Electronic Supplementary Material (ESI) for RSC Advances.

An integrated flow and microwave approach to a broad spectrum kinase inhibitor

Cecilia Russell, Andrew J. S. Lin Peter Haines, Michela I Simone, Phillip J Robinson and Adam McCluskey*

Electronic supporting information

Contents

Experimental for batch synthesis approaches to compounds described in the main text.

All reagents were purchased from Sigma-Aldrich, Matrix Scientific or Lancaster Synthesis and were used without purification. With the exception of THF (anhydrous > 99%) obtained from Sigma-Aldrich, all solvents were re-distilled from glass prior to use.

^{1}H and ^{13}C NMR spectra were recorded using Brüker Avance™ AMX 400 and 600 MHz spectrometers at 400 (or 600) and 101 MHz, respectively. Chemical shifts (δ) are reported in parts per million (ppm) measured relative to the internal standards, and coupling constants (*J*) are expressed in Hertz (Hz). Mass spectra were recorded on a Shimadzu LCMS 2010 EV using a mobile phase of 1:1 acetonitrile:H_2O with 0.1% formic acid.

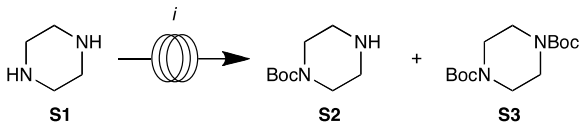
HPLC analysis was recorded using a Shimadzu 20A with Grace econosphere C18 5µ 150 x 4.6 mm column, and GCMS analysis was carried out using a Shimadzu QP 2010 GCMS.

Flow Chemistry Approaches

***tert*-Butyl piperazine-1-carboxylate (S2)**

To a chilled magnetically stirred solution of piperazine (1.60 g, 18.6 mmol) in methanol (25 mL) a solution of Boc-anhydride (3.25 g, 14.8 mmol) was introduced using the Syrris FRX-100 reaction system at a rate of 0.2 mL.min^{-1}. After completion of addition of the Boc-anhydride solution, the mixture was allowed to stir and warm to room temperature overnight. The ensuing mixture was concentrated under reduced pressure to give a white solid (1.050 g, 89%) containing a mixture of mono- and di-Boc piperazine (88:12 by GCMS). This material was used without further purification.

^{1}H NMR (400 MHz, $CDCl_3$) δ 3.45 – 3.36 (4H, m), 2.89 – 2.76 (4H, m), 2.20 (2H, s), 1.46 (9H, s). ^{13}C NMR (101 MHz, $CDCl_3$) δ 154.9, 79.9 (2C), 45.9 (2C), 28.6. GCMS (EI) m/z 186 (100%). IR ν_{max} (cm^{-1}): 3274, 2974, 2869, 1665, 1420, 1364, 1235, 1165, 1109, 1001, 865.12, 656, 593, 548.



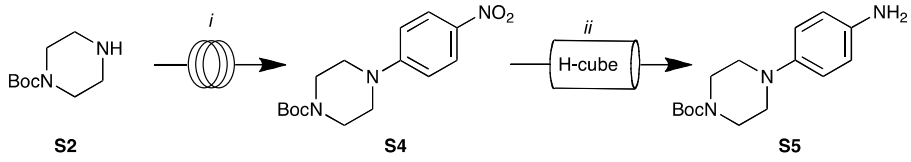
Scheme 1. Reagents and conditions. (i) Syrris FRX-100: Boc_2O, MeOH 0.2 mL.min^{-1}, 0 → 19 °C., 19 h.

Table S1. Flow optimisation of the synthesis of Boc-piperazine **S2**.

Piperazine : Boc_2O		Temp (°C)	Flow Rate (mL.min^{-1})	**S1**:**S2**	Yield (%)
1.0	0.8	30	0.2	-[a]	-
1.0	0.8	40	0.2	-[a]	-
1.0	0.8	50	0.2	-[a]	-
1.0	0.5	0	0.2	88:12	64%
1.0	0.7	0	0.2	80:20	ND
1.0	0.8	0	0.2	82:18	89%
1.0	0.9	0	0.2	75:25	>95%

[a] '-' = no **S2** or **S3** detected by GC MS

***tert*-Butyl 4-(4-aminophenyl)piperazine-1-carboxylate (S5)**



tert-Butyl 4-(4-nitrophenyl)piperazine-1-carboxylate (**S4**)

A stream of crude *tert*-butyl piperazine-1-carboxylate **S2** (0.93 g, 5.0 mmol) in DMF (100 mL) and another stream of 4-fluoronitrobenzene (352 mg, 2.5 mmol) in DMF (100 mL) was passed through a Vapourtec R2+ reaction system at 0.5 mL.min^{-1}. The instrument was fitted with two 10 mL PFA coils, maintained at 120 °C and 8 bar of pressure. The resulting product stream was taken up in CH_2Cl_2 (200 mL) and washed with water (2 × 100 mL) and saturated NaCl (1 × 100 mL). The organic layer was then dried ($MgSO_4$) and concentrated *in vacuo* to give a yellow solid (277 mg, 36% yield).

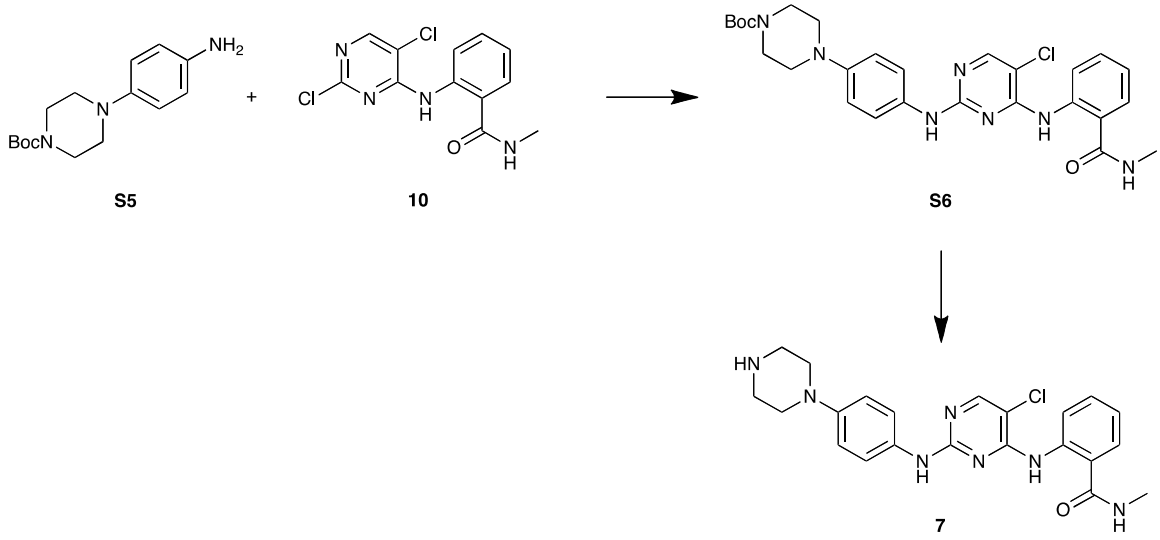
^{1}H NMR ($CDCl_3$, 400 MHz): δ 8.13 (2H, d, *J* = 9.3 Hz), 6.82 (2H, d, *J* = 9.3 Hz), 3.61 (4H, m), 3.42 (4H, m), 1.49 (9H, s); ^{13}C NMR ($CDCl_3$, 101 MHz): δ 154.6, 154.6, 138.8, 126.0 (2C), 112.9 (2C), 80.4, 46.9 (2), 43.9-42.1 (bs, 2C), 28.4 (3C); Mass spectrum (ESI, +ve) 308 *m/z* [$(M + H)^+$, 20%], 252 (100), 208 (7), 146 (7), 100 (13); FTIR ν_{max} (cm^{-1}): 3007, 2970, 2865, 167, 1585, 1485, 1417, 1367, 1318, 1238, 1162, 1112, 1040, 1081, 1001, 919, 830, 774, 754, 714, 691, 666, 640, 538, 500.

tert-Butyl 4-(4-aminophenyl)piperazine-1-carboxylate (**S5**)

A solution of *tert*-butyl 4-(4-nitrophenyl)piperazine-1-carboxylate **S4** (116 mg, 0.378 mmol) in methanol (100 mL) was passed through a ThalesNano H-Cube Pro® using 30 mm 10% Pd-C CatCart® catalyst at 1 mL.min^{-1} at 50 °C and 50 bar of pressure. The resulting reactant stream was concentrated under reduced pressure. This material was deemed pure by ^{1}H NMR spectroscopy and used in the subsequent step without further purification.

^{1}H NMR ($CDCl_3$, 400 MHz): δ 6.81 (2H, d, J = 12 Hz), 6.86 (2H, d, J = 12 Hz), 3.62 – 3.59 (4H, m), 3.43 – 3.41 (2H, bs), 2.96 (4H, m), 1.49 (9H, s); ^{13}C NMR ($CDCl_3$, 101 MHz): δ 154.8, 144.5, 140.6, 119.2 (2C), 116.17 (2C), 79.8, 51.2 (2C), 43.9 (2C), 28.5 (3C); Mass spectrum (ESI, +ve) 278 *m/z* [$(M + H)^+$, 100%], 279 (33), 222 (22); IR (cm^{-1}) 3355, 2973, 2929, 2813, 1682, 1628, 1513, 1477, 1453, 1365, 1391, 1280, 1325, 1263, 1248, 1225, 1163, 1122, 1083, 1042, 912, 862, 823, 769, 705, 641, 528.

2-((5-Chloro-2-((4-(piperazin-1-yl)phenyl)amino)pyrimidin-4-yl)amino)-*N*-methylbenzamide (7)



tert-Butyl 4-(4-(5-chloro-4-(2-(methylcarbamoyl)phenylamino)pyrimidin-2-ylamino)phenyl)piperazine-1-carboxylate (**S6**)

To a quartz walled Smith tube containing a magnetic stirrer bar was charged with 2-(2,5-dichloropyrimidin-4-ylamino)-*N*-methylbenzamide **10** (160 mg, 0.54 mmol), *tert*-butyl 4-(4-aminophenyl)piperazine-1-carboxylate **S5** (1 mL of a 0.3 M *n*-butanol solution; 0.3 mmol) and then *n*-butanol (2 mL). The mixture was heated in the microwave (Biotage) at 150 °C (200W) for 18 min. After cooling to room temperature, the solvent was removed *in vacuo*, and purified by flash chromatography (silica gel, 0:1 ⪡ 1:9 *v*/*v* methanol/dichloromethane gradient elution) and concentration of the relevant fractions (R_f = 0.2 in 5:95 *v*/*v* methanol/dichloromethane) gave the title compound (240 mg, 47%) as an off-white coloured solid (slow decomposition at 208 °C).

^{1}H NMR ($CDCl_3$ + d_4-MeOD, 400 MHz): 11.07 (1H, s), 8.66 (1H, d, J = 8.4 Hz), 7.48 – 7.43 (1H, dd, J = 7.8, 1.4 Hz), 7.43 – 7.41 (3H, m), 7.06 (1H, m), 6.90 (2H, d, J = 8.9 Hz), 6.85 (1H, s), 3.59 (4H, m), 3.98 (4H, m), 3.03 (3H, d, J = 4.9 Hz), 1.49 (9H, s); ^{13}C NMR ($CDCl_3$ + d_4-MeOD, 101 MHz): δ ^{13}C NMR ($CDCl_3$ + d_4-MeOD, 101 MHz): δ 169.9 (rotamer A), 169.6 (rotamer B), 158.1 (rotamer A+B), 155.8 (rotamer A+B), 155.0 (rotamer A+B), 154.3 (rotamer A+B), 147.4 (rotamer A+B), 139.4 (rotamer A+B), 132.7 (rotamer A+B), 131.7 (rotamer A+B), 126.9 (rotamer A+B), 122.4 (bs, rotamer A+B), 122.3 (rotamer A+B), 122.1 (2C, rotamer A+B), 121.8 (rotamer A) 121.7 (rotamer B), 117.6 (2C, rotamer A+B), 106.2 (rotamer A+B), 80.2 (rotamer A+B), 50.3 (2C, rotamer A+B), 44.2-43.1 (broad singlet, 2C, rotamer A+B), 28.5 (3C, rotamer A+B), 26.9 (rotamer A), 26.8 (rotamer B); Mass spectrum (ESI, +ve) 539 *m/z* [$(M + H)^+$, 23%], 538 (67), 198 (27), 152 (5), 126 (93), 85 (100); FTIR ν_{max} (cm^{-1}) 3374, 2923, 2854, 1682, 1601, 1562, 1515, 1448, 1416, 1228, 1161, 1081, 1048, 1024, 1001, 824, 759, 593, 531.

Batch Chemistry Approaches

tert-Butyl 4-(4-nitrophenyl)piperazine-1-carboxylate (**S4**)

To a magnetically stirred solution of mono-Boc protected piperazine (**S2**) (1.05 g, 5.62mmol) in DMSO (20 mL), maintained at 18 °C, was charged with potassium carbonate (1.17 g, 8.43 mmol) and 4-fluoronitrobenzene (0.91 g, 6.47 mmol). The ensuing slurry was stirred and heated to 80 °C for 19 h. After cooling to 18 °C, the reaction mixture was dilute with water (1 × 200 mL) and, then, extracted with ethyl acetate (4 × 20 mL). The combined organic extracts were washed with water (2 × 100 mL), brine (1 × 100 mL), dried ($MgSO_4$), filtered and, then concentrated under reduced pressure to afford a dark orange solid. Subjection of this material to flash chromatography (silica, 1:9 ⪡ 3:1 *v*/*v* ethyl acetate/hexane gradient elution) and concentration of the relevant fractions (R_f = 0.8 in 1:3 *v*/*v* ethyl acetate/hexane) gave the title compound (1.56 g, 90%) as an orange solid.

***tert*-Butyl 4-(4-aminophenyl)piperazine-1-carboxylate (S5)**

To a magnetically stirred solution of *tert*-butyl 4-(4-nitrophenyl)piperazine-1-carboxylate (**S4**) (1.46 g, 4.75 mmol) in methanol, maintained at 0 °C, was charged with, in this order, 10% *w*/*w* palladium on carbon (146 mg, 10%. wt), sodium borohydride (720 mg, 19 mmol) and aqueous sodium hydroxide (1 drop of a 1 M solution). The resulting black slurry was stirred at 18 °C for 2 h, before filtering through a pad of Celite that was then washed with ethanol. The combined filtrates were concentrated under reduced pressure to afford a reddish-purple oil (1.25 g, 96 %).

2-amino-*N*-methylbenzamide (16)

A flask containing isatoic anhydride (1.0 g, 6.1 mmol), maintained at 0 °C, was charged, dropwise, with methylamine (10 ml of 40% *w*/*v* aqueous solution). The ensuing mixture was stirred vigorously for 2 hours at room temperature before it was dilute with ethyl acetate (1×100 ml). The separated aqueous layer was extracted further with ethyl acetate (4×100 ml), and the combined organic extracts were washed with water (1 × 200 ml), brine (2 × 200 mL), dried ($MgSO_4$), filtered and then concentrated under reduce pressure to afford the title compound (749 mg, 81%), as a creamy solid.

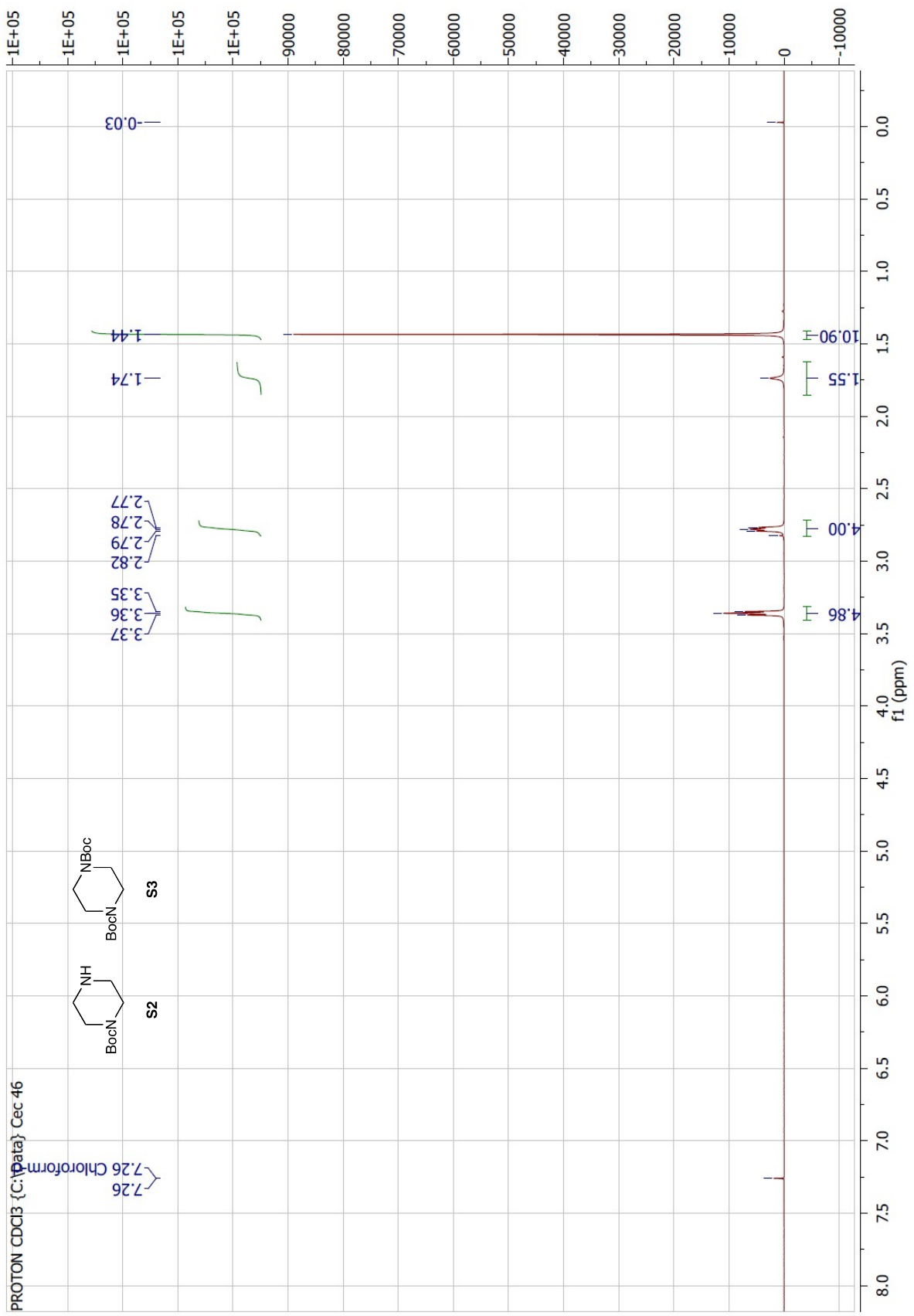
2-(2,5-dichloropyrimidin-4-ylamino)-*N*-methylbenzamide (10)

To a magnetically stirred solution of 2-amino-*N*-benzeneamide (**11**) (10.17 g, 37.0 mmol) in *iso*-propanol (200 mL), maintained at 18 °C, charged with 2,4,5 trichloropyrimidine (7.4 ml, 40.0 mmol) and DIPEA (9.77 ml, 54.9 mmol). The ensuing mixture was heated to reflux and at this temperature for 19 h. After cooling to room temperature, the resulting slurry was filtered and the filter cake was washed with cold *iso*-propanol (2 × 20 mL) and ether (2 × 20 mL). The filter cake was dried, under vacuum, to afford the title compound (12.6 g, 67 %) as a creamy coloured fine powder.

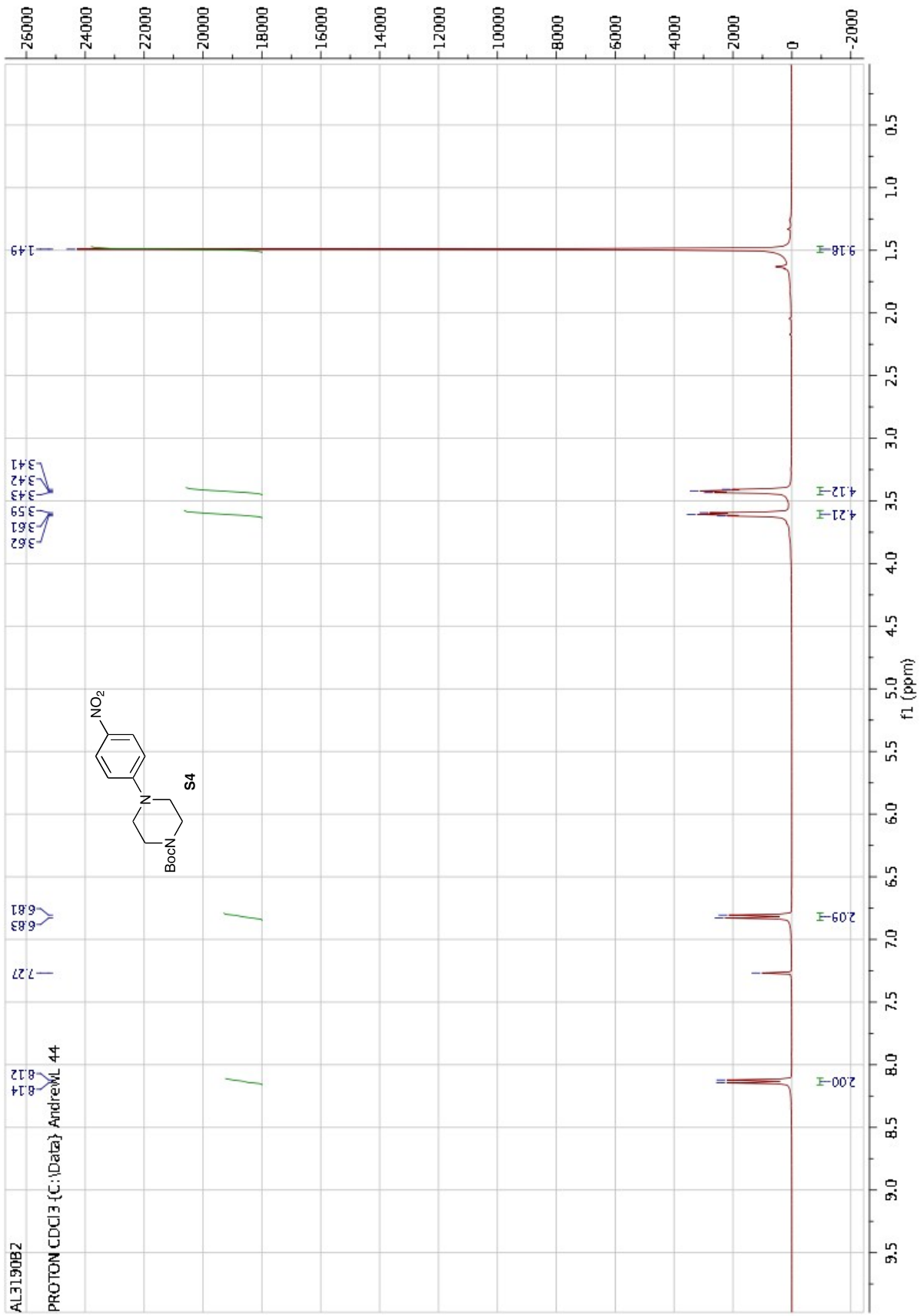
2-((5-chloro-2-((4-(piperazin-1-yl)phenyl)amino)pyrimidin-4-yl)amino)-*N*-methylbenzamide (7)

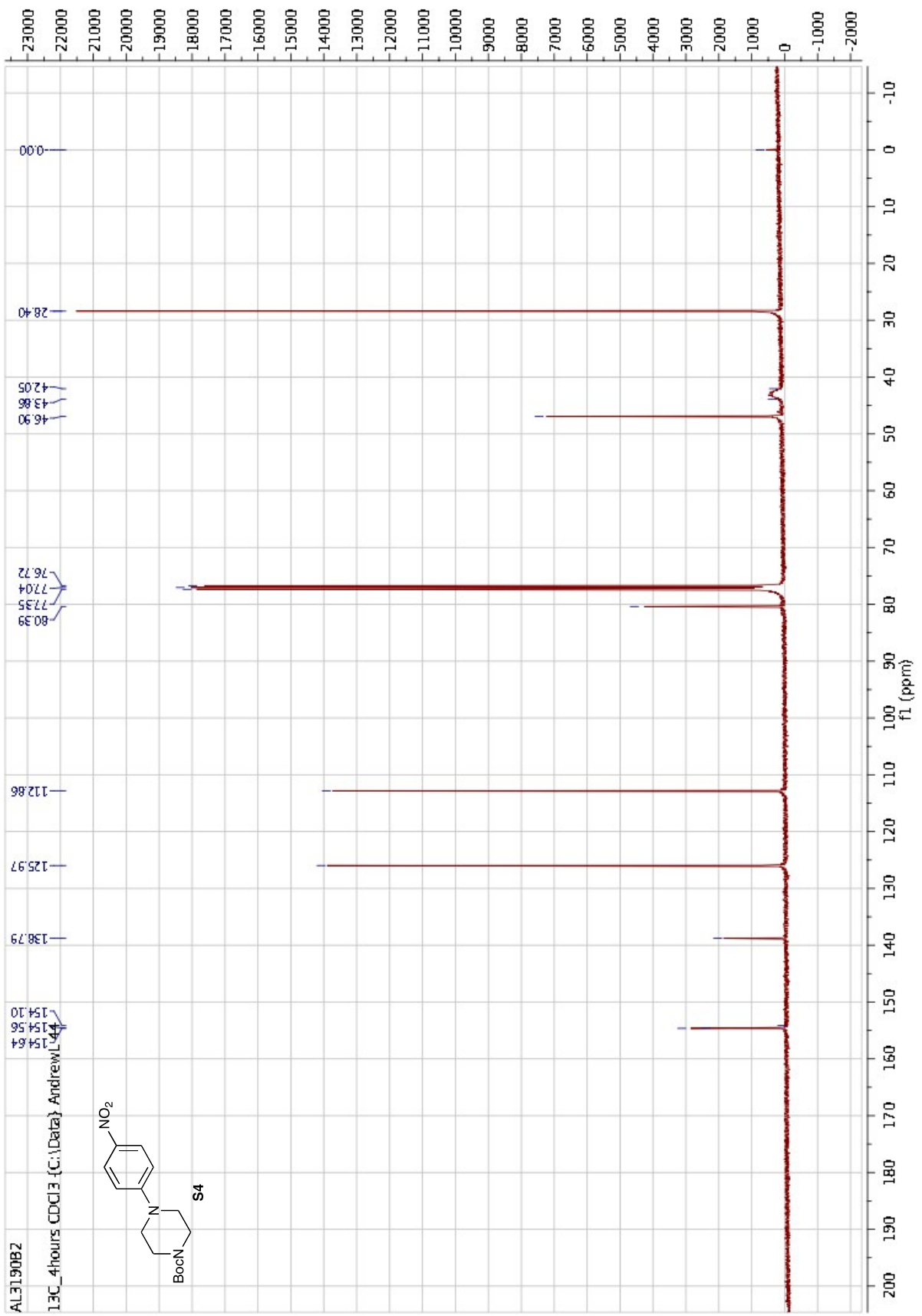
To a flask containing a solution of Boc protected piperazine (56.7 mg, 0.1 mmol) in dichloromethane (10 mL), maintained at 18 °C, was charged, dropwise, with TFA (2 mL). *–CAUTION: CO_2 evolution–* The ensuing mixture was sonicated for 0.5 h and, then, concentrated under reduced pressure to afford a yellow gum. This material was diluted with saturated aqueous sodium bicarbonate (1×20 mL) and, then, extracted with ethyl acetate (3 × 20 mL). The combined organic extracts were washed with water (1 × 50 mL), brine (1 × 50 mL), dried ($MgSO_4$), filtered and, then, concentrated to afford a light orange solid. Subjection of this material to flash chromatography (Grace Reveleris® Amino Flash Cartridges, 0:1 ⩤ 1:5 *v*/*v* methanol/dichloromethane) and concentration of the relevant fractions (R_f = 0.1 in 1:9 *v*/*v* methanol/dichloromethane) gave the title compound (8 mg, 18%) as a pale solid.

[1]H spectra of products **S2** and **S3**

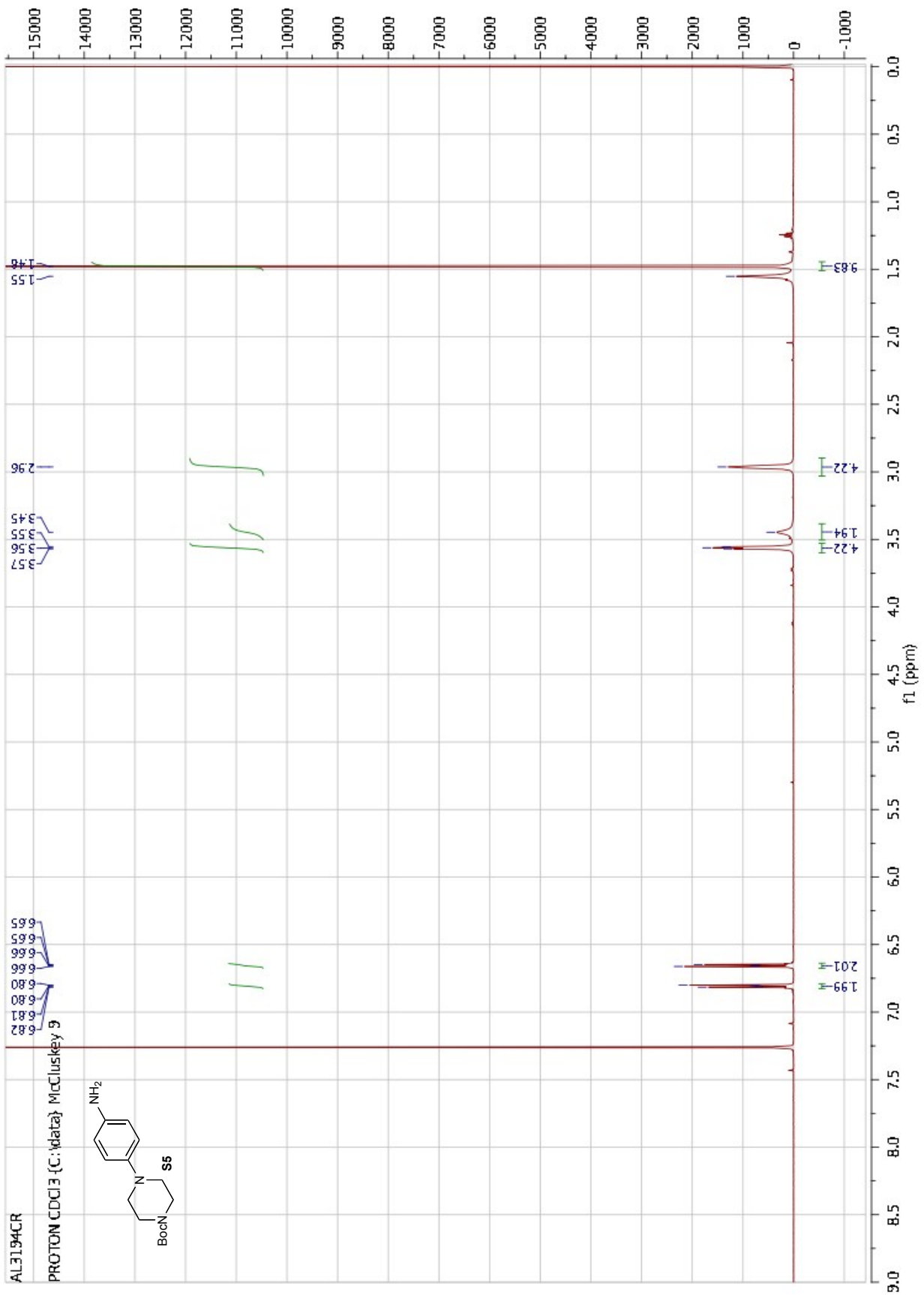


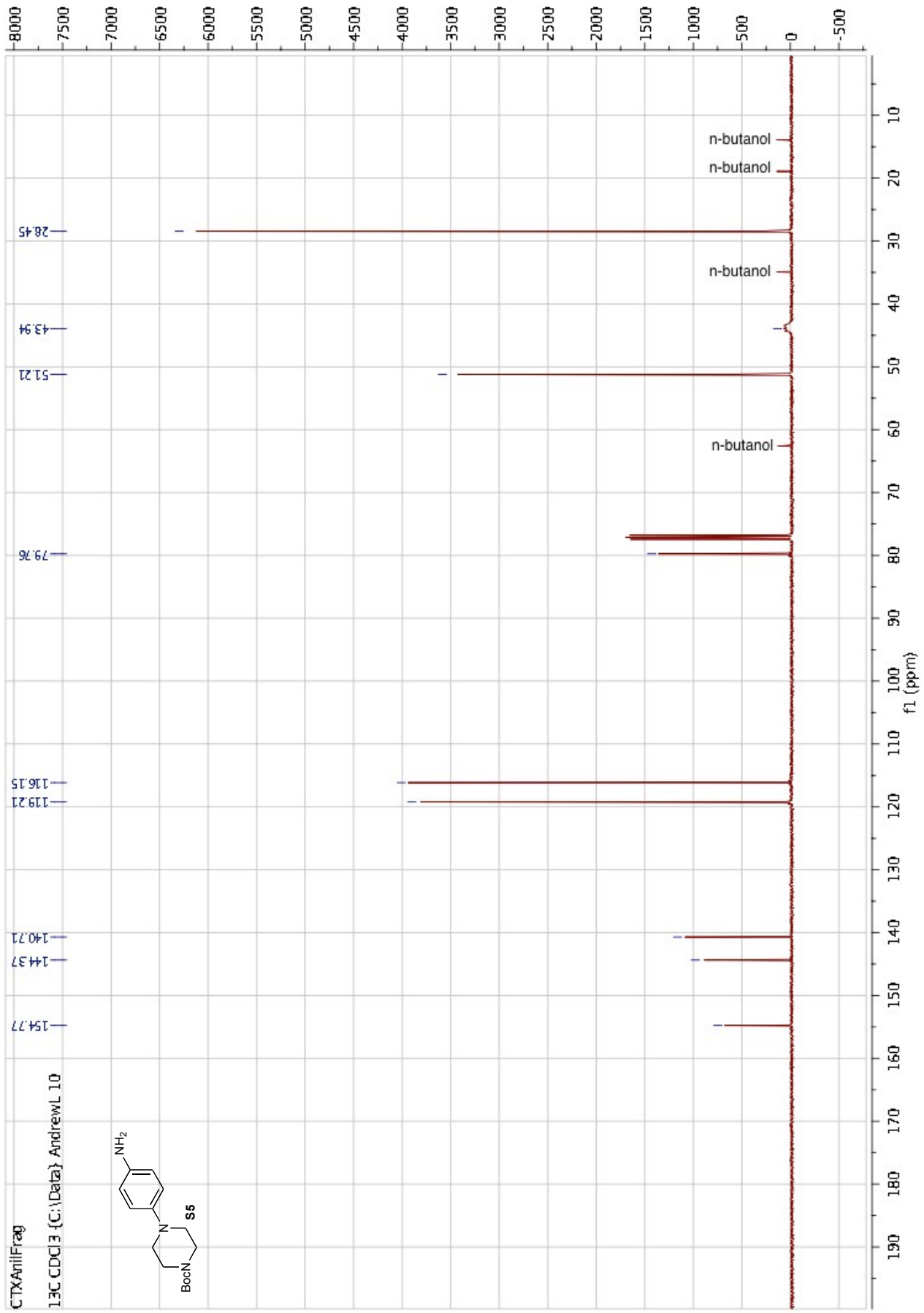
^{1}H and ^{13}C NMR spectra of product **S4**



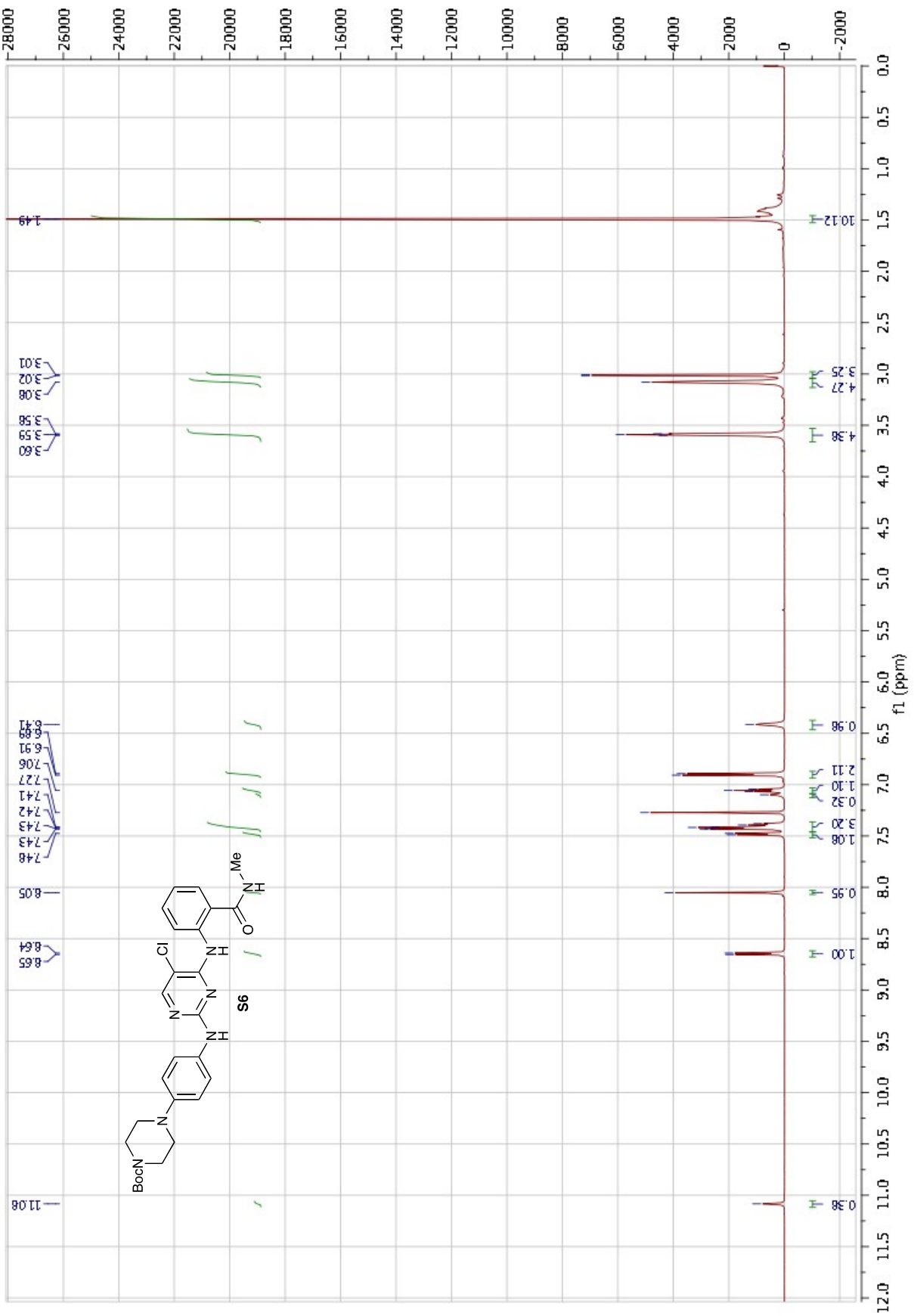

AL3190B2
13C_4hours CDCl3 {C:\Data} AndrewL 44
154.64
154.56
154.10
138.79
125.97
112.86
80.39
77.35
77.04
76.72
46.90
43.86
42.05
28.40
0.00
NO2
N
BocN
S4
f1 (ppm)

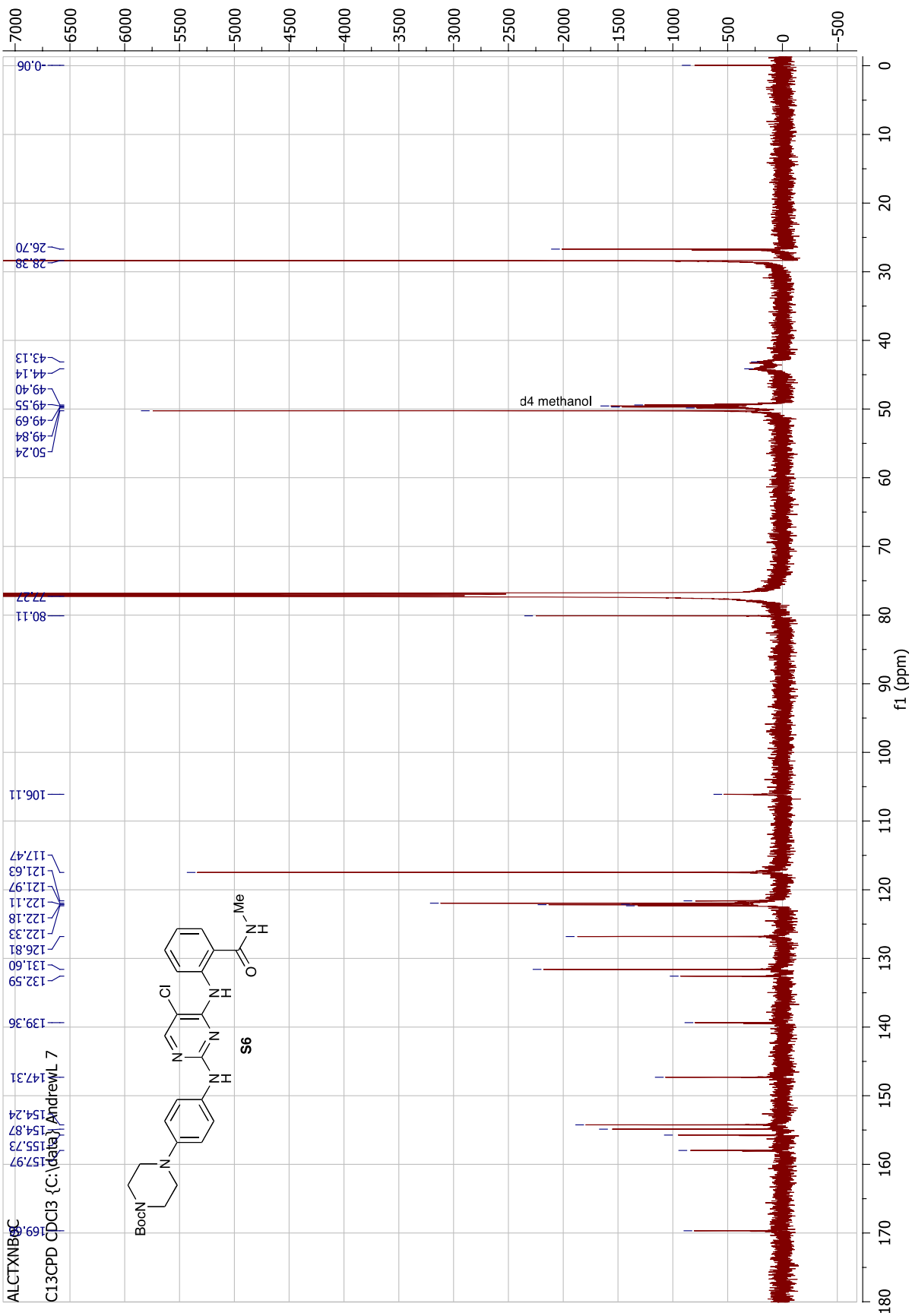
^{1}H and ^{13}C NMR spectra of product **S5**



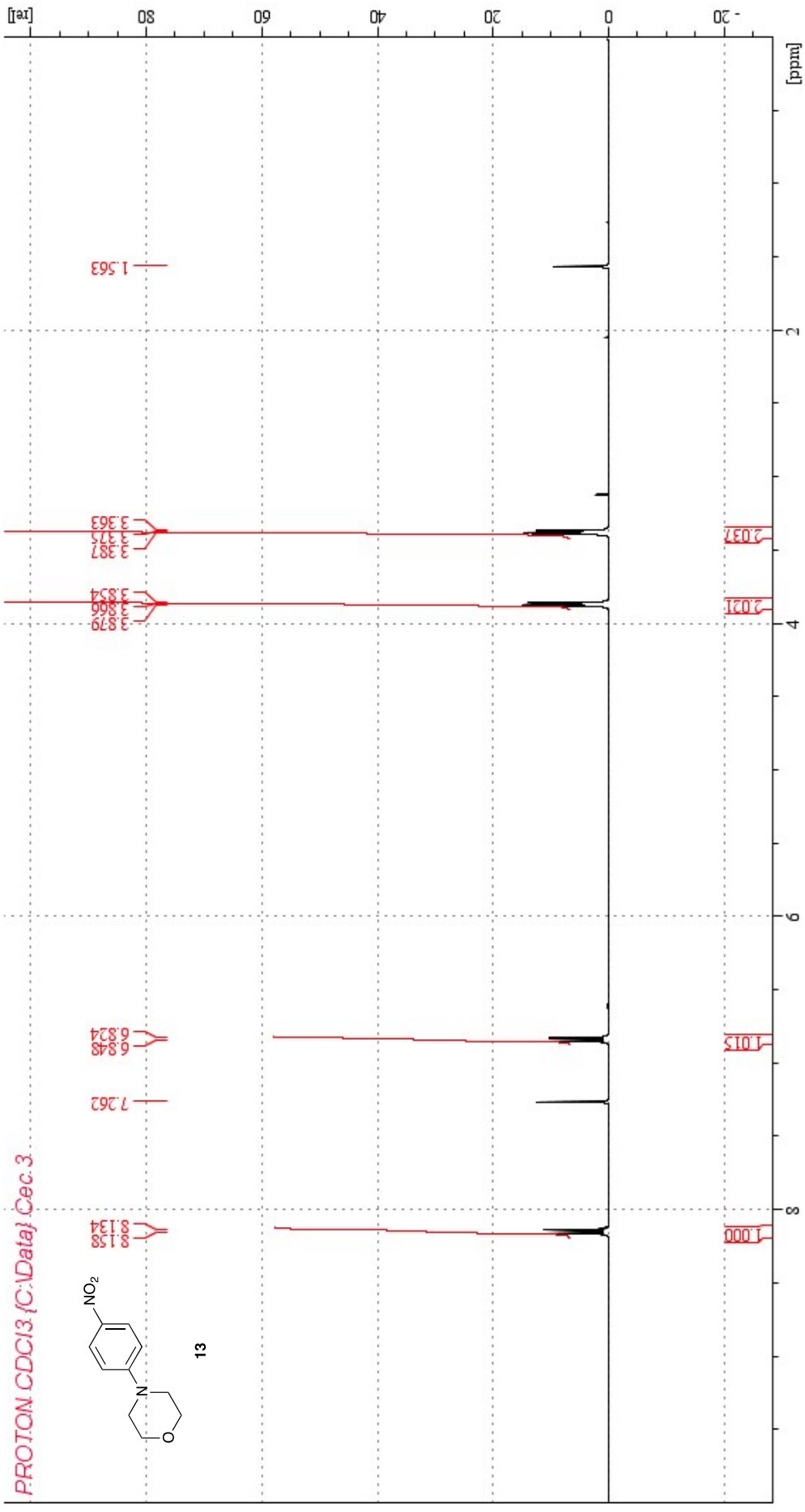

CTXAnilFrag
13C CDCl3 {C:\Data} AndrewL 10
28.45
43.94
51.21
79.76
116.15
119.21
140.71
144.37
154.77
n-butanol
n-butanol
n-butanol
f1 (ppm)
S5
BocN
NH2

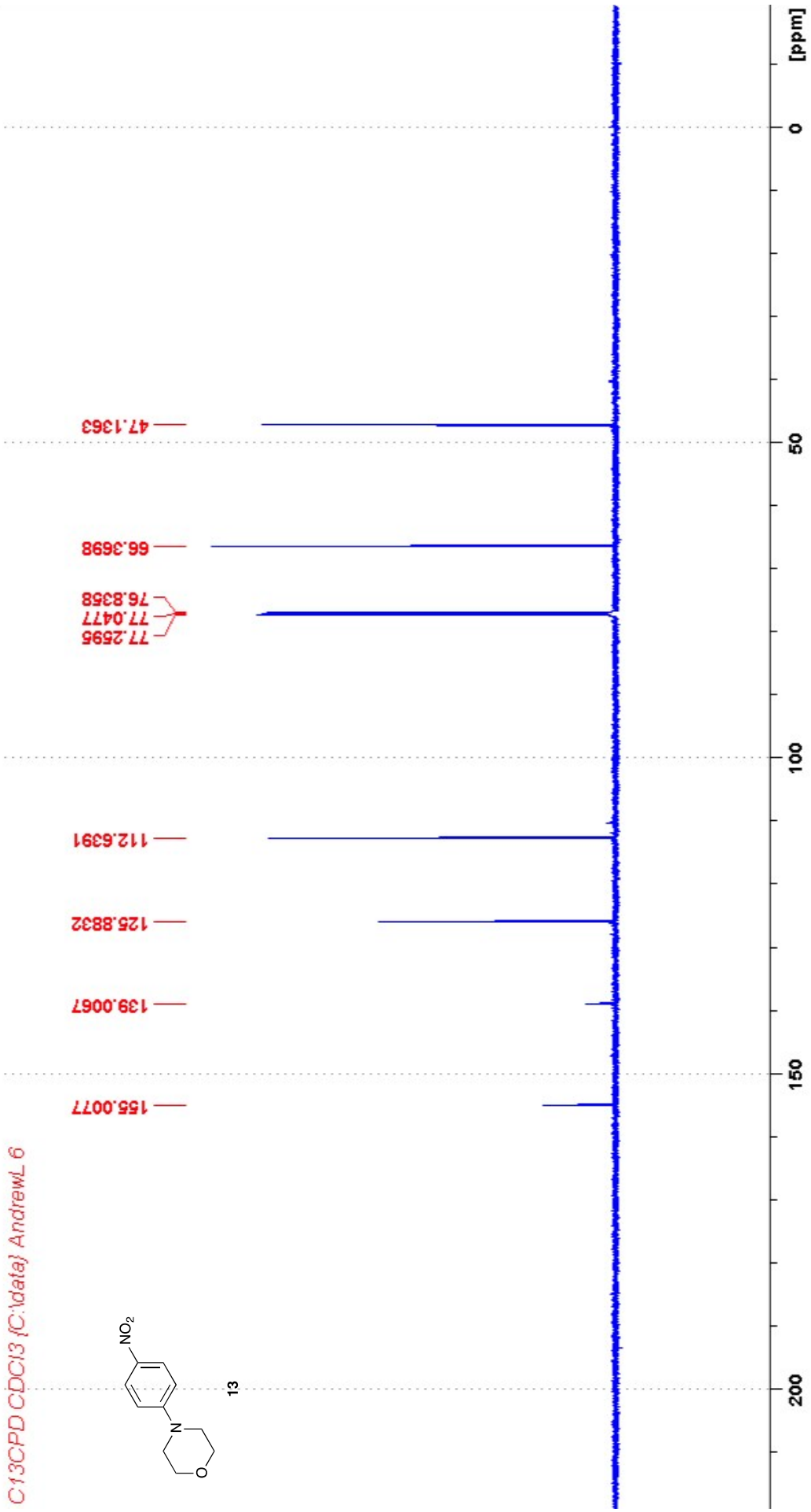
^{1}H and ^{13}C NMR spectra of product **S6**.



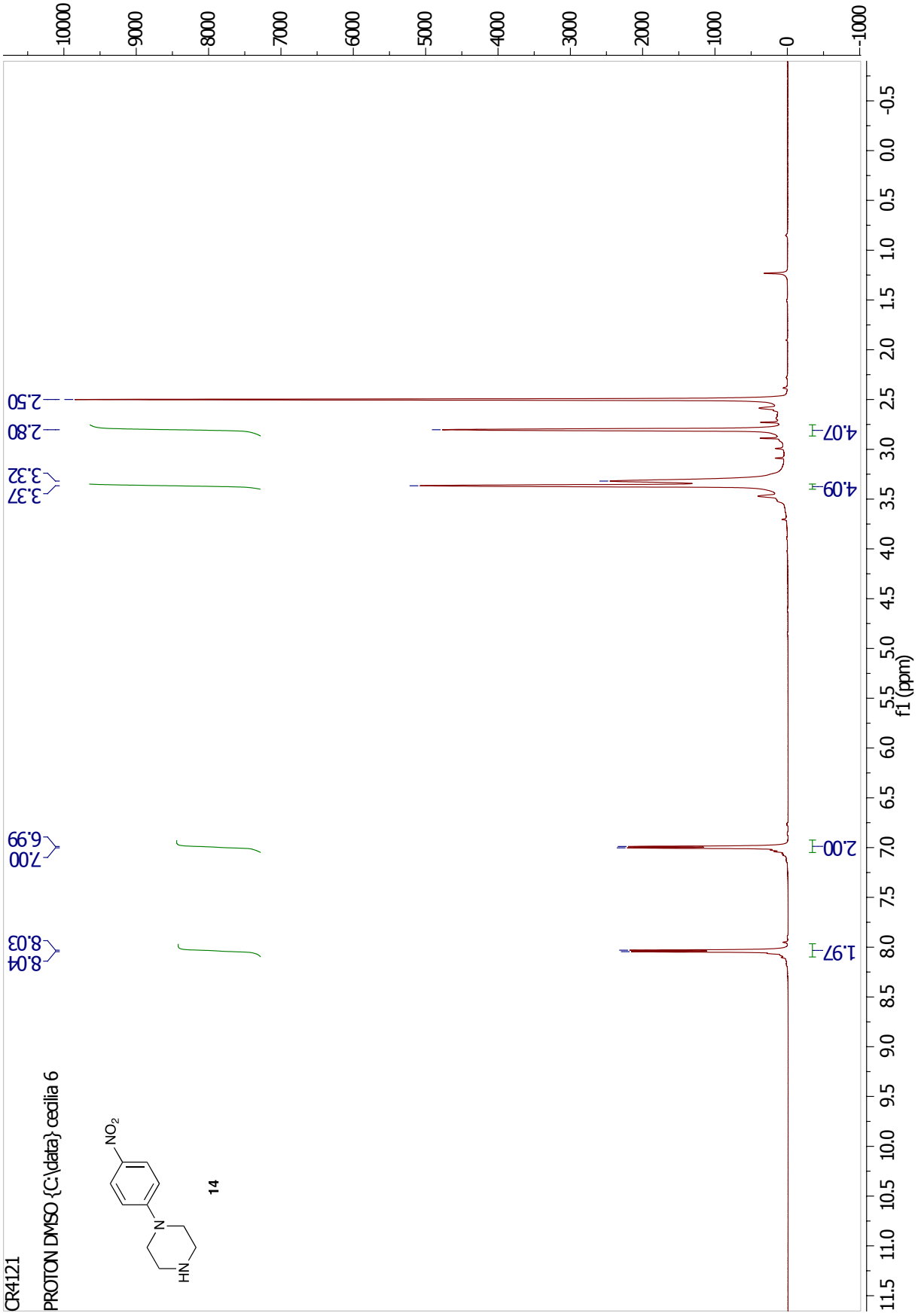

ALCTXNBOC
C13CPD CDCl3 {C:\data} AndrewL 7
d4 methanol
S6
Cl
BocN
Me
-0.06
26.70
28.38
43.13
44.14
49.40
49.55
49.69
49.84
50.24
77.27
80.11
106.11
117.47
121.63
121.97
122.11
122.18
122.33
126.81
131.60
132.59
139.36
147.31
154.24
154.87
155.73
157.97
169.68
f1 (ppm)

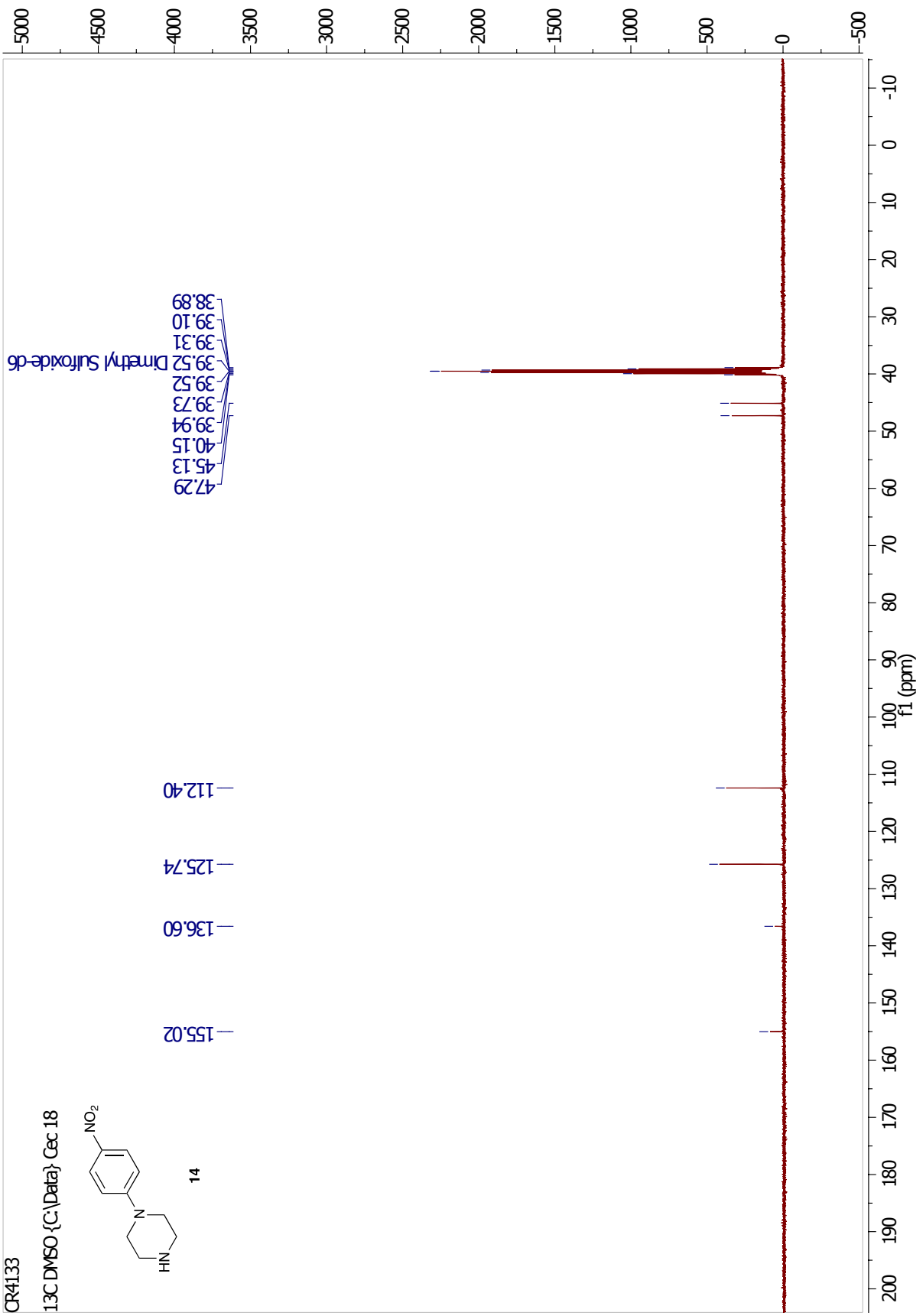
^{1}H and ^{13}C NMR spectra of product **13**



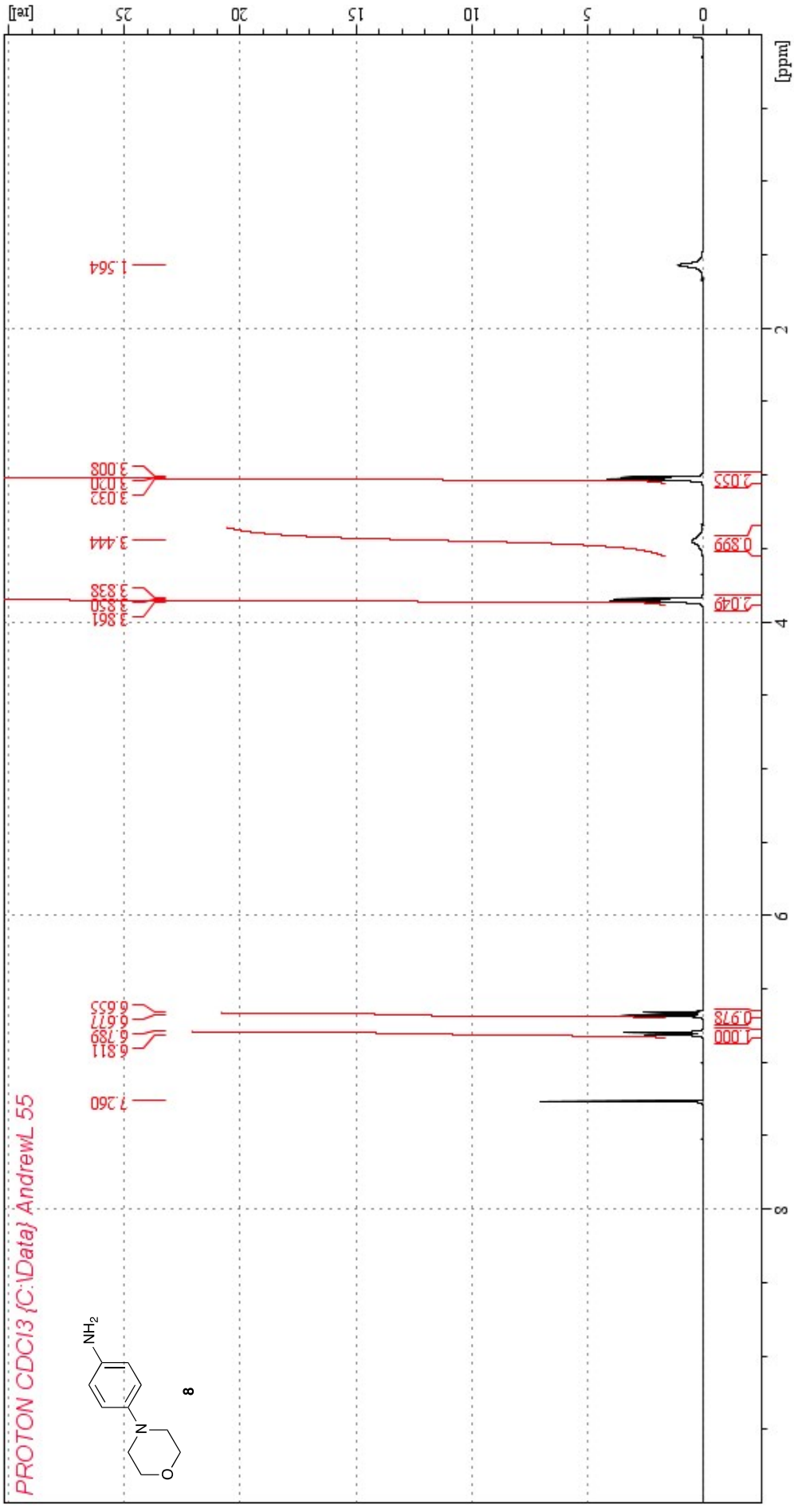

C13CPD CDCl3 {C:\data} AndrewL 6
155.0077
139.0067
125.8832
112.6391
77.2595
77.0477
76.8358
66.3698
47.1363
[ppm]
0
50
100
150
200
13
NO2
N
O

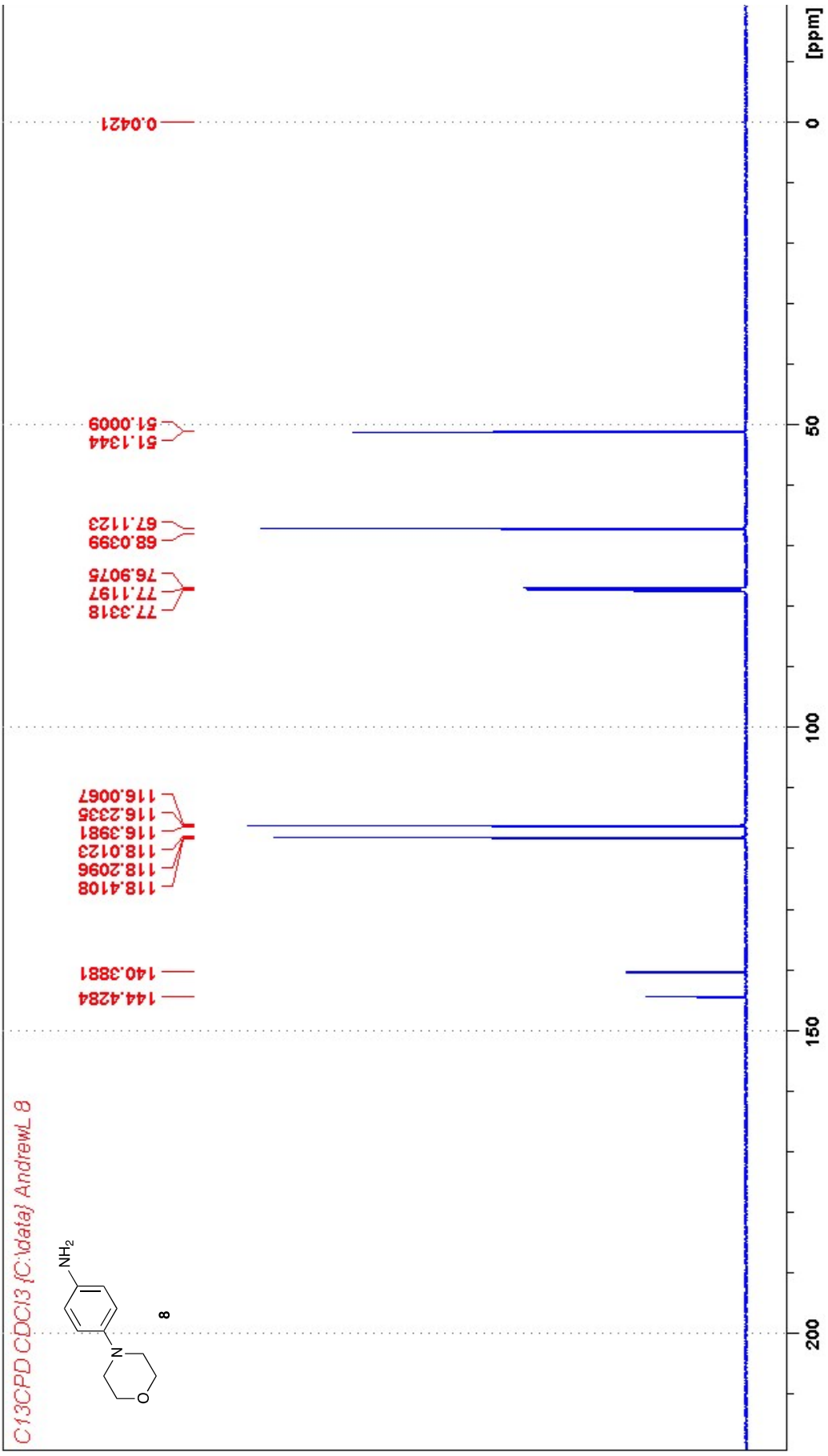
^{1}H and ^{13}C NMR spectra of product **14**



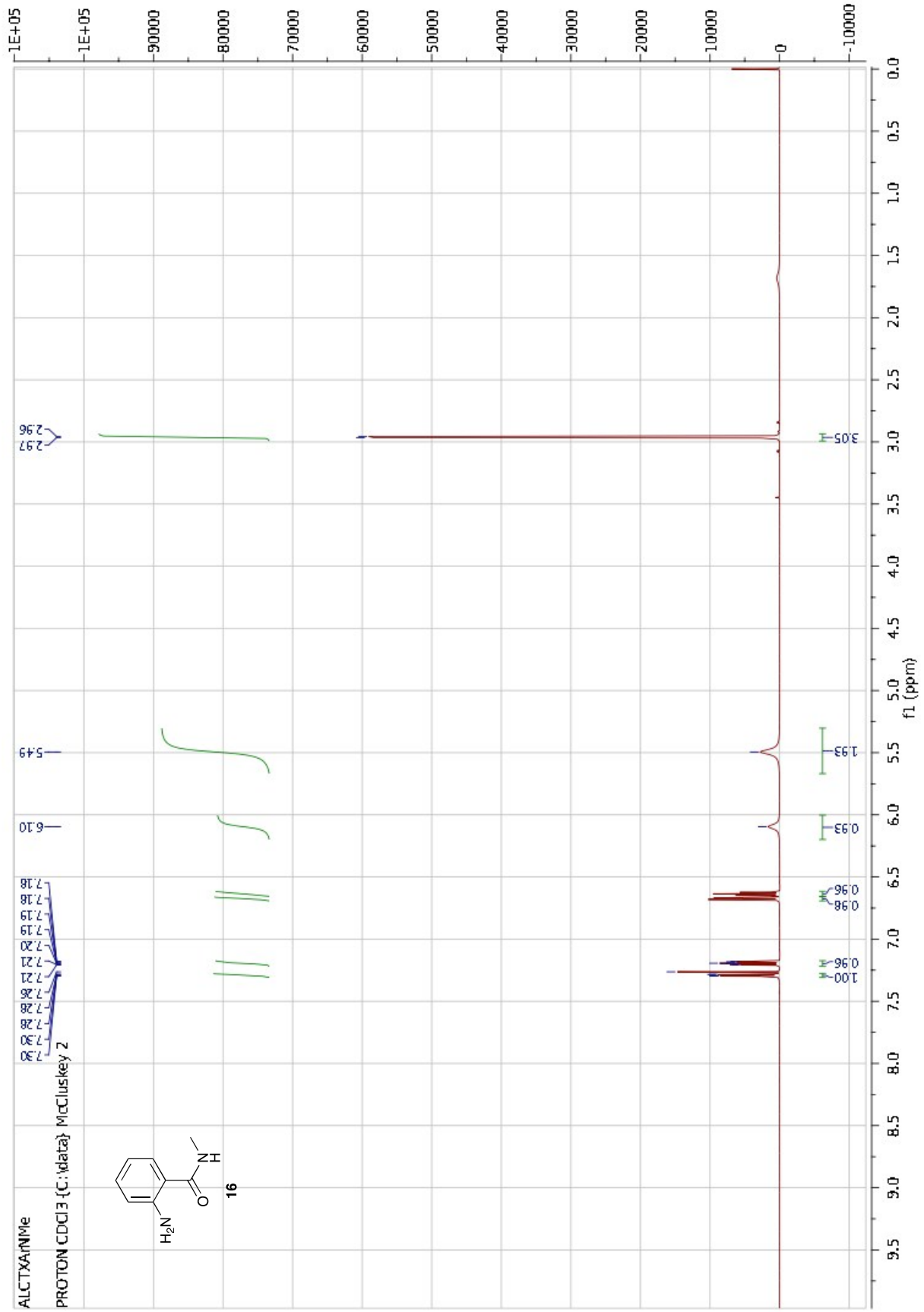

CR4133
13C DMSO {C:\Data} Cec 18
14
155.02
136.60
125.74
112.40
47.29
45.13
40.15
39.94
39.73
39.52
39.52 Dimethyl Sulfoxide-d6
39.31
39.10
38.89
f1 (ppm)

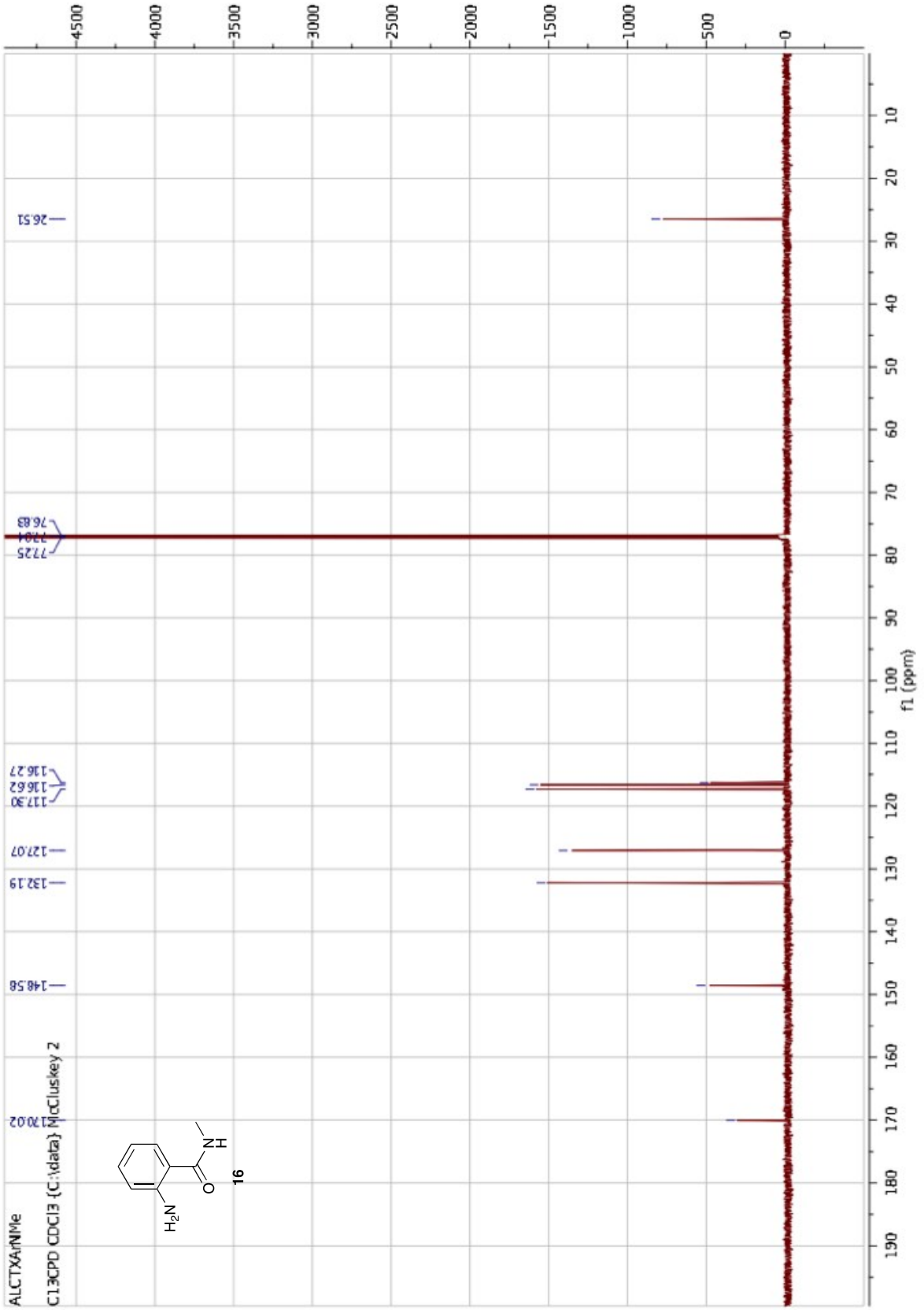
^{1}H and ^{13}C NMR spectra of product **8**



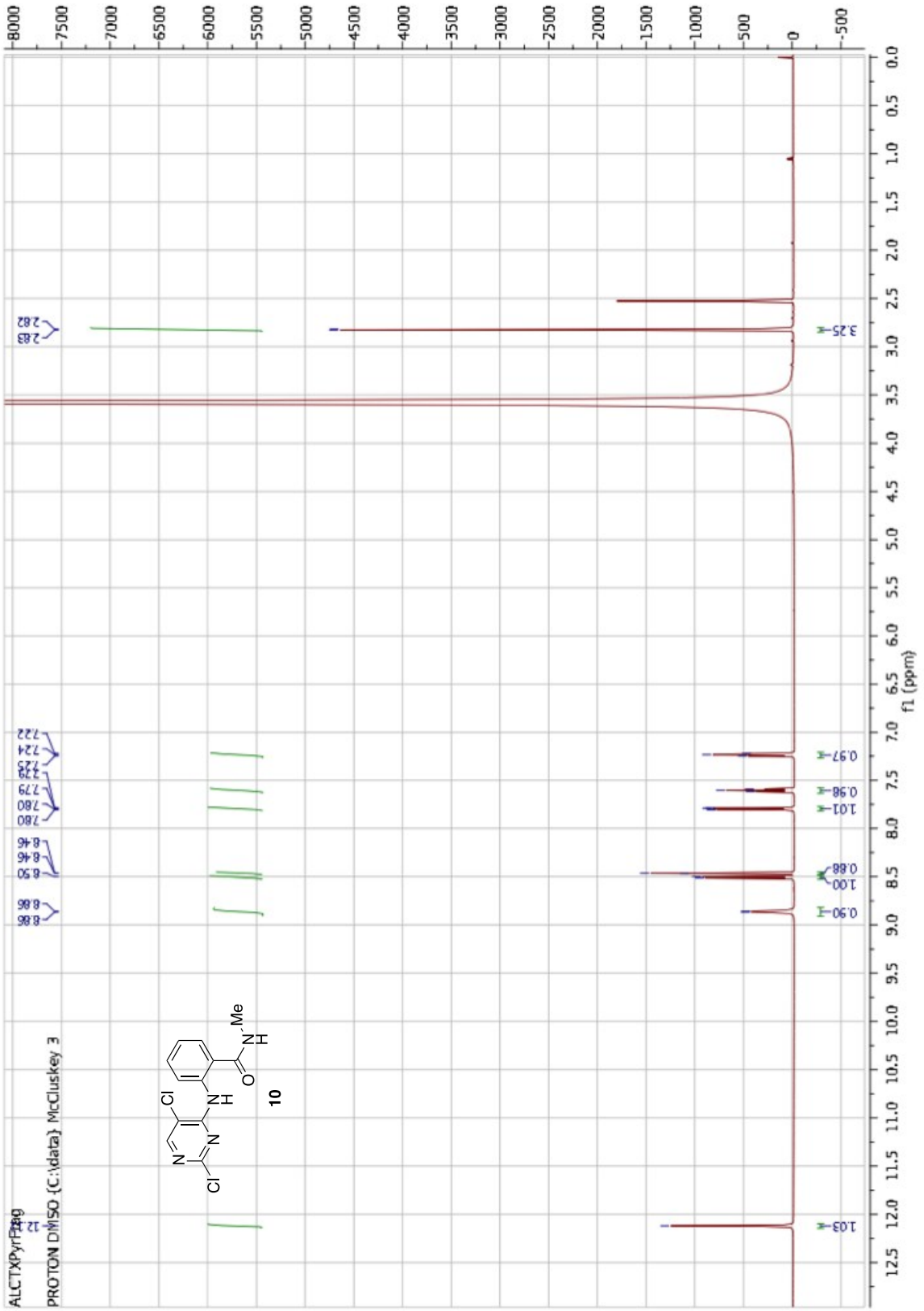

C13CPD CDCl3 (C:\data) AndrewL 8
8
NH2
N
O
0.0421
51.0009
51.1344
67.1123
68.0399
76.9075
77.1197
77.3318
116.0067
116.2335
116.3981
118.0123
118.2096
118.4108
140.3881
144.4284
200
150
100
50
0
[ppm]

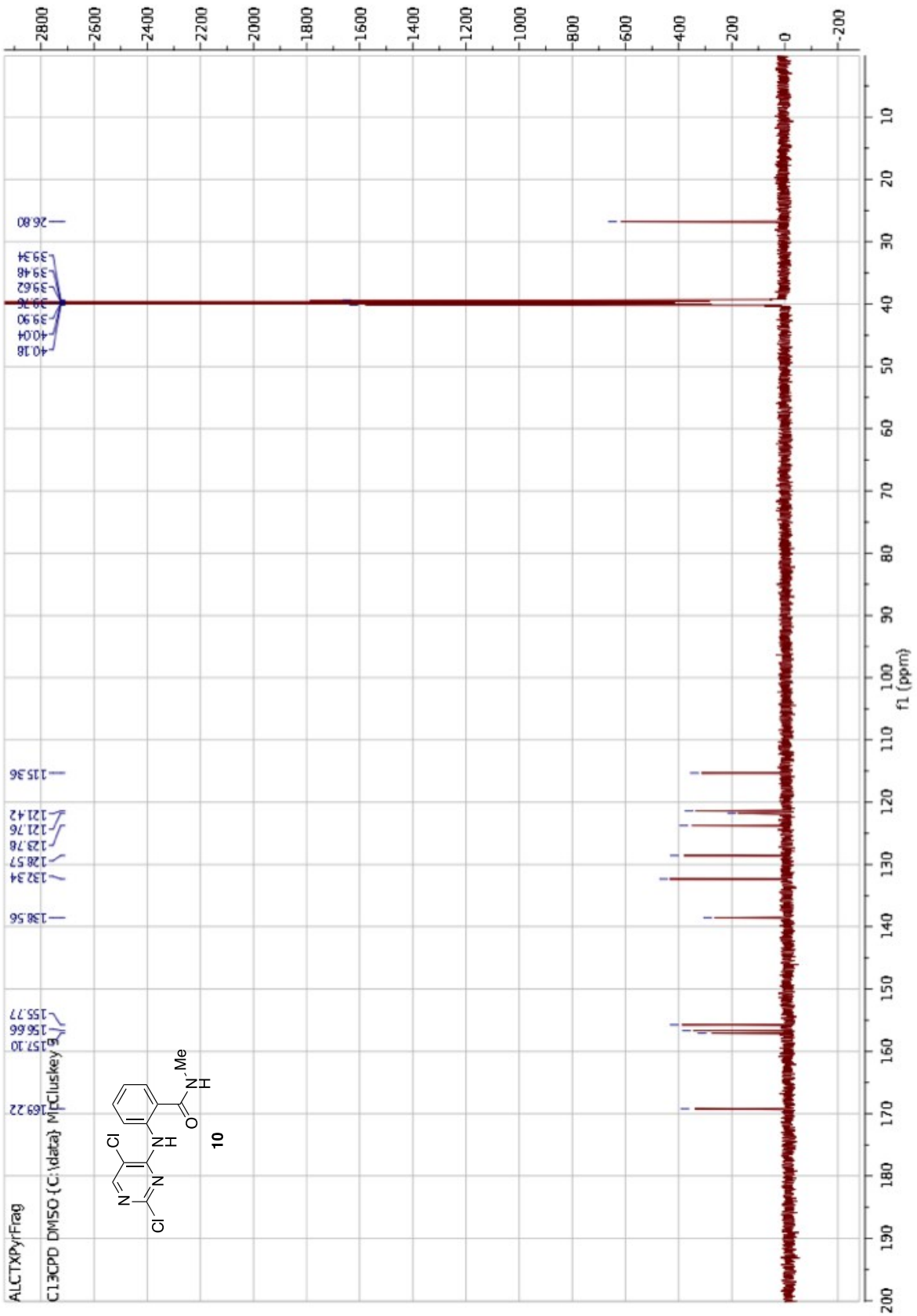
^{1}H and ^{13}C NMR spectra of product **16**



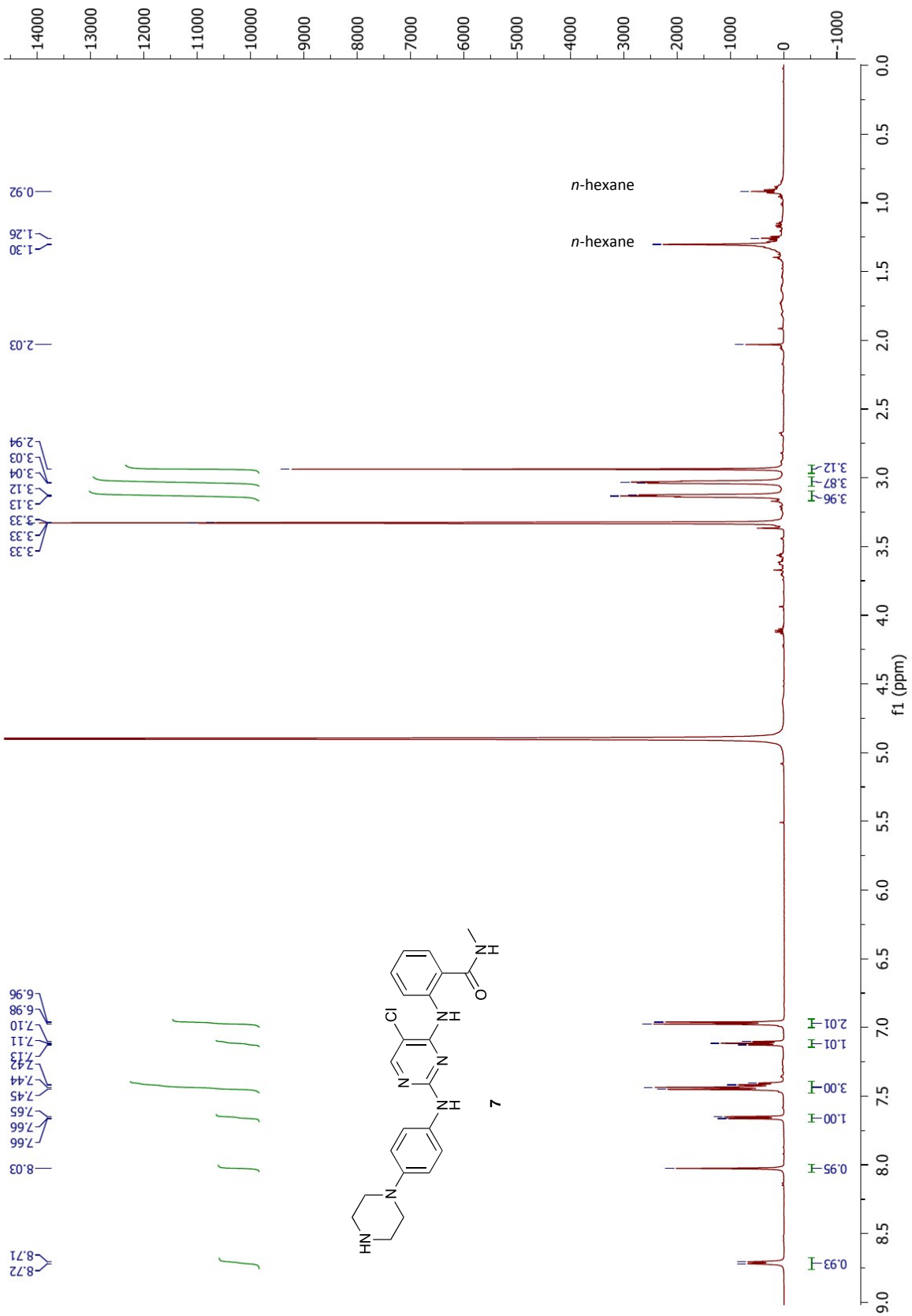

ALCTXArNMe
C13CPD CDCl3 {C:\data} McCluskey 2
170.02
148.58
132.19
127.07
117.30
116.62
116.27
77.25
77.04
76.83
26.51
16
H2N
O
N
H
f1 (ppm)

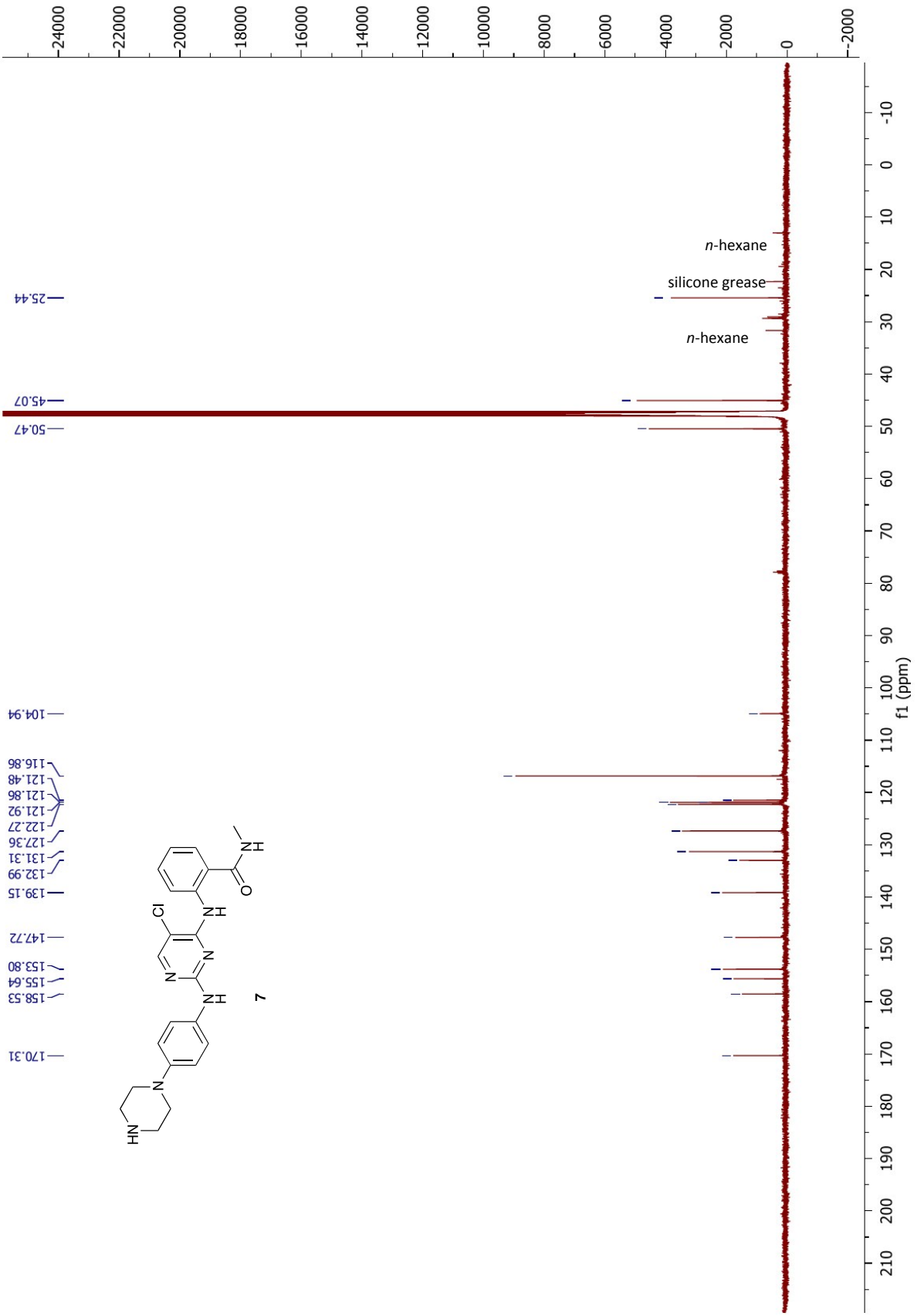
^{1}H and ^{13}C NMR spectra of products **10**



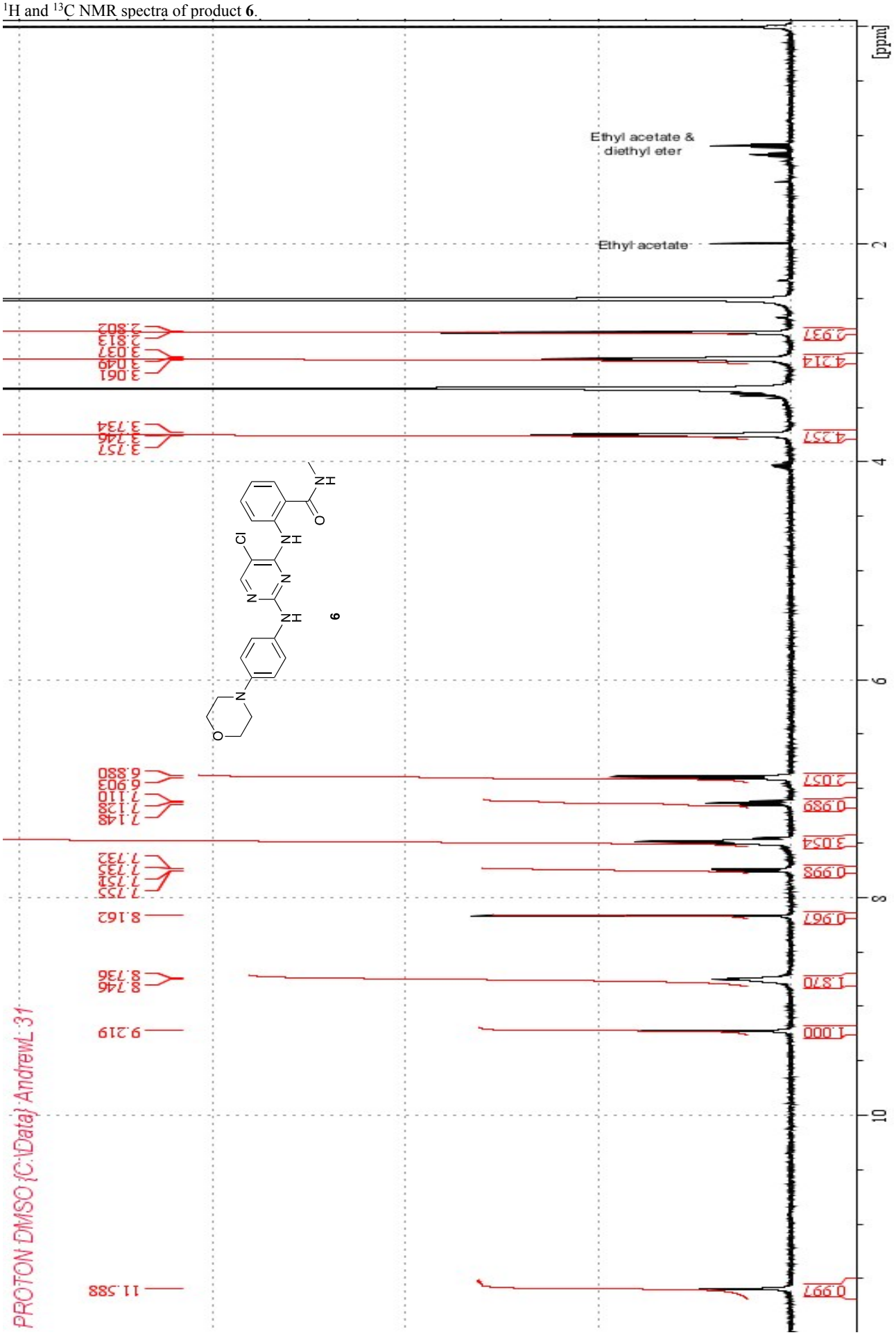

ALCTXPyrFrag
C13CPD DMSO (C:\data) MCcluskey 9
169.22
157.10
156.66
155.77
138.56
132.34
128.57
123.76
121.76
121.42
115.36
40.18
40.04
39.90
39.76
39.62
39.48
39.34
26.80
f1 (ppm)
10

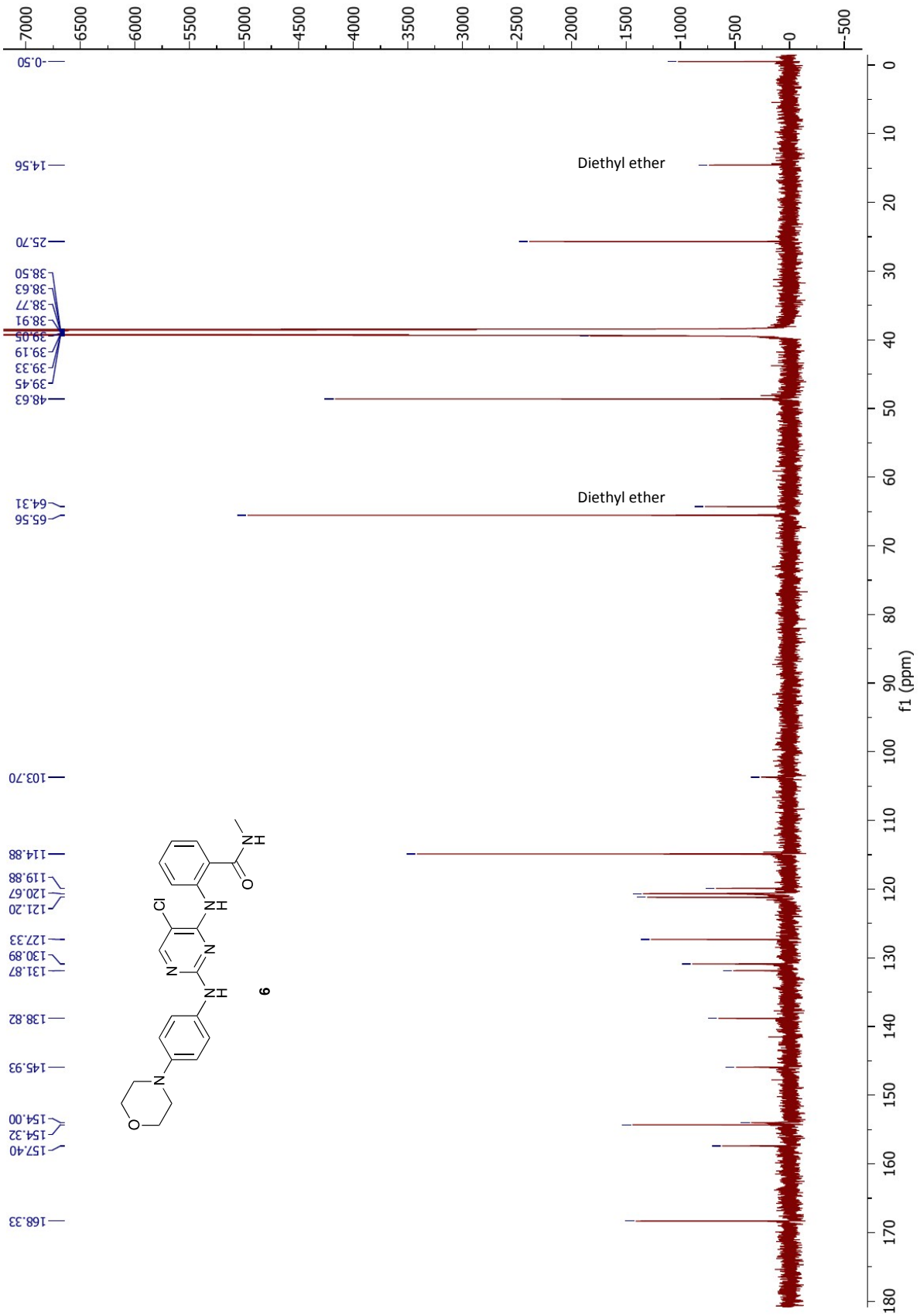
^{1}H and ^{13}C NMR spectra of product **7**.



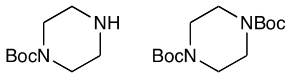

f1 (ppm)
25.44
45.07
50.47
104.94
116.86
121.48
121.86
121.92
122.27
127.36
131.31
132.99
139.15
147.72
153.80
155.64
158.53
170.31
n-hexane
silicone grease
n-hexane
7

^{1}H and ^{13}C NMR spectra of product **6**.




Diethyl ether
Diethyl ether
f1 (ppm)
6

GC Mass Spectrum of **S2** and **S3**

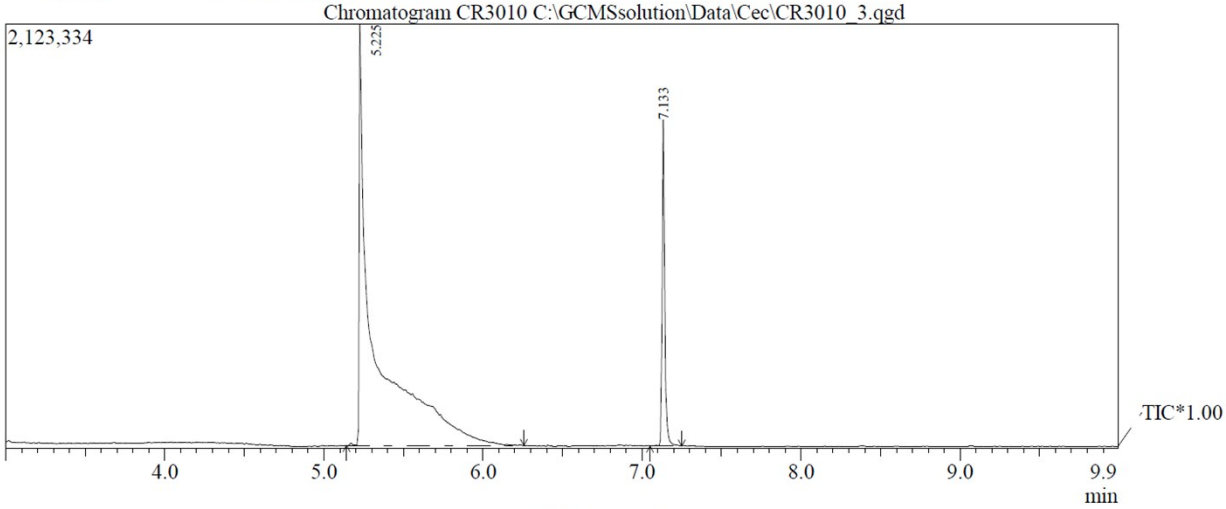


S2 **S3**

Sample Information

Analyzed by	: Admin
Analyzed	: 2/3/2014 10:37:28 AM
Sample Type	: Unknown
Level #	: 1
Sample Name	: CR3010
Sample ID	: CR3010
IS Amount	: [1]=1.000
Sample Amount	: 1.000
Dilution Factor	: 1.000
Vial #	: 15
Injection Volume	: 1.000
Data File	: C:\GCMSsolution\Data\Cec\CR3010_3.qgd
Org Data File	: C:\GCMSsolution\Data\Cec\CR3010_3.qgd
Method File	: C:\GCMSsolution\Data\Project1\Snar by flow high split.qgm
Org Method File	: C:\GCMSsolution\Data\Project1\Snar by flow high split.qgm
Report File	:
Tuning File	: C:\GCMSsolution\System\Tune1_Default.qgt
Modified by	: Admin
Modified	: 2/5/2014 7:06:45 AM

Chromatogram CR3010 C:\GCMSsolution\Data\Cec\CR3010_3.qgd

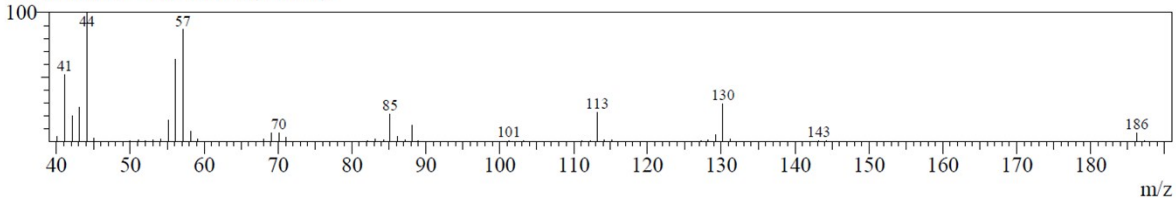


Peak Report TIC

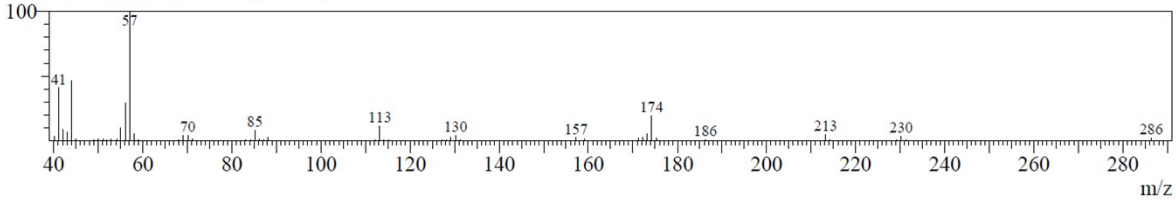
Peak#	R.Time	I.Time	F.Time	Area	Area%	Height	Height%	A/H	Mark	Name
1	5.225	5.142	6.258	13599204	87.96	2108819	56.36	6.45	MI	
2	7.133	7.050	7.250	1861610	12.04	1632630	43.64	1.14	MI	
				15460813	100.00	3741449	100.00			

Spectrum

Peak#:1 R.Time:5.2(Scan#:268)
MassPeaks:44 BasePeak:44(408553)



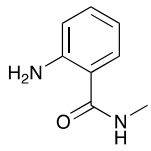
Peak#:2 R.Time:7.1(Scan#:497)
MassPeaks:50 BasePeak:57(478673)



GC Mass Spectrum of **16**.

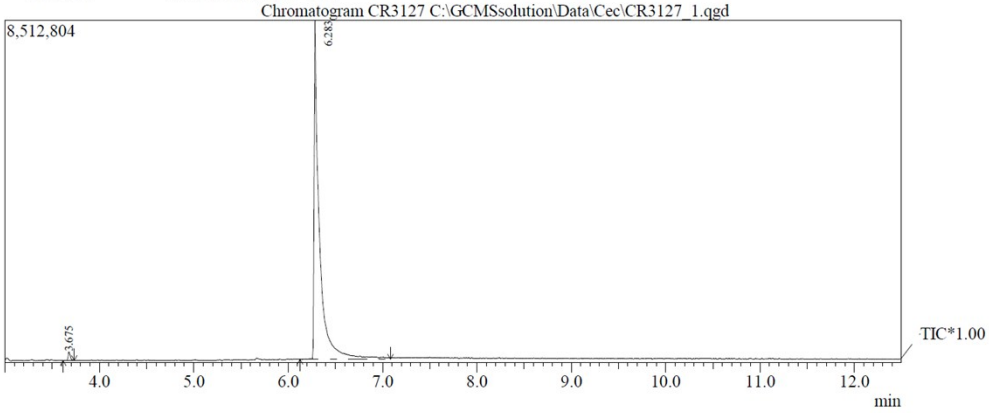
Sample Information

Analyzed by	: Admin
Analyzed	: 7/29/2014 10:19:26 AM
Sample Type	: Unknown
Level #	: 1
Sample Name	: CR3127
Sample ID	: CR3127
IS Amount	: [1]=1.000
Sample Amount	: 1.000
Dilution Factor	: 1.000
Vial #	: 2
Injection Volume	: 1.000
Data File	: C:\GCMSsolution\Data\Cec\CR3127_1.qgd
Org Data File	: C:\GCMSsolution\Data\Cec\CR3127_1.qgd
Method File	: C:\GCMSsolution\Data\Cec\Ellipitcine flow 1.qgm
Org Method File	: C:\GCMSsolution\Data\Cec\Ellipitcine flow 1.qgm
Report File	:
Tuning File	: C:\GCMSsolution\System\Tune1_Default.qgt
Modified by	: Admin
Modified	: 7/29/2014 12:00:54 PM



16

Chromatogram CR3127 C:\GCMSsolution\Data\Cec\CR3127_1.qgd

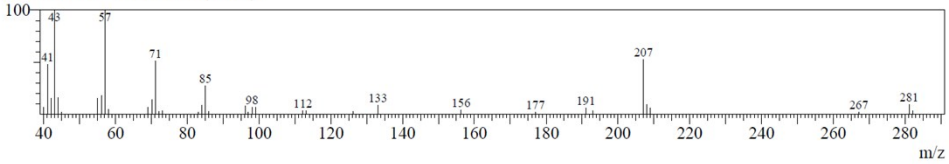


Peak Report TIC

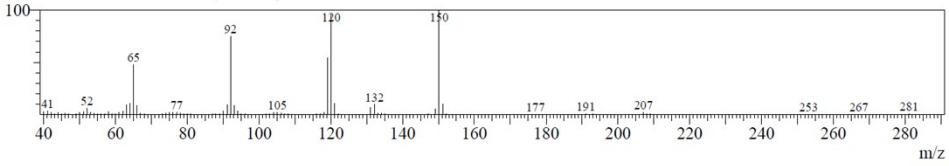
Peak#	R.Time	I.Time	F.Time	Area	Area%	Height	Height%	A/H	Mark	Name
1	3.675	3.617	3.733	338967	1.04	210189	2.43	1.61	MI	
2	6.283	6.125	7.083	32404066	98.96	8426677	97.57	3.85	MI	
				32743033	100.00	8636866	100.00			

Spectrum

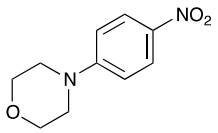
Peak#:1 R.Time:3.7(Scan#:82)
MassPeaks:37 BasePeak:57(45828)



Peak#:2 R.Time:6.3(Scan#:395)
MassPeaks:86 BasePeak:150(1603350)



GC Mass Spectrum **13**.

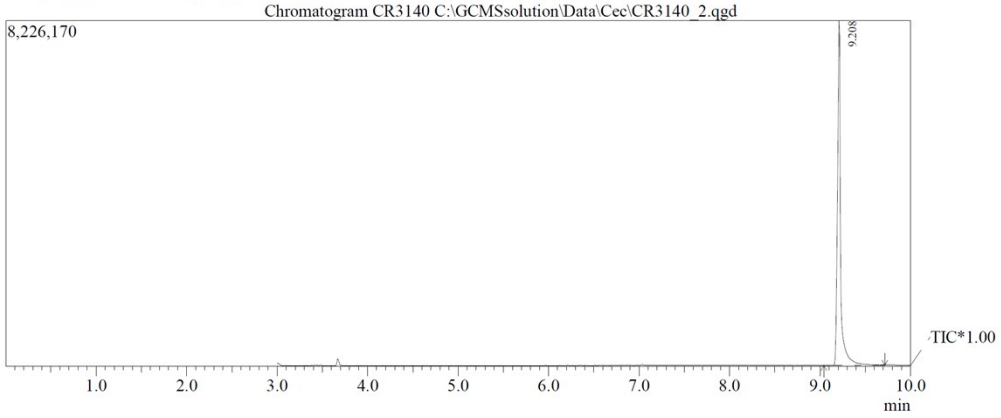


13

Sample Information

Analyzed by	: Admin
Analyzed	: 8/21/2007 3:26:33 AM
Sample Type	: Unknown
Level #	: 1
Sample Name	: CR3140
Sample ID	:
IS Amount	: [1]=1.000
Sample Amount	: 1.000
Dilution Factor	: 1.000
Vial #	: 17
Injection Volume	: 1.000
Data File	: C:\GCMSsolution\Data\Cec\CR3140_2.qgd
Org Data File	: C:\GCMSsolution\Data\Cec\CR3140_2.qgd
Method File	: C:\GCMSsolution\Data\Cec\Ellipticine flow 1.qgm
Org Method File	: C:\GCMSsolution\Data\Cec\Ellipticine flow 1.qgm
Report File	:
Tuning File	: C:\GCMSsolution\System\Tune1_Default.qgt
Modified by	: Admin
Modified	: 8/13/2014 2:17:04 PM

Chromatogram CR3140 C:\GCMSsolution\Data\Cec\CR3140_2.qgd

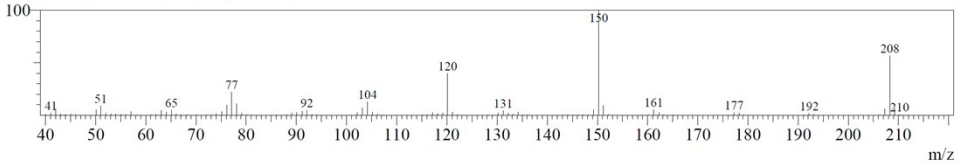


Peak Report TIC

Peak#	R.Time	I.Time	F.Time	Area	Area%	Height	Height%	A/H	Mark	Name
1	9.208	9.042	9.717	20446281	100.00	8203541	100.00	2.49	MI	
				20446281	100.00	8203541	100.00			

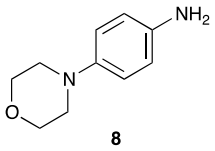
Spectrum

Peak#:1 R.Time:9.2(Scan#:746)
MassPeaks:110 BasePeak:150(1979465)



GC mass spectrum of **8**.

C:\GCMSsolution\Data\Cec\CR3141_1.qgd 15/09/2014

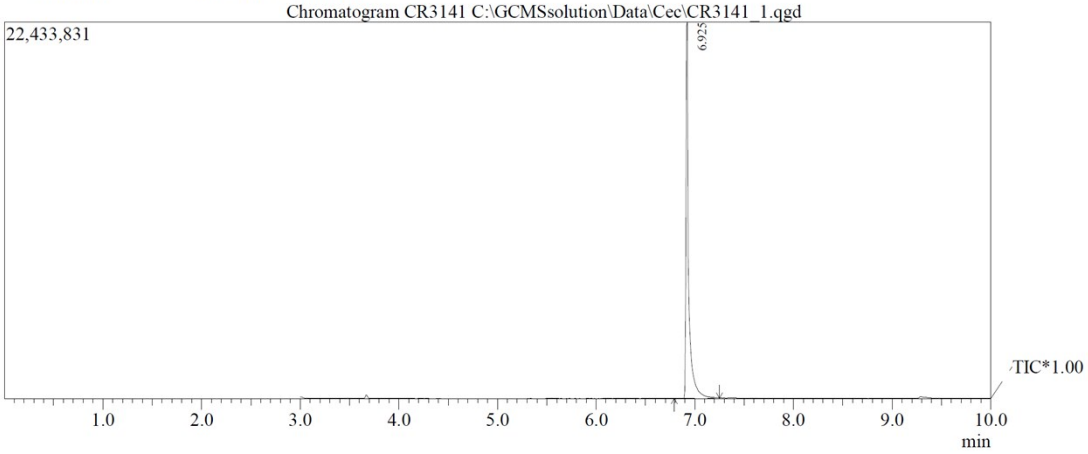


8

Sample Information

Analyzed by	: Admin
Analyzed	: 8/21/2007 6:52:43 AM
Sample Type	: Unknown
Level #	: 1
Sample Name	: CR3141
Sample ID	:
IS Amount	: [1]=1.000
Sample Amount	: 1.000
Dilution Factor	: 1.000
Vial #	: 18
Injection Volume	: 1.000
Data File	: C:\GCMSsolution\Data\Cec\CR3141_1.qgd
Org Data File	: C:\GCMSsolution\Data\Cec\CR3141_1.qgd
Method File	: C:\GCMSsolution\Data\Cec\Ellipiteine flow 1.qgm
Org Method File	: C:\GCMSsolution\Data\Cec\Ellipiteine flow 1.qgm
Report File	:
Tuning File	: C:\GCMSsolution\System\Tune1_Default.qgt
Modified by	: Admin
Modified	: 8/12/2014 2:26:38 PM

Chromatogram CR3141 C:\GCMSsolution\Data\Cec\CR3141_1.qgd

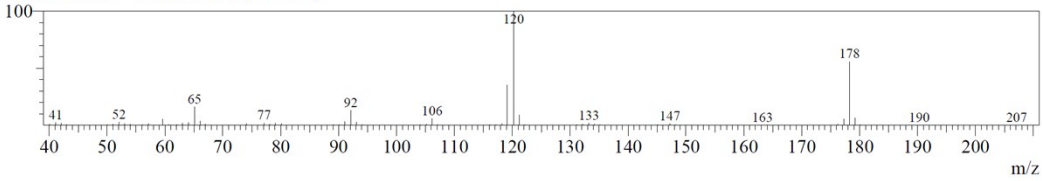


Peak Report TIC

Peak#	R.Time	I.Time	F.Time	Area	Area%	Height	Height%	A/H	Mark	Name
1	6.925	6.792	7.250	42701355	100.00	22415407	100.00	1.91	MI	
				42701355	100.00	22415407	100.00			

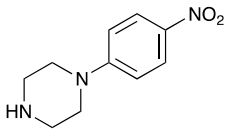
Spectrum

Peak#:1 R.Time:6.9(Scan#:472)
MassPeaks:111 BasePeak:120(7057024)



GC mass spectrum of **14**

C:\GCMSsolution\Data\Cec\CR4094 recryst_2.qgd 16/02/2008

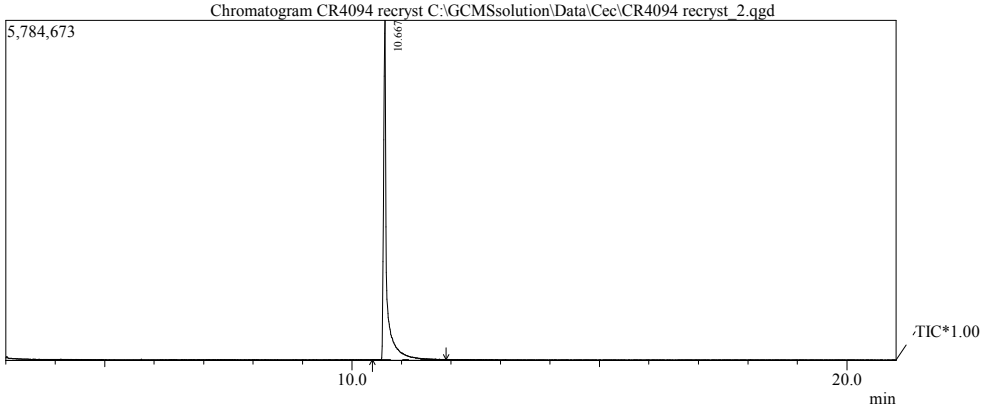


14

Sample Information

Analyzed by	: Admin
Analyzed	: 2/12/2008 6:52:01 AM
Sample Type	: Unknown
Level #	: 1
Sample Name	: CR4094 recryst
Sample ID	:
IS Amount	: [1]=1.000
Sample Amount	: 1.000
Dilution Factor	: 1.000
Vial #	: 11
Injection Volume	: 2.000
Data File	: C:\GCMSsolution\Data\Cec\CR4094 recryst_2.qgd
Org Data File	: C:\GCMSsolution\Data\Cec\CR4094 recryst_2.qgd
Method File	: C:\GCMSsolution\Data\Project1\Ellipitcine flow extended.qgm
Org Method File	: C:\GCMSsolution\Data\Project1\Ellipitcine flow extended.qgm
Report File	:
Tuning File	: C:\GCMSsolution\System\Tune1_Default.qgt
Modified by	: Admin
Modified	: 2/12/2008 7:13:01 AM

Chromatogram CR4094 recryst C:\GCMSsolution\Data\Cec\CR4094 recryst_2.qgd

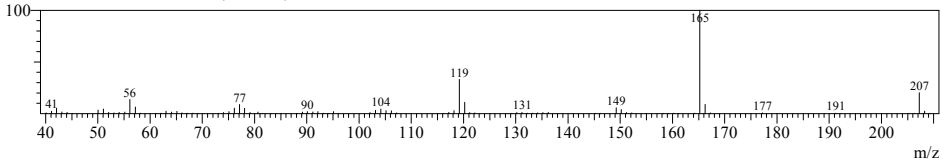


Peak Report TIC

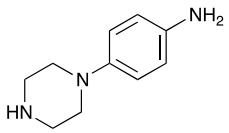
Peak#	R.Time	I.Time	F.Time	Area	Area%	Height	Height%	A/H	Mark	Name
1	10.667	10.408	11.900	25008284	100.00	5771473	100.00	4.33	MI	
				25008284	100.00	5771473	100.00			

Spectrum

Peak#:1 R.Time:10.7(Scan#:921)
MassPeaks:108 BasePeak:165(1871520)



GC mass spectrum of **9**

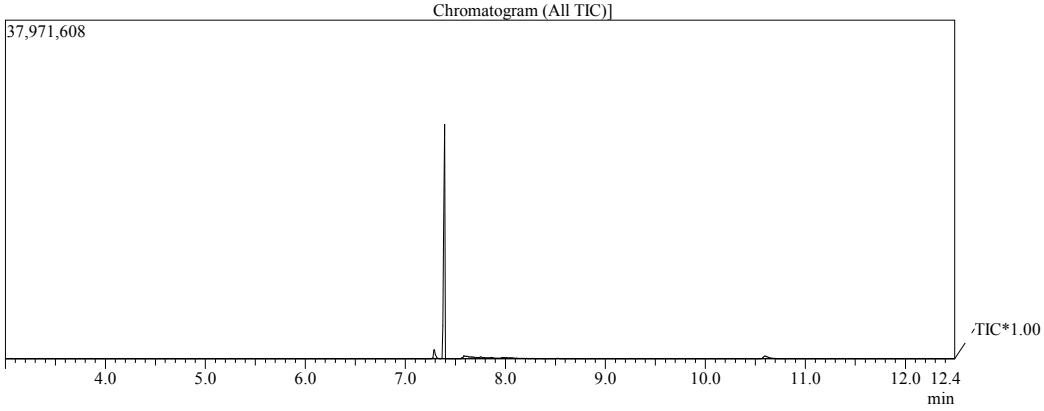


9

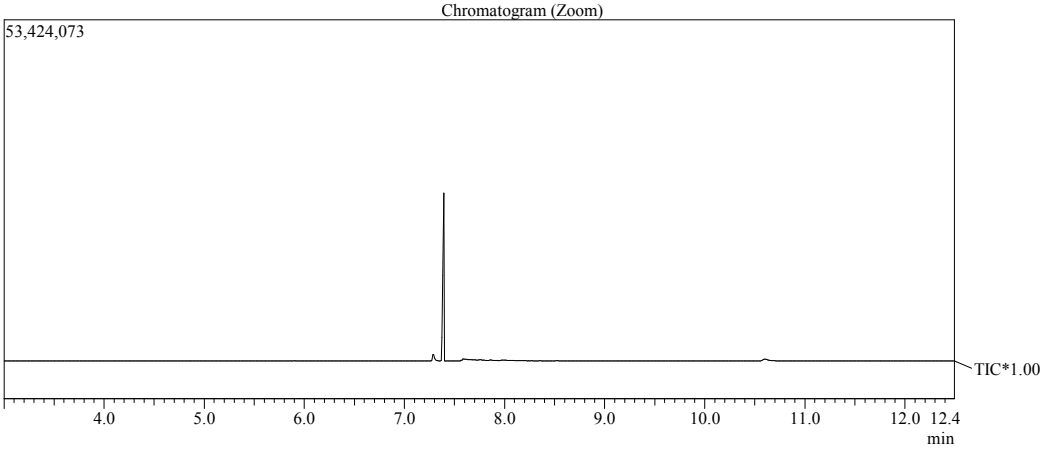
24/10/2007 19:57:35

C:\GCMSsolution\Data\Cec\SP3182_2.qgd

Chromatogram (All TIC)]

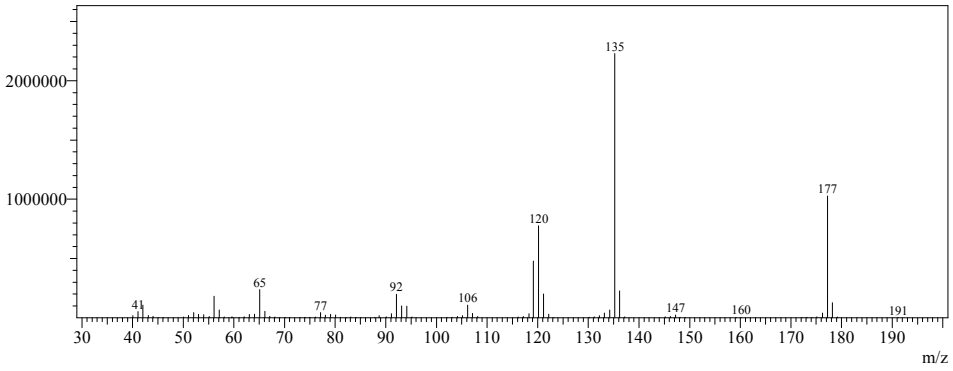


Chromatogram (Zoom)

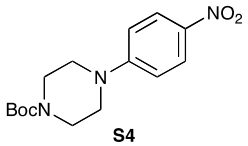


Spectrum

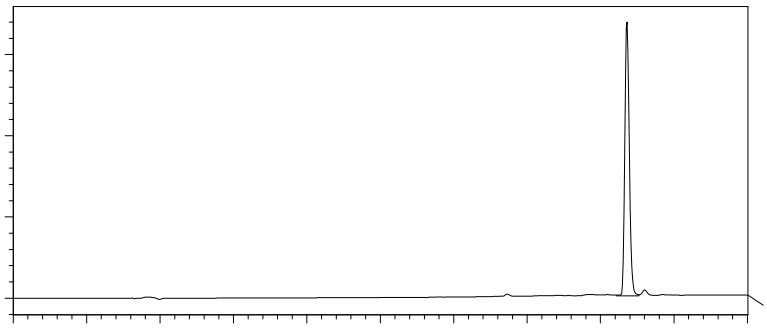
Line#:1 R.Time:7.392(Scan#:528)
MassPeaks:109 BasePeak:135.20(2228420)
RawMode:Averaged 7.367-7.408(525-530)
BG Mode:Averaged 7.092-7.142(492-498)



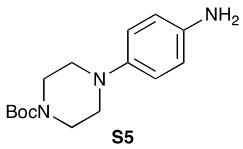
HPLC trace of **S4**.



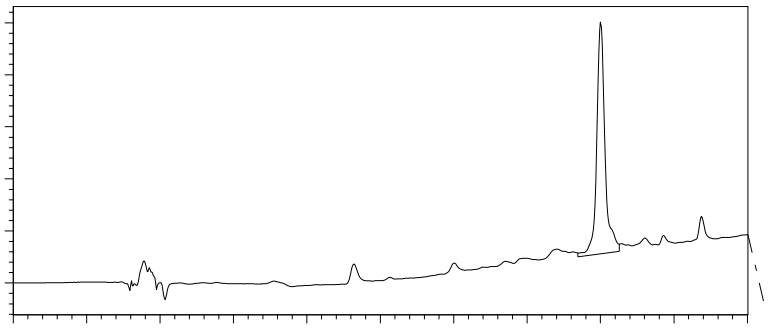
S4



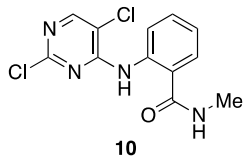
HPLC trace of product **S5**.



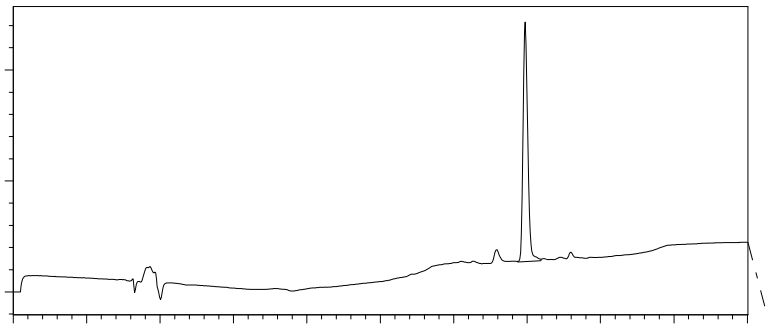
S5



HPLC trace of products **10**.



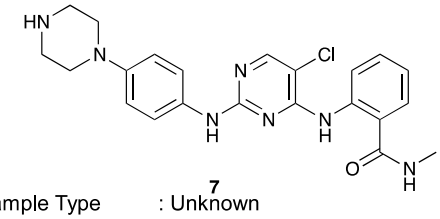
10



HPLC trace of product **7**.

SHIMADZU LabSolutions

Analysis Report

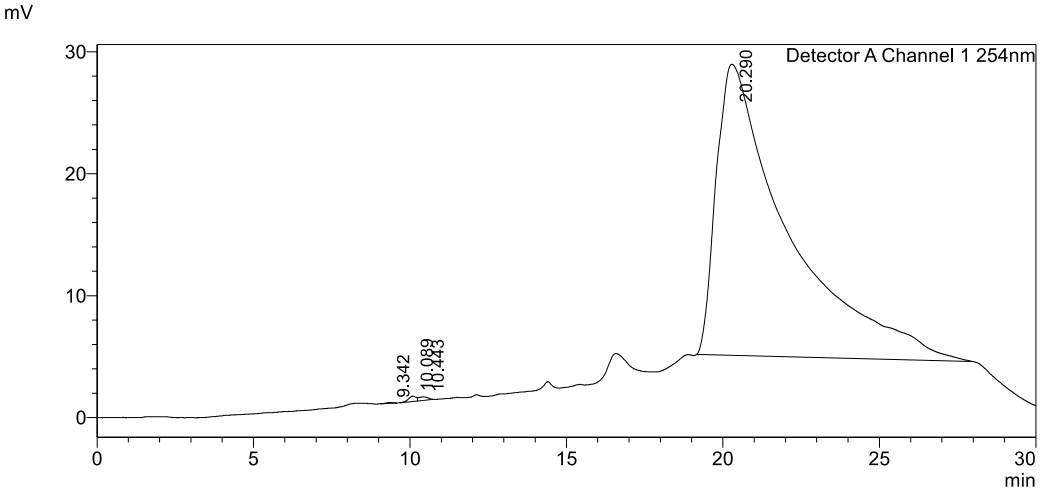


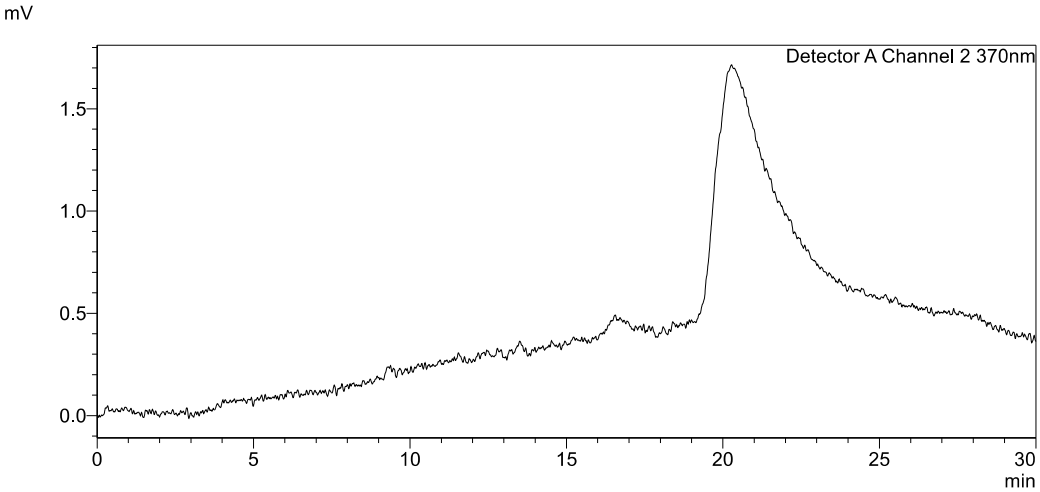
7

<Sample Information>

Sample Name	: CR3173
Sample ID	:
Data Filename	: CR3173_1.lcd
Method Filename	: 10-100 over 15 mins.lcm
Batch Filename	: CR2014.lcb
Vial #	: 1-1
Injection Volume	: 10 uL
Date Acquired	: 29/09/2014 1:57:22 PM
Date Processed	: 29/09/2014 2:27:23 PM
Sample Type	: Unknown
Acquired by	: System Administrator
Processed by	: System Administrator

<Chromatogram>





<Peak Table>

Detector A Channel 1 254nm