NAME _____

ID # _____

INTERPRETATION OF ORGANIC SPECTRA (4361/8361)

9:05 – 9:55 am, October 24, 2012

Exam 2

This exam is open book and open note. You are permitted to use any written materials you have brought as aids on this exam. You may also use a simple calculator. Other than this, please do not use any other electronic devices (cell phones, computers, recording devices, etc.) during the exam.

You may use pen or pencil. However, re-grades will be considered only for exams completed in pen.

Please write your answers in the boxes/spaces provided. If your answer is not in the appropriate space (say, for example, it's on the back of the page), draw us an arrow and/or note telling us where to look.

Feel free to remove the corner staple if this helps you analyze the spectra; you will have the opportunity to re-staple your exam at the end. You will be given 50 minutes total to finish the test. This exam contains one problem, which is split into parts. Many of these parts can be answered independently. *Do not get stuck* on one part and then assume that you will be unable to answer the rest of the question—move on. In addition, partial credit will be given for incorrect but still plausible answers, so *guess* on problems you cannot answer perfectly.

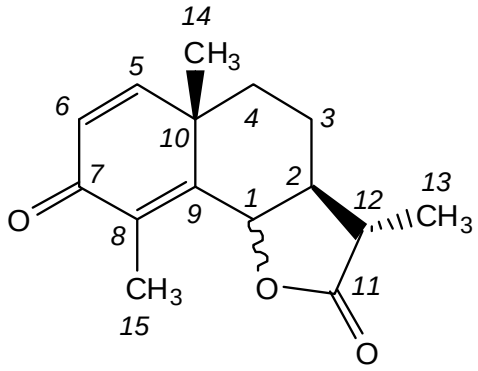
At the end of the 50 minute exam period you will be asked to return your exam to the proctor. Please do not take any part of the exam packet with you when you are done; everything will be returned to you after the exams are graded. This packet should contain 15 pages, including this one. Please check to make sure that your packet contains 15 pages before beginning your exam.

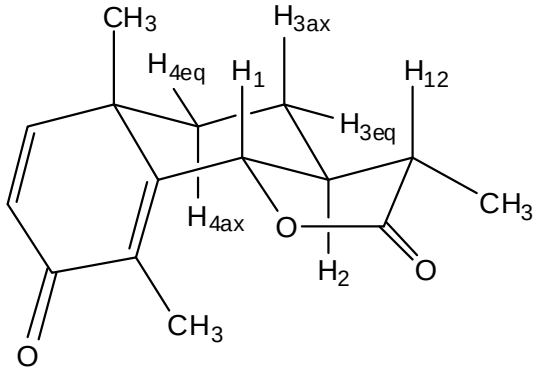
NAME _____

Scoring:	1. _____ / 66	5. _____ / 4
	2. _____ / 4	6. _____ / 4
	3. _____ / 6	7. _____ / 6
	4. _____ / 4	8. _____ / 6

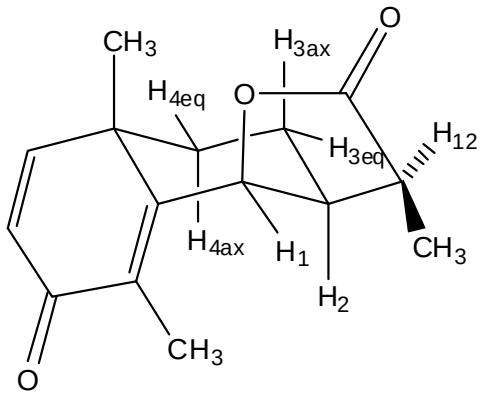
Total Score: _____ / 100

Santonins, extracted from wormwood, were once commonly used as anthelmintics (drugs that treat against parasitic worms). Different santonins possess different stereochemistries at C_1, C_2, and C_{12}. In this exam, you will try to determine the stereochemistry of an unknown santonin at C_1 (shown at right, with the unknown stereochemistry denoted with a squiggle-bond), using the ^{1}H, ^{13}C, ^{1}H-^{1}H COSY, and ^{1}H-^{13}C HSQC spectra attached to the back of this exam. Molecular modeling of either C1 stereochemistry gives the two possible configurations shown below; so, in this exam, you will be choosing between one of these two configurations.





or



?

1. In the charts on the next page, list chemical shifts for the listed proton atoms (to within 0.05 ppm) and carbon atoms (to within 5 ppm) according to the numbering schemes on the structures above. *Note:* The chart asks for assignments on all protons in santonin, but not on all carbons.

proton	δ (ppm)
H1	
H2	
H3ax	
H3eq	

proton	δ (ppm)
H4ax	
H4eq	
H5	
H6	

proton	δ (ppm)
H12	
H13	
H14	
H15	

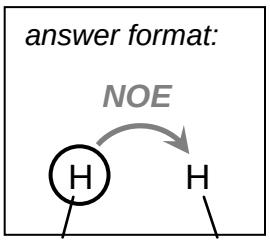
carbon	δ (ppm)
C1	
C2	
C3	
C4	

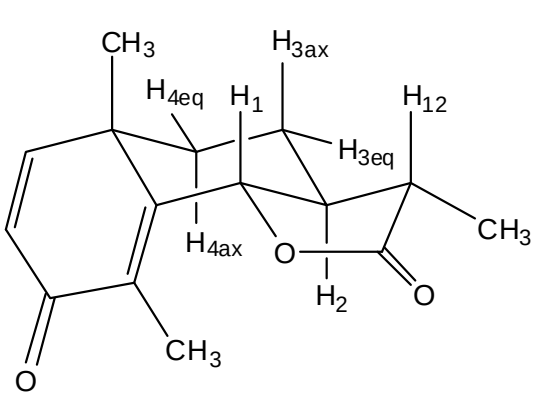
carbon	δ (ppm)
C5	
C6	
C12	

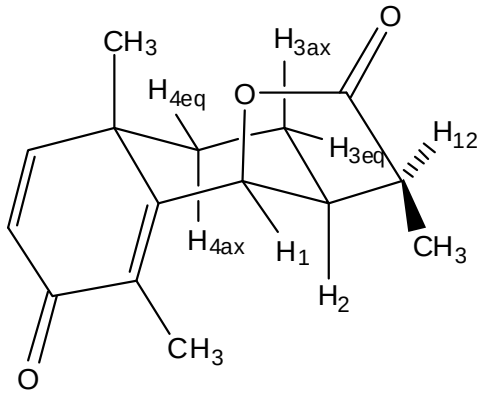
carbon	δ (ppm)
C13	
C14	
C15	

2. Based on the spectra you have, which santonin configuration shown on the previous page is the correct one? Circle the correct configuration on page 2.

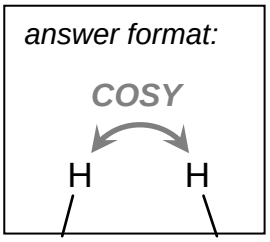
3. One-dimensional, nuclear Overhauser effect (NOE) experiments would help confirm your choice of configuration. On each of the structures on the next page:
   a. Propose one ^{1}H resonance to irradiate in an NOE experiment by circling the corresponding proton. Circle the same proton in <u>both</u> structures.
   b. On each structure, draw an intramolecular NOE that you would expect to see in that configuration but not the other configuration as a curved arrow. (In other words, draw an NOE that would lead you to pick that configuration over the other one. This means that, even though you circled the *same* proton to excite in each structure, you will be drawing *different* NOEs in each.) Label each curved arrow "NOE".



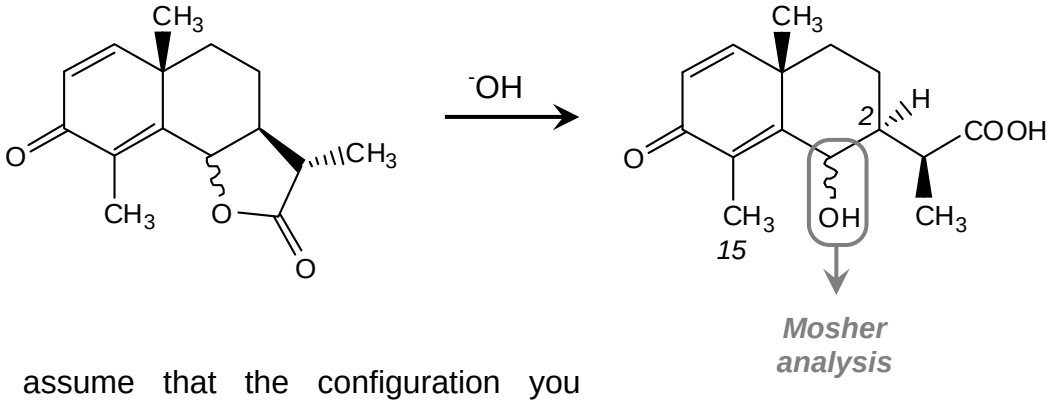




4. One crosspeak is circled in grey on the ^{1}H-^{1}H COSY spectrum. What correlation does this crosspeak represent? On one of the structures above (doesn't matter which one), draw this correlation as a double-headed arrow marked "COSY".



5. The absolute configuration (stereochemistry) of santonin can't be directly confirmed by derivative analysis, because there are no easily modified functional groups in the molecule. However, hydrolysis of the ester in base yields an alcohol (with retention of stereochemistry at C1) that could be analyzed by Mosher's (MTPA ester) method.



Let's assume that the configuration you circled in problem 2 was subjected to base hydrolysis and then Mosher analysis. Given $\Delta\delta = \delta_S - \delta_R$, would you predict that

$\Delta\delta$ **(H15) > 0** *or* $\Delta\delta$ **(H15) < 0** *?* *(Circle one.)*

$\Delta\delta$ **(H2) > 0** *or* $\Delta\delta$ **(H2) < 0** *?* *(Circle one.)*

6. This exam doesn't include 1-D TOCSY data. But if a 1-D TOCSY experiment were conducted by irradiating at 6.25 ppm, which of the following protons would *not* appear as a positive peak in the TOCSY spectrum? (*Circle one answer.*)

H4 **H6** **H14** **all of these would appear as a positive peak**

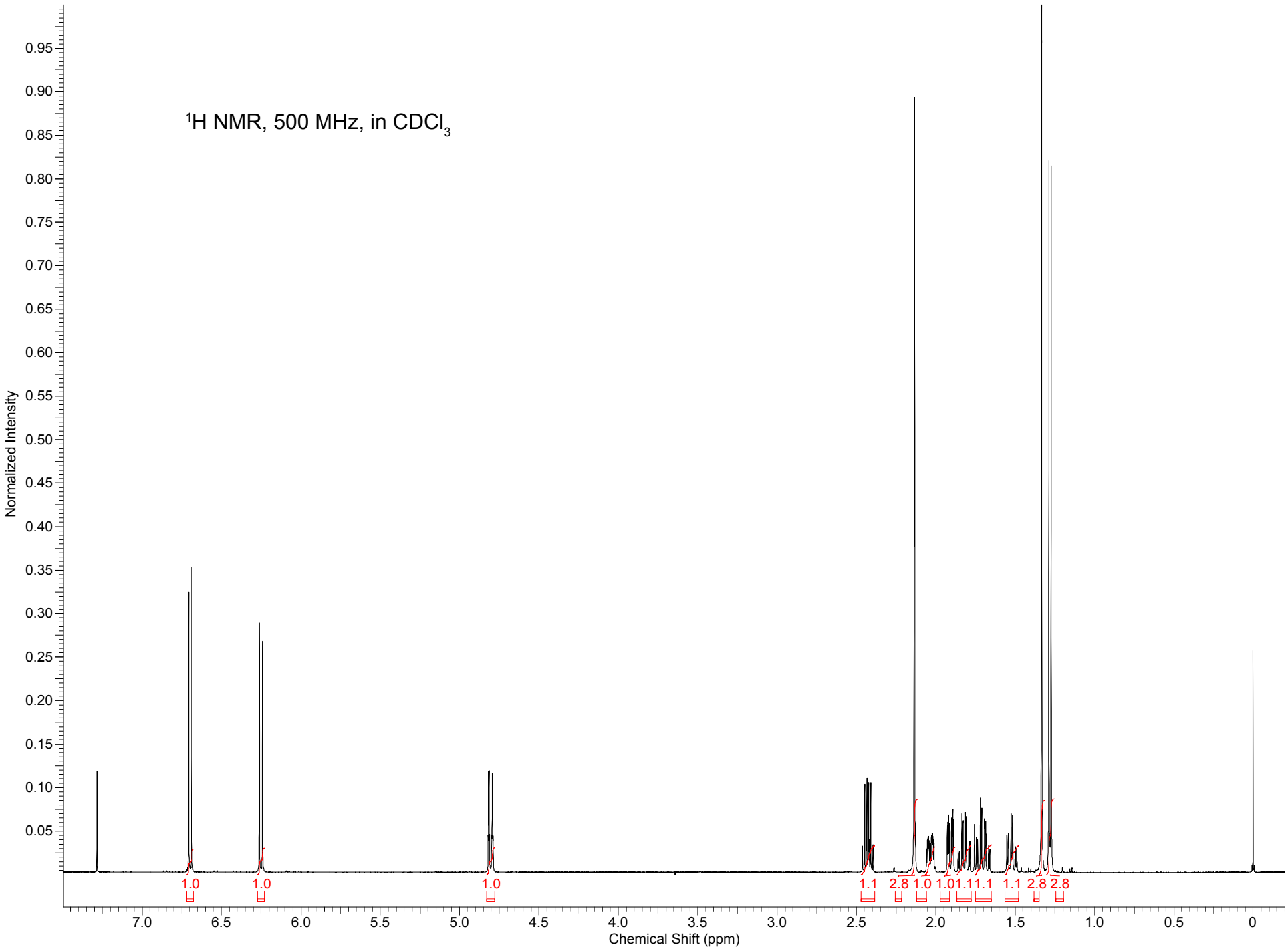
7. The exam also doesn't include a DEPT spectrum. But if there was one, would it show a positive-intensity peak (**+**), a negative-intensity peak (**–**), or no peak (**0**) for each of the following carbon atoms? (Circle one answer in each box.)

carbon	DEPT-135	DEPT-90
C11	**+** **–** *or* **0** ?	**+** **–** *or* **0** ?
C12	**+** **–** *or* **0** ?	**+** **–** *or* **0** ?
C13	**+** **–** *or* **0** ?	**+** **–** *or* **0** ?

8. The ^{1}H-^{13}C H**S**QC spectrum shown in this exam provides the same information as an ^{1}H-^{13}C H**M**QC spectrum. Name one advantage and one disadvantage of the HSQC method relative to HMQC.

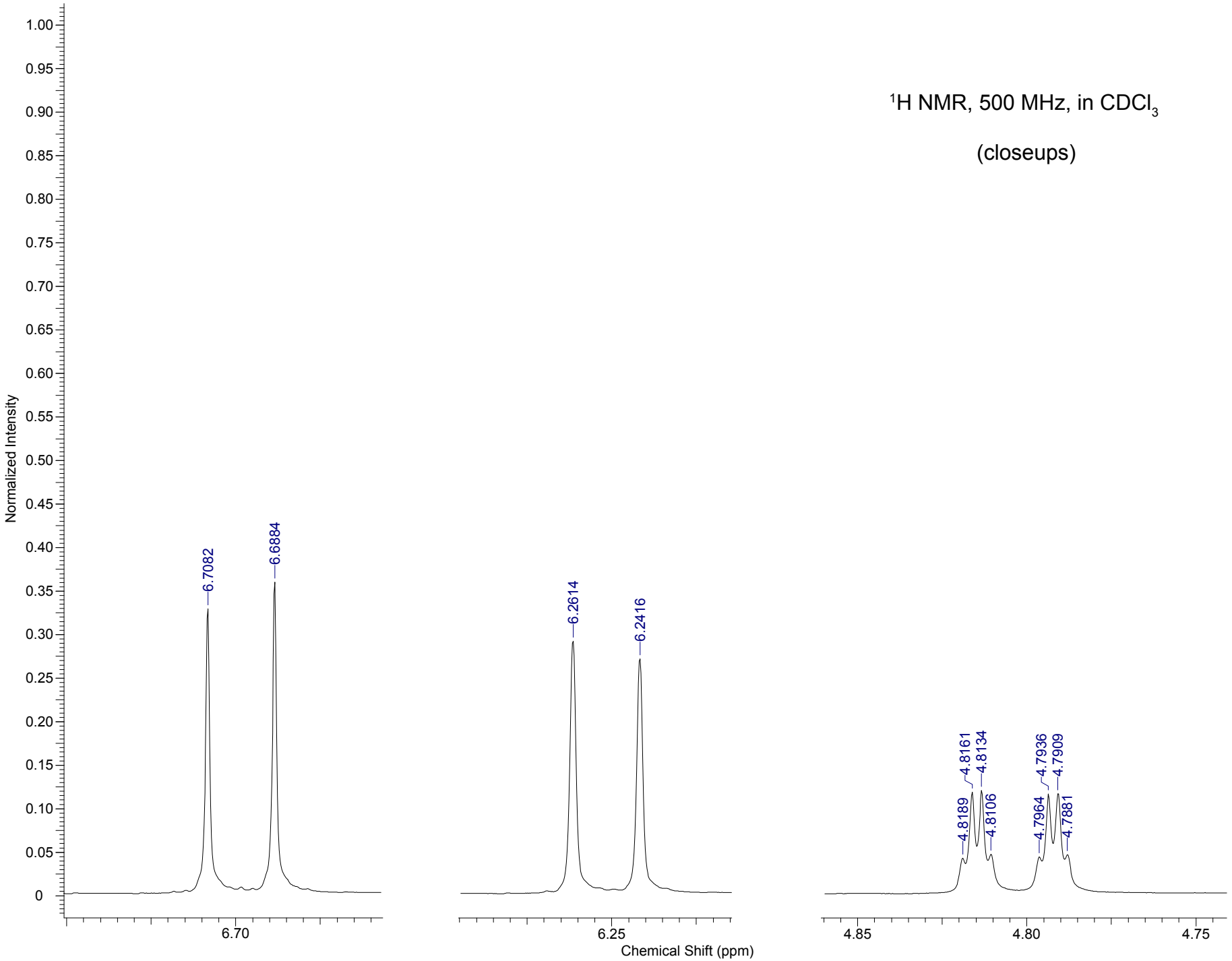
advantage of HSQC:

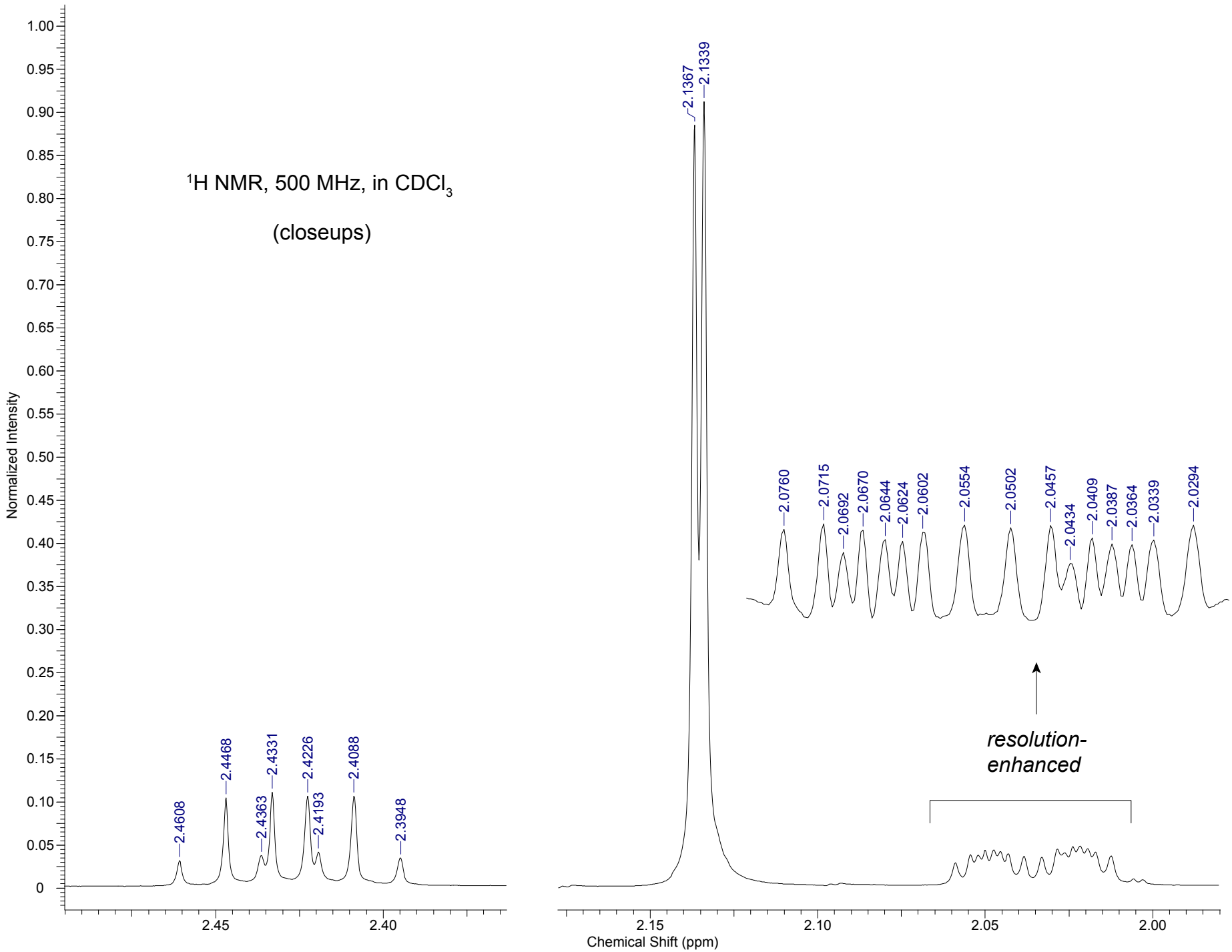
disadvantage of HSQC:

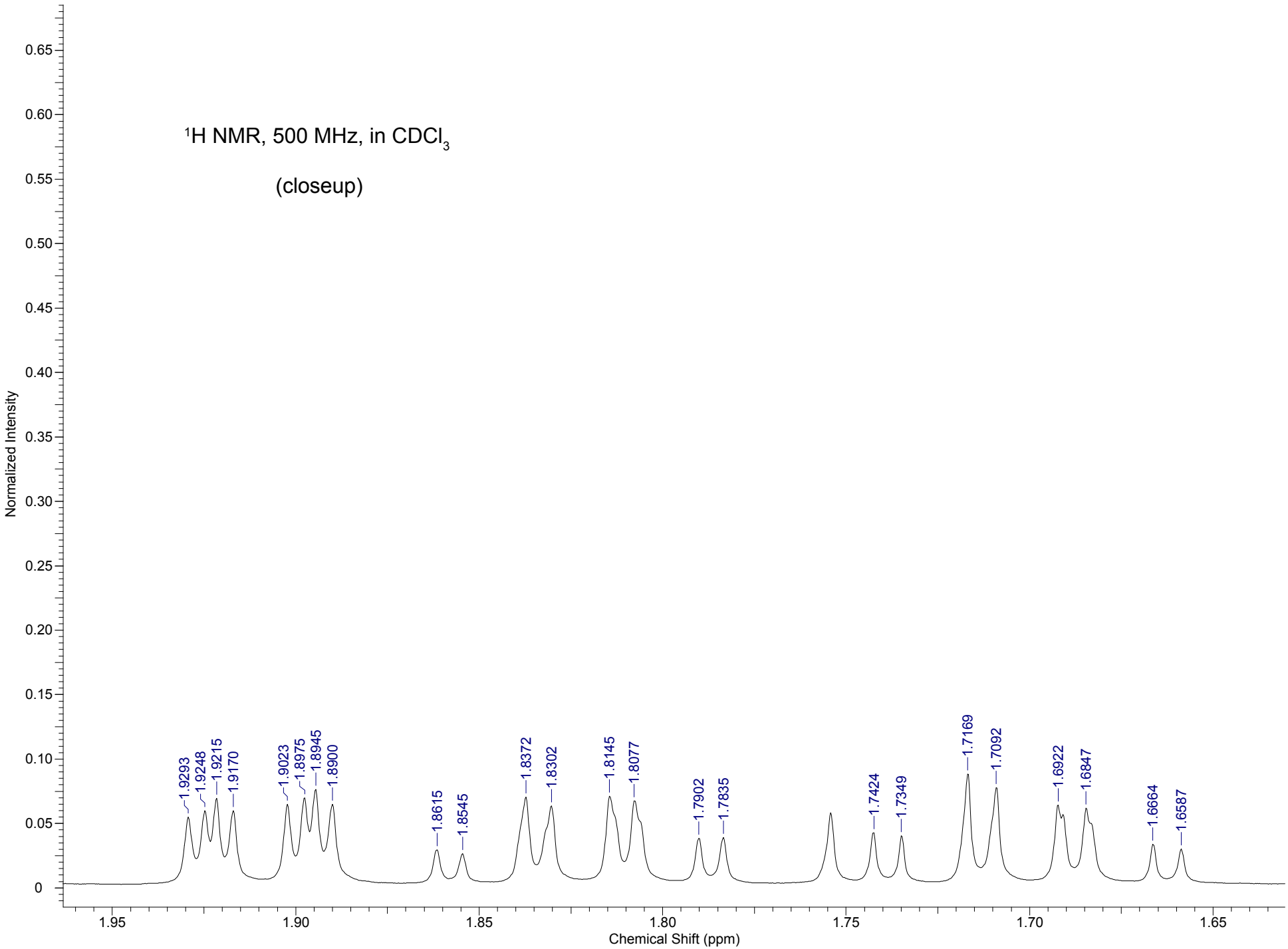

^{1}H NMR, 500 MHz, in $CDCl_3$
Normalized Intensity
Chemical Shift (ppm)
1.0
1.0
1.0
1.1
2.8
1.0
1.0
1.1
1.1
1.1
2.8
2.8

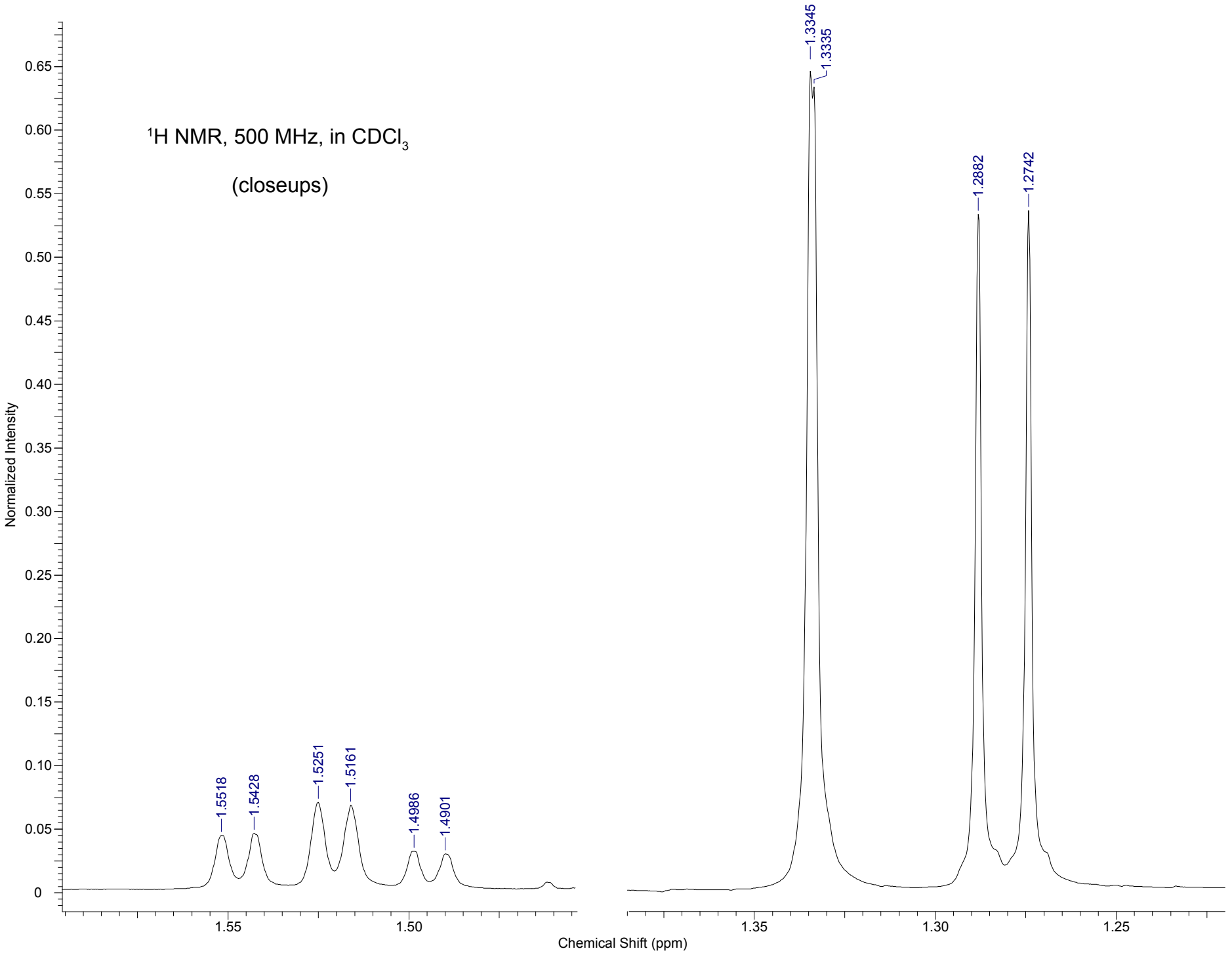
^{1}H NMR, 500 MHz, in $CDCl_3$

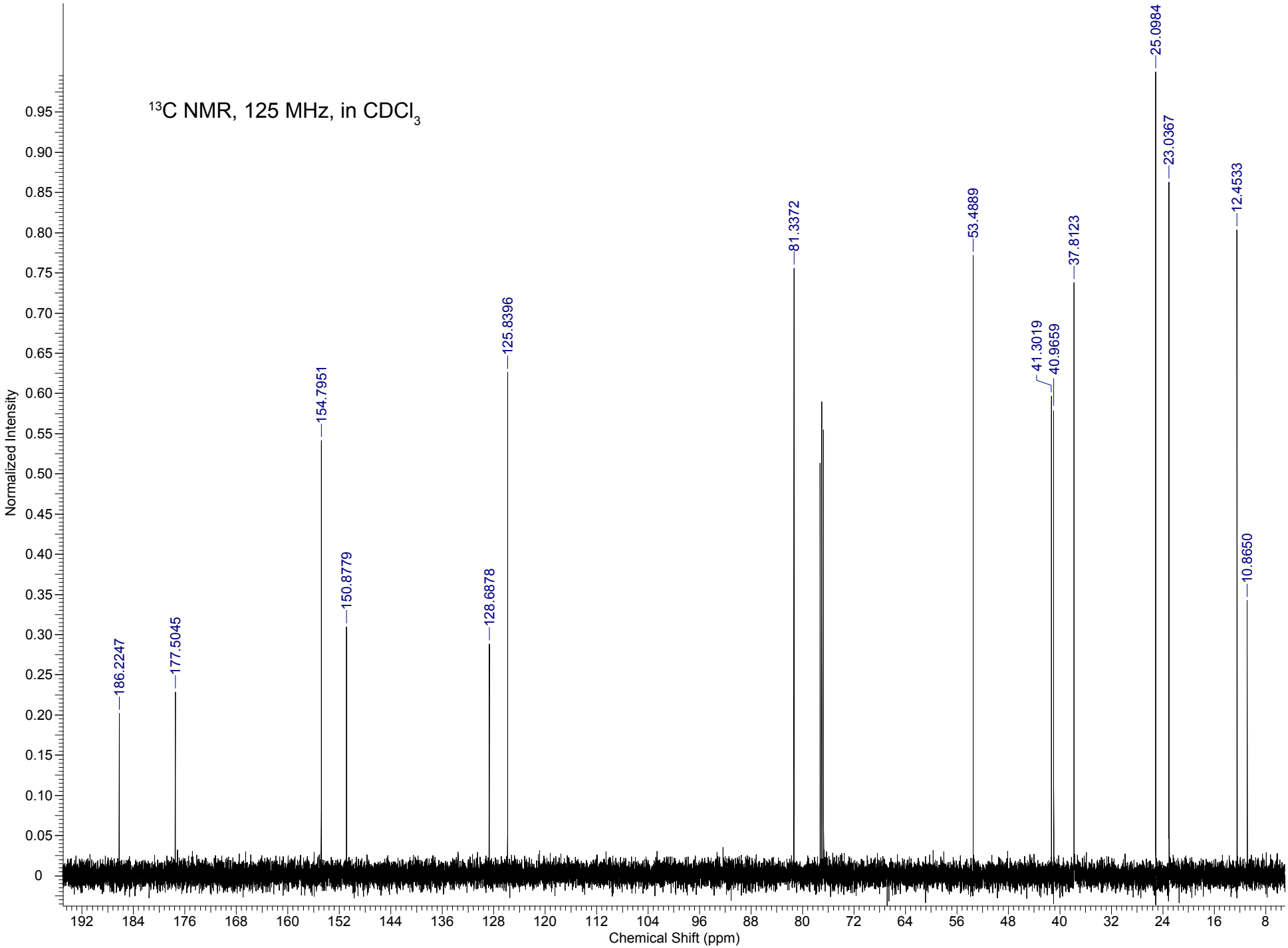
(closeups)



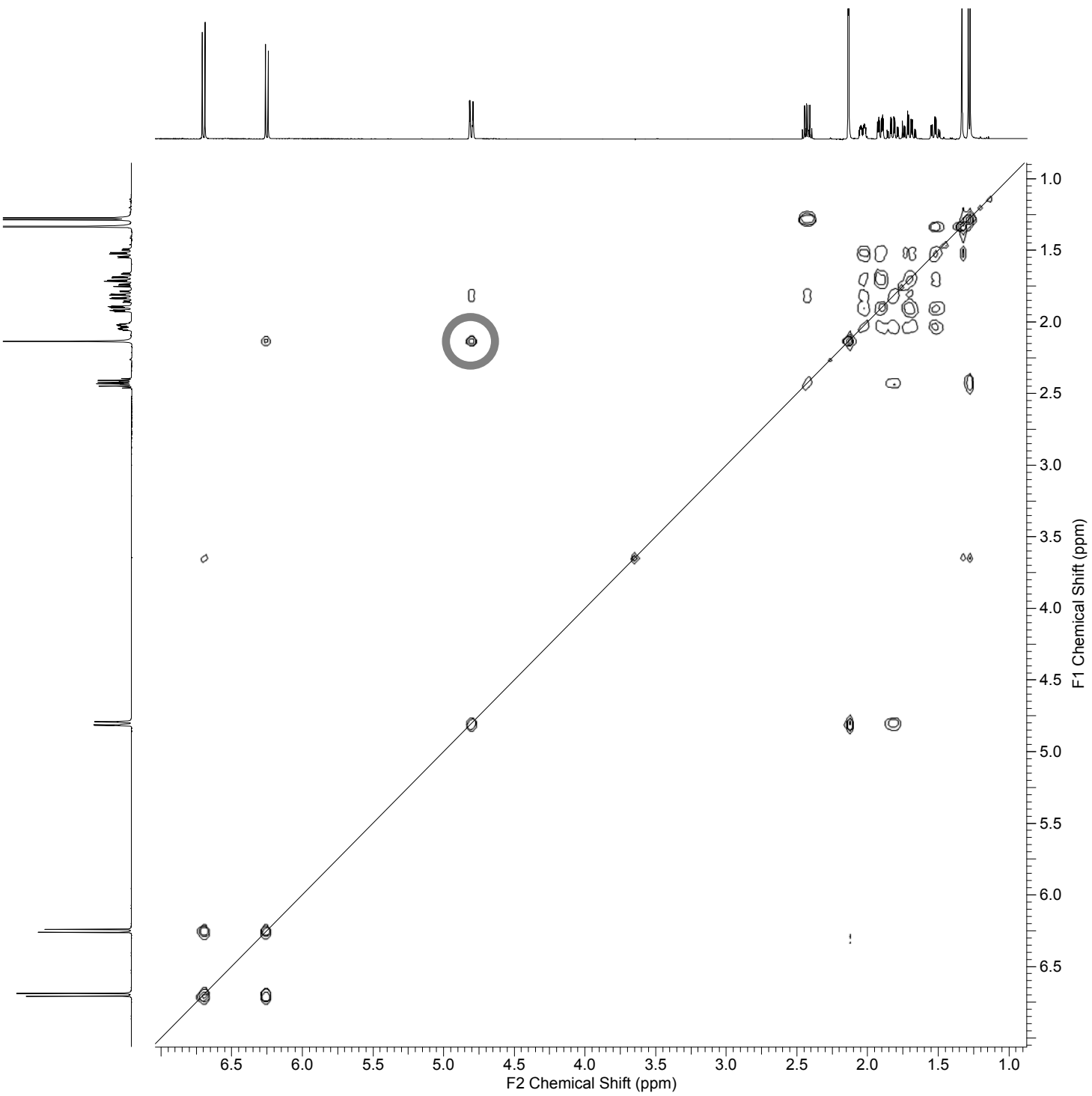

^{1}H NMR, 500 MHz, in $CDCl_3$
(closeups)
Normalized Intensity
1.00
0.95
0.90
0.85
0.80
0.75
0.70
0.65
0.60
0.55
0.50
0.45
0.40
0.35
0.30
0.25
0.20
0.15
0.10
0.05
0
2.4608
2.4468
2.4363
2.4331
2.4226
2.4193
2.4088
2.3948
2.45
2.40
2.1367
2.1339
2.0760
2.0715
2.0692
2.0670
2.0644
2.0624
2.0602
2.0554
2.0502
2.0457
2.0434
2.0409
2.0387
2.0364
2.0339
2.0294
resolution-
enhanced
2.15
2.10
2.05
2.00
Chemical Shift (ppm)


^{1}H NMR, 500 MHz, in $CDCl_3$
(closeup)
Normalized Intensity
0.65
0.60
0.55
0.50
0.45
0.40
0.35
0.30
0.25
0.20
0.15
0.10
0.05
0
1.9293
1.9248
1.9215
1.9170
1.9023
1.8975
1.8945
1.8900
1.8615
1.8545
1.8372
1.8302
1.8145
1.8077
1.7902
1.7835
1.7424
1.7349
1.7169
1.7092
1.6922
1.6847
1.6664
1.6587
1.95
1.90
1.85
1.80
1.75
1.70
1.65
Chemical Shift (ppm)


^{1}H NMR, 500 MHz, in $CDCl_3$
(closeups)
Normalized Intensity
0.65
0.60
0.55
0.50
0.45
0.40
0.35
0.30
0.25
0.20
0.15
0.10
0.05
0
1.5518
1.5428
1.5251
1.5161
1.4986
1.4901
1.3345
1.3335
1.2882
1.2742
1.55
1.50
1.35
1.30
1.25
Chemical Shift (ppm)

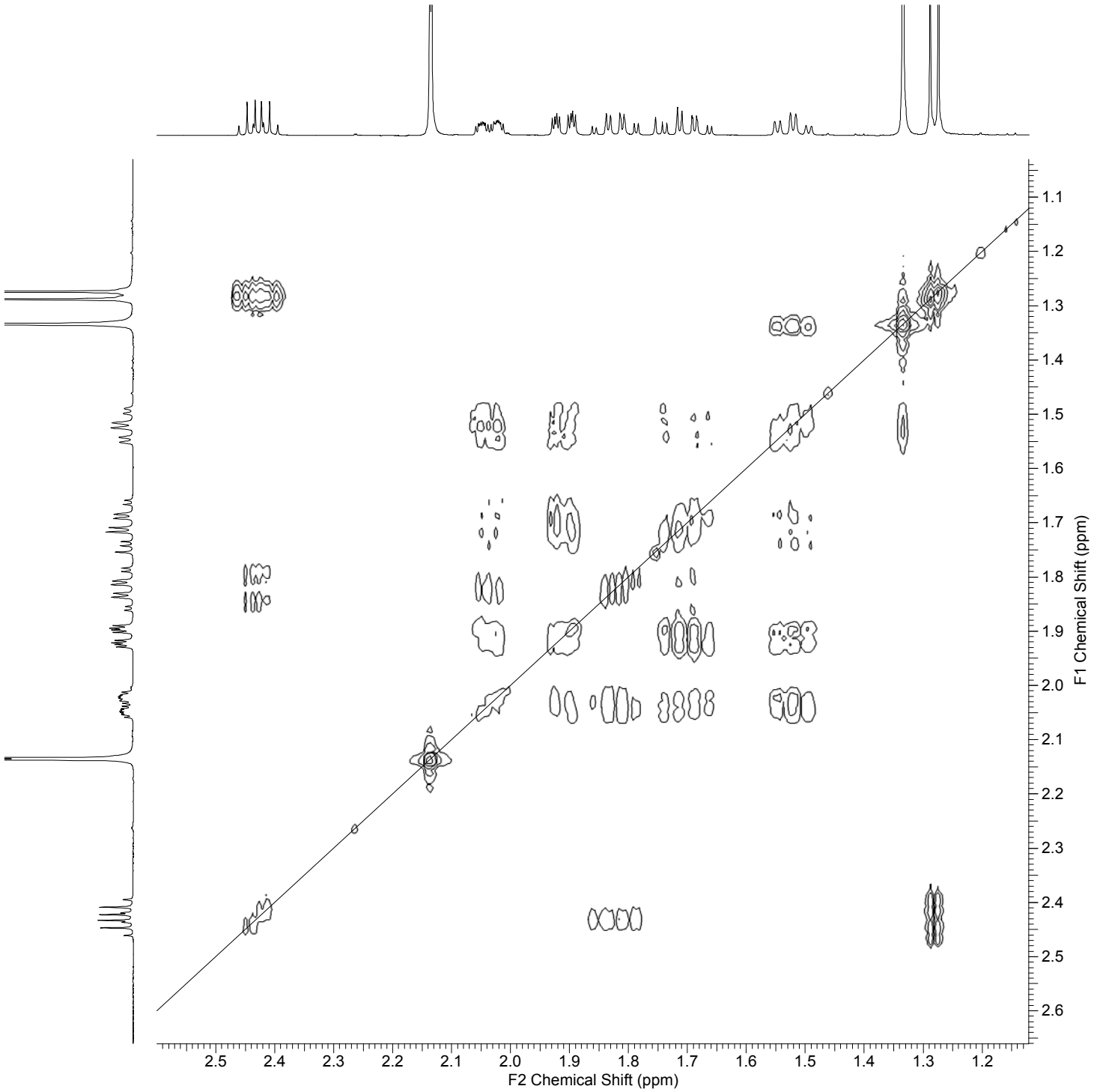

^{13}C NMR, 125 MHz, in $CDCl_3$
Normalized Intensity
Chemical Shift (ppm)
186.2247
177.5045
154.7951
150.8779
128.6878
125.8396
81.3372
53.4889
41.3019
40.9659
37.8123
25.0984
23.0367
12.4533
10.8650

^{1}H-^{1}H COSY, 500 MHz, in $CDCl_3$

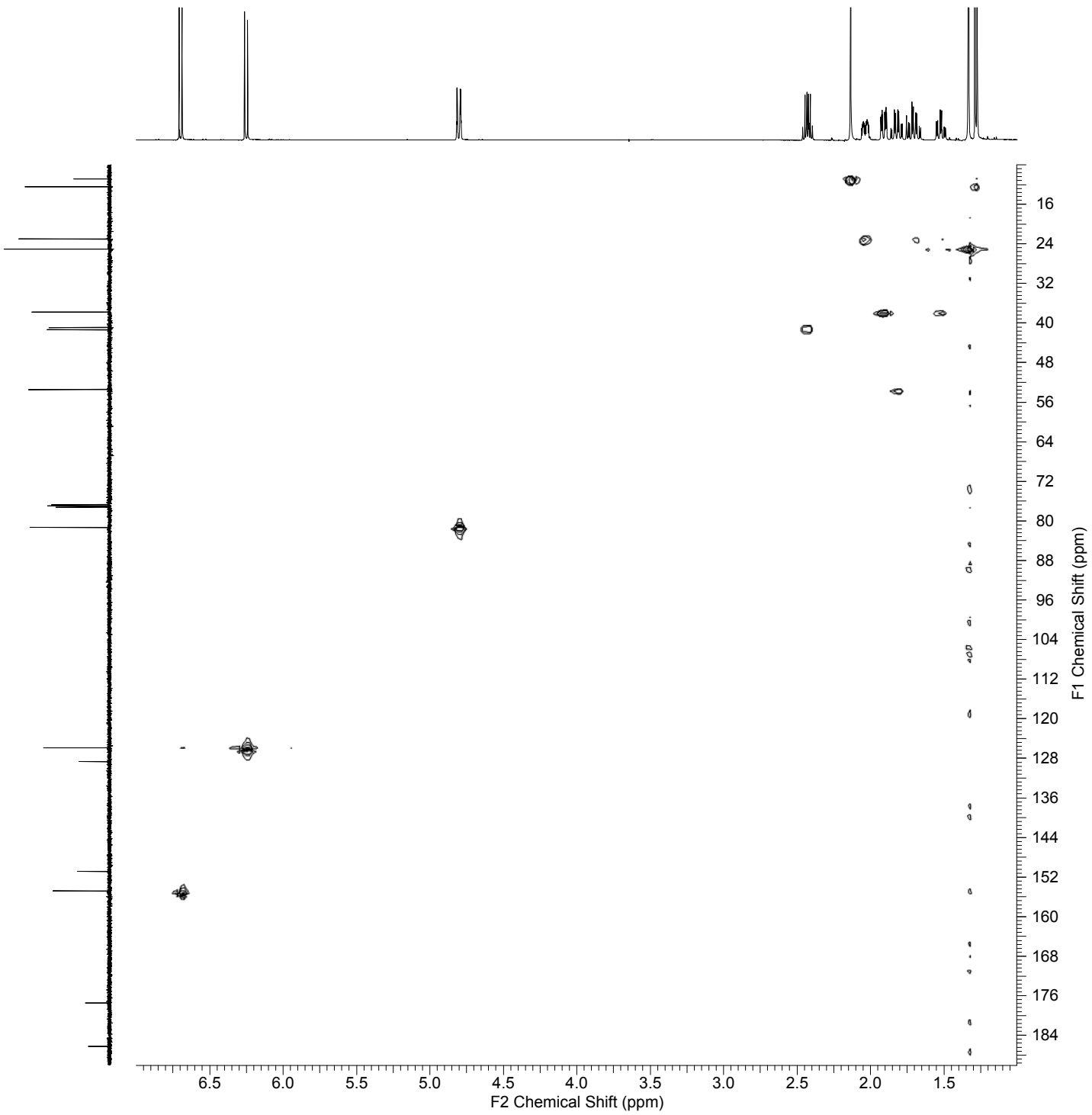


^{1}H-^{1}H COSY, 500 MHz, in $CDCl_3$

(closeup)



^{1}H-^{13}C HSQC, 500/125 MHz, in $CDCl_3$



^{1}H-^{13}C HSQC, 500/125 MHz, in $CDCl_3$

(closeup)