Electronic Supporting Information

3-Aminothiophenecarboxylic acid (3-Atc)-induced folding in peptides

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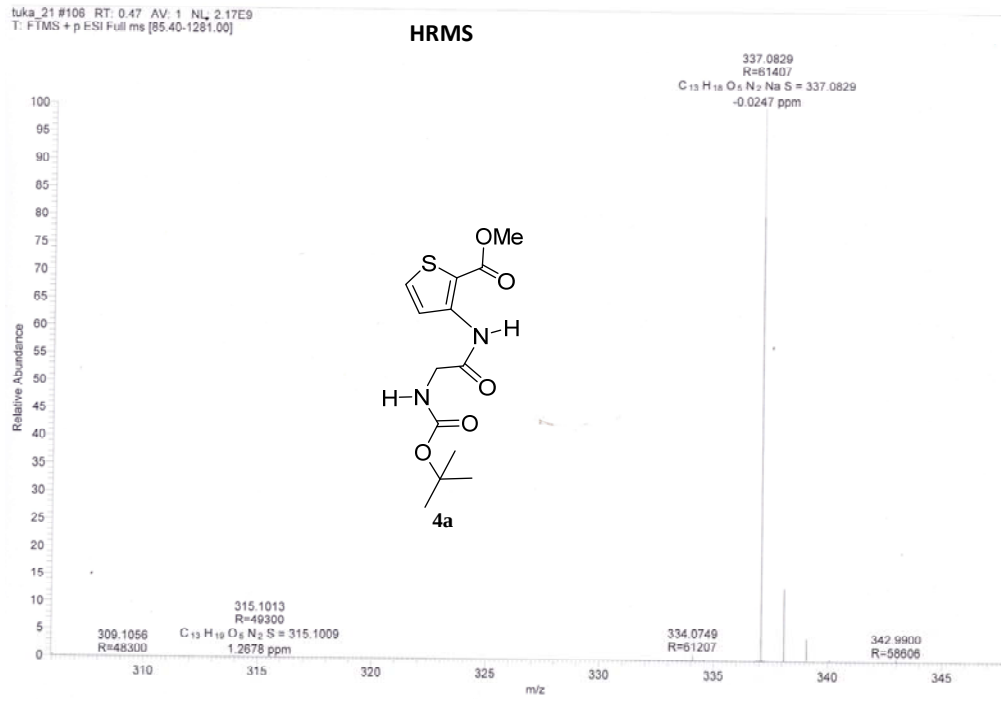
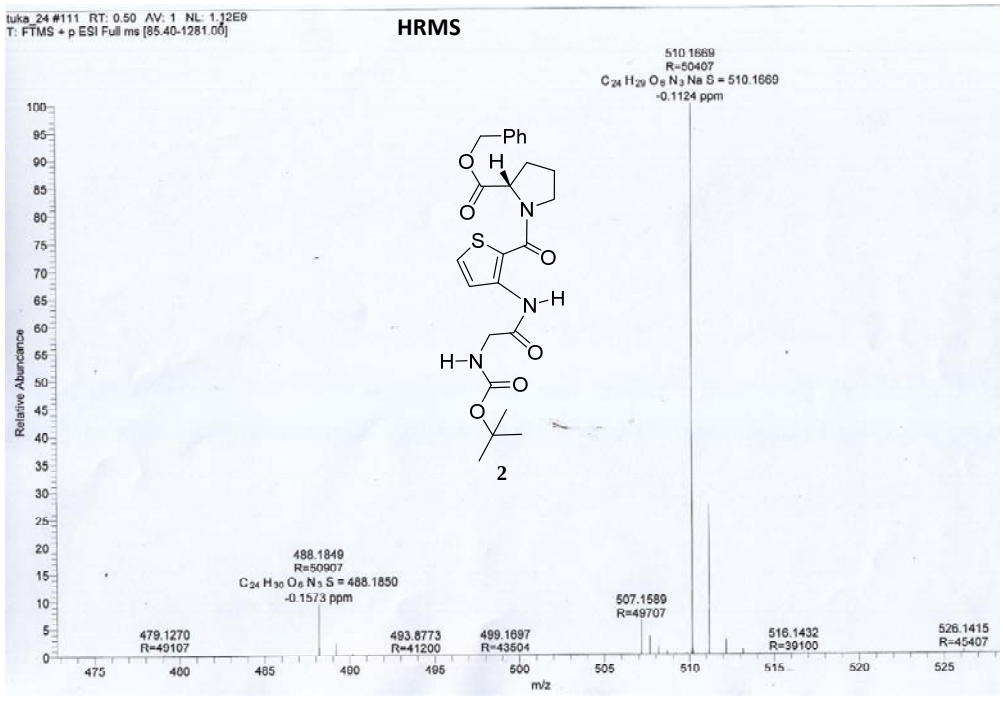

tuka_21 #106 RT: 0.47 AV: 1 NL: 2.17E9
T: FTMS + p ESI Full ms [85.40-1281.00]
HRMS
337.0829
R=61407
C13 H18 O5 N2 Na S = 337.0829
-0.0247 ppm
OMe
S
O
N-H
O
H-N
O
O
315.1013
R=49300
C13 H19 O5 N2 S = 315.1009
1.2678 ppm
309.1056
R=48300
334.0749
R=61207
342.9900
R=58606
Relative Abundance
m/z

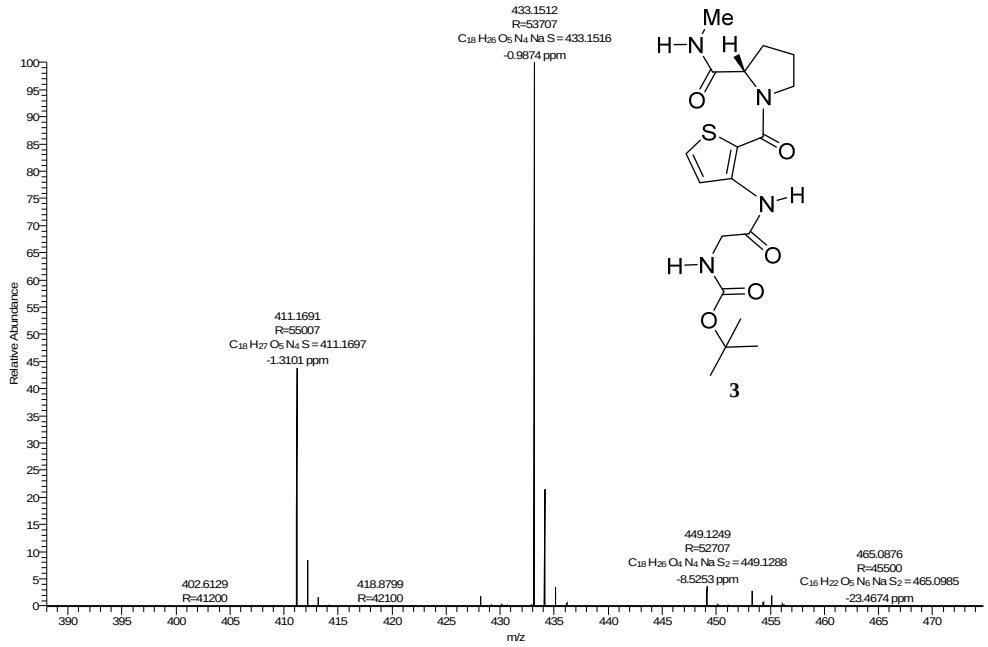
4a


tuka_24 #111 RT: 0.50 AV: 1 NL: 1.12E9
T: FTMS + p ESI Full ms [85.40-1281.00]
HRMS
510.1669
R=50407
C24 H29 O6 N3 Na S = 510.1669
-0.1124 ppm
Ph
O
H
O
N
S
O
N-H
O
H-N
O
O
488.1849
R=50907
C24 H30 O6 N3 S = 488.1850
-0.1573 ppm
507.1589
R=49707
479.1270
R=49107
493.8773
R=41200
499.1697
R=43504
516.1432
R=39100
526.1415
R=45407
Relative Abundance
m/z

2

TUKA-4-TRINHME #884 RT: 3.94 AV: 1 NL: 1.14E9
T: FTMS + p ESI Full ms [150.00-2250.00]

HRMS



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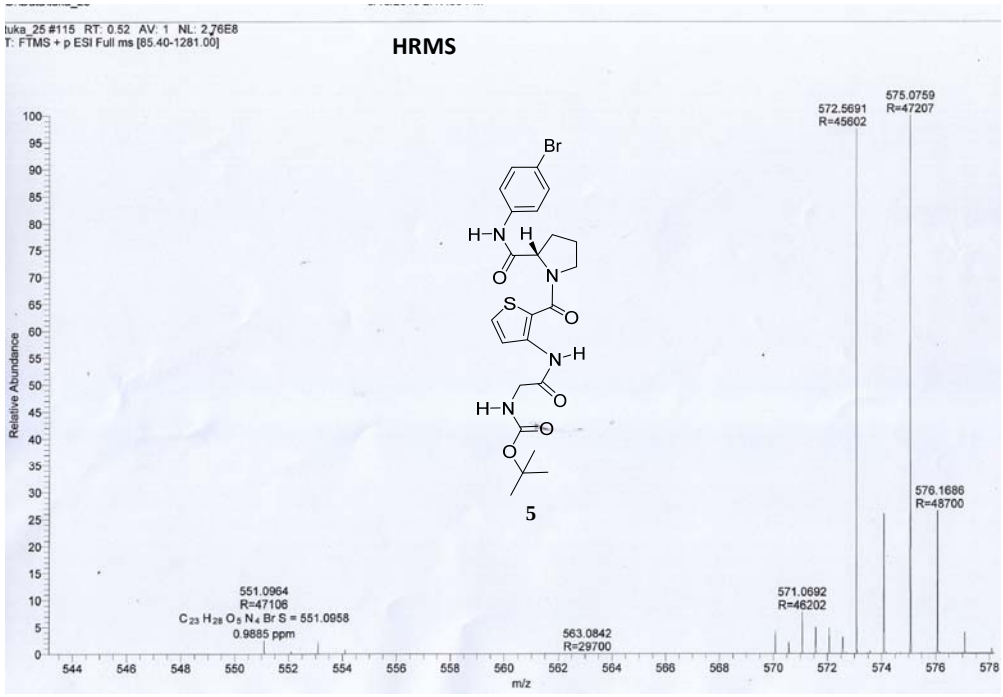

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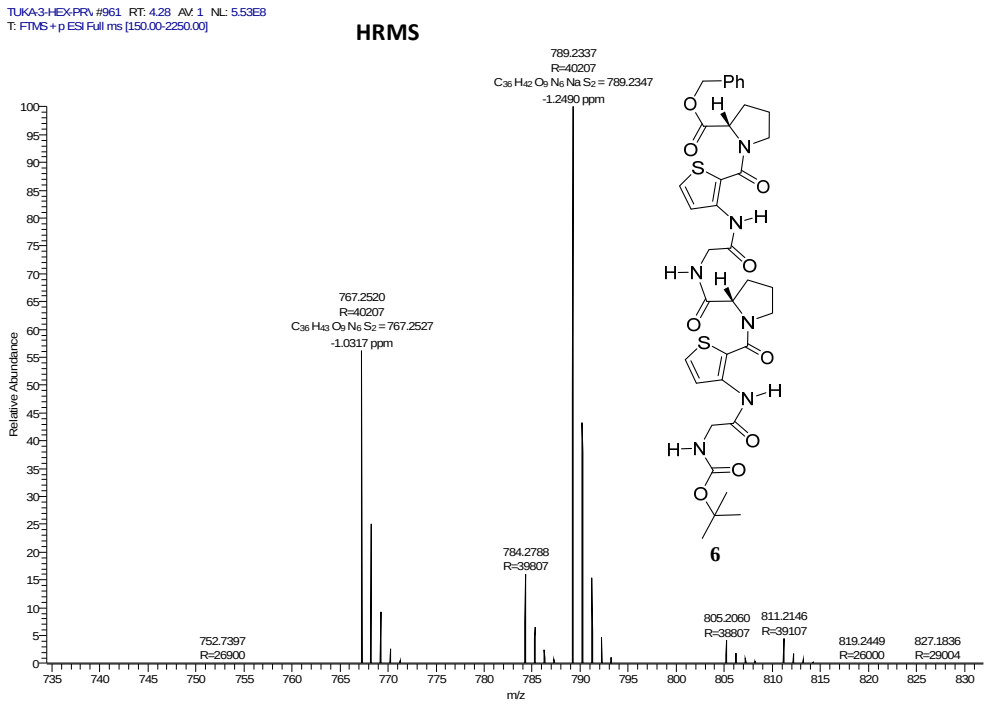
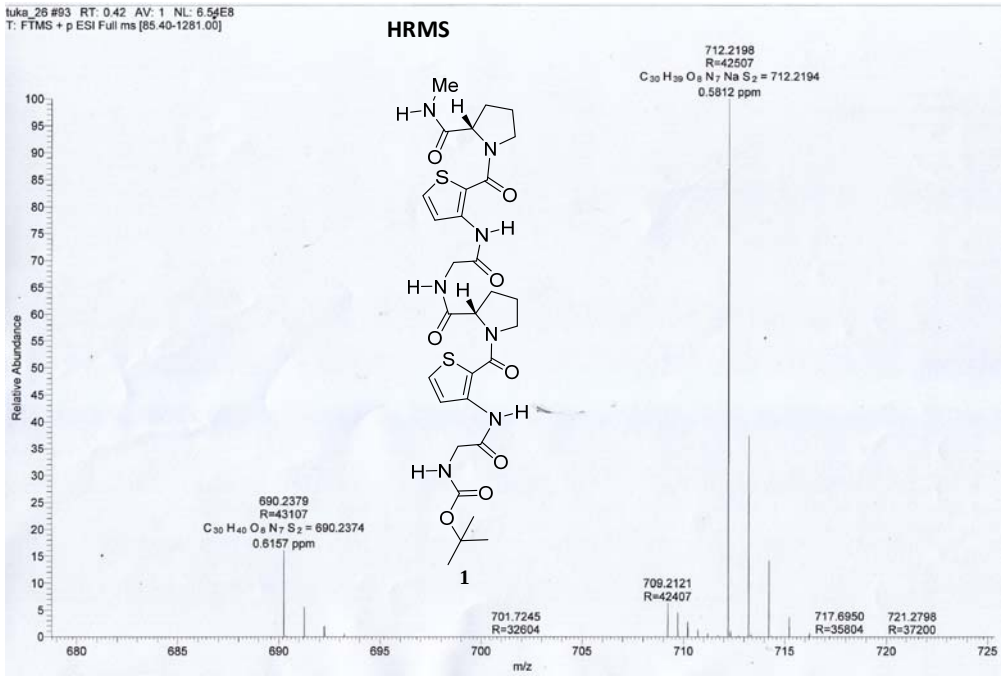
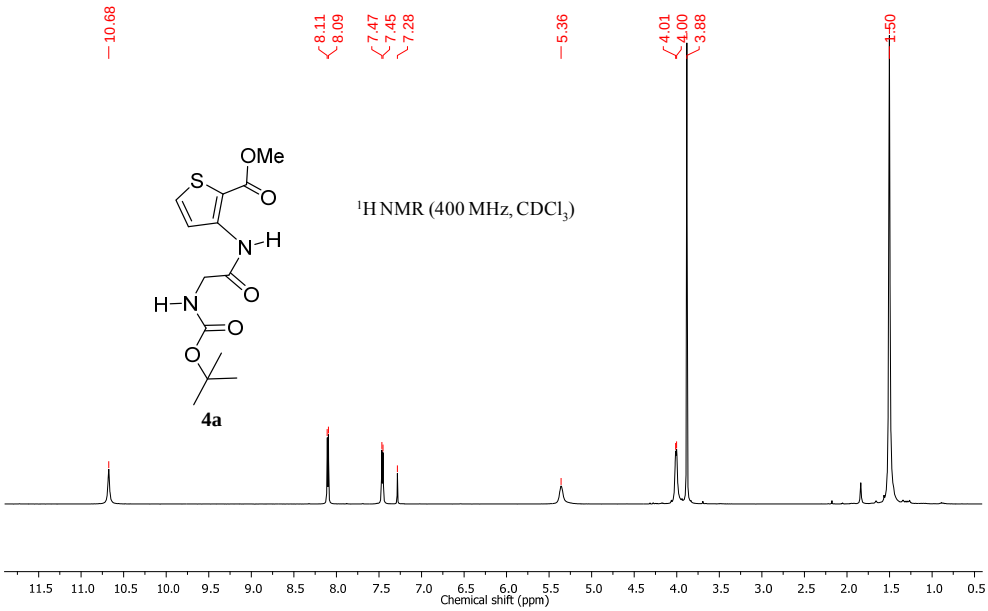
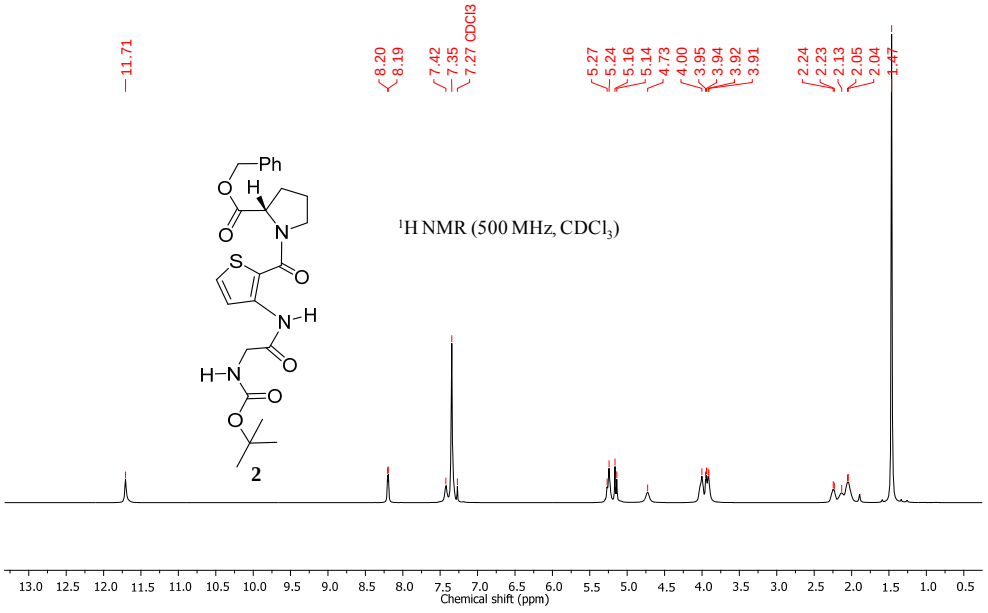
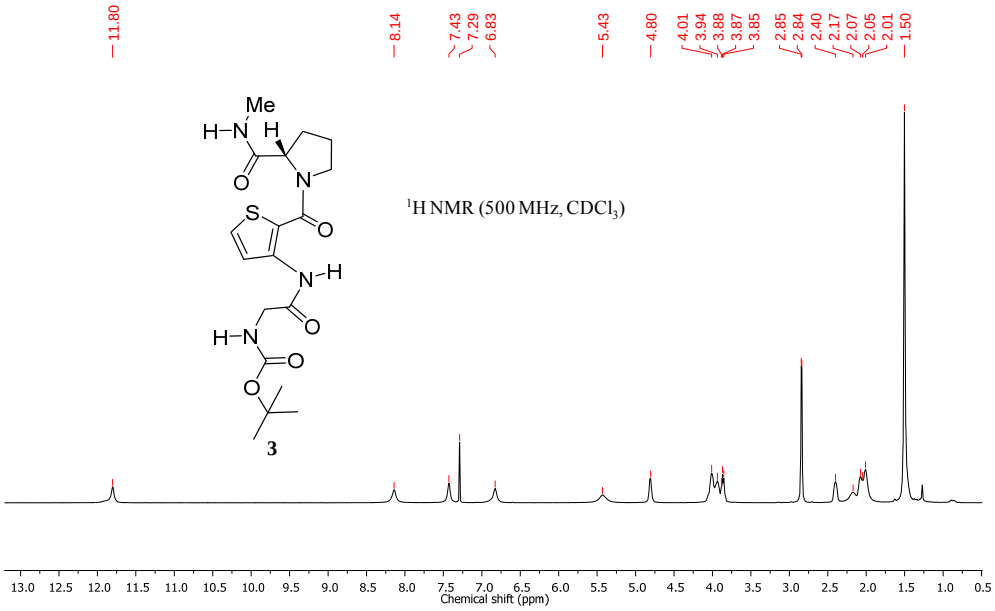
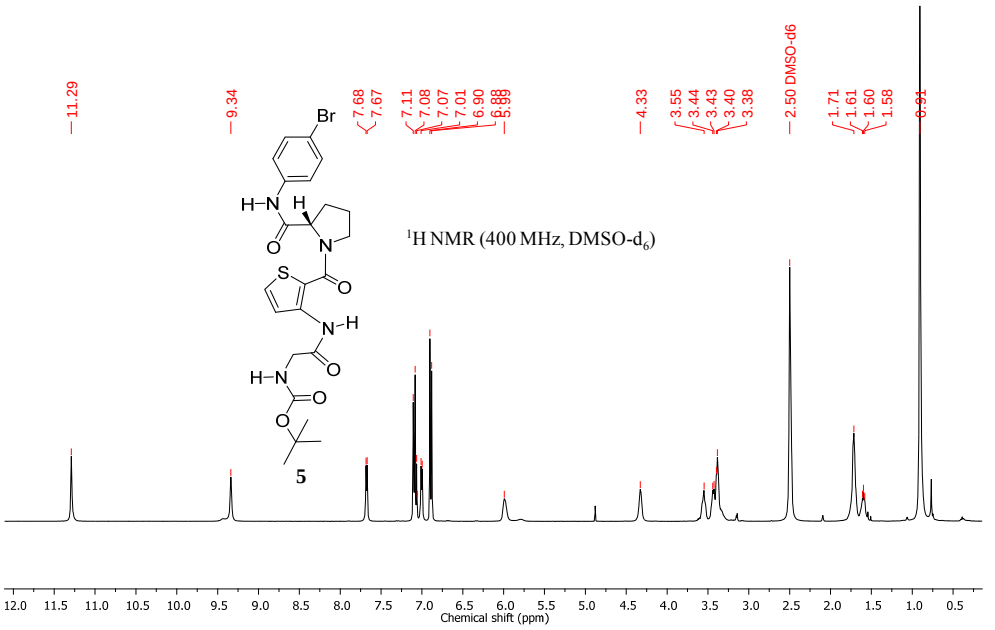

TUKA-3-HEX-PRV #961 RT: 4.28 AV: 1 NL: 5.53E8
T: FTMS + p ESI Full ms [150.00-2250.00]
HRMS
789.2337
R=40207
C36 H42 O9 N6 Na S2 = 789.2347
-1.2490 ppm
767.2520
R=40207
C36 H43 O9 N6 S2 = 767.2527
-1.0317 ppm
784.2788
R=39807
752.7397
R=26900
805.2060
R=38807
811.2146
R=39107
819.2449
R=26000
827.1836
R=29004
Relative Abundance
m/z
6

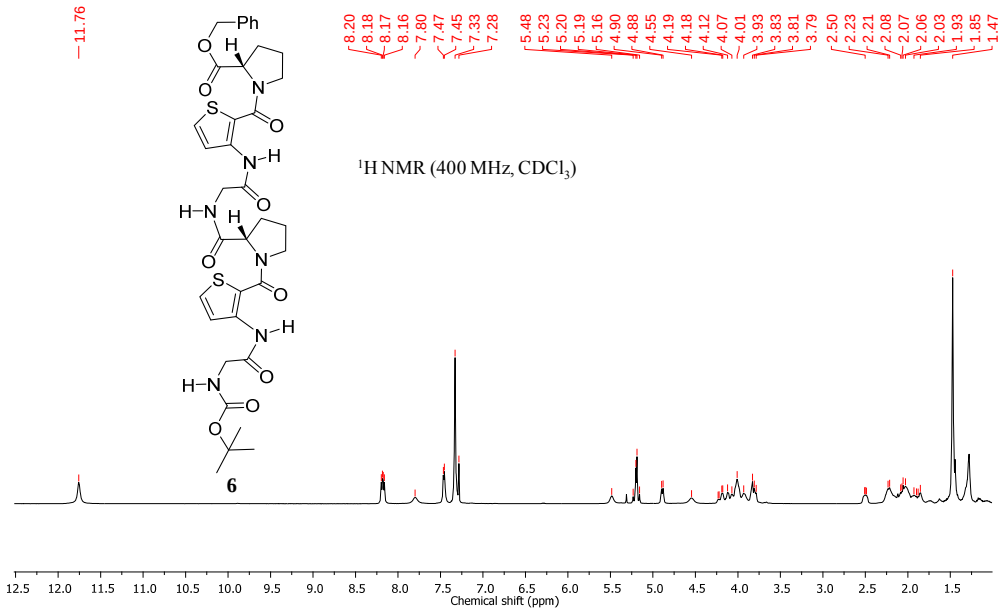

tuka_26 #93 RT: 0.42 AV: 1 NL: 6.54E8
T: FTMS + p ESI Full ms [85.40-1281.00]
HRMS
712.2198
R=42507
C30 H39 O8 N7 Na S2 = 712.2194
0.5812 ppm
690.2379
R=43107
C30 H40 O8 N7 S2 = 690.2374
0.6157 ppm
709.2121
R=42407
701.7245
R=32604
717.6950
R=35804
721.2798
R=37200
Relative Abundance
m/z
1

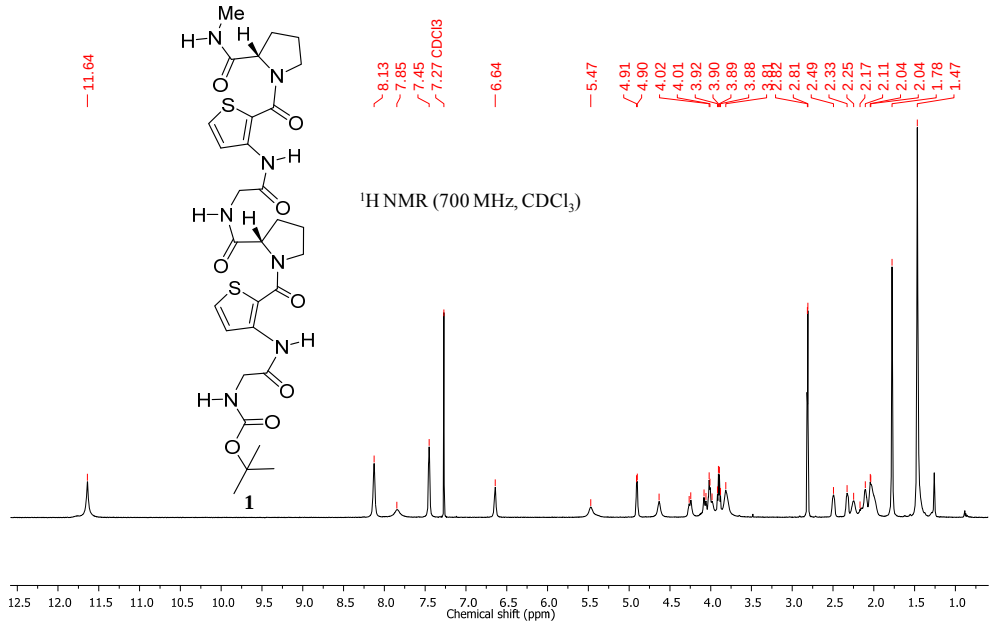

10.68
8.11
8.09
7.47
7.45
7.28
5.36
4.01
4.00
3.88
1.50
OMe
S
O
N–H
O
H–N
O
O
4a
^{1}H NMR (400 MHz, $CDCl_3$)
11.5 11.0 10.5 10.0 9.5 9.0 8.5 8.0 7.5 7.0 6.5 6.0 5.5 5.0 4.5 4.0 3.5 3.0 2.5 2.0 1.5 1.0 0.5
Chemical shift (ppm)

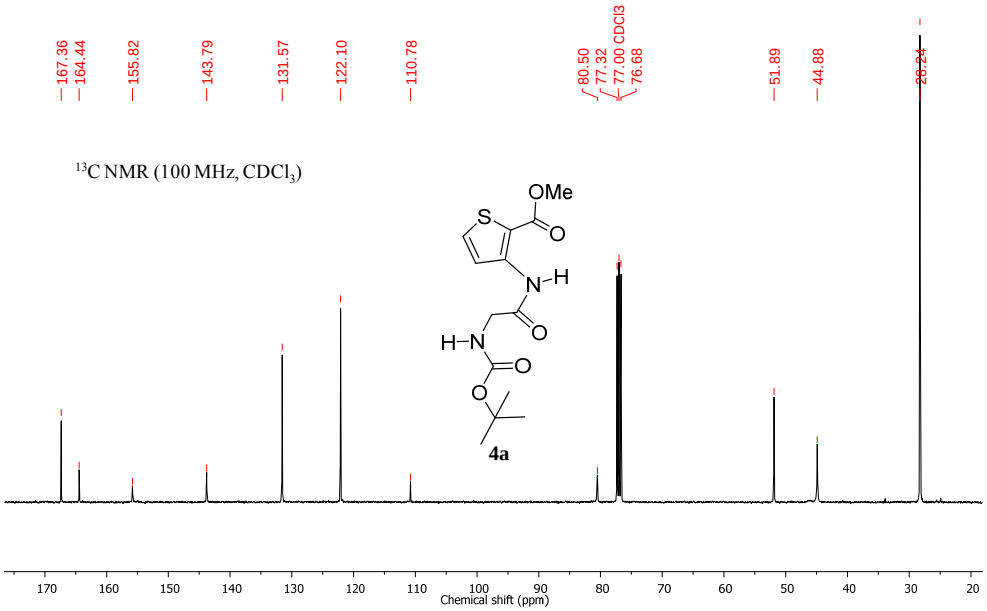

11.71
8.20
8.19
7.42
7.35
7.27 CDCl3
5.27
5.24
5.16
5.14
4.73
4.00
3.95
3.94
3.92
3.91
2.24
2.23
2.13
2.05
2.04
1.47
Ph
O
H
O
N
S
O
N–H
O
H–N
O
O
2
^{1}H NMR (500 MHz, $CDCl_3$)
13.0 12.5 12.0 11.5 11.0 10.5 10.0 9.5 9.0 8.5 8.0 7.5 7.0 6.5 6.0 5.5 5.0 4.5 4.0 3.5 3.0 2.5 2.0 1.5 1.0 0.5
Chemical shift (ppm)

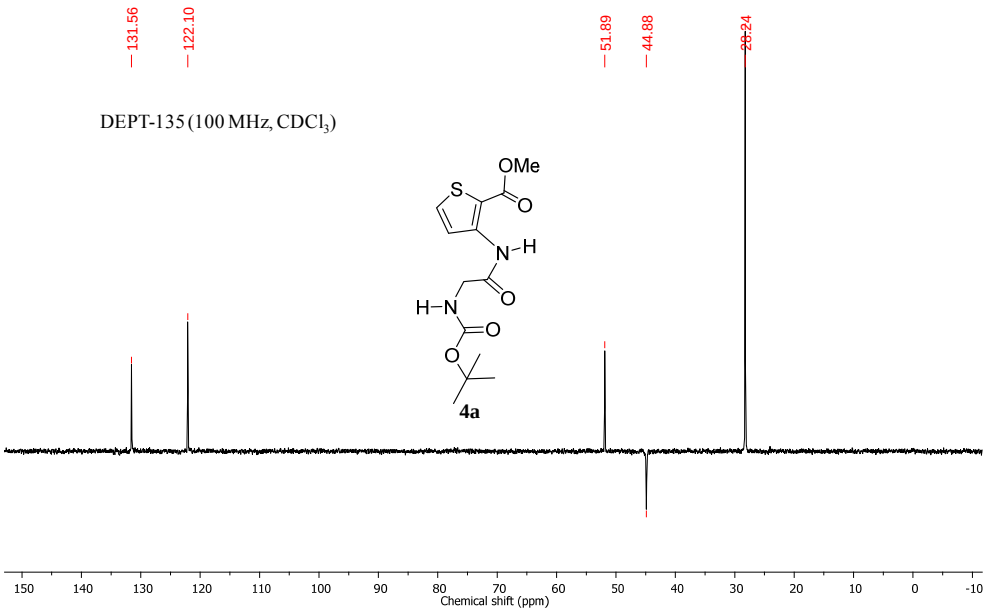

11.80
8.14
7.43
7.29
6.83
5.43
4.80
4.01
3.94
3.88
3.87
3.85
2.85
2.84
2.40
2.17
2.07
2.05
2.01
1.50
Me
H–N H
O
N
S
O
N–H
H–N
O
O
O
3
^{1}H NMR (500 MHz, CDCl$_3$)
13.0 12.5 12.0 11.5 11.0 10.5 10.0 9.5 9.0 8.5 8.0 7.5 7.0 6.5 6.0 5.5 5.0 4.5 4.0 3.5 3.0 2.5 2.0 1.5 1.0 0.5
Chemical shift (ppm)

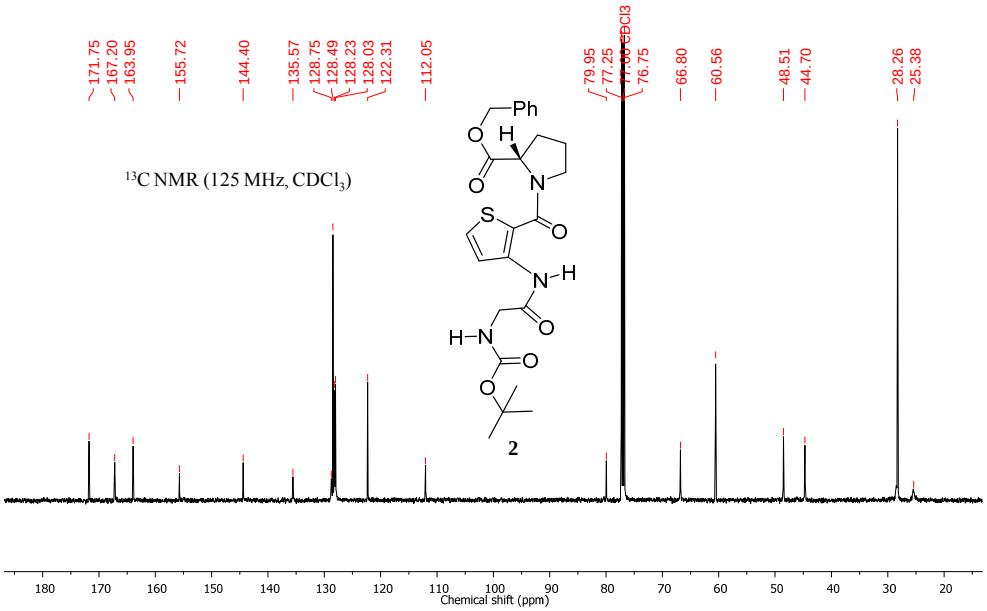

11.29
9.34
7.68
7.67
7.11
7.08
7.07
7.01
6.90
4.33
3.55
3.44
3.43
3.40
3.38
2.50 DMSO-d6
1.71
1.61
1.60
1.58
0.91
Br
H–N H
O
N
S
O
N–H
H–N
O
O
O
5
^{1}H NMR (400 MHz, DMSO-d$_6$)
12.0 11.5 11.0 10.5 10.0 9.5 9.0 8.5 8.0 7.5 7.0 6.5 6.0 5.5 5.0 4.5 4.0 3.5 3.0 2.5 2.0 1.5 1.0 0.5
Chemical shift (ppm)

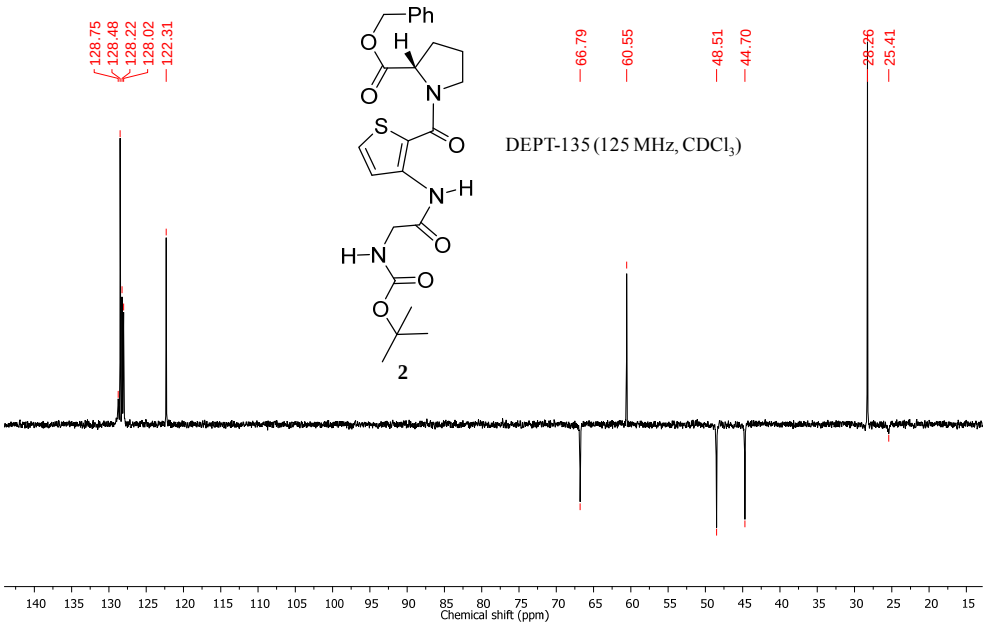

11.76
8.20
8.18
8.17
8.16
7.80
7.47
7.45
7.33
7.28
5.48
5.23
5.20
5.19
5.16
4.90
4.88
4.55
4.19
4.18
4.12
4.07
4.01
3.93
3.83
3.81
3.79
2.50
2.23
2.21
2.08
2.07
2.06
2.03
1.93
1.85
1.47
Ph
^{1}H NMR (400 MHz, CDCl$_3$)
6
12.5 12.0 11.5 11.0 10.5 10.0 9.5 9.0 8.5 8.0 7.5 7.0 6.5 6.0 5.5 5.0 4.5 4.0 3.5 3.0 2.5 2.0 1.5
Chemical shift (ppm)

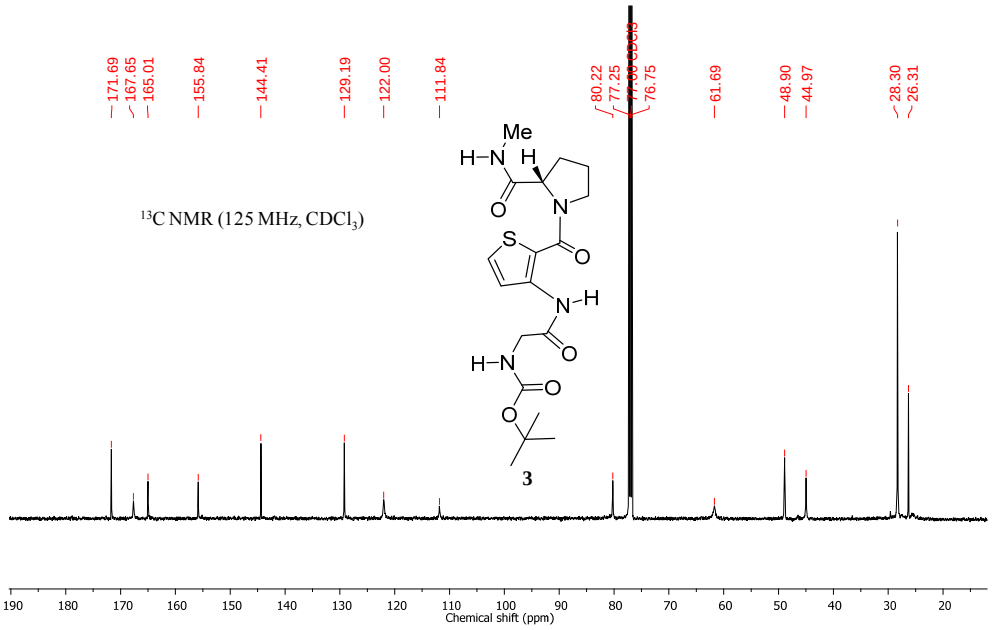

11.64
8.13
7.85
7.45
7.27 CDCl3
6.64
5.47
4.91
4.90
4.02
4.01
3.92
3.90
3.89
3.88
2.81
2.49
2.33
2.25
2.17
2.11
2.04
2.04
1.78
1.47
Me
^{1}H NMR (700 MHz, CDCl$_3$)
1
12.5 12.0 11.5 11.0 10.5 10.0 9.5 9.0 8.5 8.0 7.5 7.0 6.5 6.0 5.5 5.0 4.5 4.0 3.5 3.0 2.5 2.0 1.5 1.0
Chemical shift (ppm)


167.36
164.44
155.82
143.79
131.57
122.10
110.78
80.50
77.32
77.00 CDCl3
76.68
51.89
44.88
28.24
13C NMR (100 MHz, CDCl3)
OMe
S
O
N-H
O
H-N
O
O
4a
170
160
150
140
130
120
110
100
90
80
70
60
50
40
30
20
Chemical shift (ppm)

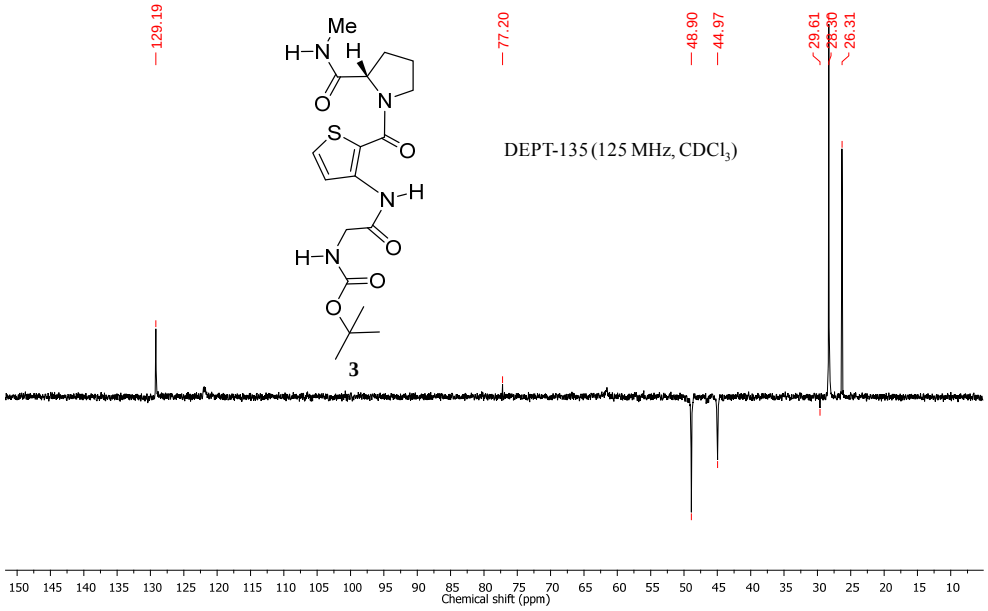

131.56
122.10
51.89
44.88
28.24
DEPT-135 (100 MHz, CDCl3)
OMe
S
O
N-H
O
H-N
O
O
4a
150
140
130
120
110
100
90
80
70
60
50
40
30
20
10
0
-10
Chemical shift (ppm)


171.75
167.20
163.95
155.72
144.40
135.57
128.75
128.49
128.23
128.03
122.31
112.05
79.95
77.25
77.00
CDCl3
76.75
66.80
60.56
48.51
44.70
28.26
25.38
13C NMR (125 MHz, CDCl3)
Ph
O
H
N
O
S
O
N-H
O
H-N
O
O
2
180 170 160 150 140 130 120 110 100 90 80 70 60 50 40 30 20
Chemical shift (ppm)

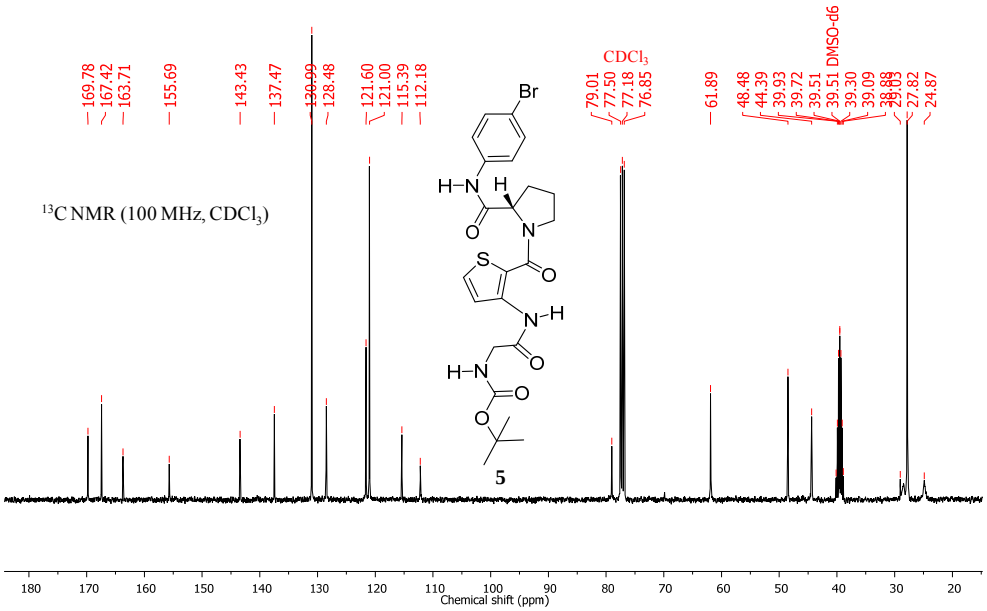

128.75
128.48
128.22
128.02
122.31
66.79
60.55
48.51
44.70
28.26
25.41
Ph
O
H
N
O
S
O
N-H
O
H-N
O
O
2
DEPT-135 (125 MHz, CDCl3)
140 135 130 125 120 115 110 105 100 95 90 85 80 75 70 65 60 55 50 45 40 35 30 25 20 15
Chemical shift (ppm)

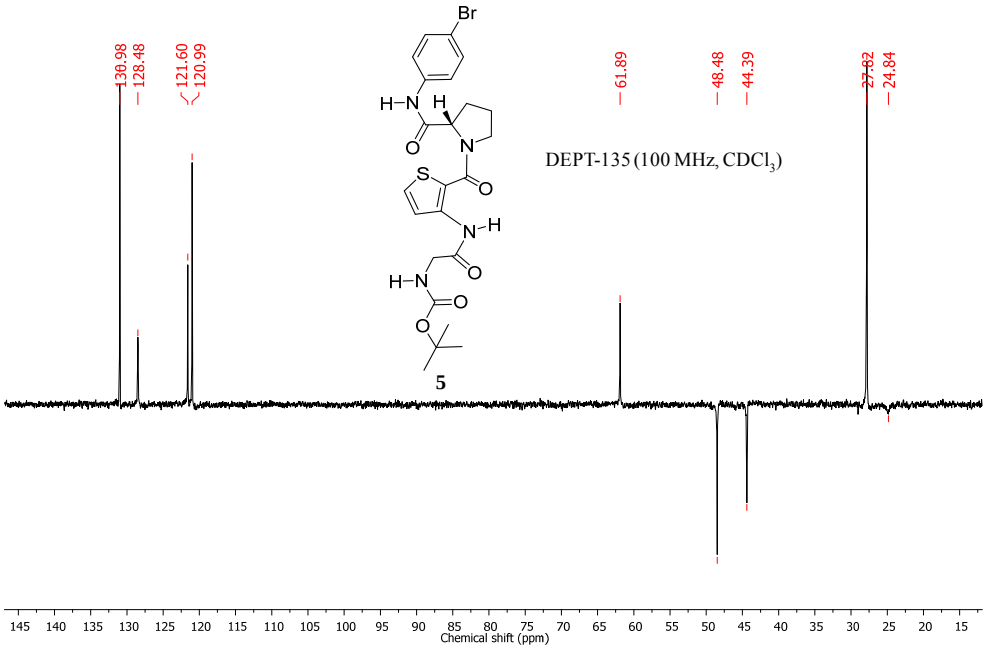


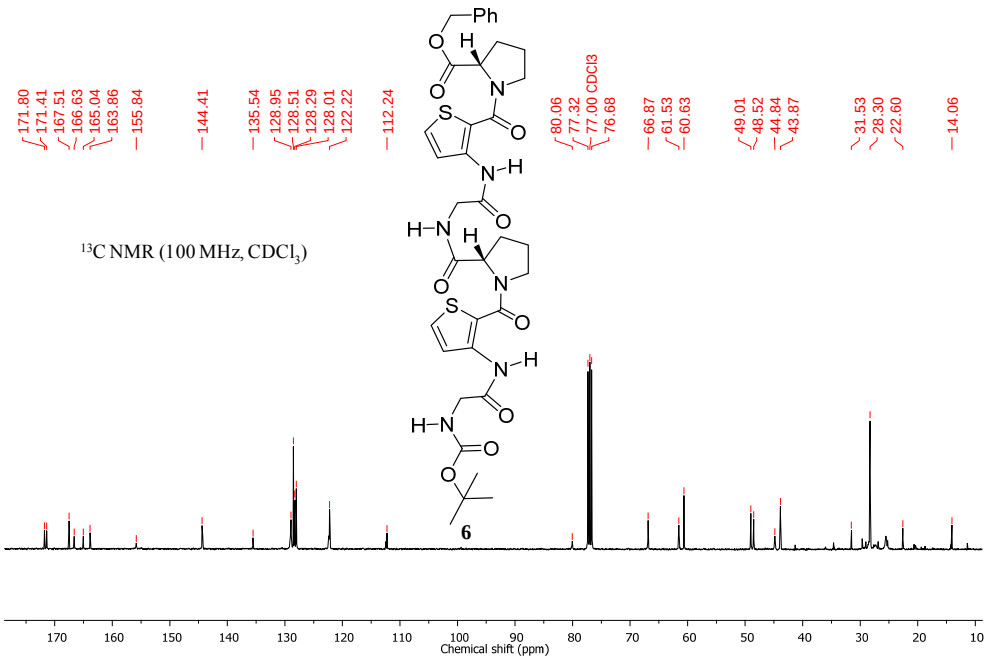
^{13}C NMR (125 MHz, $CDCl_3$)

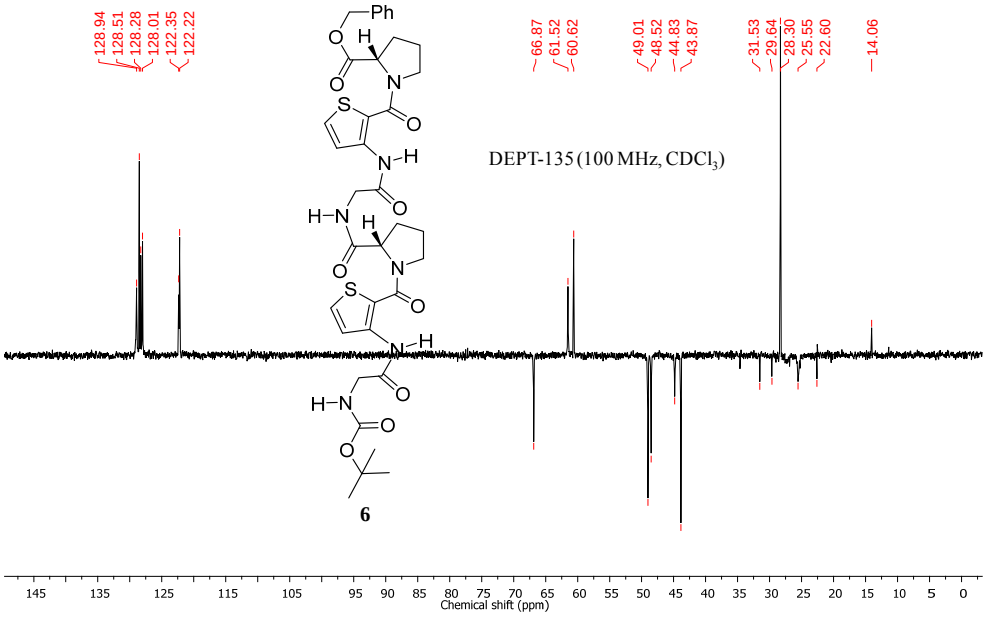


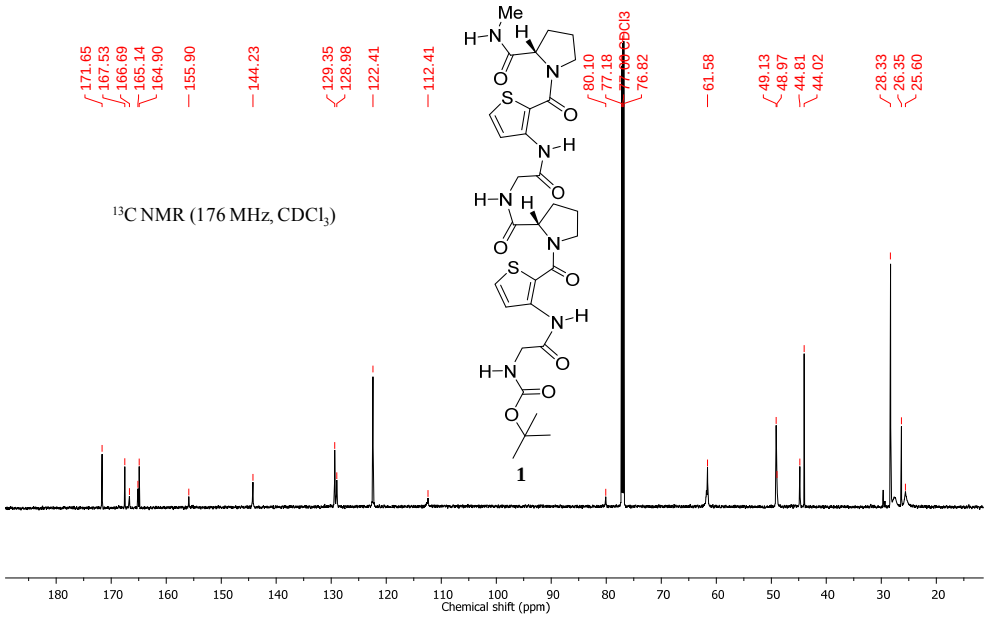
DEPT-135 (125 MHz, $CDCl_3$)


169.78
167.42
163.71
155.69
143.43
137.47
130.99
128.48
121.60
121.00
115.39
112.18
CDCl3
79.01
77.50
77.18
76.85
61.89
48.48
44.39
39.93
39.72
39.51
39.51 DMSO-d6
39.30
39.09
28.88
28.03
27.82
24.87
13C NMR (100 MHz, CDCl3)
Br
H–N H
O
N
S
O
N–H
H–N
O
O
O
5
180 170 160 150 140 130 120 110 100 90 80 70 60 50 40 30 20
Chemical shift (ppm)


130.98
128.48
121.60
120.99
61.89
48.48
44.39
27.82
24.84
Br
H–N H
O
N
S
O
N–H
H–N
O
O
O
5
DEPT-135 (100 MHz, CDCl3)
145 140 135 130 125 120 115 110 105 100 95 90 85 80 75 70 65 60 55 50 45 40 35 30 25 20 15
Chemical shift (ppm)


171.80
171.41
167.51
166.63
165.04
163.86
155.84
144.41
135.54
128.95
128.51
128.29
128.01
122.22
112.24
80.06
77.32
77.00 CDCl3
76.68
66.87
61.53
60.63
49.01
48.52
44.84
43.87
31.53
28.30
22.60
14.06
13C NMR (100 MHz, CDCl3)
6
Chemical shift (ppm)


128.94
128.51
128.28
128.01
122.35
122.22
66.87
61.52
60.62
49.01
48.52
44.83
43.87
31.53
29.64
28.30
25.55
22.60
14.06
DEPT-135 (100 MHz, CDCl3)
6
Chemical shift (ppm)


171.65
167.53
166.69
165.14
164.90
155.90
144.23
129.35
128.98
122.41
112.41
80.10
77.18
77.00 CDCl3
76.82
61.58
49.13
48.97
44.81
44.02
28.33
26.35
25.60
13C NMR (176 MHz, CDCl3)
1
Chemical shift (ppm)

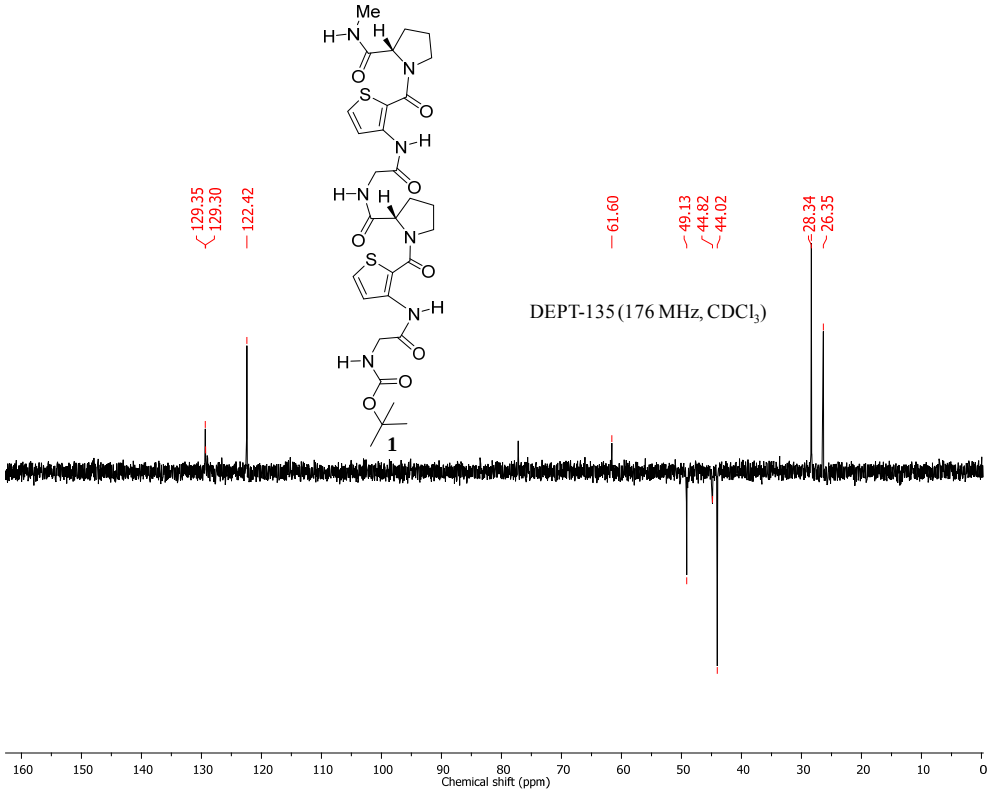
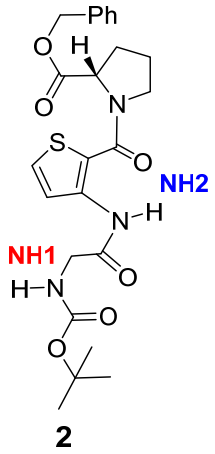

129.35
129.30
122.42
61.60
49.13
44.82
44.02
28.34
26.35
DEPT-135 (176 MHz, CDCl3)
1
Chemical shift (ppm)

Table S1. Titration study of 2 in $CDCl_3$ (5 mM, 400 MHz) with DMSO-d_6 (Volume of DMSO- d_6 added at each addition = 5 μL)

No	Volume of DMSO-d6 (μL)	Chemical Shift δ (ppm)	
		NH1	NH2
1	0	5.15	11.69
2	5	5.2	11.68
3	10	5.25	11.67
4	15	5.3	11.66
5	20	5.38	11.64
6	25	5.43	11.64
7	30	5.48	11.62
8	35	5.54	11.61
9	40	5.6	11.6
10	45	5.65	11.59
11	50	5.7	11.58



2

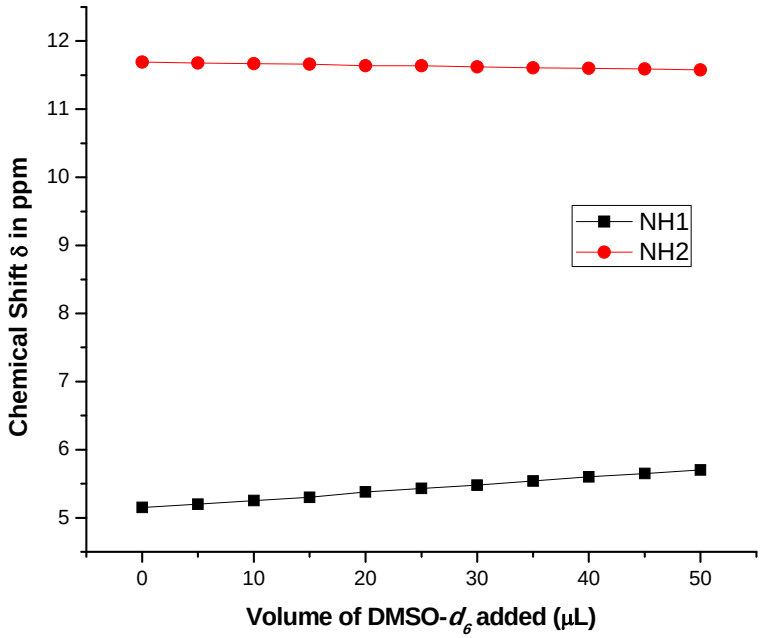
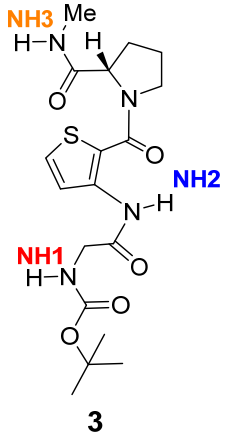


Table S2. Titration study of 3 in $CDCl_3$ (5 mM, 400 MHz) with DMSO-d_6 (Volume of DMSO- d_6 added at each addition = 5 μL)

No	Volume of DMSO-d6 (μL)	Chemical Shift δ (ppm)		
		NH1	NH2	NH3
1	0	5.2	11.77	6.69
2	5	5.27	11.75	6.72
3	10	5.32	11.75	6.75
4	15	5.42	11.73	6.8
5	20	5.48	11.71	6.83
6	25	5.57	11.69	6.87
7	30	5.63	11.68	6.9
8	35	5.7	11.66	6.93
9	40	5.74	11.65	6.95
10	45	5.81	11.63	6.97
11	50	5.84	11.62	6.99



3

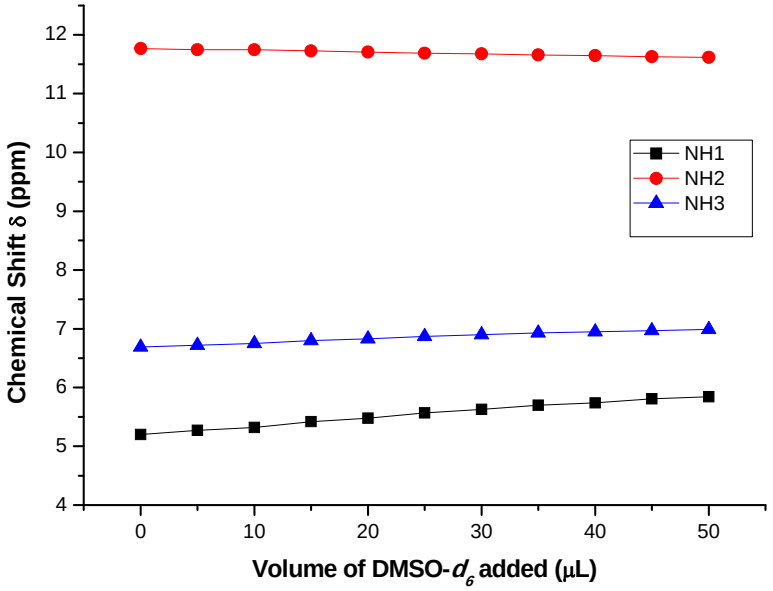


Table S3. Titration study of 1 in $CDCl_3$ (5 mM, 400 MHz) with DMSO-d_6 (Volume of DMSO- d_6 added at each addition = 5 μL)

No	Volume of DMSO-d6 (μL)	Chemical Shift δ (ppm)				
		NH1	NH2	NH3	NH4	NH5
1	0	5.43	11.69	7.85	11.69	6.58
2	5	5.48	11.66	7.85	11.66	6.66
3	10	5.53	11.63	7.87	11.63	6.72
4	15	5.59	11.6	7.87	11.6	6.78
5	20	5.62	11.59	7.87	11.59	6.82
6	25	5.68	11.56	7.88	11.58	6.86
7	30	5.72	11.54	7.88	11.57	6.89
8	35	5.75	11.52	7.88	11.56	6.93
9	40	5.81	11.5	7.89	11.54	6.95
10	45	5.84	11.49	7.89	11.53	6.98
11	50	5.87	11.47	7.89	11.52	7

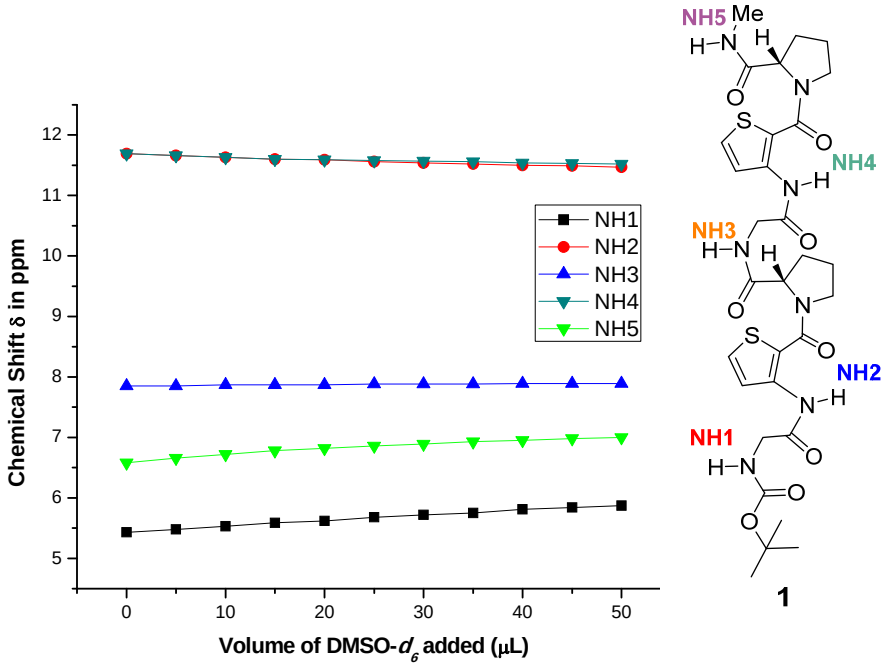
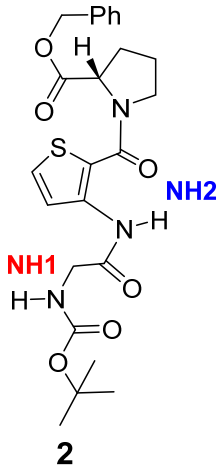


Table S4. Variable temperature study of 2 (5 mM, 400 MHz, $CDCl_3$)

No	Temperature (K)	Chemical Shift δ in ppm	
		NH1	NH2
1	268	5.19	11.78
2	273	5.18	11.76
3	278	5.17	11.75
4	283	5.16	11.74
5	288	5.15	11.72
6	293	5.15	11.71
7	298	5.14	11.69
8	303	5.13	11.68
9	308	5.13	11.66
10	313	5.12	11.65
11	318	5.1	11.63
12	323	5.09	11.62



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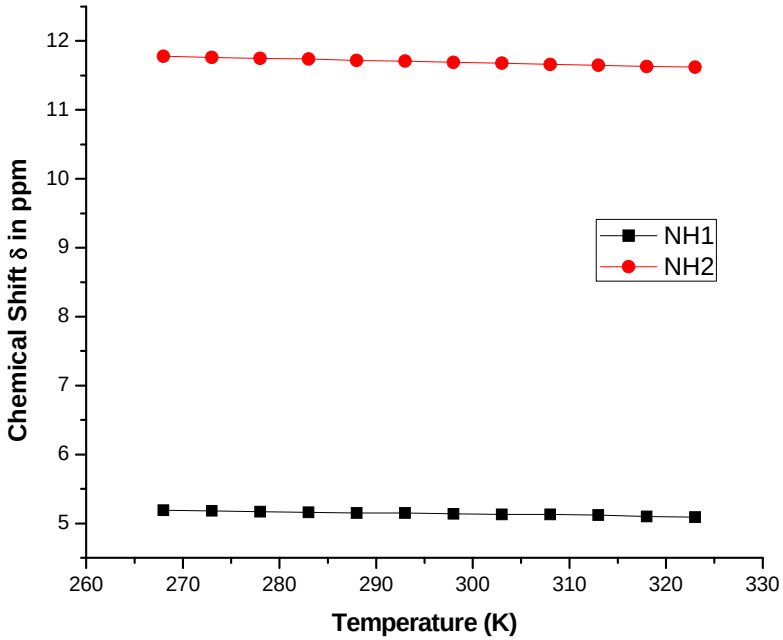
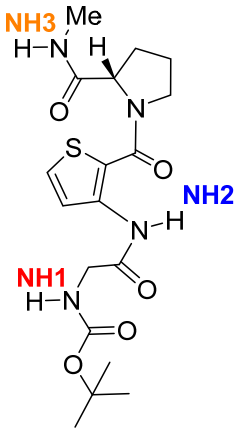


Table S5. Variable temperature study of 3 (5 mM, 400 MHz, $CDCl_3$)

No	Temperature (K)	Chemical Shift δ in ppm		
		NH1	NH2	NH3
1	268	5.25	11.88	6.79
2	273	5.25	11.87	6.78
3	278	5.24	11.85	6.76
4	283	5.24	11.83	6.74
5	288	5.23	11.81	6.72
6	293	5.22	11.8	6.71
7	298	5.2	11.77	6.69
8	303	5.19	11.76	6.67
9	308	5.18	11.74	6.65
10	313	5.18	11.73	6.64
11	318	5.15	11.71	6.63
12	323	5.14	11.69	6.61



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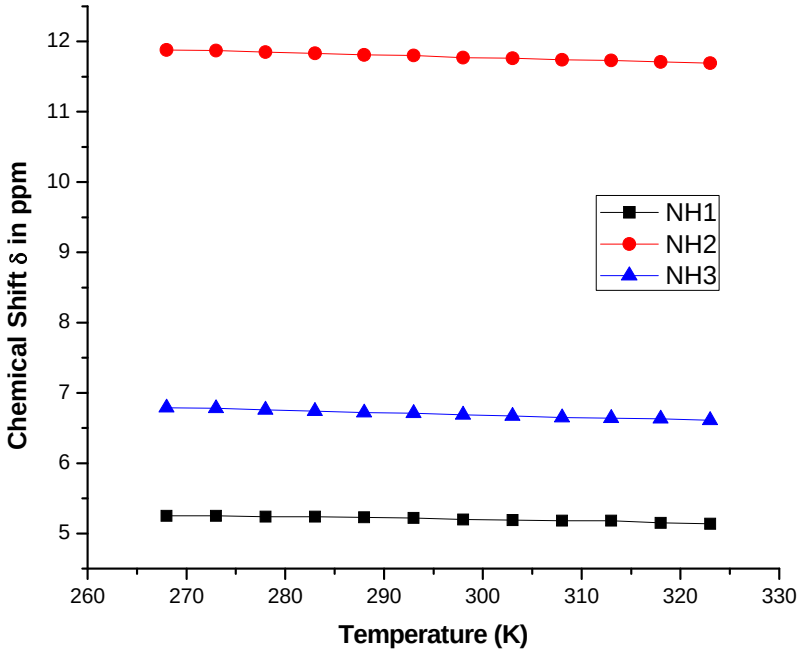
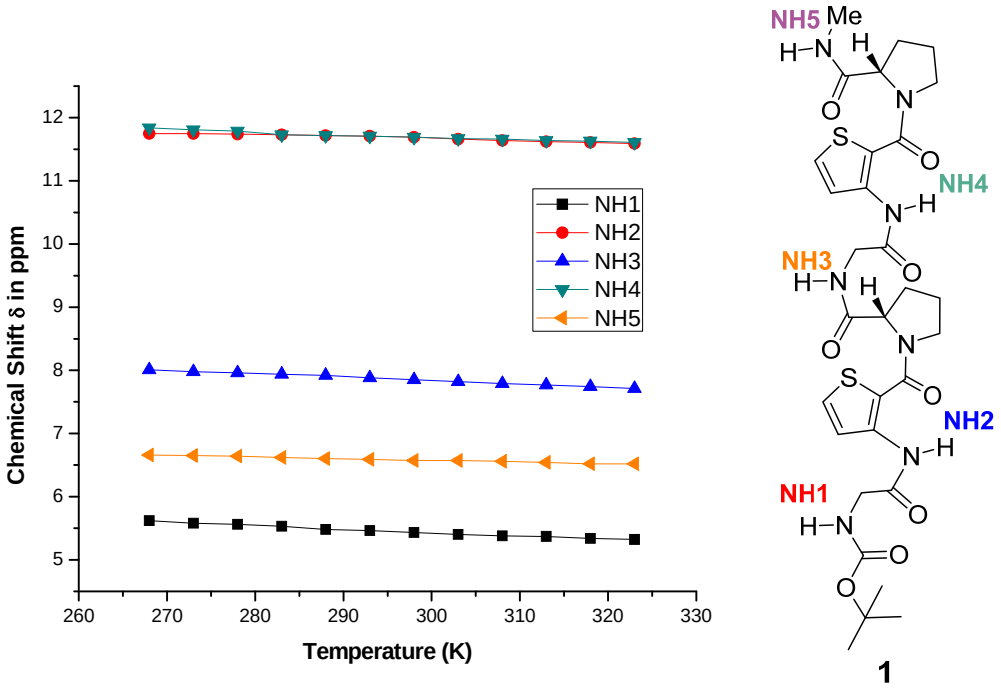


Table S6. Variable temperature study of 1 (5 mM, 400 MHz, $CDCl_3$)

No	Temperature (K)	Chemical Shift δ in ppm				
		NH1	NH2	NH3	NH4	NH5
1	268	5.62	11.75	8.01	11.84	6.66
2	273	5.58	11.75	7.98	11.81	6.65
3	278	5.56	11.74	7.96	11.79	6.64
4	283	5.53	11.73	7.94	11.73	6.62
5	288	5.48	11.72	7.92	11.72	6.6
6	293	5.46	11.71	7.88	11.71	6.59
7	298	5.43	11.69	7.85	11.69	6.57
8	303	5.4	11.66	7.82	11.67	6.57
9	308	5.38	11.64	7.79	11.66	6.56
10	313	5.37	11.62	7.77	11.64	6.54
11	318	5.34	11.61	7.74	11.63	6.52
12	323	5.32	11.59	7.71	11.61	6.52



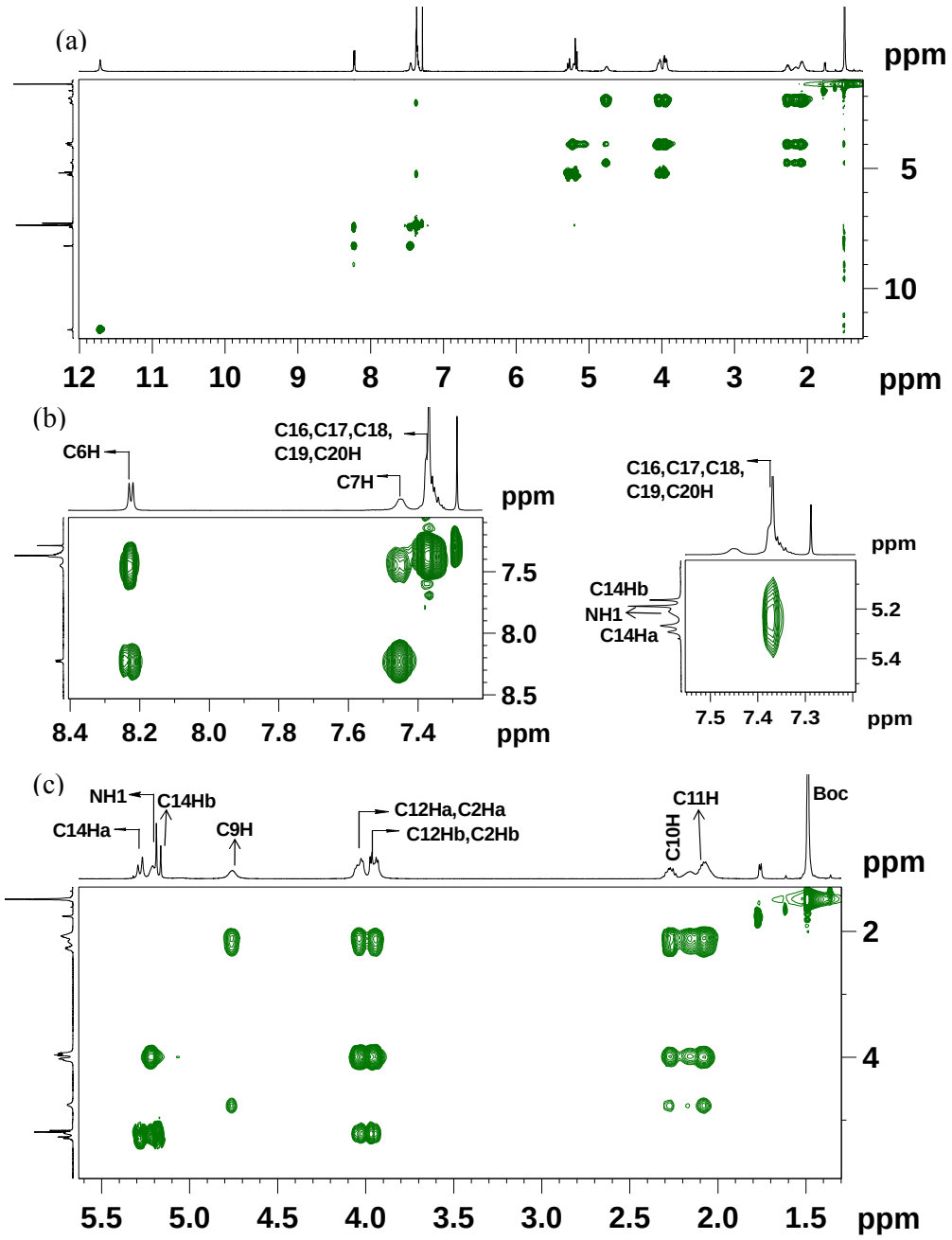


Figure S1: TOCSY full spectrum (a) of **2** (25 mM, 500 MHz, $CDCl_3$, 298 K); aromatic (b) and aliphatic (c) regions shown separately.

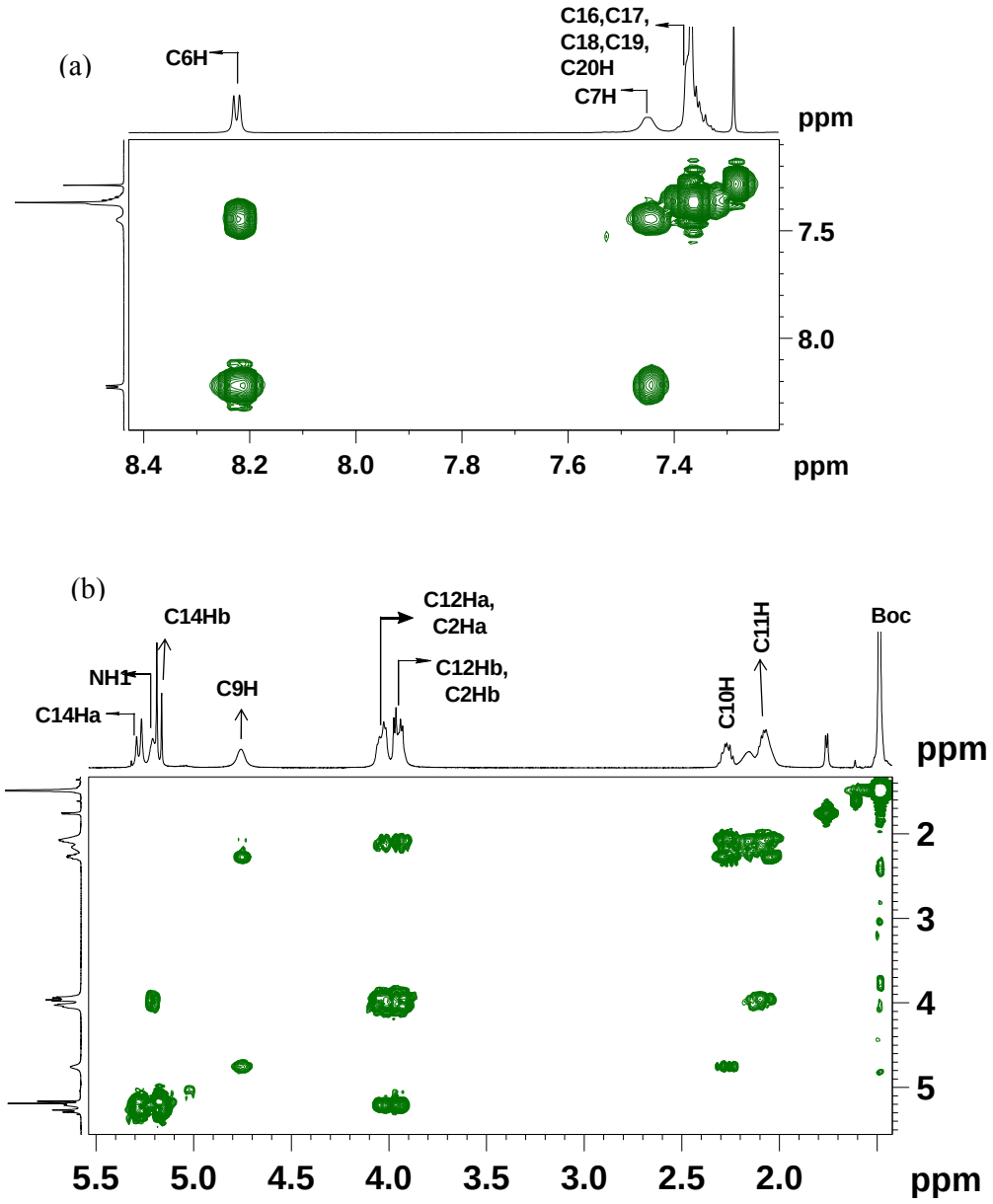


Figure S2: Partial COSY spectra of **2** (25 mM, 500 MHz, $CDCl_3$, 298 K); aromatic (a) and aliphatic (b) regions shown separately.

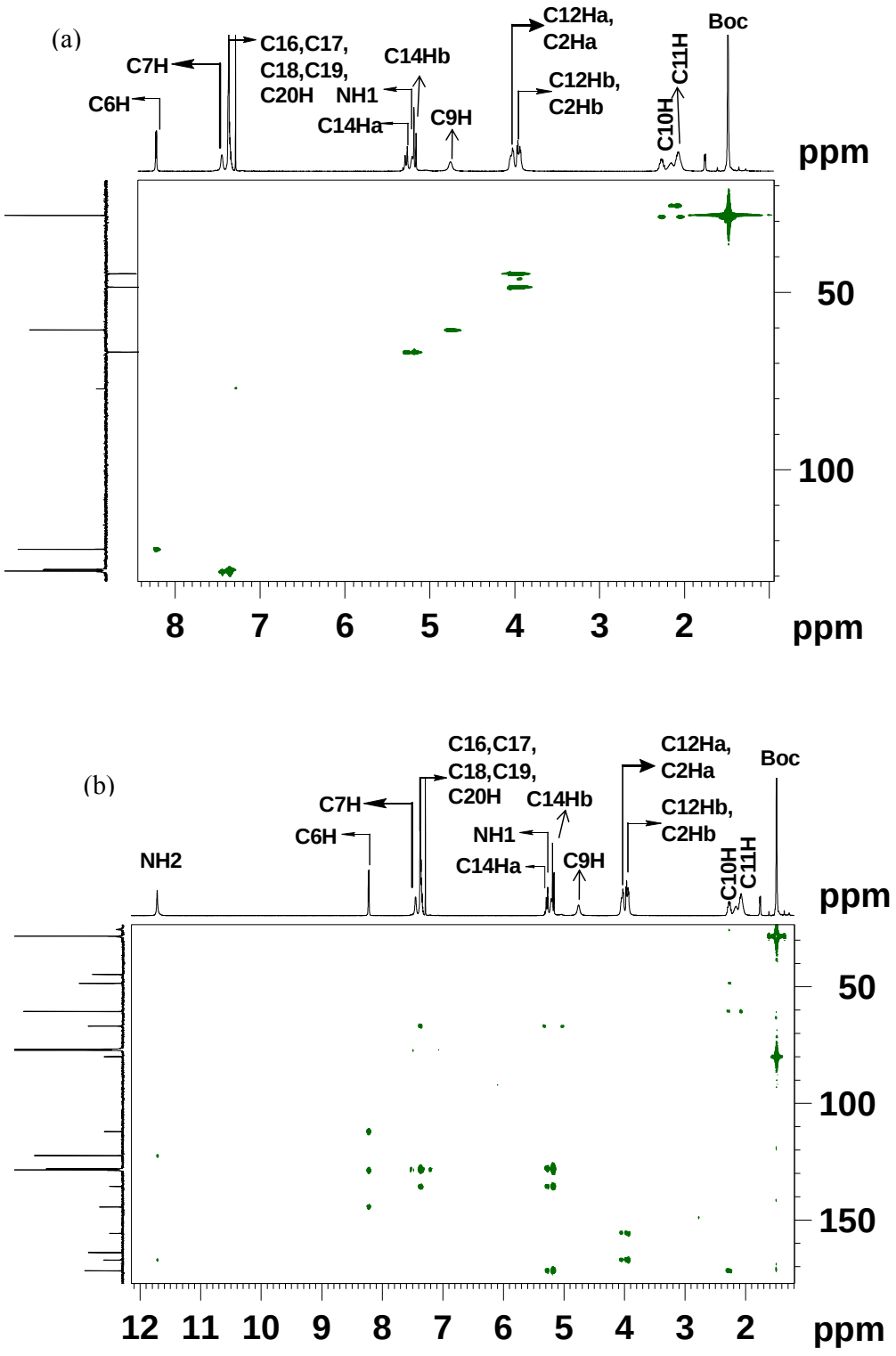


Figure S3: HSQC (a) and HMBC (b) full spectra of **2** (25 mM, 500 MHz, $CDCl_3$, 298 K).

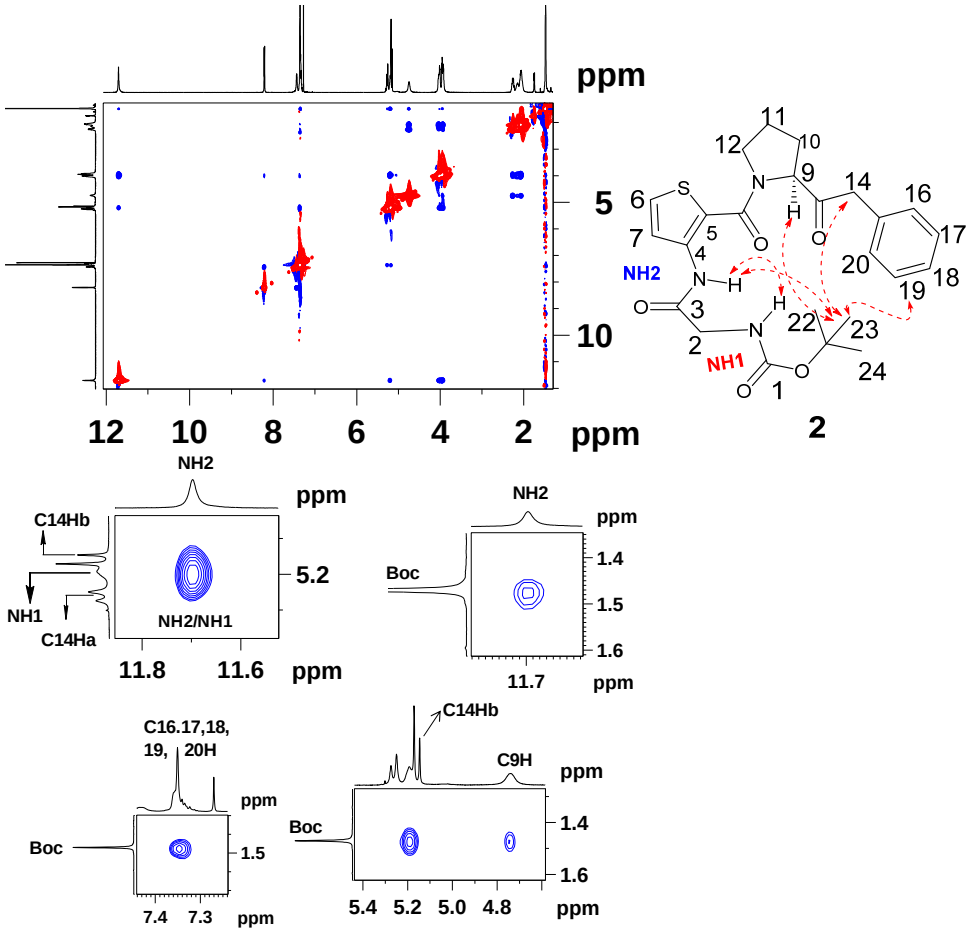


Figure S4: 2D NOESY full spectrum and excerpts of **2** (25 mM, 500 MHz, $CDCl_3$, 298 K).

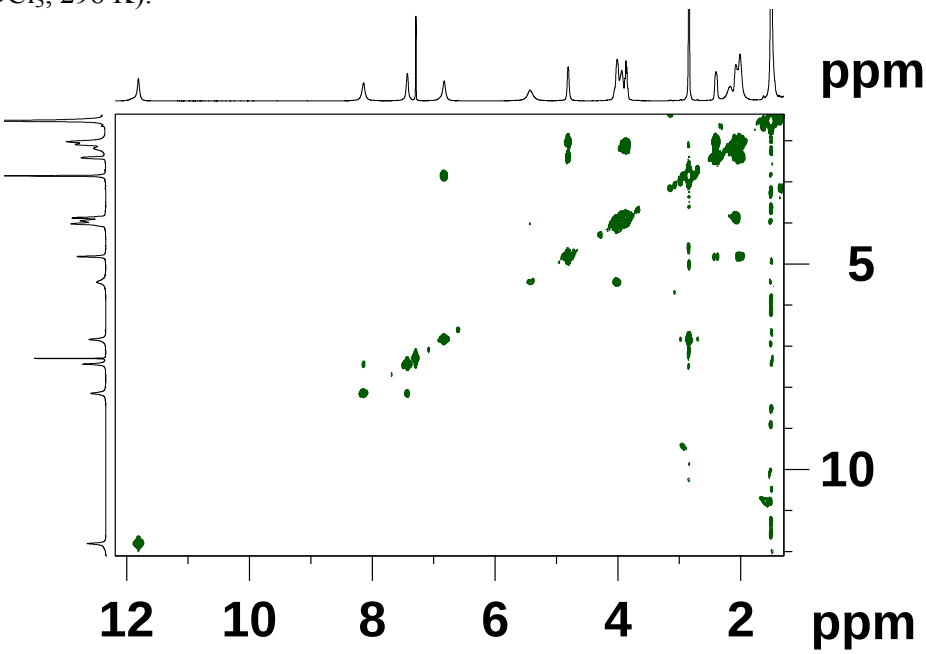


Figure S5: COSY full spectrum (a) of **3** (25 mM, 500 MHz, $CDCl_3$, 298 K).

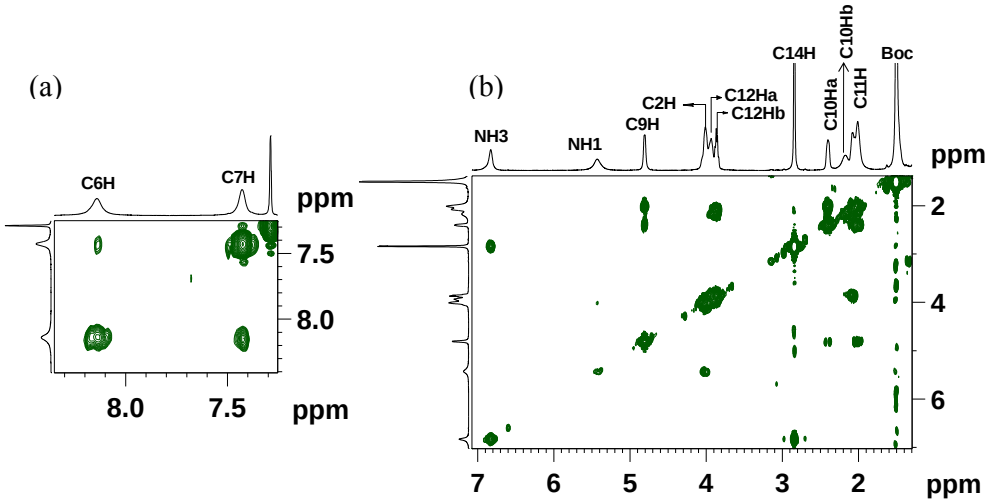


Figure S6: Partial COSY spectra of **3** (25 mM, 500 MHz, $CDCl_3$, 298 K); aromatic (a) and aliphatic (b) regions shown separately.

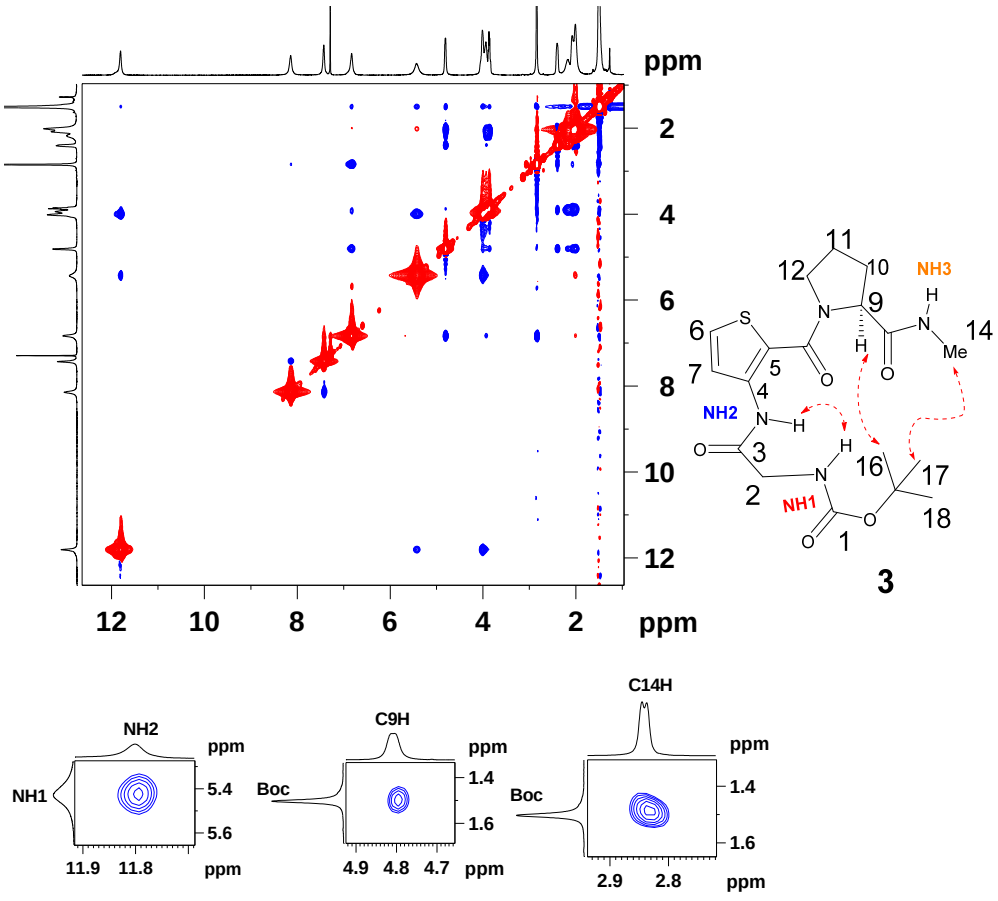


Figure S7: 2D NOESY full spectrum and excerpts of **3** (25 mM, 500 MHz, $CDCl_3$, 298 K).

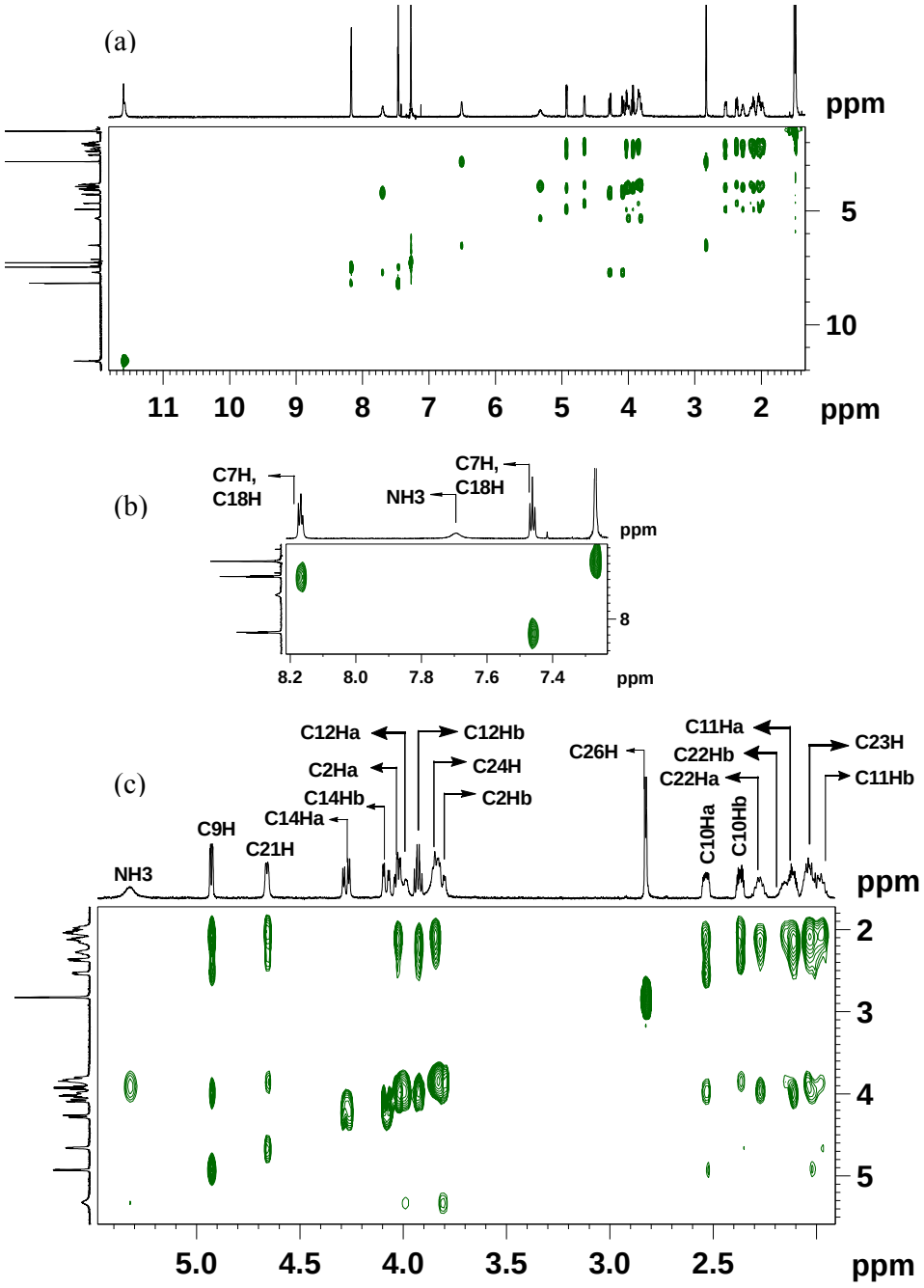


Figure S8: TOCSY full spectrum (a) of **1** (6 mM, 700 MHz, $CDCl_3$, 328 K); aromatic (b) and aliphatic (c) regions shown separately.

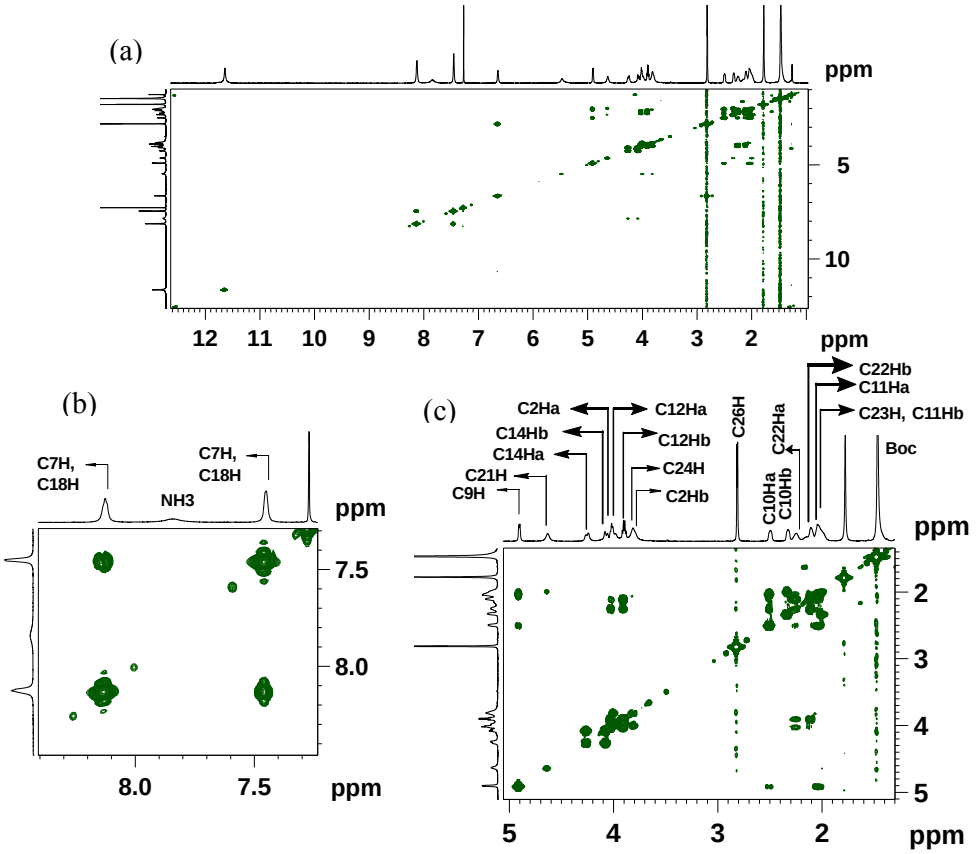


Figure S9. COSY full spectrum (a) of **1** (23 mM, 700MHz, $CDCl_3$, 298 K); aromatic (b) and aliphatic (c) regions shown separately.

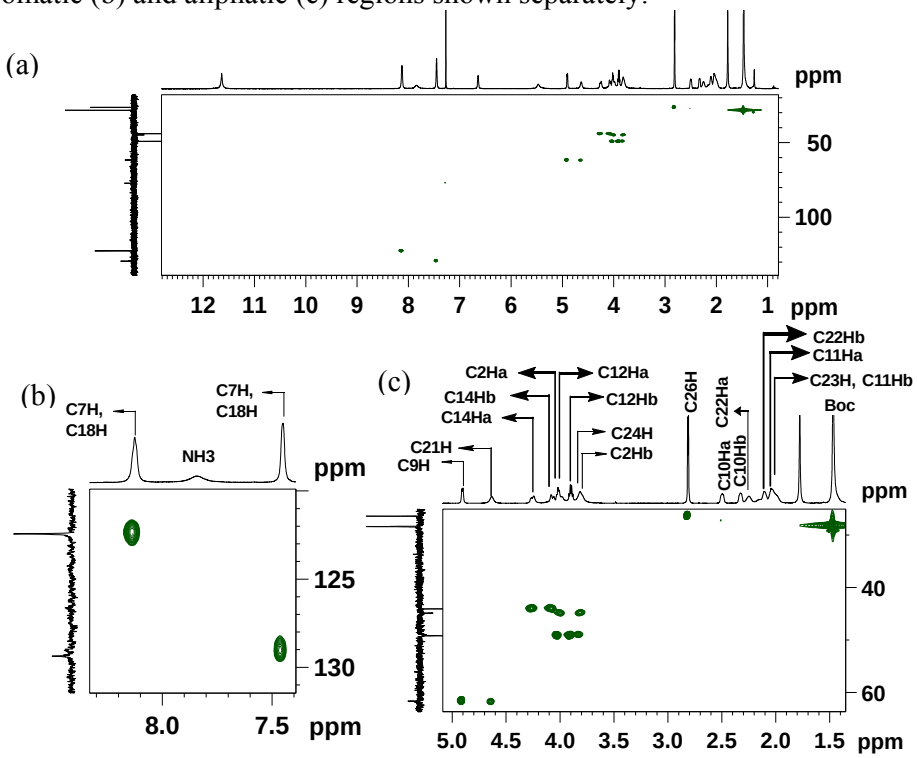


Figure S10. HSQC full spectrum (a) of **1** (23 mM, 700MHz, $CDCl_3$, 298 K); aromatic (b) and aliphatic (c) regions shown separately.

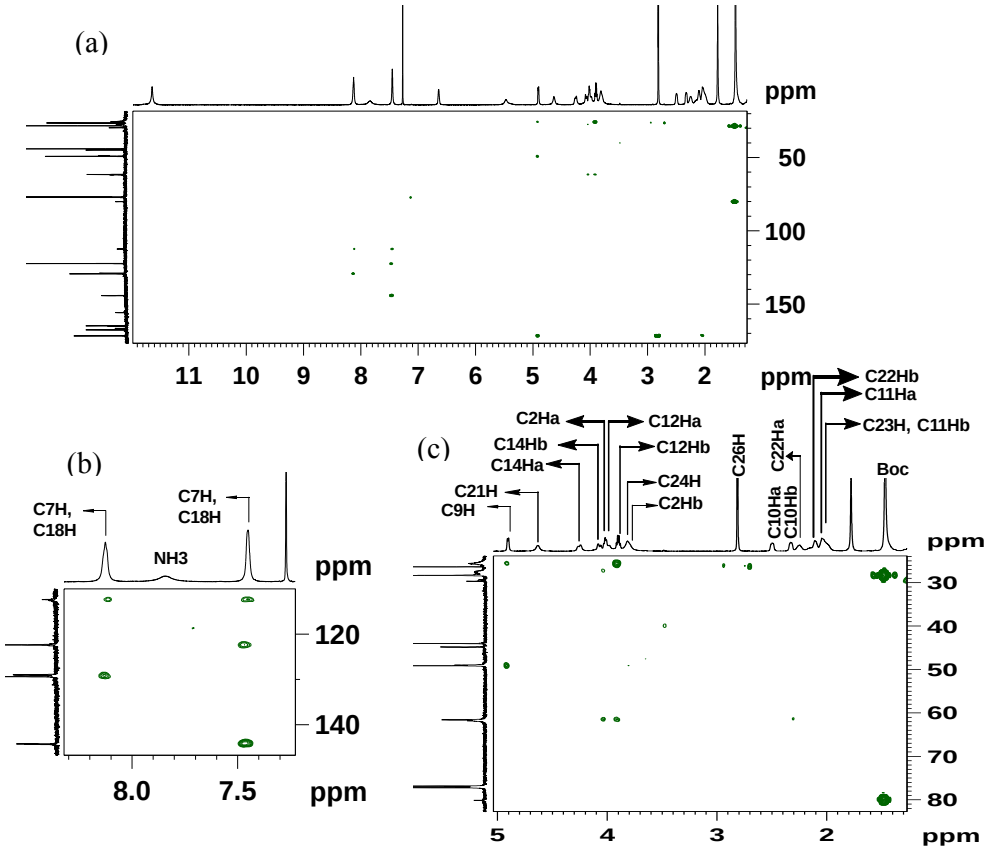


Figure S11. HMBC full spectrum (a) of **1** (23 mM, 700MHz, $CDCl_3$, 298 K); aromatic (b) and aliphatic (c) regions shown separately.

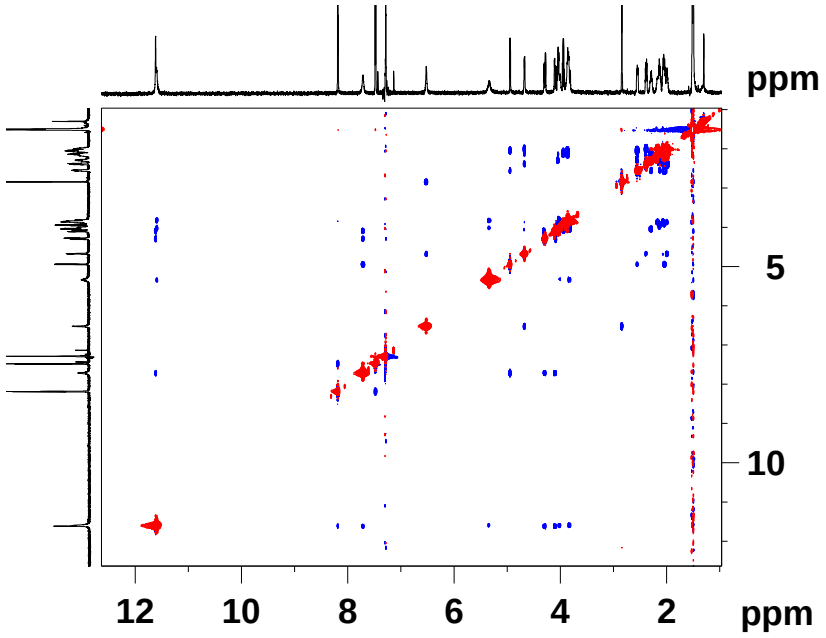


Figure S12. NOESY full spectrum of **1** (6 mM, 700MHz, $CDCl_3$, 328 K).

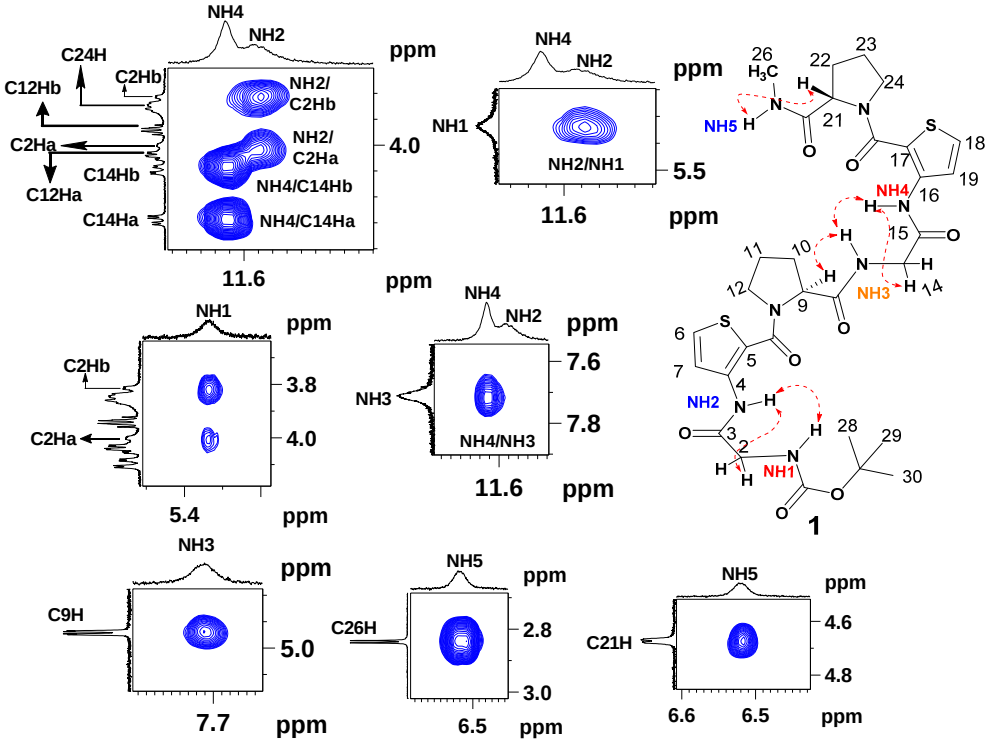


Figure S13. 2D NOESY extracts of **1** (6 mM, 700MHz, $CDCl_3$, 328 K).

X-ray Crystallography: Single crystal structure of compound **2** was determined by measuring X-ray intensity data on a Bruker SMART APEX II single crystal X-ray CCD diffractometer having graphite-monochromatised (Mo-Kα = 0.71073 Å) radiation. The X-ray generator was operated at 50 kV and 30 mA. A preliminary set of cell constants and an orientation matrix were calculated from total 36 frames. The optimized strategy used for data collection consisted different sets of φ and ω scans with 0.5° steps in φ/ω. Data were collected keeping the sample-to-detector distance fixed at 5.00 cm. The X-ray data acquisition was monitored by APEX2 program suit. All the data were corrected for Lorentz-polarization and absorption effects using SAINT and SADABS programs integrated in APEX2 package. The structures were solved by direct methods and refined by full matrix least squares, based on F^2, using SHELX-97. Molecular diagrams were generated using ORTEP-3 and Mercury programs. Geometrical calculations were performed using SHELXTL and PLATON.

Table 7: X-ray crystallographic data of trimer **2**.

Crystal Data	**2**
Formula	$C_{24}\ H_{29}\ N_3\ O_6\ S$
M_r	487.56
Crystal Size, mm	0.32×0.25×0.10
Temp. (K)	150(2)
Crystallizing solvent	Ethyl acetate-petroleum ether
Crystal Syst.	Orthorhombic
Space Group	$P2_12_12_1$
a/Å	8.8665(3)
b/Å	12.6487(5)
c/Å	21.9234(9)
$\alpha/^0$	90
$\beta/^0$	90
$\gamma/^0$	90
V/Å^3	2458.70(16)
Z	4
D_{calc}/g cm^{-3}	1.317
μ/mm^{-1}	0.176
F(000)	1032
Ab. Correct.	multi-scan
$2\theta_{max}$	50
Total reflns.	41420
unique reflns.	4322
h, k, l (min, max)	(-10,10),(-15,15),(-23,26)
R_{int}	0.0292

No. of para	311
R1 [*I*> 2σ(*I*)]	0.0315
wR2[*I*> 2σ(*I*)]	0.0793
R1 [all data]	0.0330
wR2 [all data]	0.0801
goodness-of-fit	1.067
$\Delta\rho_{max}$,$\Delta\rho_{min}$(eÅ^{-3})	0.218,-0.177
CCDC no.	1435889

Table 8: nOe-derived distance constraints used in molecular modeling for structural elucidation of oligomer **1**.

Atom I	Atom II	Chemical Shift I	Chemical Shift II	Upper Bound	Lower Bound
C19H	NH4	8.178	11.614	3.615	2.958
NH3	NH4	7.721	11.614	3.229	2.642
NH1	NH2	5.327	11.601	3.473	2.842
C14Ha	NH4	4.292	11.614	3.206	2.623
C14Hb	NH4	4.100	11.614	3.264	2.670
C2Ha	NH2	3.987	11.601	3.175	2.598
C2Hb	NH2	3.828	11.601	3.326	2.721
C9H	NH3	4.935	7.721	2.822	2.309
C14Ha	NH3	4.292	7.721	3.433	2.809
C14Hb	NH3	4.100	7.721	3.187	2.607
C21H	NH5	4.663	6.514	3.204	2.622
C2Ha	NH1	3.987	5.327	3.418	2.797
C2Hb	NH1	3.828	5.327	3.227	2.640
C26H	NH5	2.833	6.514	2.787	2.280
C10Ha	C9H	2.541	4.935	3.538	2.895
C23H	C21H	1.991	4.663	3.003	2.457
Boc	NH3	1.487	7.721	4.571	3.740
Boc	NH1	1.487	5.327	4.941	4.042

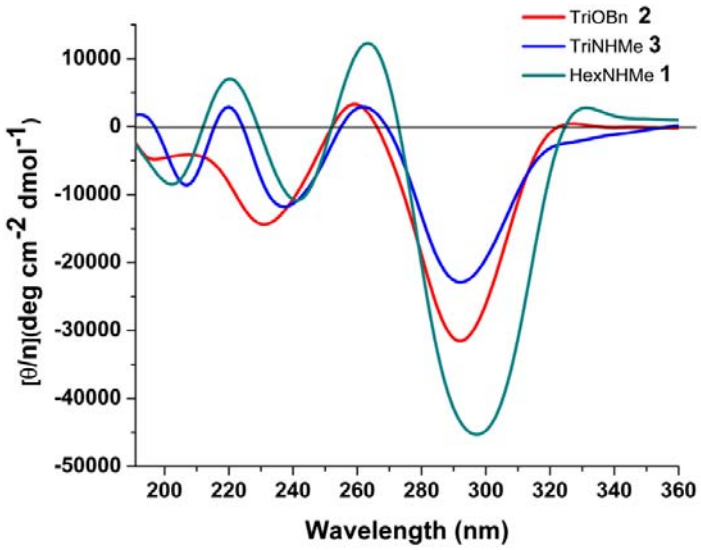


Figure S14. CD spectra of $(Gly\text{-}3\text{-}Atc\text{-}Pro)_n$ oligomers; tripeptides **2**, **3** and hexapeptide **1** at a concentration of 0.1 mM. All CD spectra were recorded in trifluoroethanol at 298 K.