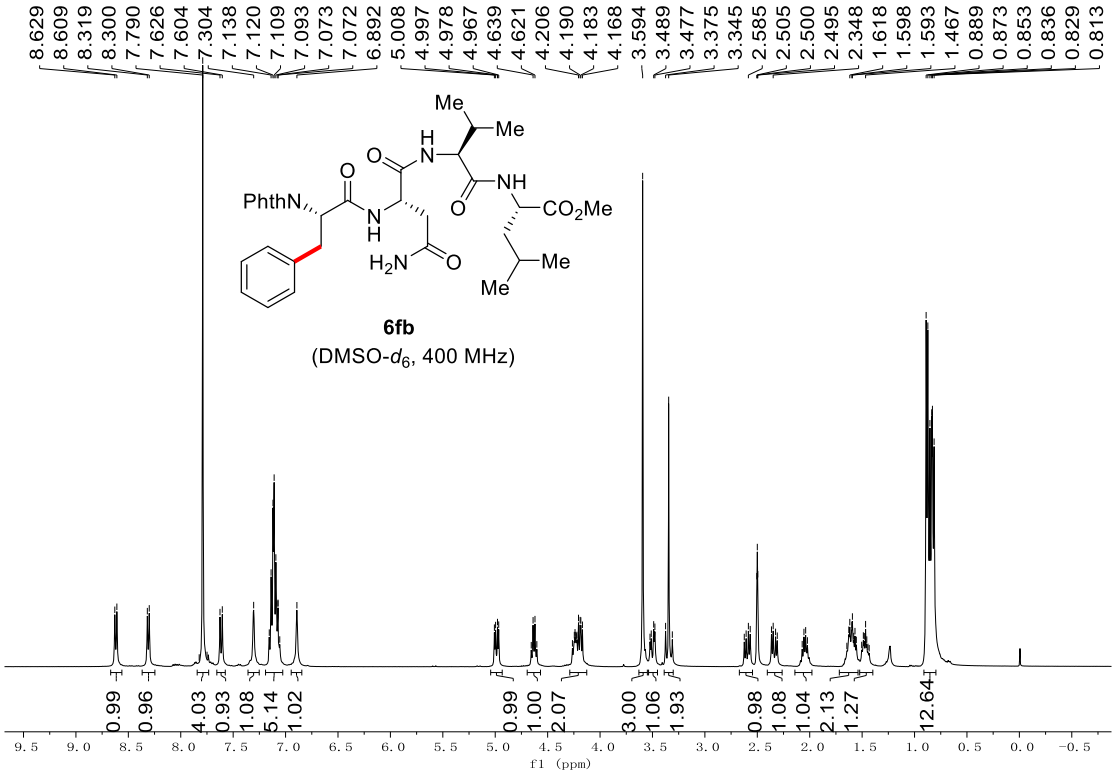
(DMSO-d_6, 100 MHz)

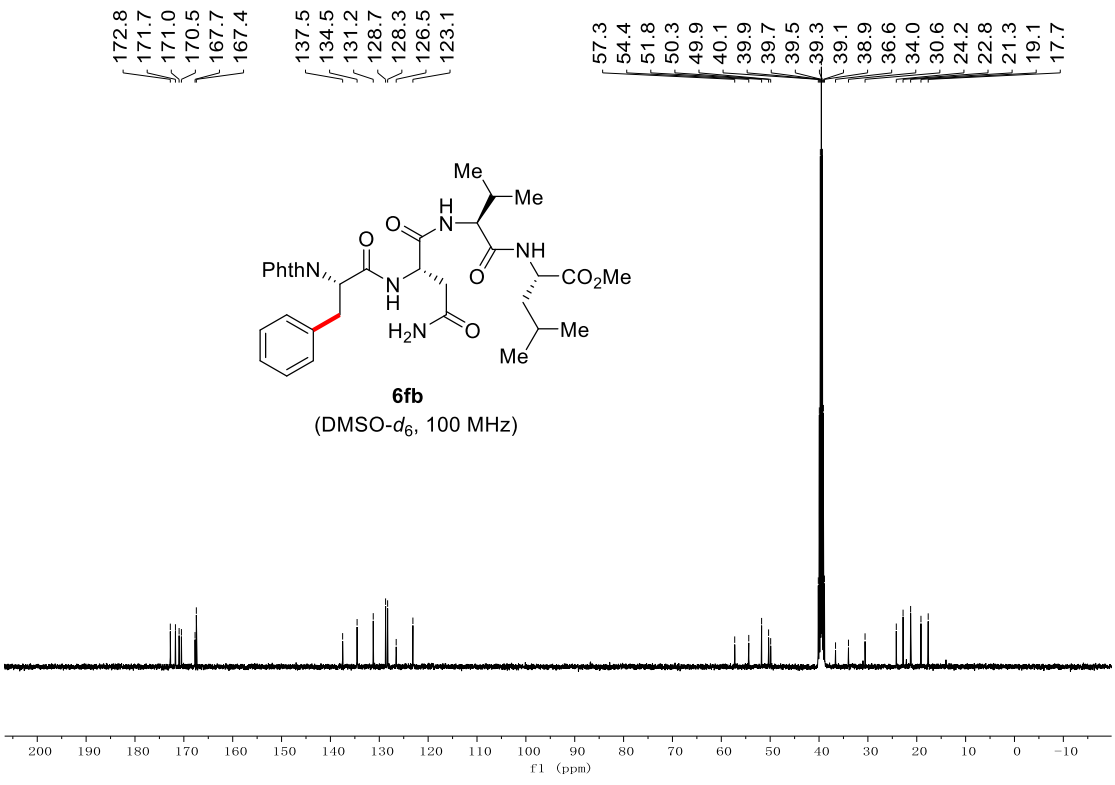


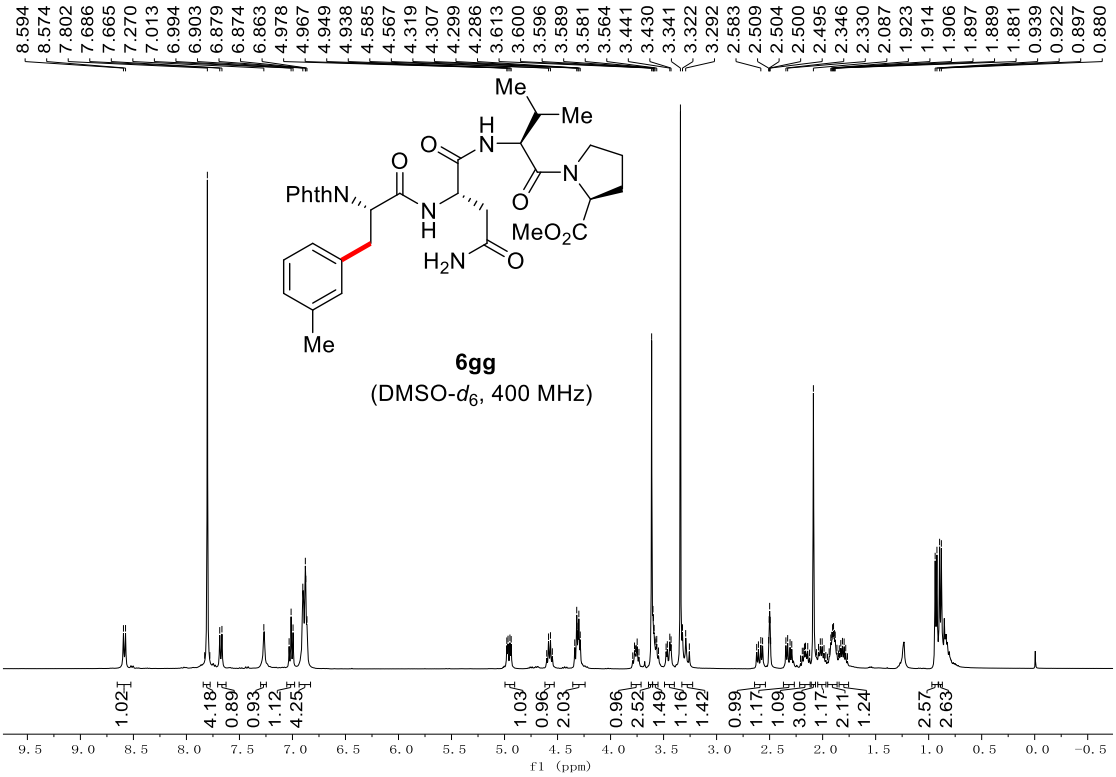
6fa
(DMSO-d_6, 400 MHz)

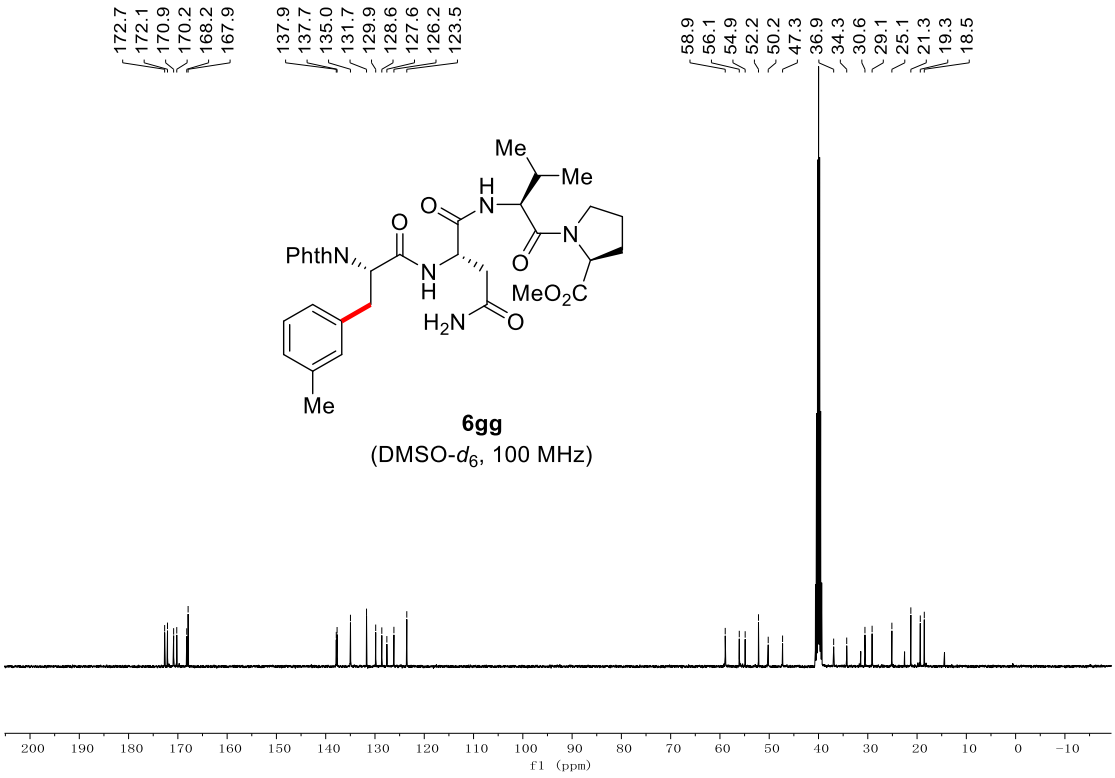


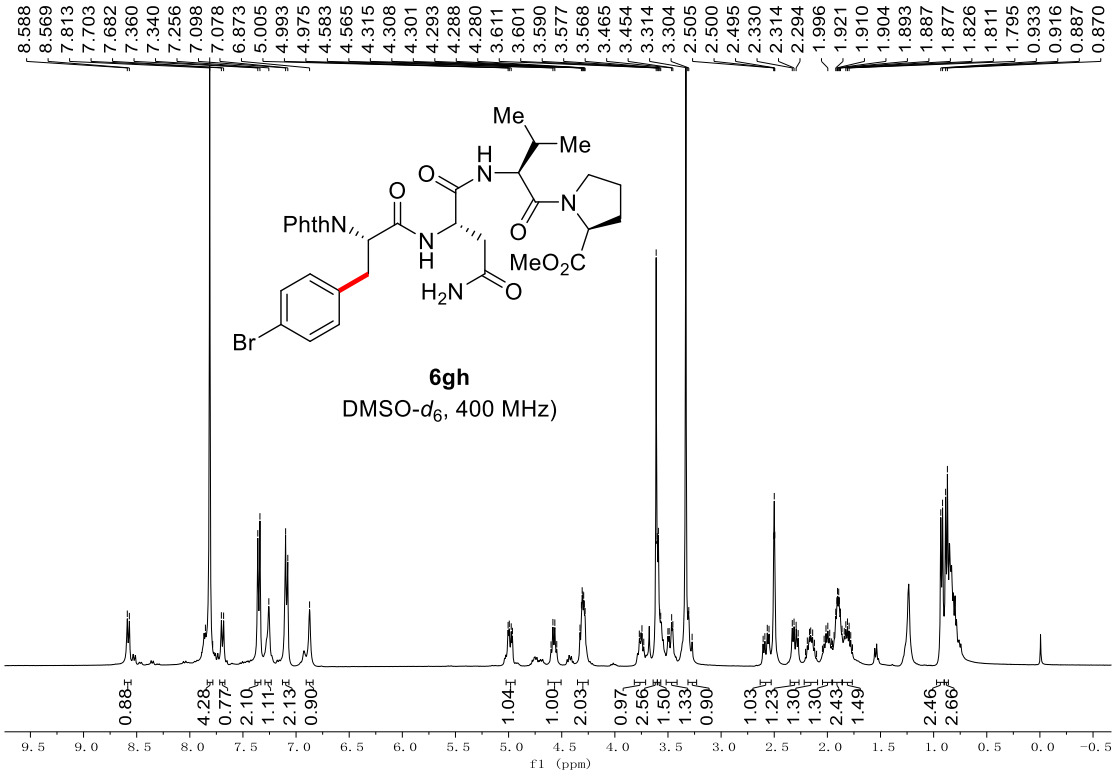
6fa
(DMSO-d_6, 100 MHz)


8.629 8.609 8.319 8.300 7.790 7.626 7.604 7.304 7.138 7.120 7.109 7.093 7.073 7.072 6.892 5.008 4.997 4.978 4.967 4.639 4.621 4.206 4.190 4.183 4.168 3.594 3.489 3.477 3.375 3.345 2.585 2.505 2.500 2.495 2.348 1.618 1.598 1.593 1.467 0.889 0.873 0.853 0.836 0.829 0.813
Me
Me
H
N
O
O
NH
O
CO2Me
PhthN
N
H
H2N
O
Me
Me
6fb
(DMSO-d6, 400 MHz)
0.99 0.96 4.03 0.93 1.08 5.14 1.02 0.99 1.00 2.07 3.00 1.06 1.93 0.98 1.08 1.04 2.13 1.27 12.64
f1 (ppm)


172.8 171.7 171.0 170.5 167.7 167.4 137.5 134.5 131.2 128.7 128.3 126.5 123.1 57.3 54.4 51.8 50.3 49.9 40.1 39.9 39.7 39.5 39.3 39.1 38.9 36.6 34.0 30.6 24.2 22.8 21.3 19.1 17.7
Me
Me
H
N
O
O
NH
O
CO2Me
PhthN
N
H
H2N
O
Me
Me
6fb
(DMSO-d6, 100 MHz)
f1 (ppm)

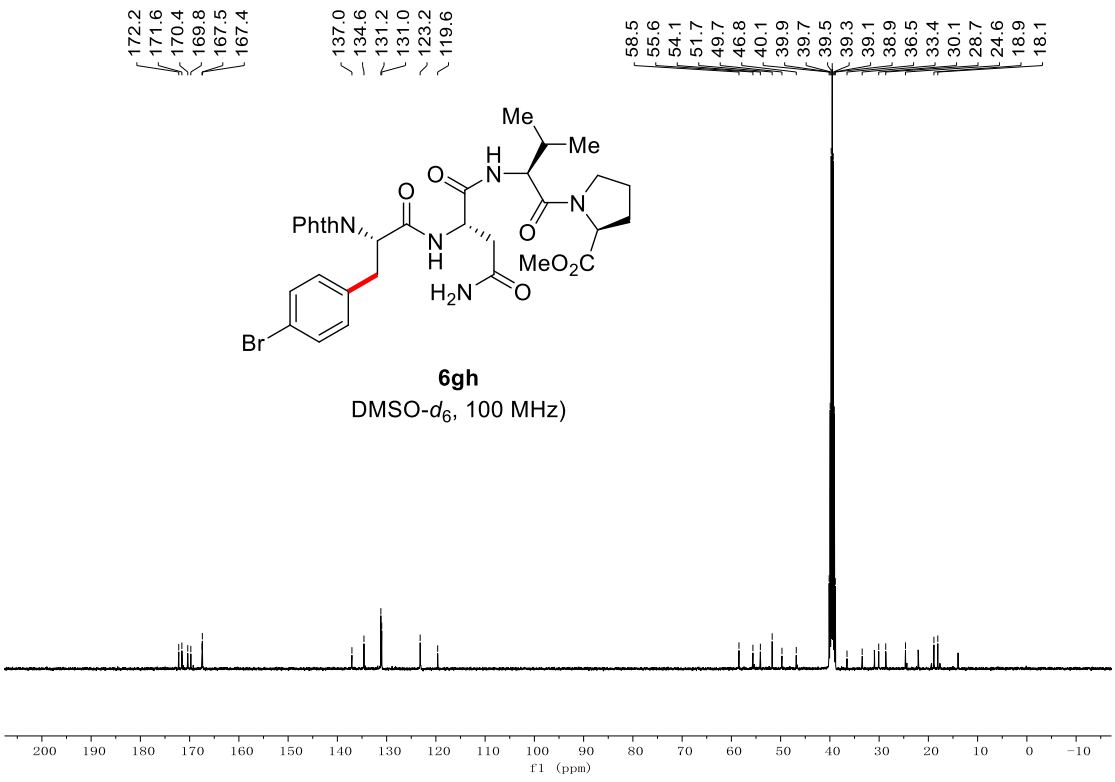

8.594
8.574
7.802
7.686
7.665
7.270
7.013
6.994
6.903
6.879
6.874
6.863
4.978
4.967
4.949
4.938
4.585
4.567
4.319
4.307
4.299
4.286
3.613
3.600
3.596
3.589
3.581
3.564
3.441
3.430
3.341
3.322
3.292
2.583
2.509
2.504
2.500
2.495
2.346
2.330
2.087
1.923
1.914
1.906
1.897
1.889
1.881
0.939
0.922
0.897
0.880
Me
Me
H
N
O
O
N
O
PhthN
N
H
MeO2C
H2N
O
Me
6gg
(DMSO-d6, 400 MHz)
1.02
4.18
0.89
0.93
1.12
4.25
1.03
0.96
2.03
0.96
2.52
1.49
1.16
1.42
0.99
1.17
1.09
3.00
1.17
2.11
1.24
2.57
2.63
f1 (ppm)


172.7
172.1
170.9
170.2
168.2
167.9
137.9
137.7
135.0
131.7
129.9
128.6
127.6
126.2
123.5
58.9
56.1
54.9
52.2
50.2
47.3
36.9
34.3
30.6
29.1
25.1
21.3
19.3
18.5
Me
Me
H
N
O
O
N
O
PhthN
N
H
MeO2C
H2N
O
Me
6gg
(DMSO-d6, 100 MHz)
f1 (ppm)



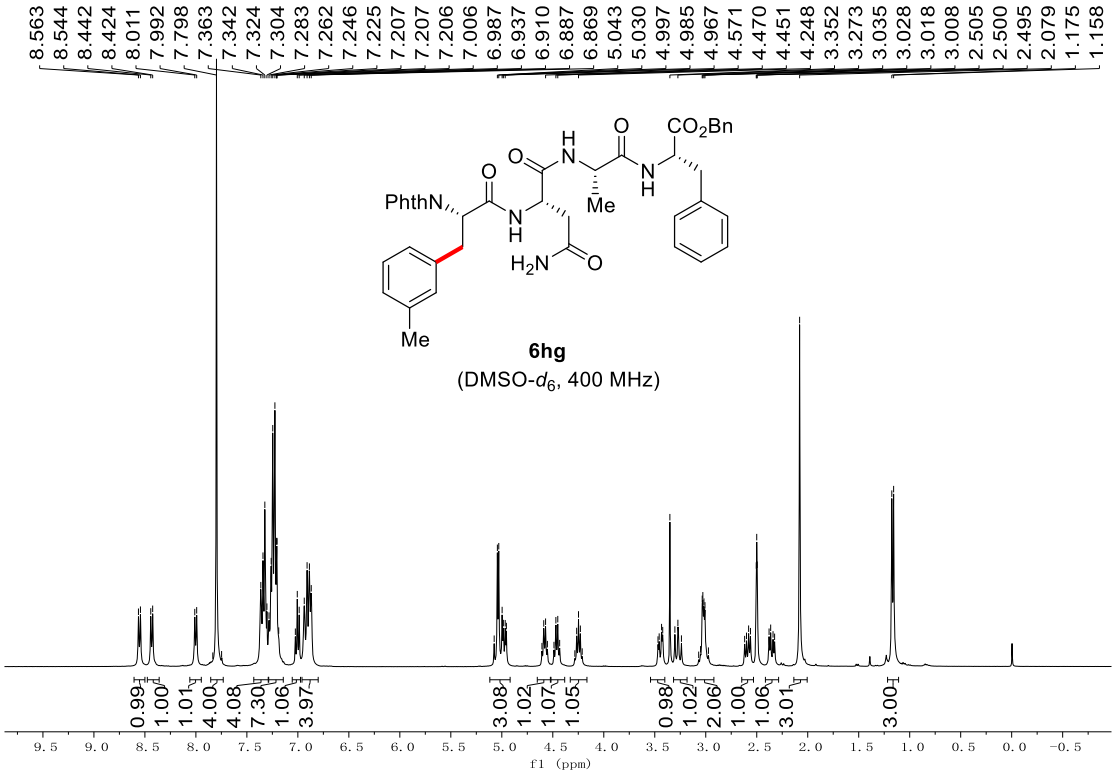
6gh

DMSO-d_6, 400 MHz)



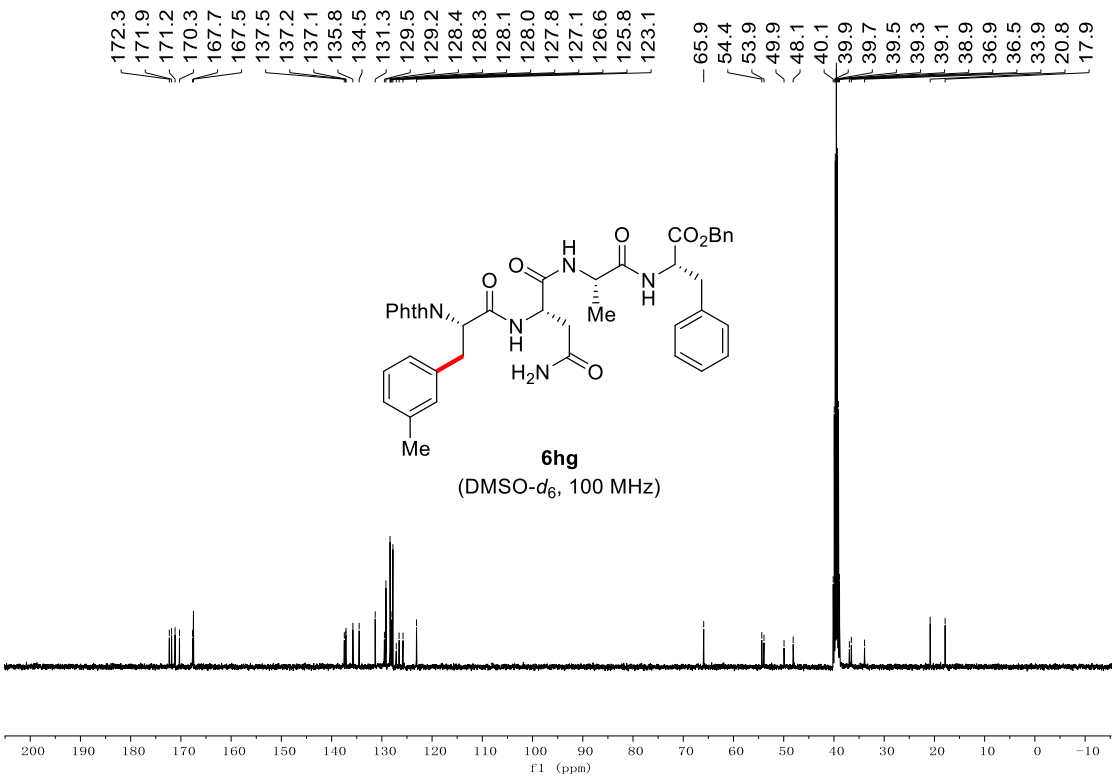
6gh

DMSO-d_6, 100 MHz)



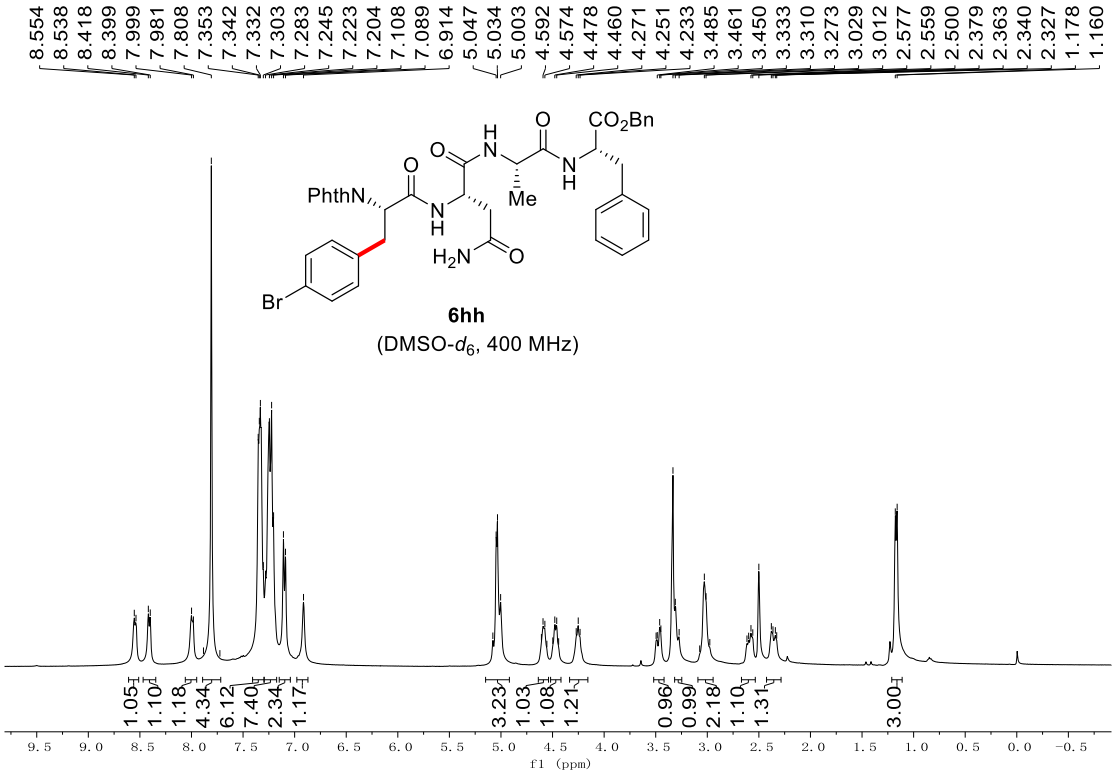
6hg

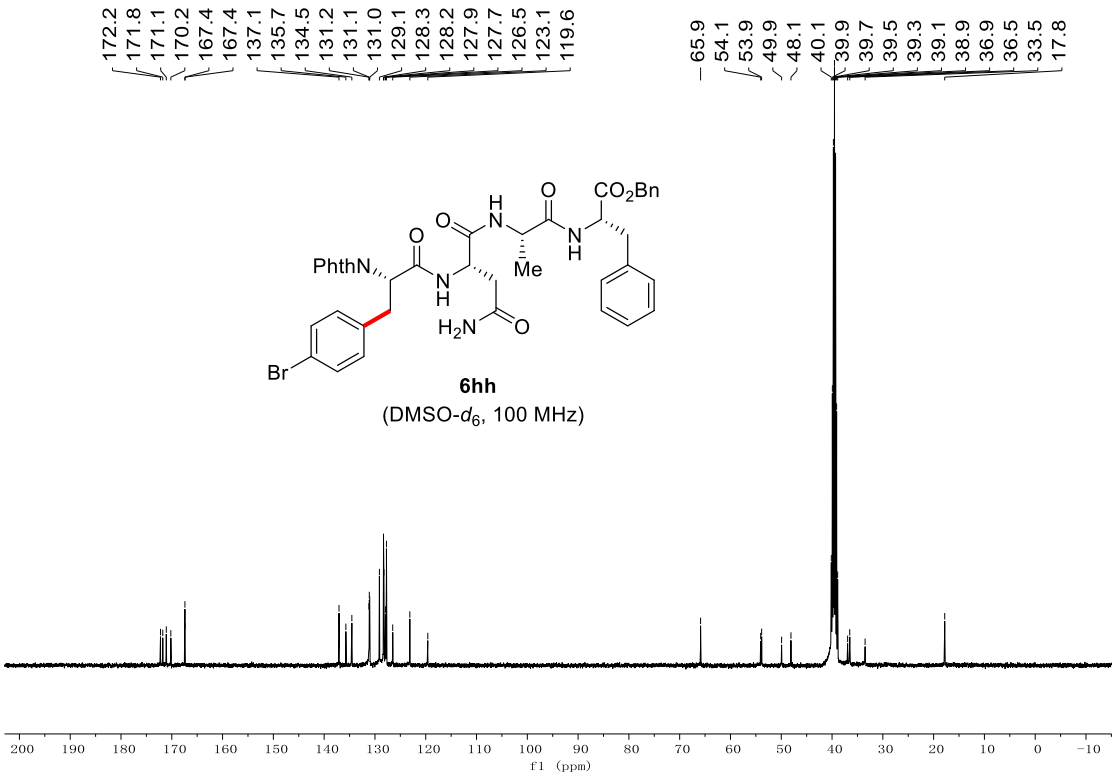
(DMSO-d_6, 400 MHz)

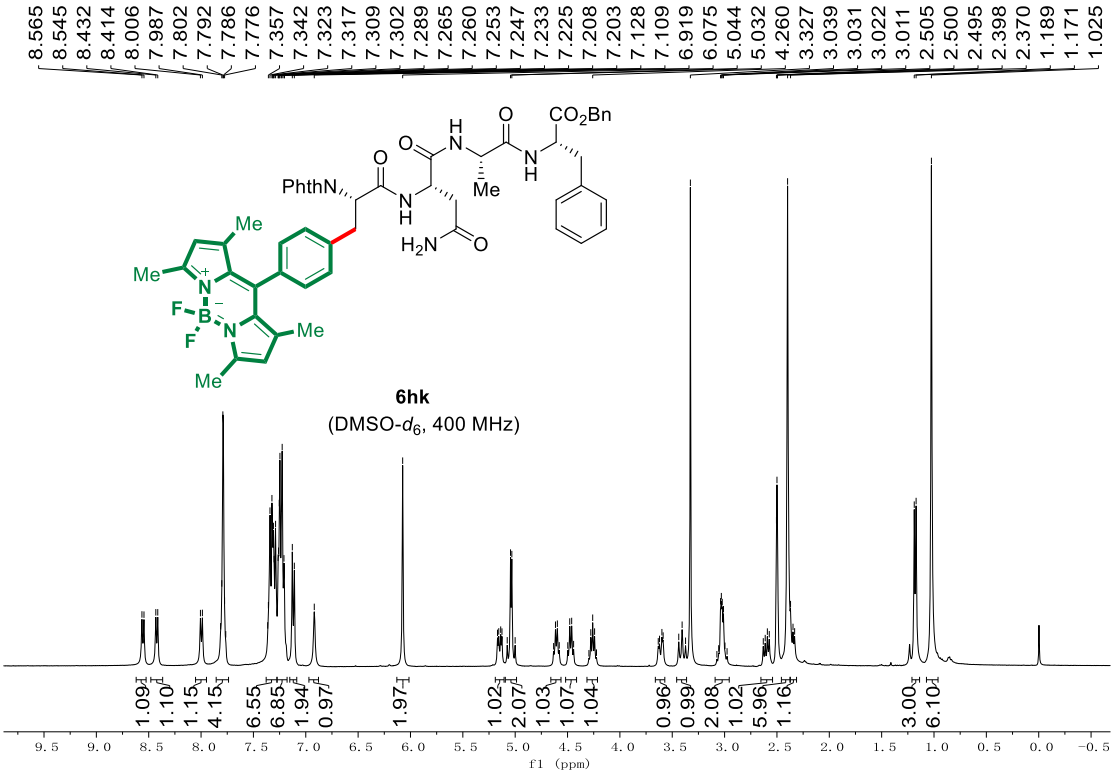


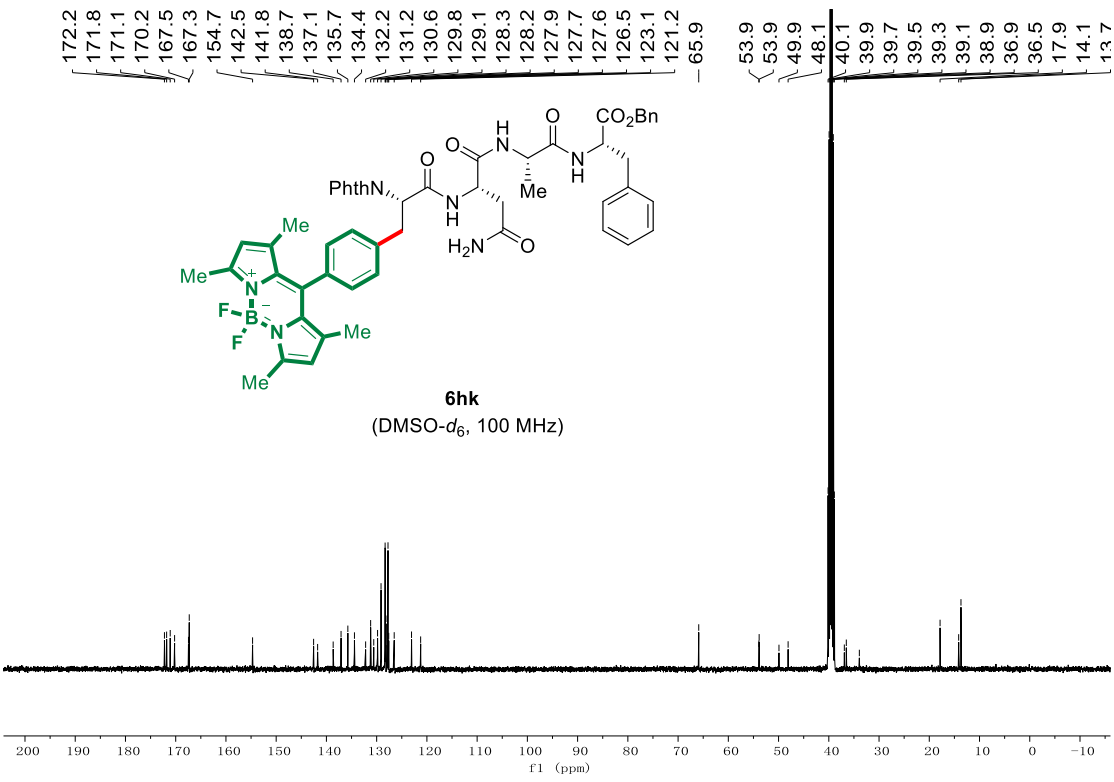
6hg

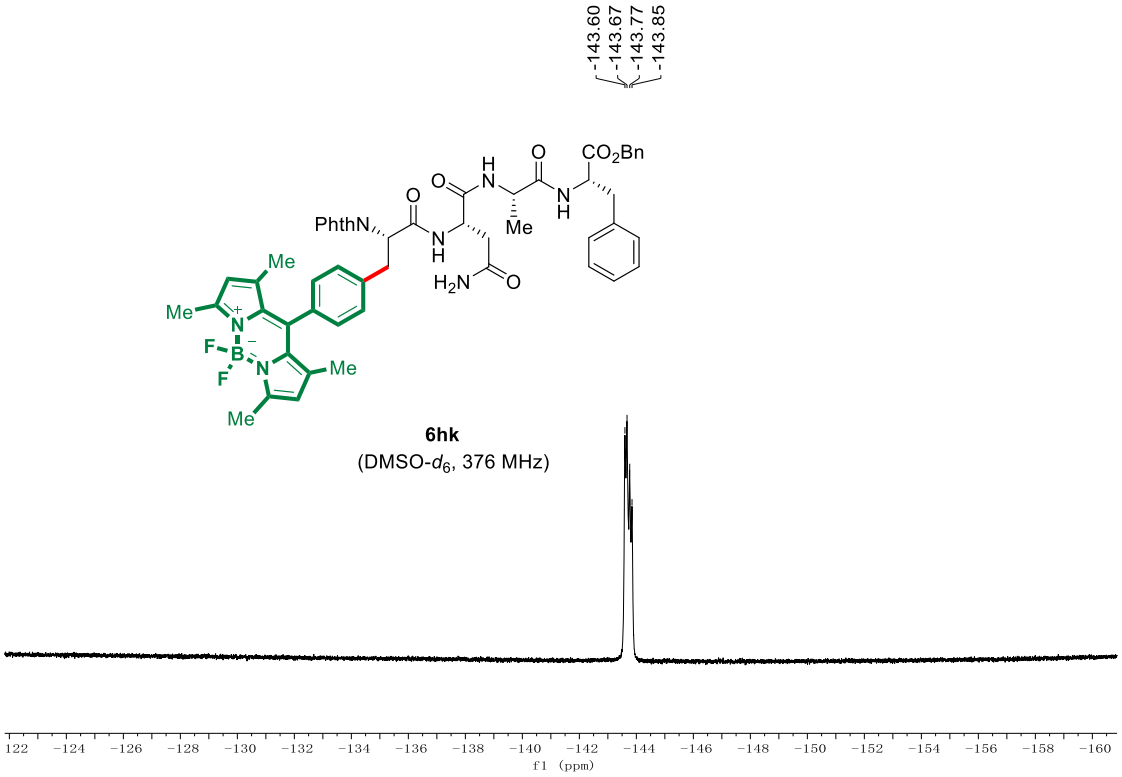
(DMSO-d_6, 100 MHz)

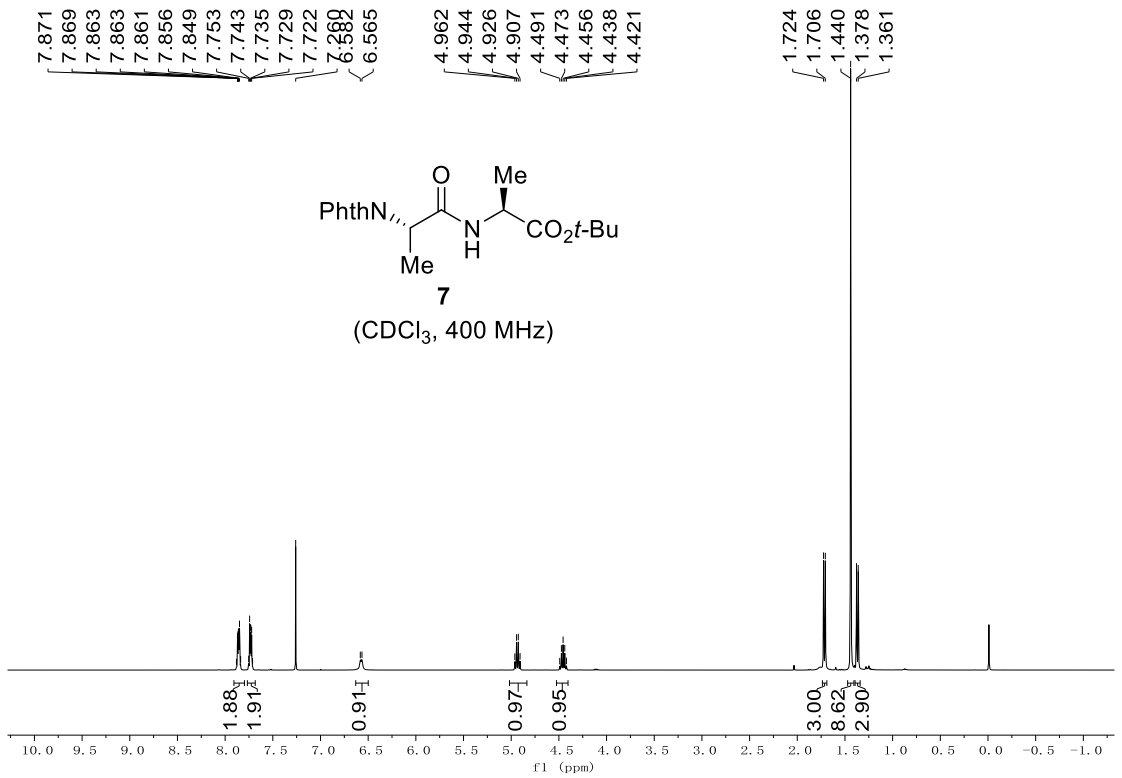

8.554
8.538
8.418
8.399
7.999
7.981
7.808
7.353
7.342
7.332
7.303
7.283
7.245
7.223
7.204
7.108
7.089
6.914
5.047
5.034
5.003
4.592
4.574
4.478
4.460
4.271
4.251
4.233
3.485
3.461
3.450
3.333
3.310
3.273
3.029
3.012
2.577
2.559
2.500
2.379
2.363
2.340
2.327
1.178
1.160
PhthN
Me
Br
6hh
(DMSO-d6, 400 MHz)
1.05
1.10
1.18
4.34
6.12
7.40
2.34
1.17
3.23
1.03
1.08
1.21
0.96
0.99
2.18
1.10
1.31
3.00
f1 (ppm)

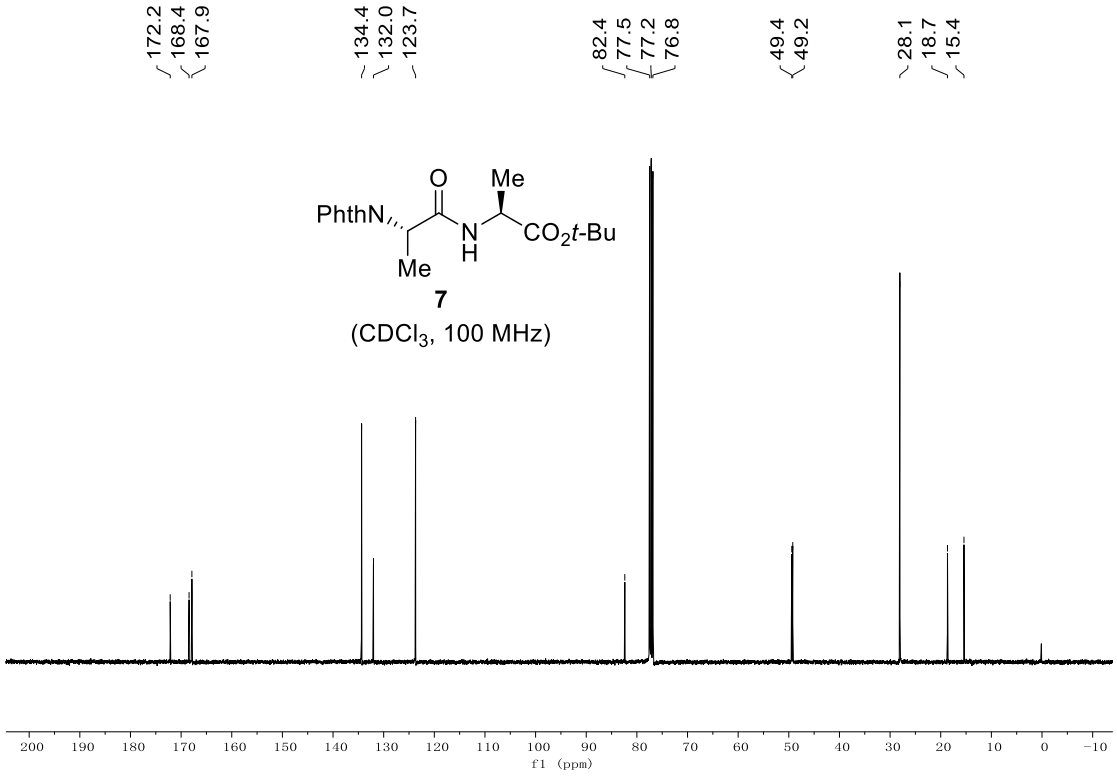

172.2
171.8
171.1
170.2
167.4
167.4
137.1
135.7
134.5
131.2
131.1
131.0
129.1
128.3
128.2
127.9
127.7
126.5
123.1
119.6
65.9
54.1
53.9
49.9
48.1
40.1
39.9
39.7
39.5
39.3
39.1
38.9
36.9
36.5
33.5
17.8
PhthN
Me
Br
6hh
(DMSO-d6, 100 MHz)
f1 (ppm)

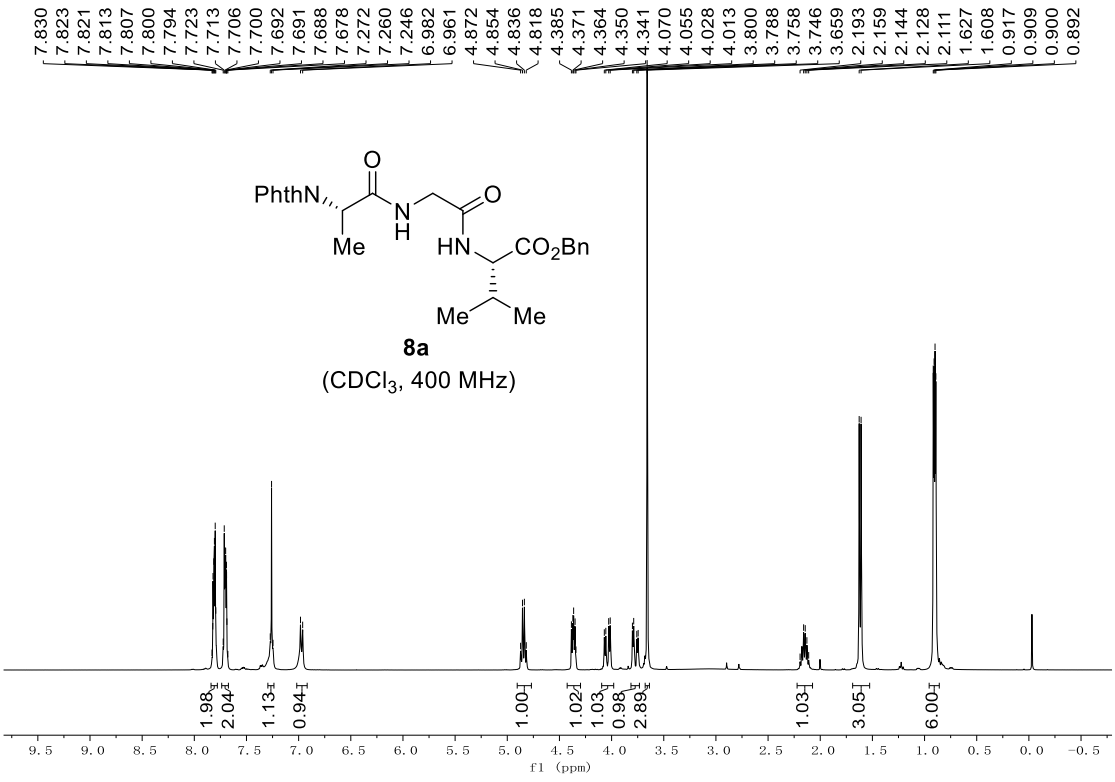

8.565 8.545 8.432 8.414 8.006 7.987 7.802 7.792 7.786 7.776 7.357 7.342 7.323 7.317 7.309 7.302 7.289 7.265 7.260 7.253 7.247 7.233 7.225 7.208 7.203 7.128 7.109 6.919 6.075 5.044 5.032 4.260 3.327 3.039 3.031 3.022 3.011 2.505 2.500 2.495 2.398 2.370 1.189 1.171 1.025
PhthN
Me
CO_2Bn
H_2N
F
B
N
6hk
(DMSO-d_6, 400 MHz)
1.09 1.10 1.15 4.15 6.55 6.85 1.94 0.97 1.97 1.02 2.07 1.03 1.07 1.04 0.96 0.99 2.08 1.02 5.96 1.16 3.00 6.10
f1 (ppm)

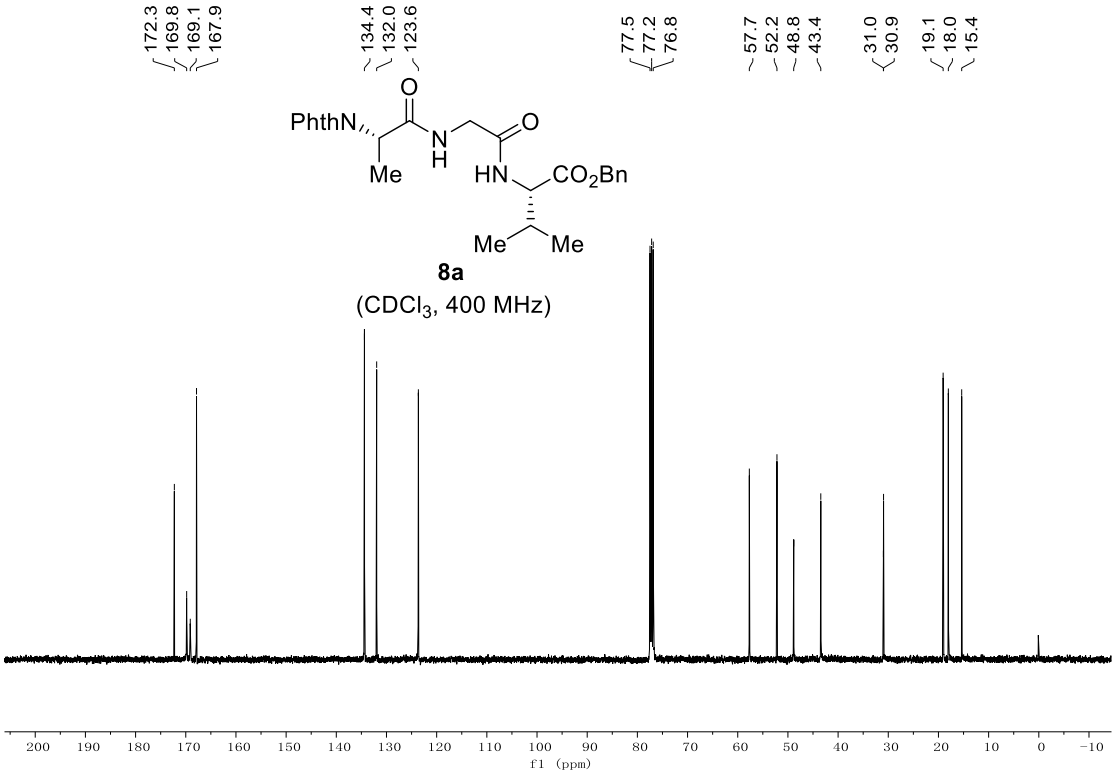

172.2 171.8 171.1 170.2 167.5 167.3 154.7 142.5 141.8 138.7 137.1 135.7 134.4 132.2 131.2 130.6 129.8 129.1 128.3 128.2 127.9 127.7 127.6 126.5 123.1 121.2 65.9 53.9 53.9 49.9 48.1 40.1 39.9 39.7 39.5 39.3 39.1 38.9 36.9 36.5 17.9 14.1 13.7
PhthN
Me
CO_2Bn
H_2N
F
B
N
6hk
(DMSO-d_6, 100 MHz)
f1 (ppm)

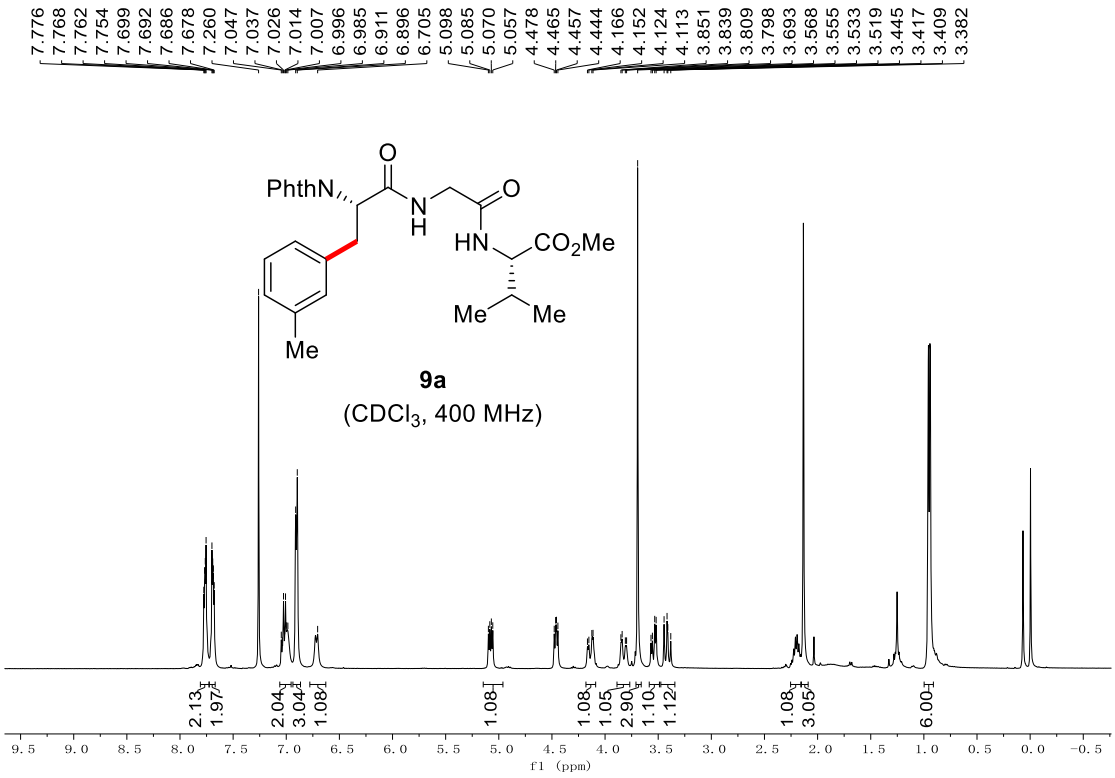

-143.60
-143.67
-143.77
-143.85
PhthN
Me
CO_2Bn
H_2N
Me
Me
Me
Me
F
F
6hk
(DMSO-d_6, 376 MHz)
f1 (ppm)

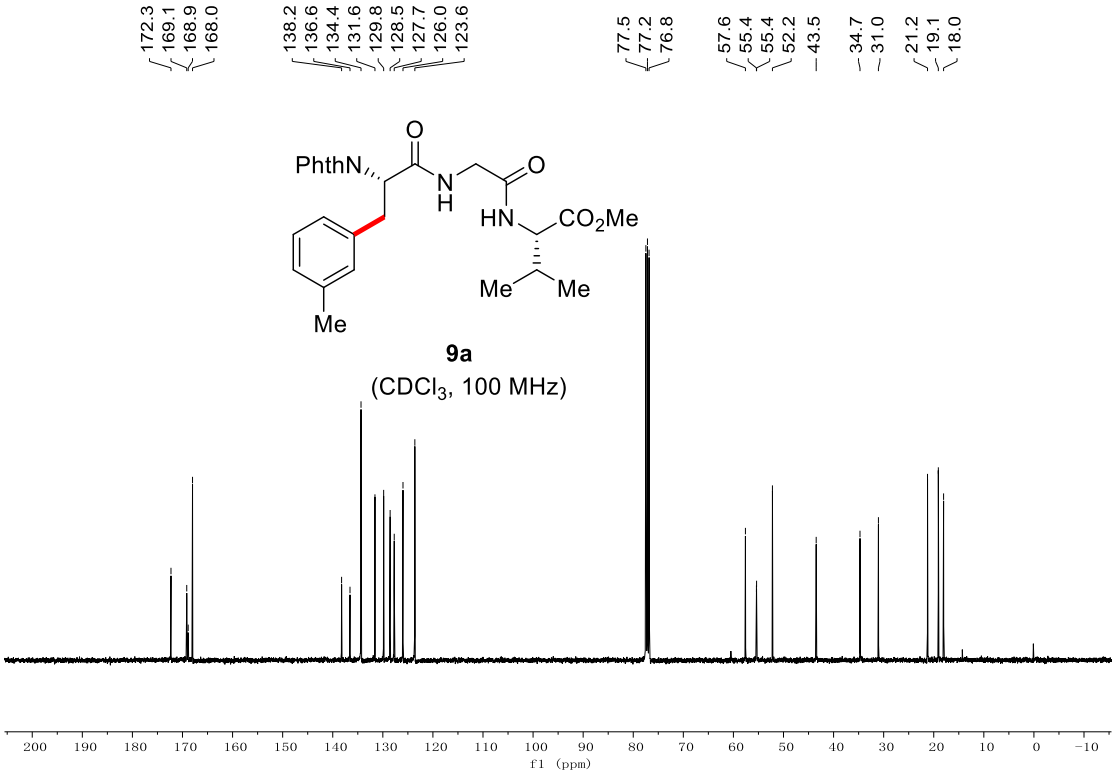

7.871
7.869
7.863
7.863
7.861
7.856
7.849
7.753
7.743
7.735
7.729
7.722
7.260
6.582
6.565
4.962
4.944
4.926
4.907
4.491
4.473
4.456
4.438
4.421
1.724
1.706
1.440
1.378
1.361
PhthN
Me
CO_2t-Bu
Me
7
($CDCl_3$, 400 MHz)
1.88
1.91
0.91
0.97
0.95
3.00
8.62
2.90
f1 (ppm)

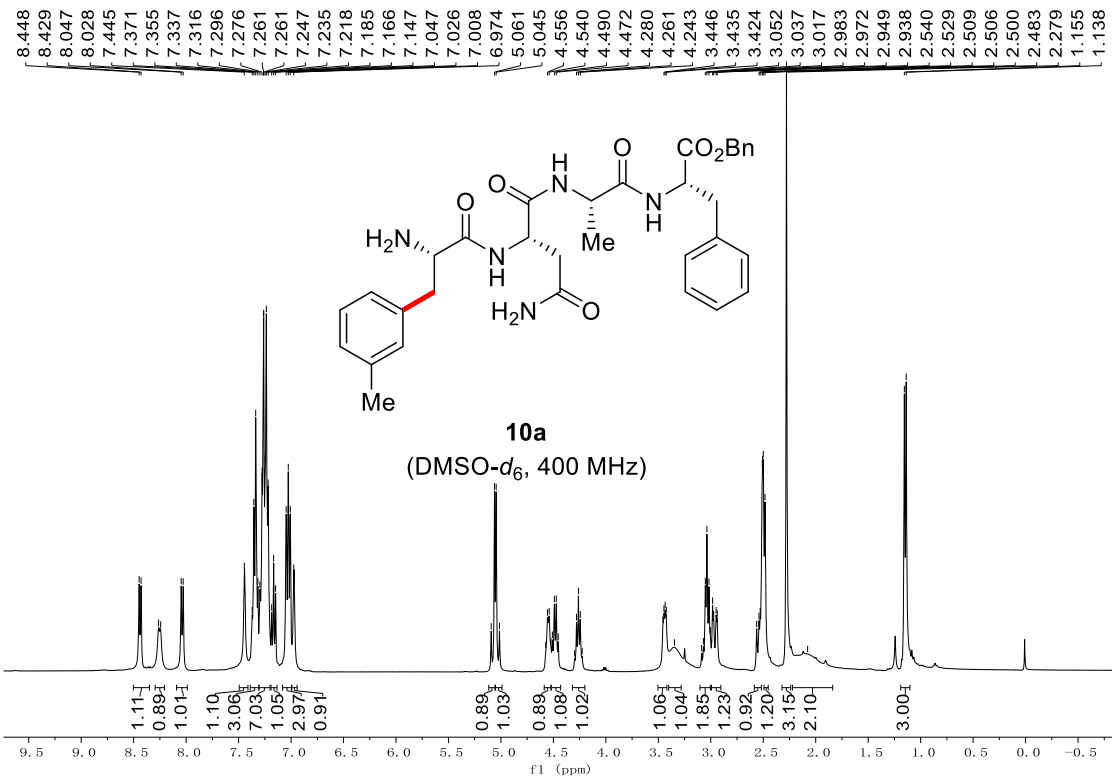

172.2
168.4
167.9
134.4
132.0
123.7
82.4
77.5
77.2
76.8
49.4
49.2
28.1
18.7
15.4
PhthN
O
Me
N
H
CO2t-Bu
Me
7
(CDCl3, 100 MHz)
f1 (ppm)

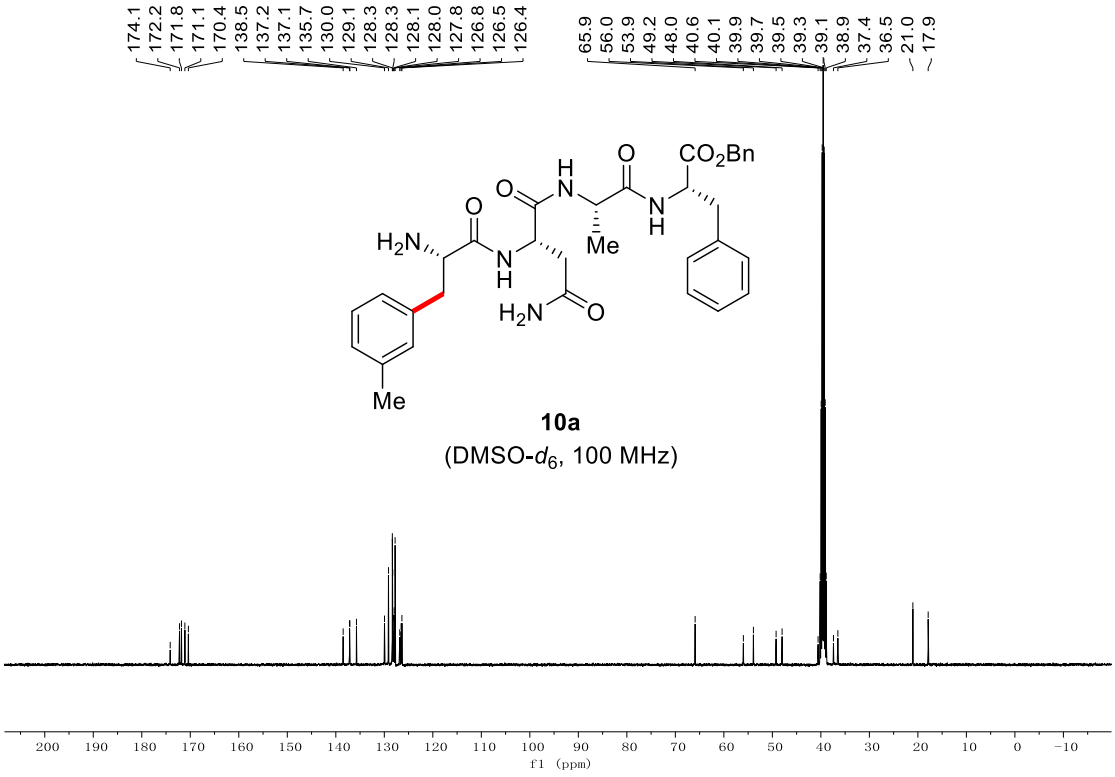

7.830
7.823
7.821
7.813
7.807
7.800
7.794
7.723
7.713
7.706
7.700
7.692
7.691
7.688
7.678
7.272
7.260
7.246
6.982
6.961
4.872
4.854
4.836
4.818
4.385
4.371
4.364
4.350
4.341
4.070
4.055
4.028
4.013
3.800
3.788
3.758
3.746
3.659
2.193
2.159
2.144
2.128
2.111
1.627
1.608
0.917
0.909
0.900
0.892
PhthN
O
N
H
O
Me
HN
CO2Bn
Me
Me
8a
(CDCl3, 400 MHz)
1.98
2.04
1.13
0.94
1.00
1.02
1.03
0.98
2.89
1.03
3.05
6.00
f1 (ppm)

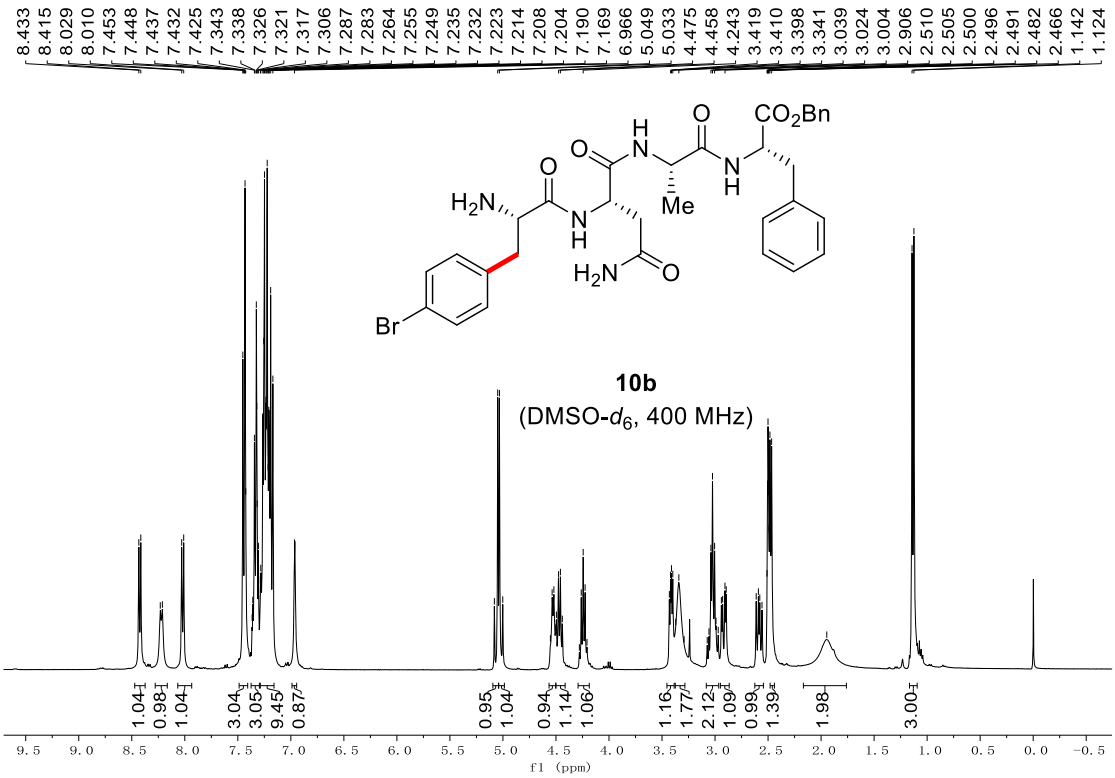

172.3
169.8
169.1
167.9
134.4
132.0
123.6
77.5
77.2
76.8
57.7
52.2
48.8
43.4
31.0
30.9
19.1
18.0
15.4
PhthN
Me
N
H
O
O
HN
CO2Bn
Me
Me
8a
(CDCl3, 400 MHz)
f1 (ppm)

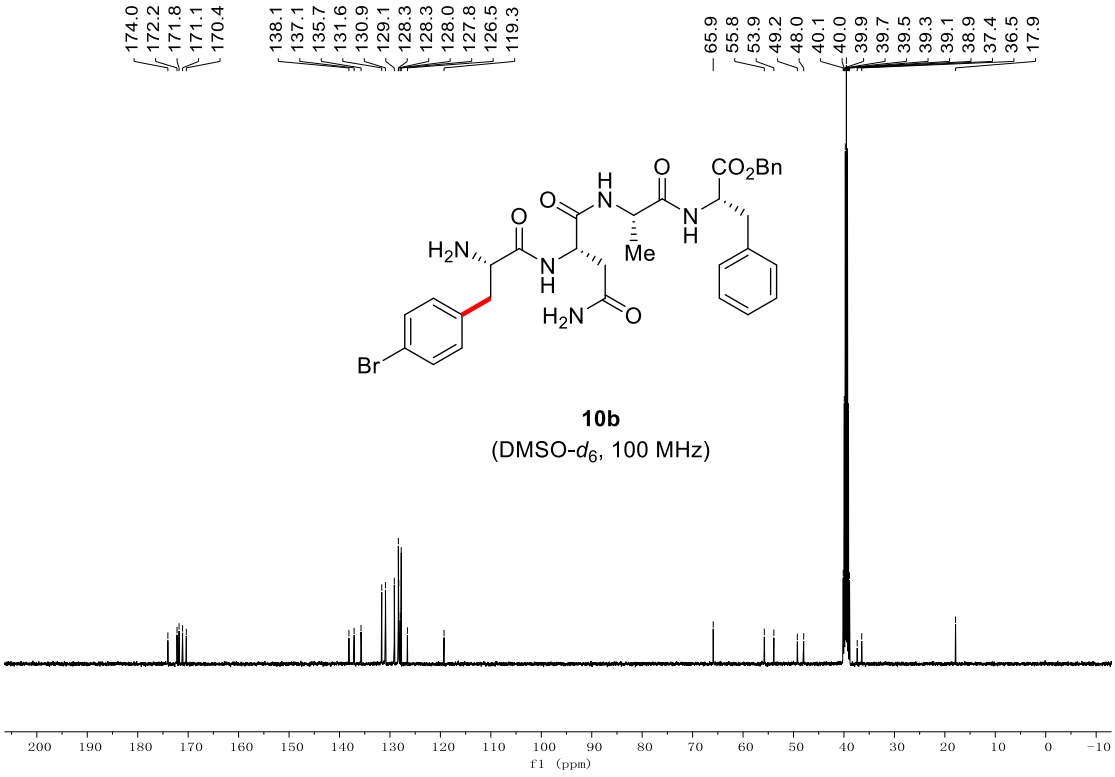

7.776
7.768
7.762
7.754
7.699
7.692
7.686
7.678
7.260
7.047
7.037
7.026
7.014
7.007
6.996
6.985
6.911
6.896
6.705
5.098
5.085
5.070
5.057
4.478
4.465
4.457
4.444
4.166
4.152
4.124
4.113
3.851
3.839
3.809
3.798
3.693
3.568
3.555
3.533
3.519
3.445
3.417
3.409
3.382
PhthN
Me
N
H
O
O
HN
CO2Me
Me
Me
9a
(CDCl3, 400 MHz)
2.13
1.97
2.04
3.04
1.08
1.08
1.08
1.05
2.90
1.10
1.12
1.08
3.05
6.00
f1 (ppm)


172.3
169.1
168.9
168.0
138.2
136.6
134.4
131.6
129.8
128.5
127.7
126.0
123.6
77.5
77.2
76.8
57.6
55.4
55.4
52.2
43.5
34.7
31.0
21.2
19.1
18.0
PhthN
O
N
H
O
HN
CO2Me
Me
Me
Me
9a
(CDCl3, 100 MHz)
200 190 180 170 160 150 140 130 120 110 100 90 80 70 60 50 40 30 20 10 0 −10
f1 (ppm)


8.448
8.429
8.047
8.028
7.445
7.371
7.355
7.337
7.316
7.296
7.276
7.261
7.261
7.247
7.235
7.218
7.185
7.166
7.147
7.047
7.026
7.008
6.974
5.061
5.045
4.556
4.540
4.490
4.472
4.280
4.261
4.243
3.446
3.435
3.424
3.052
3.037
3.017
2.983
2.972
2.949
2.938
2.540
2.529
2.509
2.506
2.500
2.483
2.279
1.155
1.138
H2N
O
N
H
O
H
N
O
CO2Bn
N
H
Me
H2N
O
Me
10a
(DMSO-d6, 400 MHz)
1.11
0.89
1.01
1.10
3.06
7.03
1.05
2.97
0.91
0.89
1.03
0.89
1.08
1.02
1.06
1.04
1.85
1.23
0.92
1.20
3.15
2.10
3.00
9.5 9.0 8.5 8.0 7.5 7.0 6.5 6.0 5.5 5.0 4.5 4.0 3.5 3.0 2.5 2.0 1.5 1.0 0.5 0.0 −0.5
f1 (ppm)

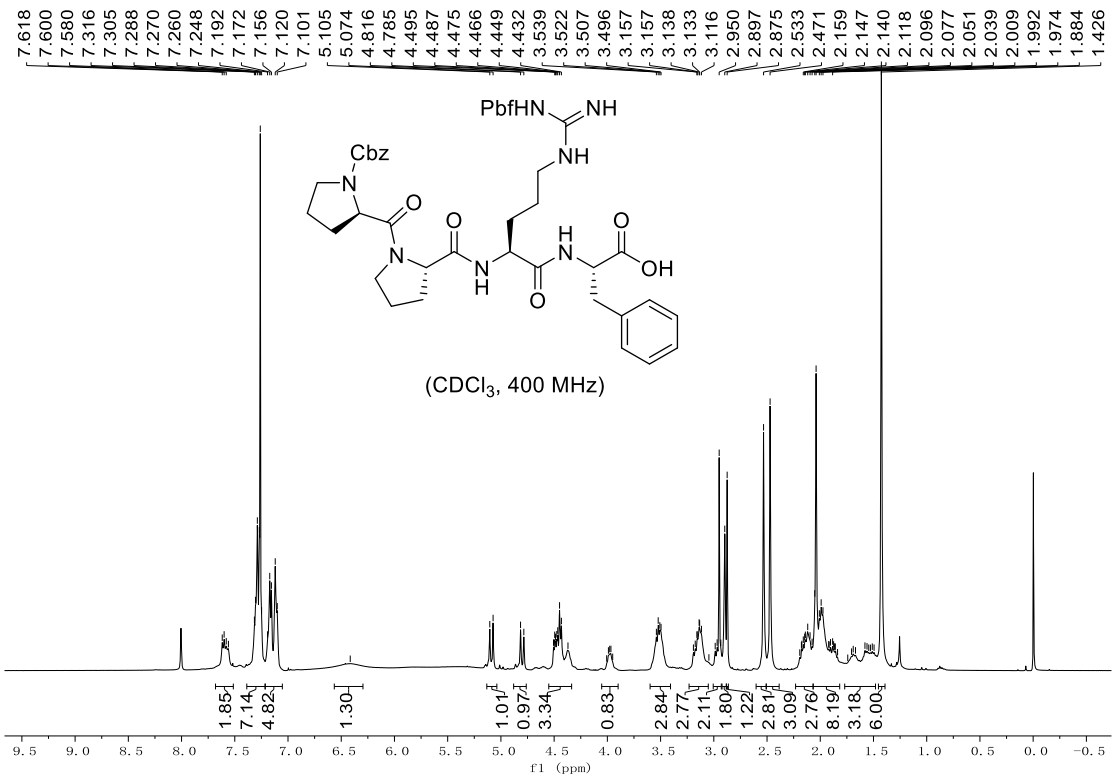

174.1
172.2
171.8
171.1
170.4
138.5
137.2
137.1
135.7
130.0
129.1
128.3
128.3
128.1
128.0
127.8
126.8
126.5
126.4
65.9
56.0
53.9
49.2
48.0
40.6
40.1
39.9
39.7
39.5
39.3
39.1
38.9
37.4
36.5
21.0
17.9
CO2Bn
H2N
Me
Me
10a
(DMSO-d6, 100 MHz)
f1 (ppm)


8.433
8.415
8.029
8.010
7.453
7.448
7.437
7.432
7.425
7.343
7.338
7.326
7.321
7.317
7.306
7.287
7.283
7.264
7.255
7.249
7.235
7.232
7.223
7.214
7.208
7.204
7.190
7.169
6.966
5.049
5.033
4.475
4.458
4.243
3.419
3.410
3.398
3.341
3.039
3.024
3.004
2.906
2.510
2.505
2.500
2.496
2.491
2.482
2.466
1.142
1.124
CO2Bn
H2N
Me
Br
10b
(DMSO-d6, 400 MHz)
1.04
0.98
1.04
3.04
3.05
9.45
0.87
0.95
1.04
0.94
1.14
1.06
1.16
1.77
2.12
1.09
0.99
1.39
1.98
3.00
f1 (ppm)

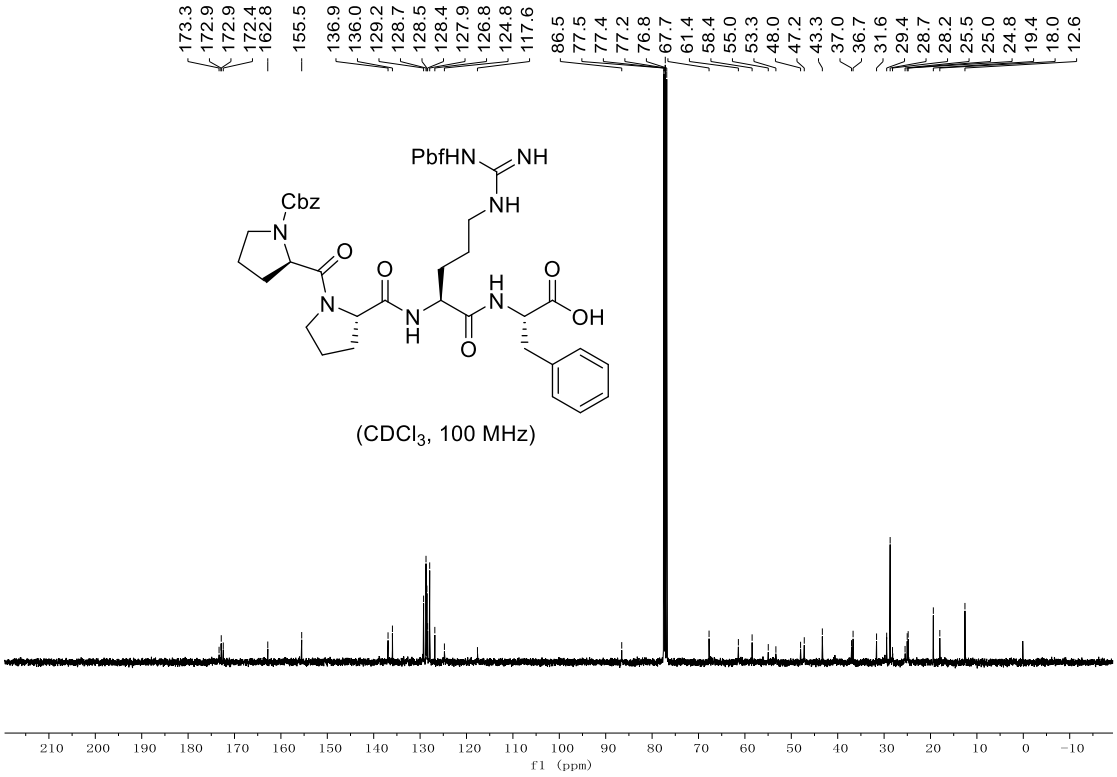


10b

(DMSO-d_6, 100 MHz)



(CDCl$_3$, 400 MHz)


173.3
172.9
172.9
172.4
162.8
155.5
136.9
136.0
129.2
128.7
128.5
128.4
127.9
126.8
124.8
117.6
86.5
77.5
77.4
77.2
76.8
67.7
61.4
58.4
55.0
53.3
48.0
47.2
43.3
37.0
36.7
31.6
29.4
28.7
28.2
25.5
25.0
24.8
19.4
18.0
12.6
PbfHN
NH
NH
Cbz
N
O
O
N
N
H
H
N
O
O
OH
O
(CDCl3, 100 MHz)
210 200 190 180 170 160 150 140 130 120 110 100 90 80 70 60 50 40 30 20 10 0 −10
f1 (ppm)