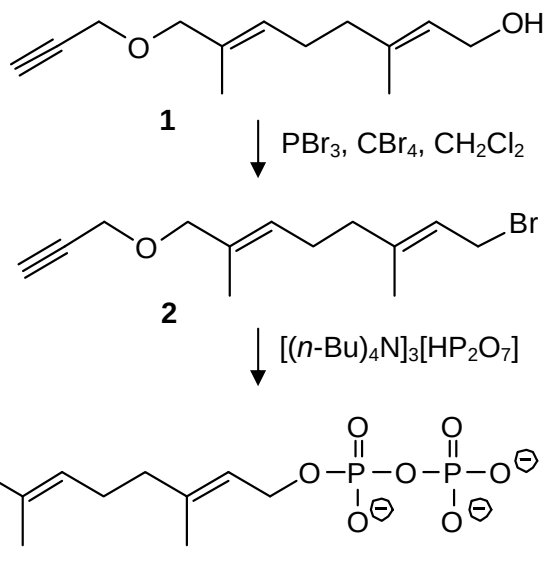
Chemistry 4361/8361 Fall 2012

Problem Set 1
Basic 1D NMR Interpretation
Due: Wednesday, September 19

1. Ed Zhang (Distefano group) attempted to synthesize the alkyne-modified farnesyl pyrophosphate **3** via the modified farnesol **1** and farnesyl bromide **2**. In this problem, you will use the NMR spectra to confirm the identity of the starting material and products in this sequence.



   (The ^{31}P NMR in this problem—like most ^{13}C and ^{31}P NMR spectra—is ^{1}H-decoupled, so that P-H coupling and splitting is not observed in the ^{31}P spectrum. We'll talk about this in class later.)

   a. The 300 MHz ^{1}H NMR spectra of **1** and **2**, taken in $CDCl_3$, are shown on the following pages. As best you can, assign ^{1}H resonances to each proton in the structures of **1** and **2**. Then, indicate which protons are coupled, and assign a coupling constant *J* to each coupled partner.

      (The ^{1}H NMR spectrum of **1** shows some hydrocarbon grease at δ = 0.6-1.3 ppm, and a couple of other small impurity peaks, that I haven't marked. Ignore them.)

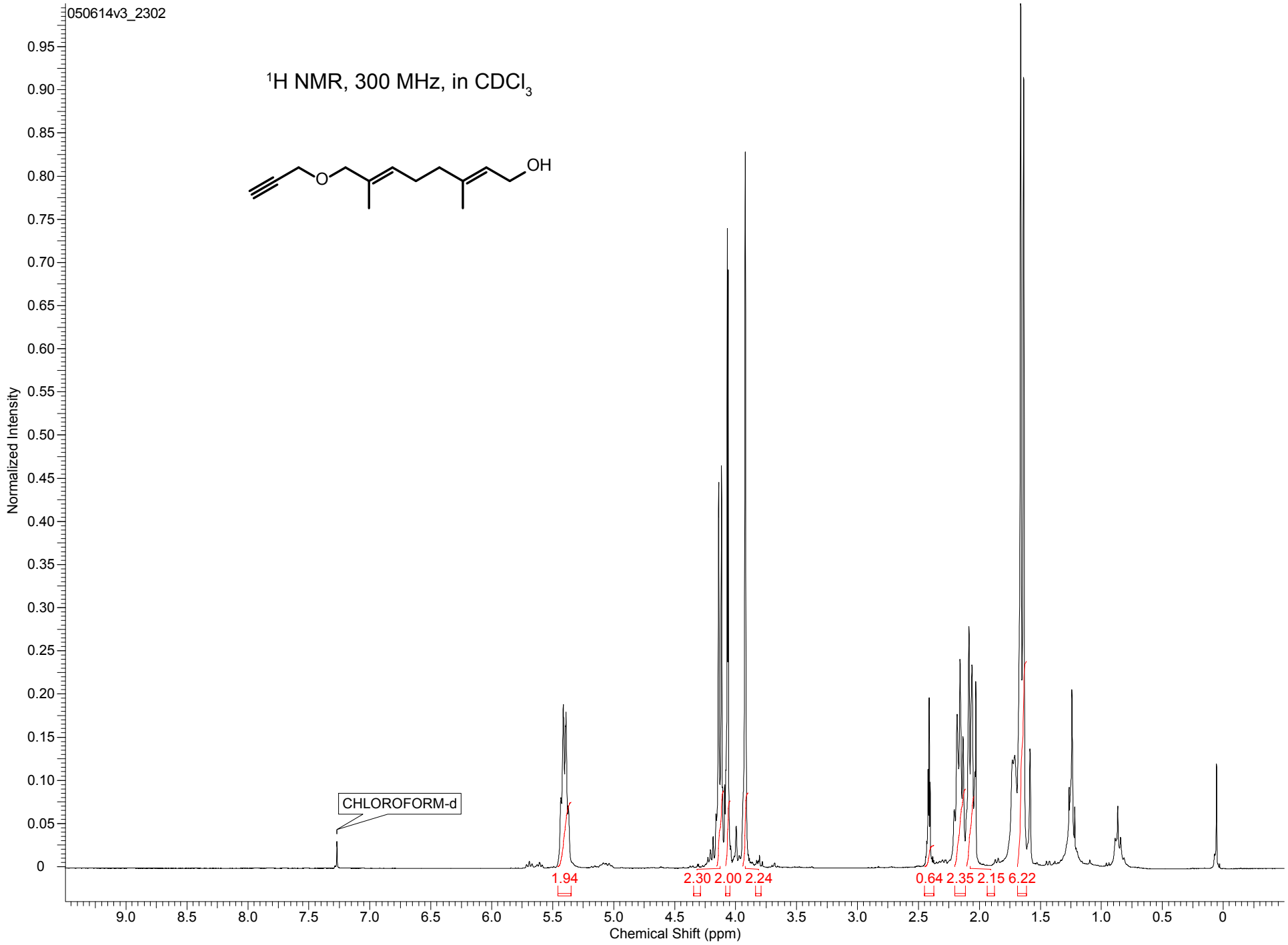
   b. Much of the ^{1}H-^{1}H coupling we'll observe in this class will be vicinal coupling (or three-bond coupling, with coupling constant ^{3}J), but we will occasionally see geminal (^{2}J) and long-range (^{4}J or ^{5}J) ^{1}H-^{1}H coupling. Do you see any geminal or long range coupling in the ^{1}H NMR spectra of **1** or **2**?

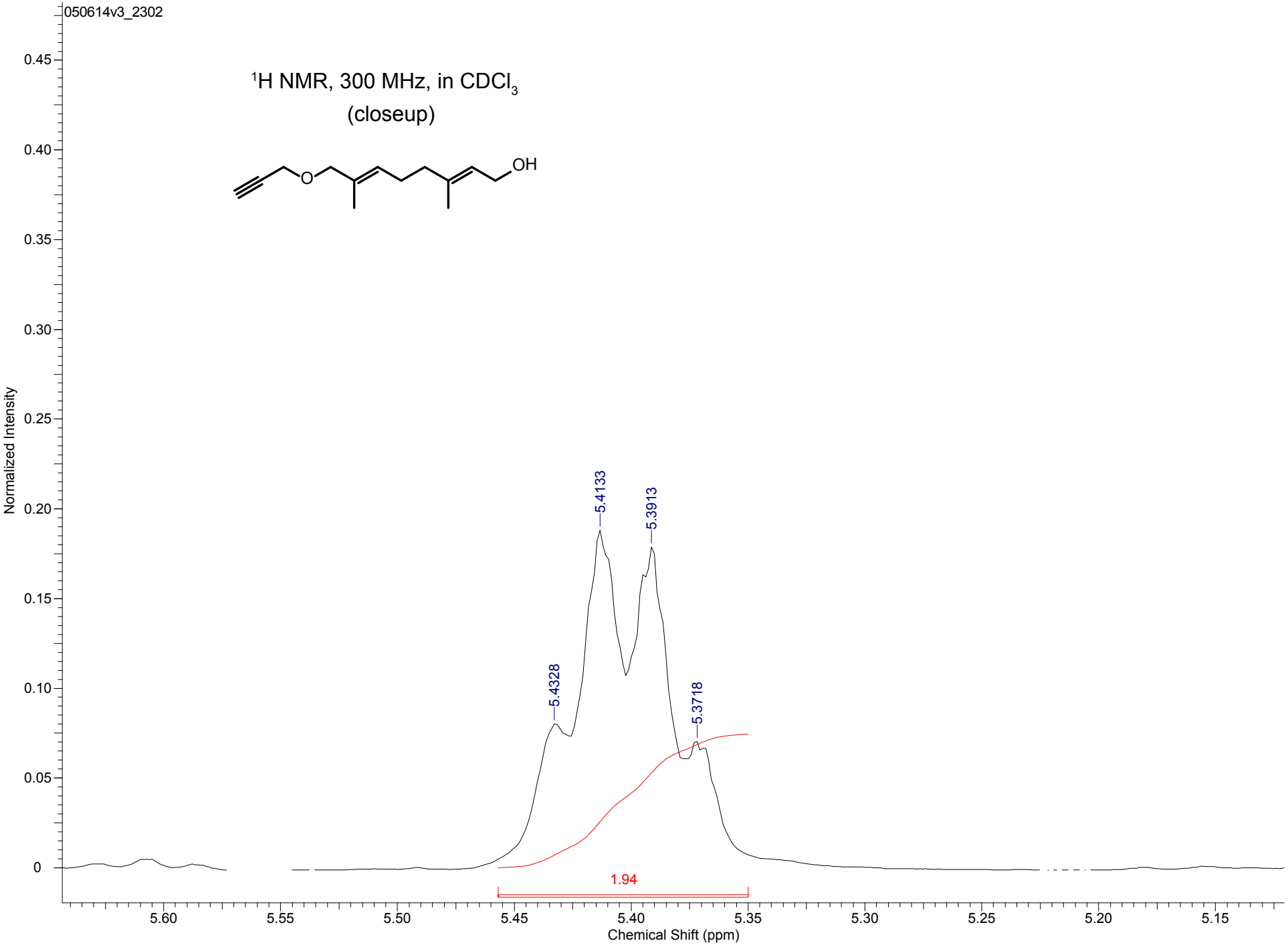
   c. The multiplet at δ = 2.41 is much smaller than the others—lower in integrated intensity that you would expect for a single proton. Why?

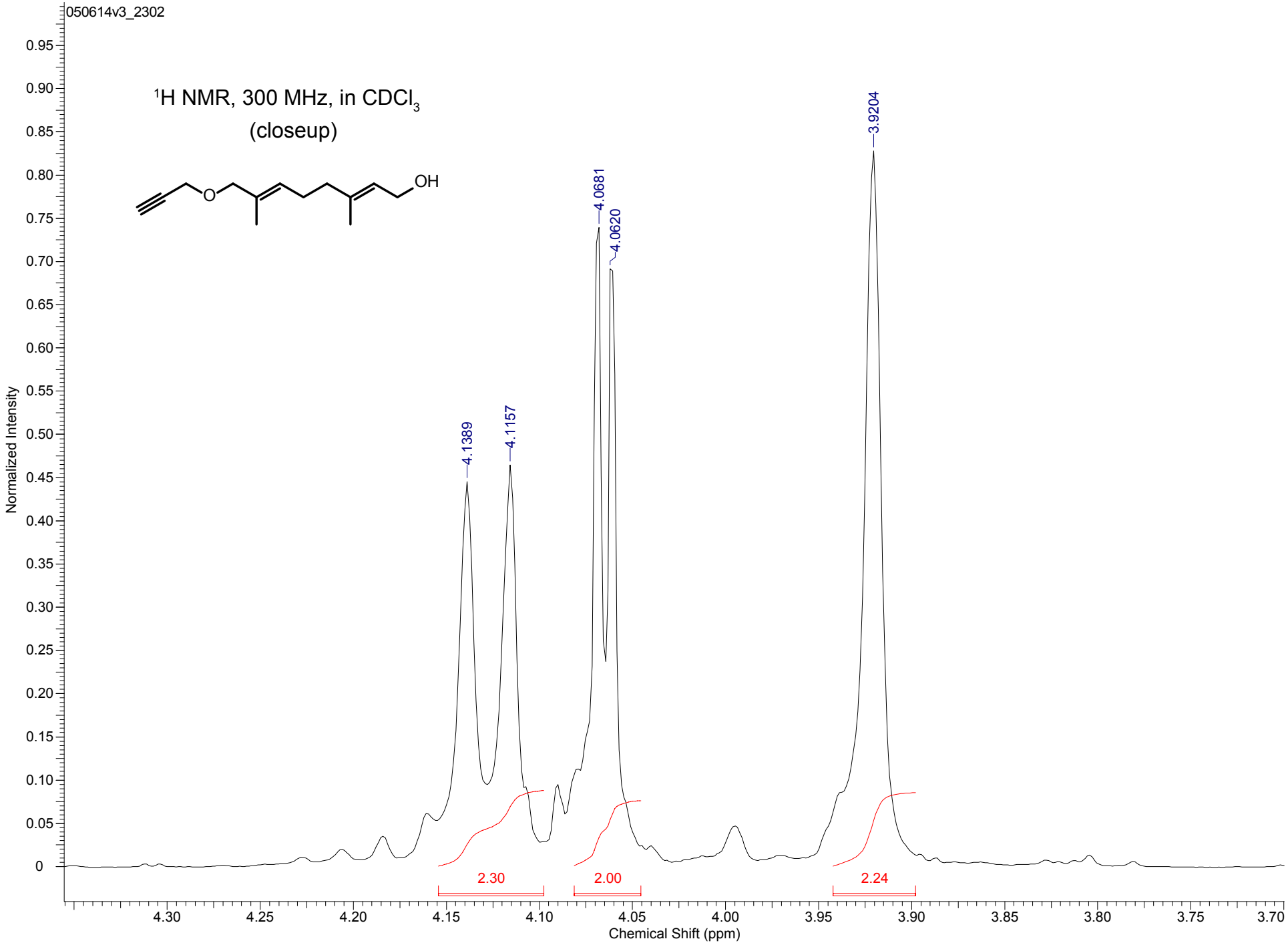
   d. A 500 MHz ^{1}H NMR and a ^{1}H-decoupled, 81 MHz ^{31}P NMR of product **3** in D_2O are shown next. (The ^{1}H NMR was obtained with solvent suppression, which is why there is a negative peak at δ = 4.7 ppm.) Based on the observed chemical shifts, do you think the reaction succeeded? If not, what do you think was made?

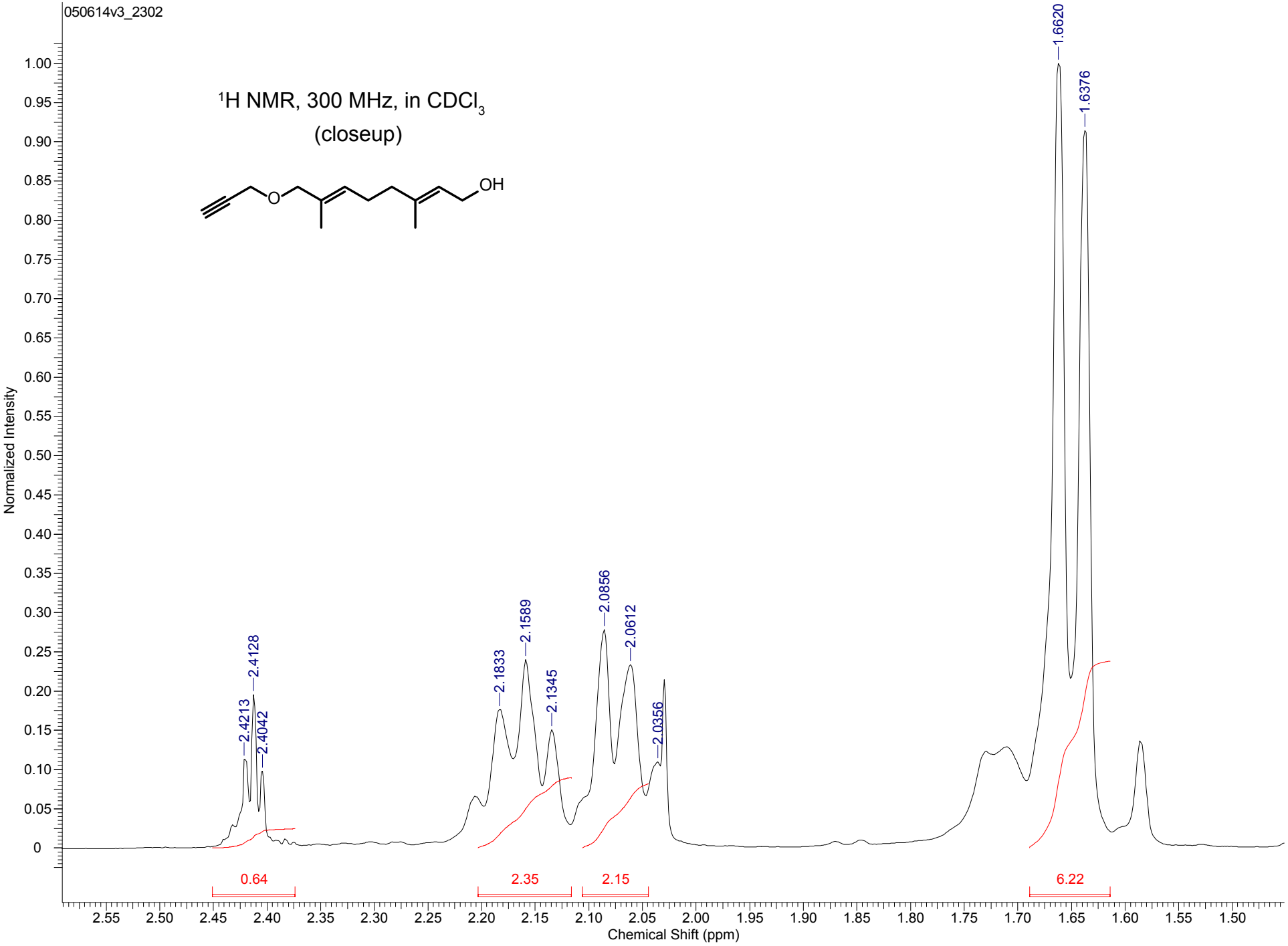
e. The final reaction was performed with a tetrabutylammonium salt, and this could in principle provide the counterions to the trianion drawn for **3**. The spectrum does contain some unmarked peaks at δ = 1.1, 2.4 and 3.0 ppm. Could these correspond to $(n\text{-Bu})_4N^+$? If not, what do these peaks correspond to?

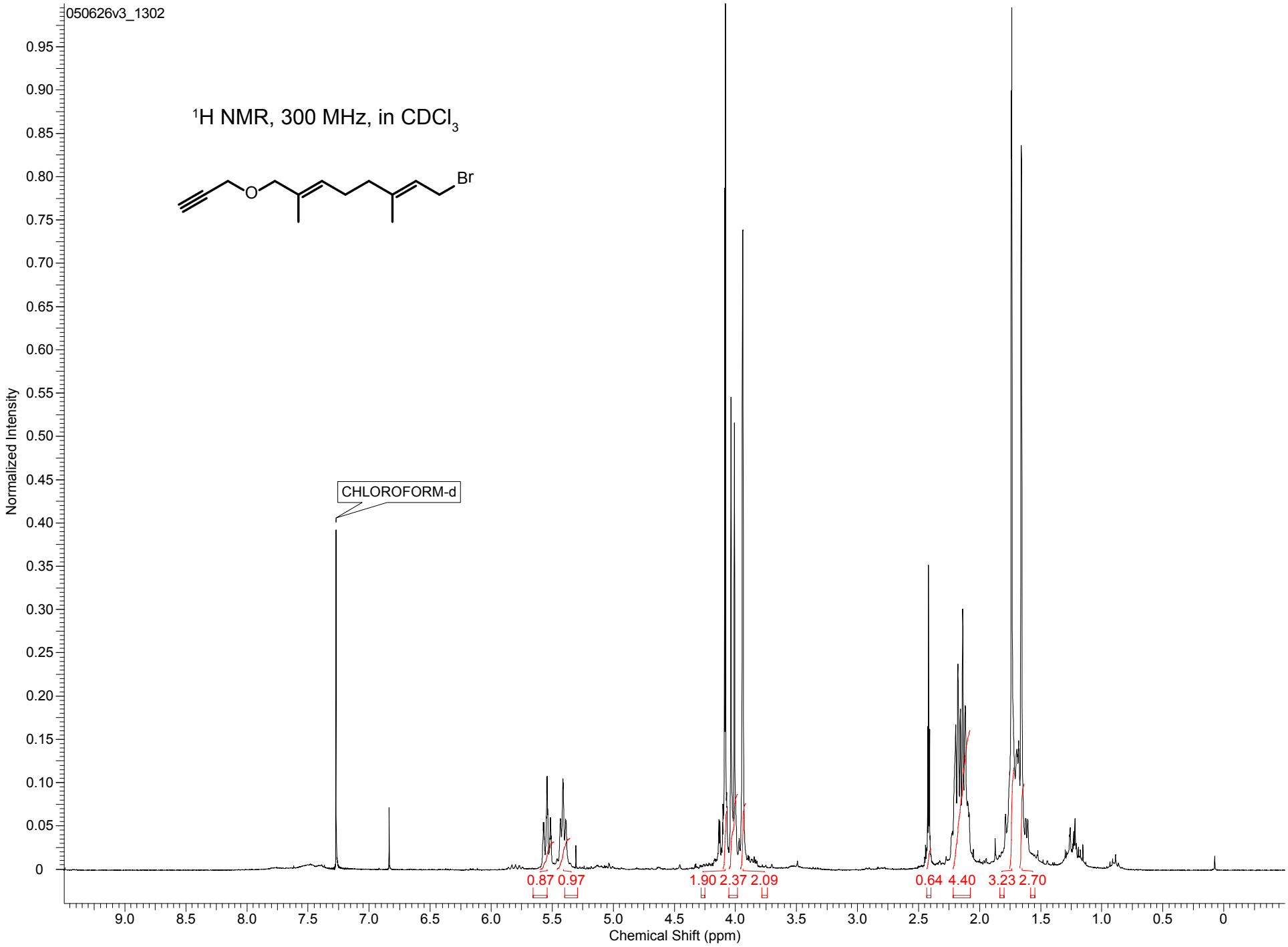
f. The ^{31}P NMR shows four peaks. Explain them in terms of your proposed product in part (e).

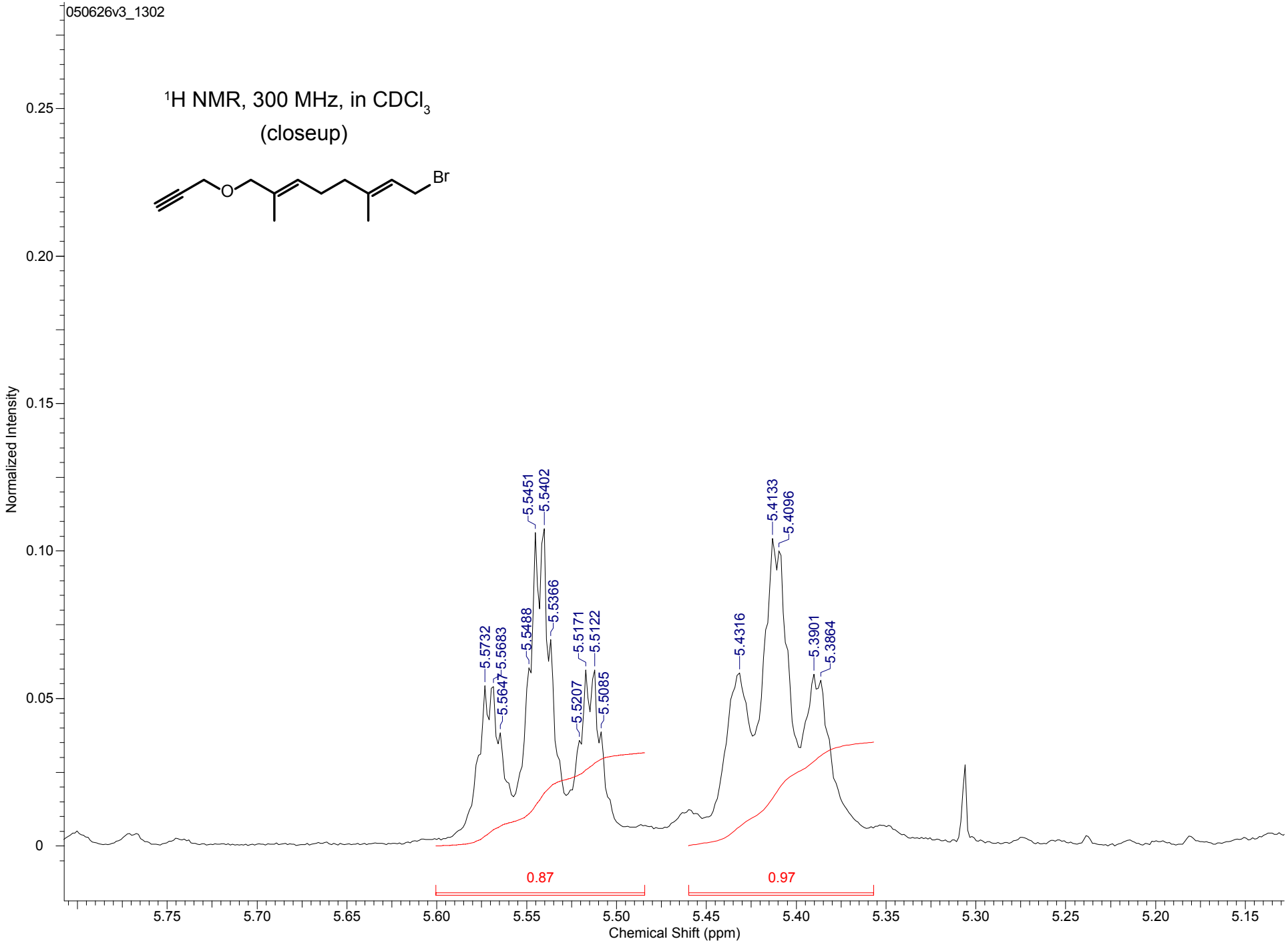

050614v3_2302
^{1}H NMR, 300 MHz, in $CDCl_3$
OH
O
CHLOROFORM-d
1.94
2.30 2.00 2.24
0.64 2.35 2.15 6.22
Normalized Intensity
Chemical Shift (ppm)

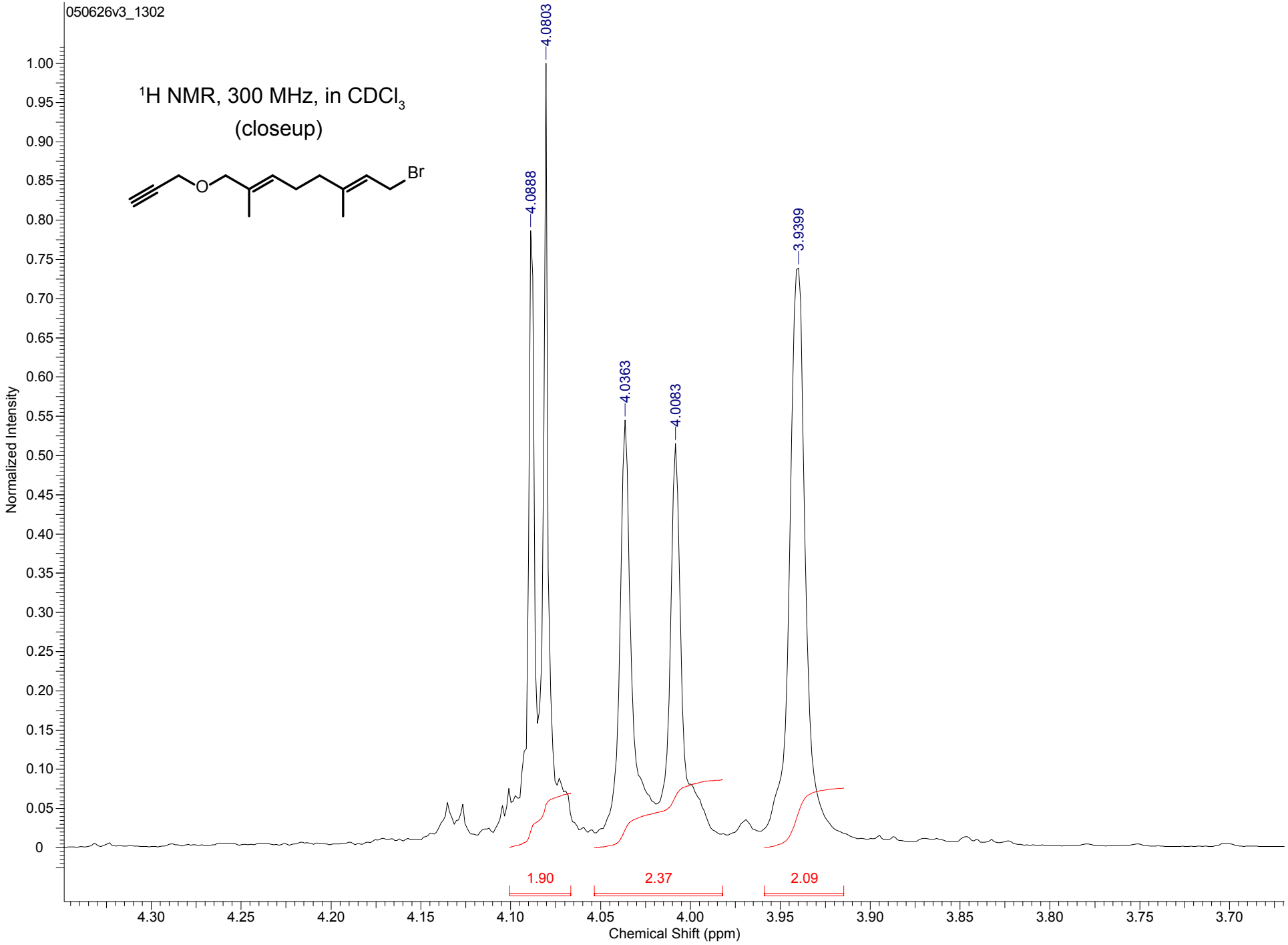

050614v3_2302
^{1}H NMR, 300 MHz, in $CDCl_3$
(closeup)
OH
O
Normalized Intensity
0.45
0.40
0.35
0.30
0.25
0.20
0.15
0.10
0.05
0
5.4328
5.4133
5.3913
5.3718
1.94
5.60
5.55
5.50
5.45
5.40
5.35
5.30
5.25
5.20
5.15
Chemical Shift (ppm)

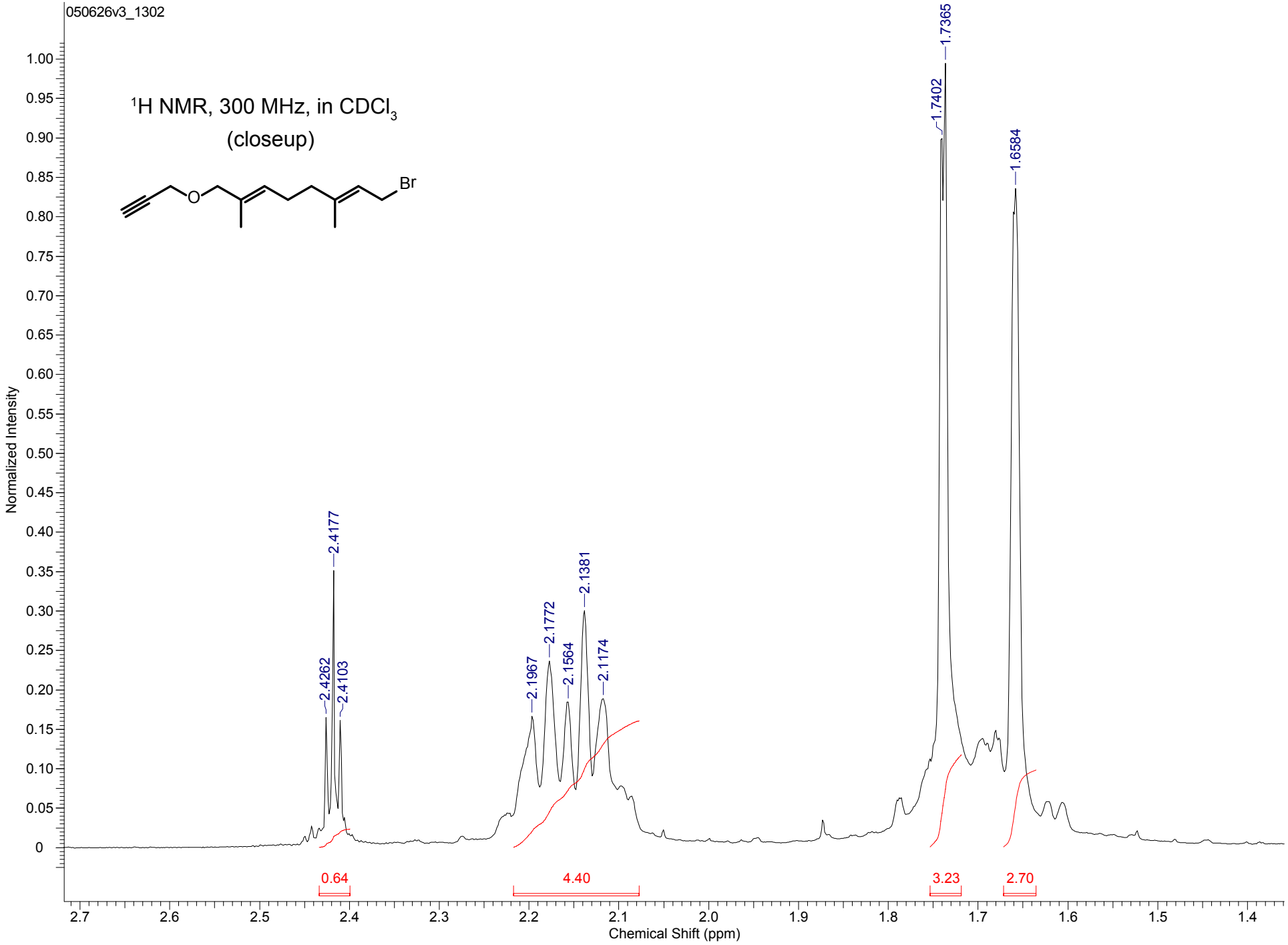

050614v3_2302
^{1}H NMR, 300 MHz, in $CDCl_3$
(closeup)
OH
O
4.1389
4.1157
4.0681
4.0620
3.9204
2.30
2.00
2.24
Normalized Intensity
Chemical Shift (ppm)
0.95
0.90
0.85
0.80
0.75
0.70
0.65
0.60
0.55
0.50
0.45
0.40
0.35
0.30
0.25
0.20
0.15
0.10
0.05
0
4.30
4.25
4.20
4.15
4.10
4.05
4.00
3.95
3.90
3.85
3.80
3.75
3.70

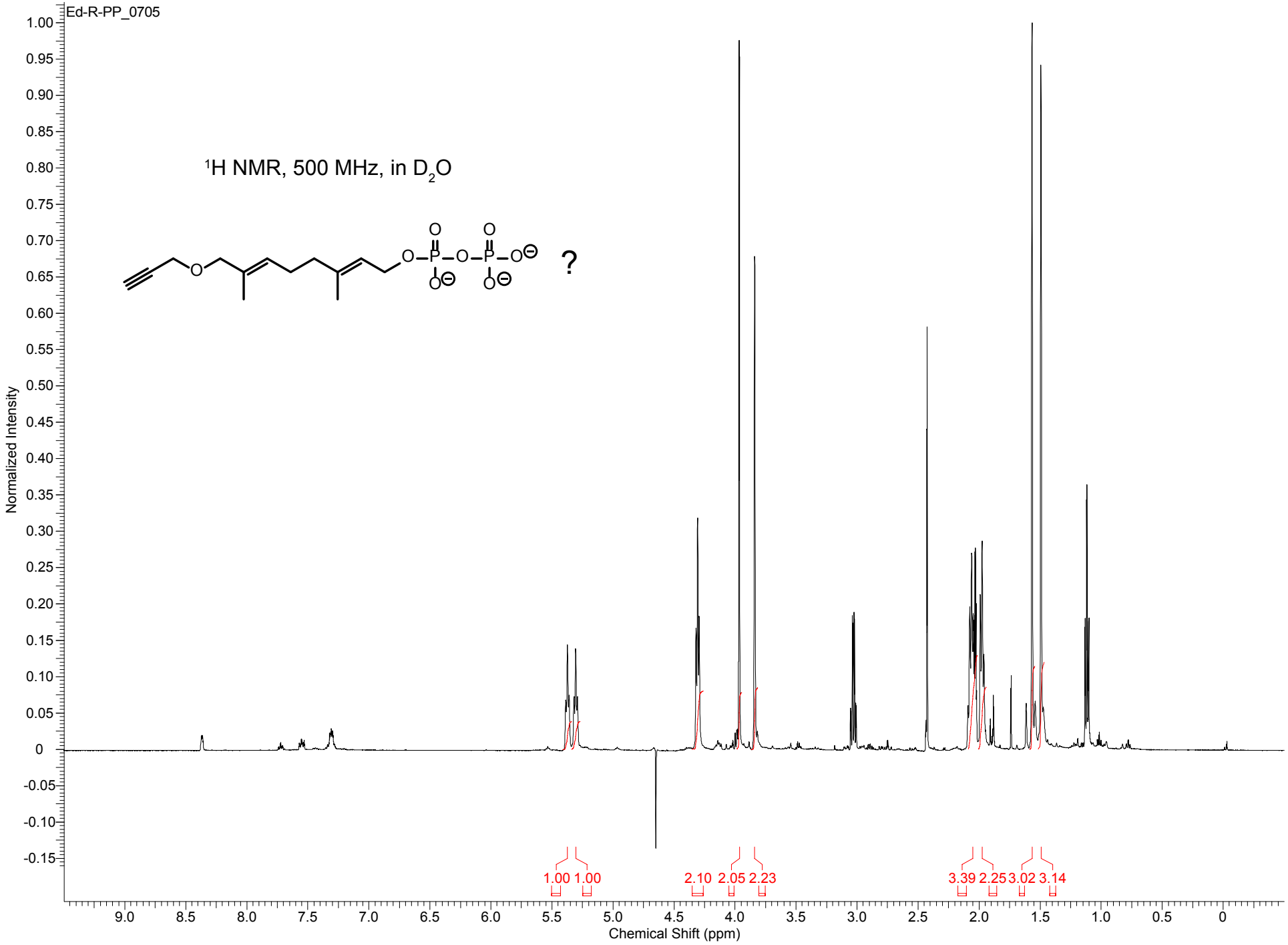

050614v3_2302
^{1}H NMR, 300 MHz, in $CDCl_3$
(closeup)
OH
O
Normalized Intensity
Chemical Shift (ppm)
2.4213
2.4128
2.4042
2.1833
2.1589
2.1345
2.0856
2.0612
2.0356
1.6620
1.6376
0.64
2.35
2.15
6.22

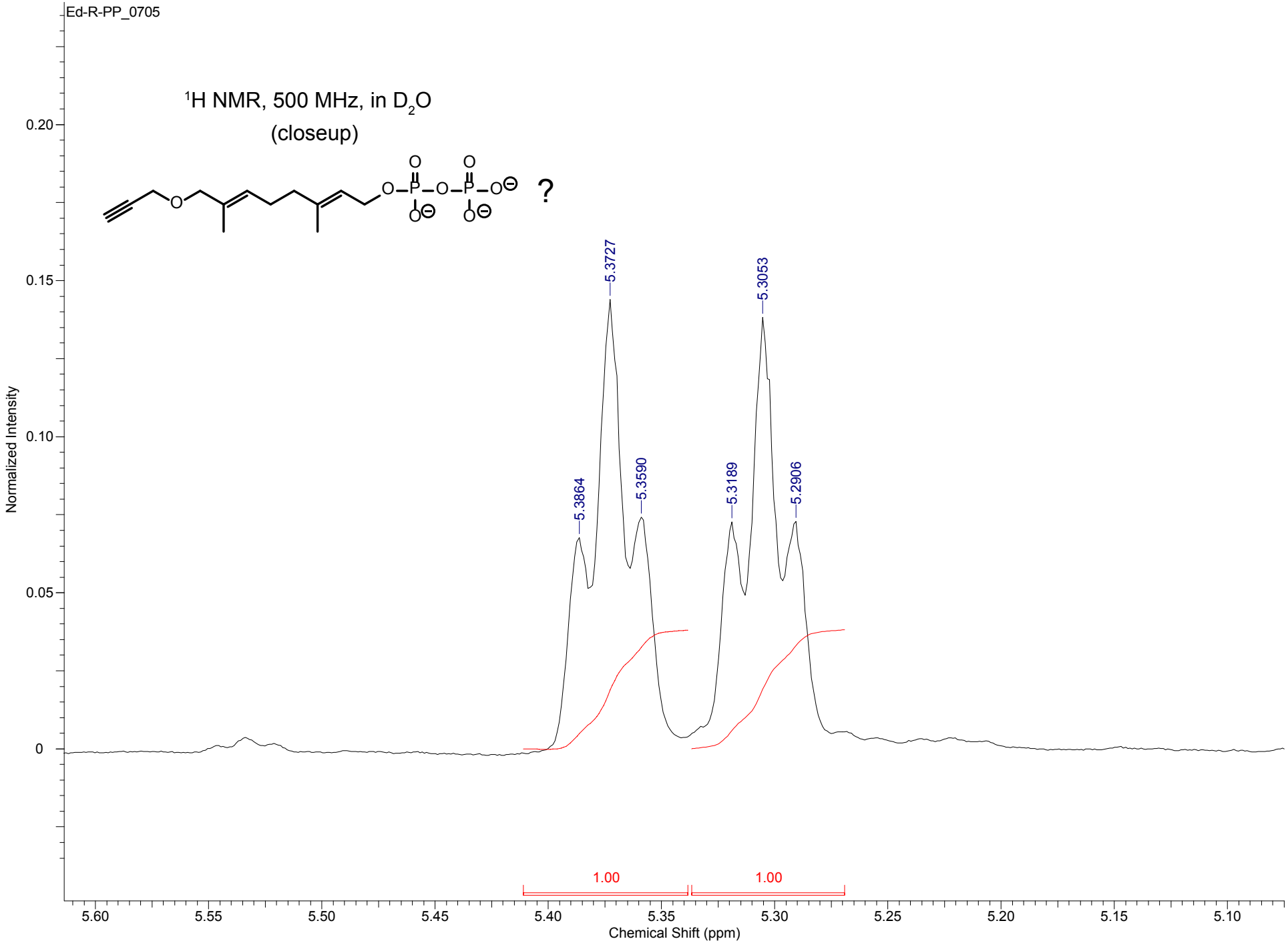

050626v3_1302
^{1}H NMR, 300 MHz, in $CDCl_3$
Br
O
CHLOROFORM-d
Normalized Intensity
Chemical Shift (ppm)
0.87 0.97
1.90 2.37 2.09
0.64 4.40
3.23 2.70

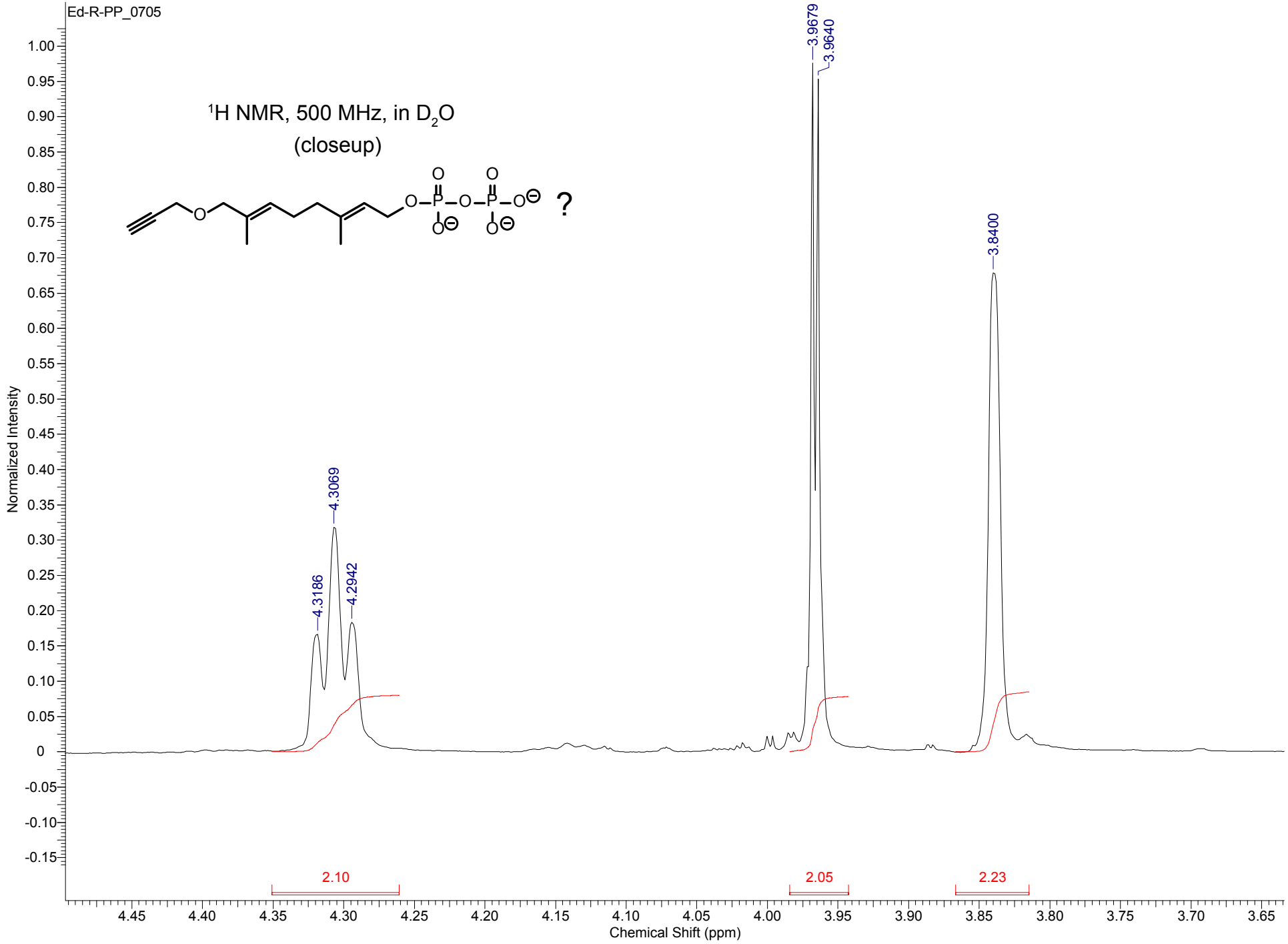

050626v3_1302
^{1}H NMR, 300 MHz, in $CDCl_3$
(closeup)
Br
O
Normalized Intensity
0.25
0.20
0.15
0.10
0.05
0
5.5732
5.5683
5.5647
5.5488
5.5451
5.5402
5.5366
5.5207
5.5171
5.5122
5.5085
5.4316
5.4133
5.4096
5.3901
5.3864
0.87
0.97
5.75
5.70
5.65
5.60
5.55
5.50
5.45
5.40
5.35
5.30
5.25
5.20
5.15
Chemical Shift (ppm)

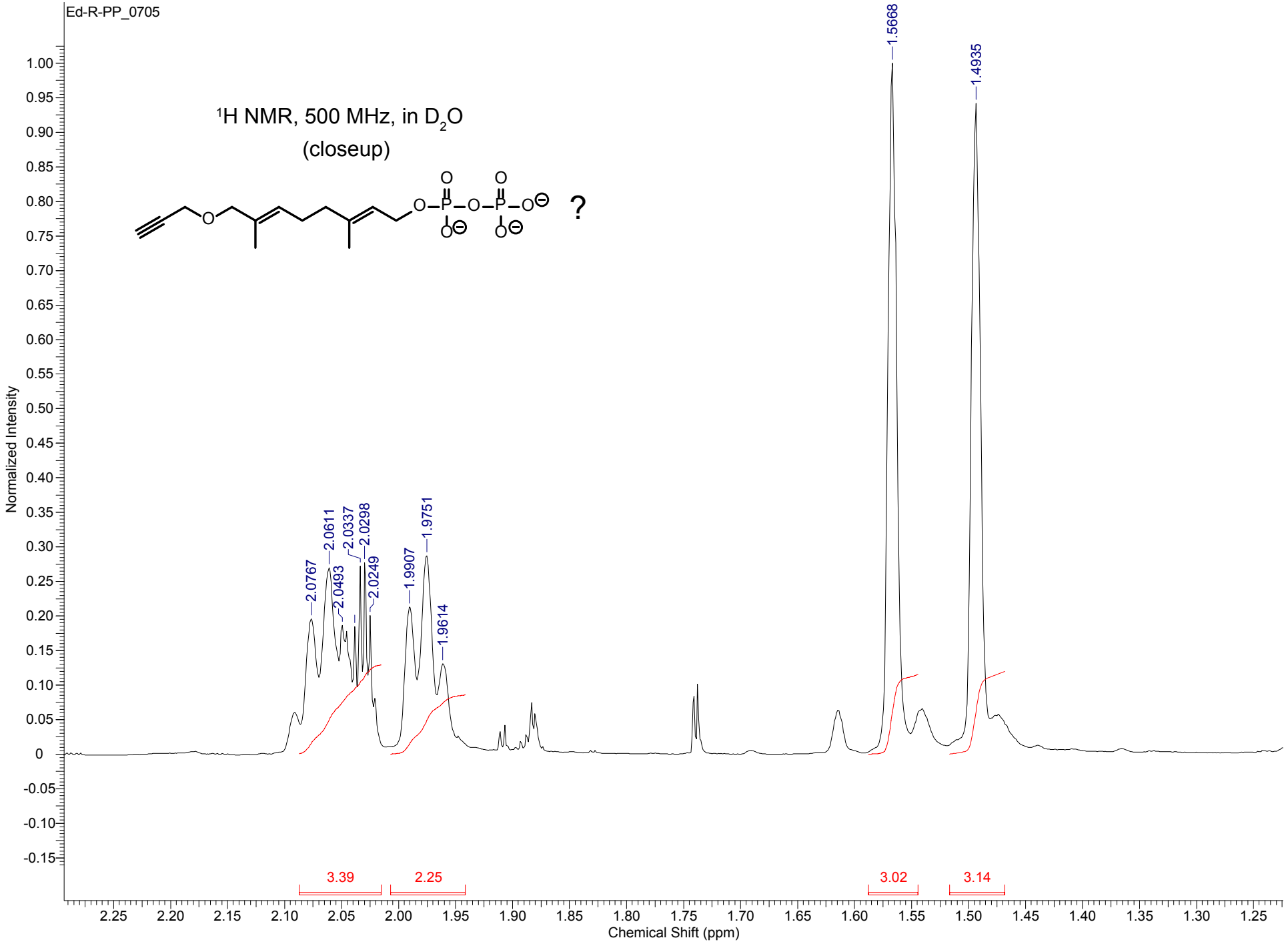

050626v3_1302
^{1}H NMR, 300 MHz, in $CDCl_3$
(closeup)
Br
O
4.0803
4.0888
4.0363
4.0083
3.9399
1.90
2.37
2.09
Normalized Intensity
Chemical Shift (ppm)

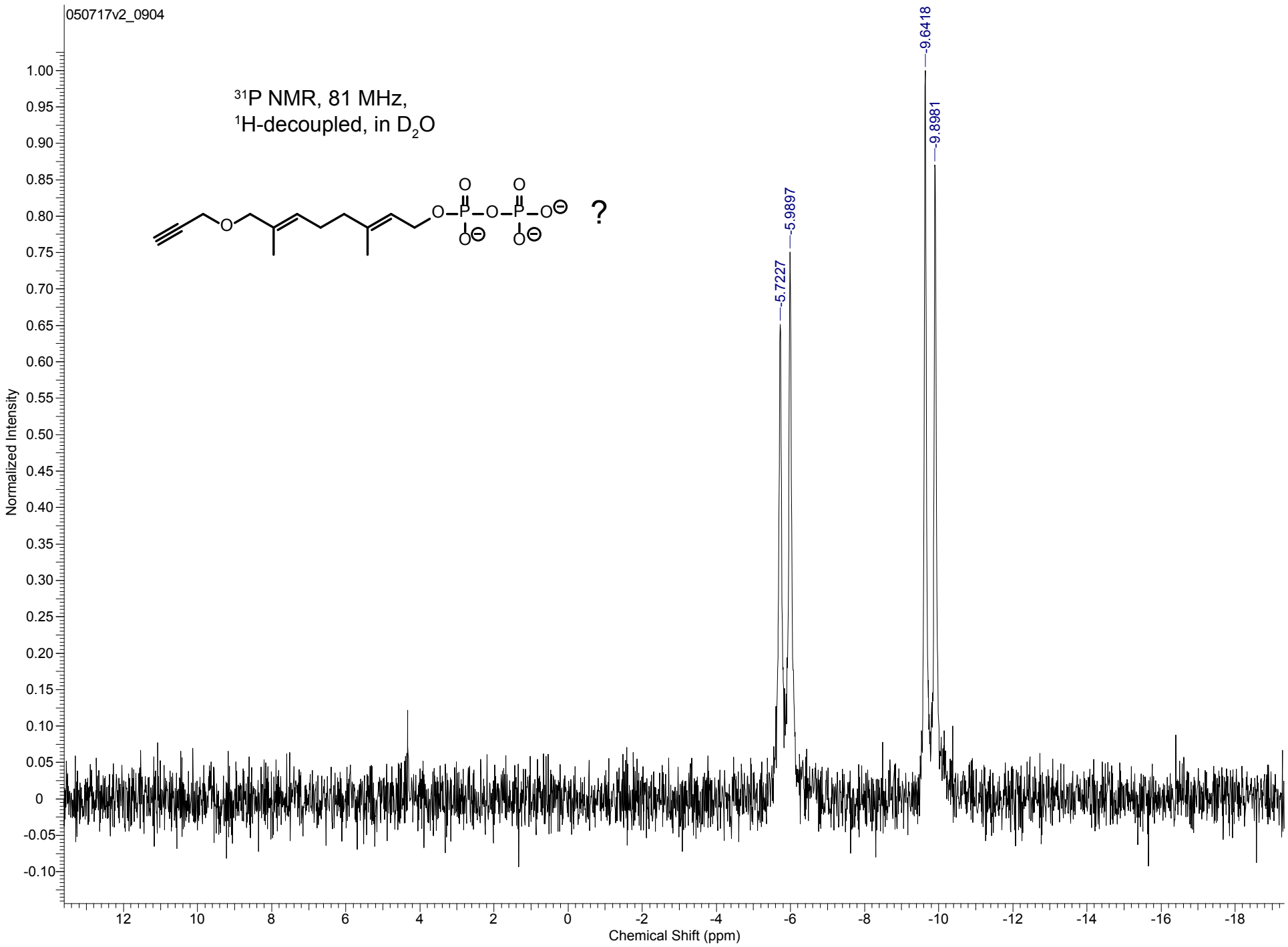

050626v3_1302
^{1}H NMR, 300 MHz, in $CDCl_3$
(closeup)
Br
O
Normalized Intensity
Chemical Shift (ppm)
2.4262
2.4177
2.4103
2.1967
2.1772
2.1564
2.1381
2.1174
1.7402
1.7365
1.6584
0.64
4.40
3.23
2.70


Ed-R-PP_0705
^{1}H NMR, 500 MHz, in D_2O
?
Normalized Intensity
Chemical Shift (ppm)
1.00 1.00
2.10 2.05 2.23
3.39 2.25 3.02 3.14

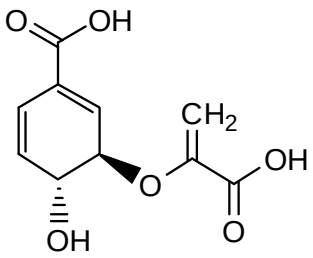

Ed-R-PP_0705
^{1}H NMR, 500 MHz, in D_2O
(closeup)
?
Normalized Intensity
0.20
0.15
0.10
0.05
0
5.3727
5.3053
5.3864
5.3590
5.3189
5.2906
1.00
1.00
5.60
5.55
5.50
5.45
5.40
5.35
5.30
5.25
5.20
5.15
5.10
Chemical Shift (ppm)


Ed-R-PP_0705
^{1}H NMR, 500 MHz, in D_2O
(closeup)
?
3.9679
3.9640
3.8400
4.3069
4.3186
4.2942
Normalized Intensity
Chemical Shift (ppm)
2.10
2.05
2.23

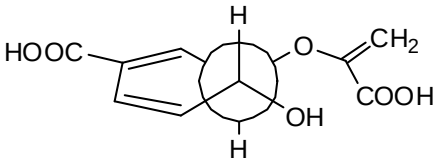

Ed-R-PP_0705
^{1}H NMR, 500 MHz, in D_2O
(closeup)
?
Normalized Intensity
Chemical Shift (ppm)
1.5668
1.4935
2.0767
2.0611
2.0493
2.0337
2.0298
2.0249
1.9907
1.9751
1.9614
3.39
2.25
3.02
3.14


050717v2_0904
^{31}P NMR, 81 MHz,
^{1}H-decoupled, in D_2O
?
-5.7227
-5.9897
-9.6418
-9.8981
Normalized Intensity
Chemical Shift (ppm)

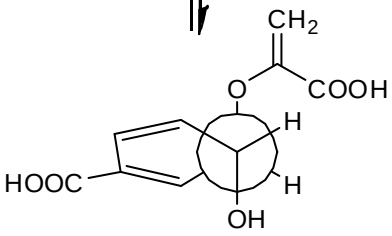
2. Chorismic acid has two pseudo-chair conformations, one of which is much more stable than the other.



chorismic acid



pseudo-diequatorial



pseudo-diaxial

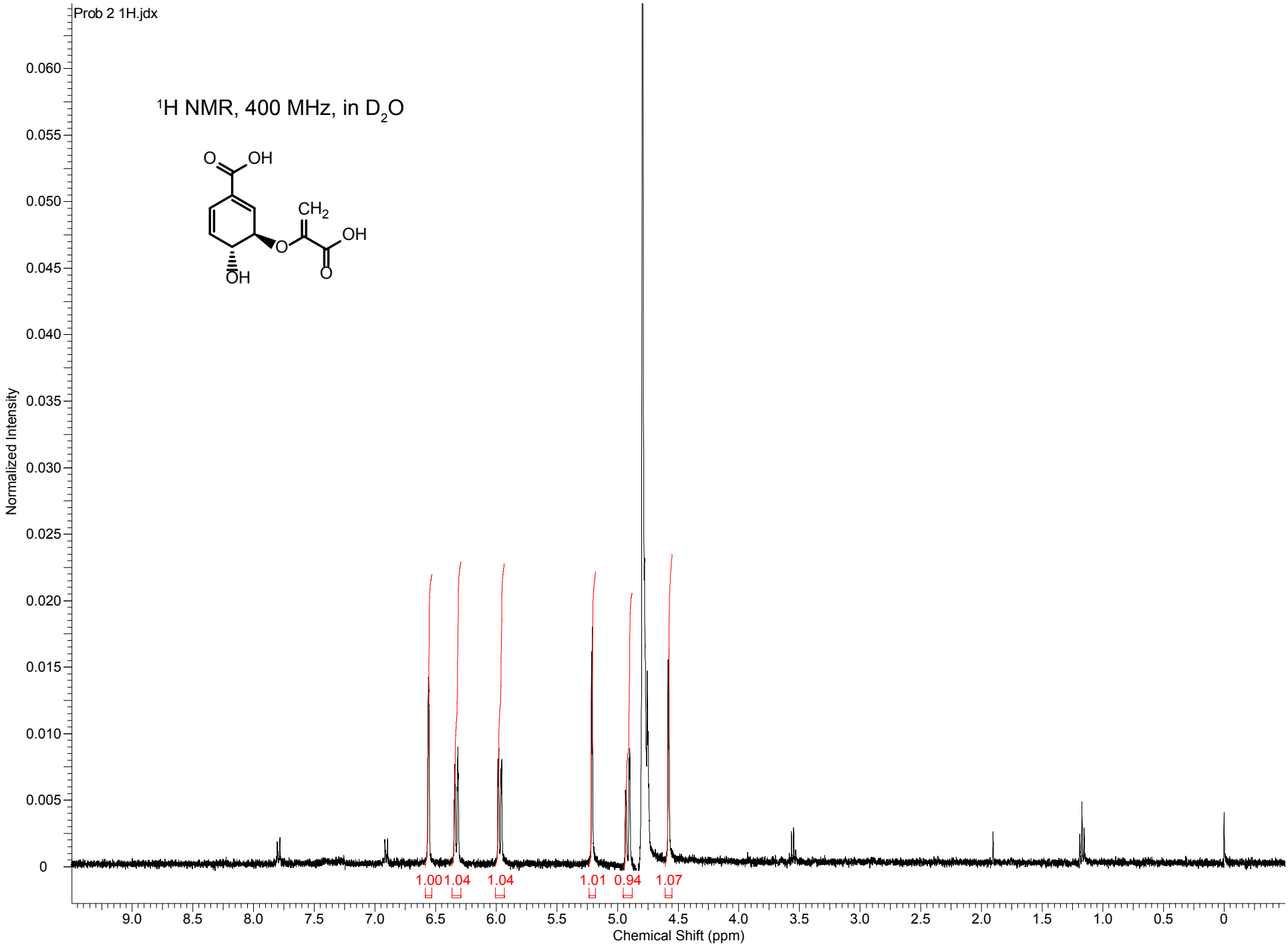
In principle, either or both of these conformations could contribute to the molecule's NMR spectra. The next three pages show the 400 MHz ^{1}H NMR spectrum of chorismic acid (the full spectrum and two close-ups) in D_2O. There are a couple of impurities in the sample—if I haven't marked a peak, then ignore it.

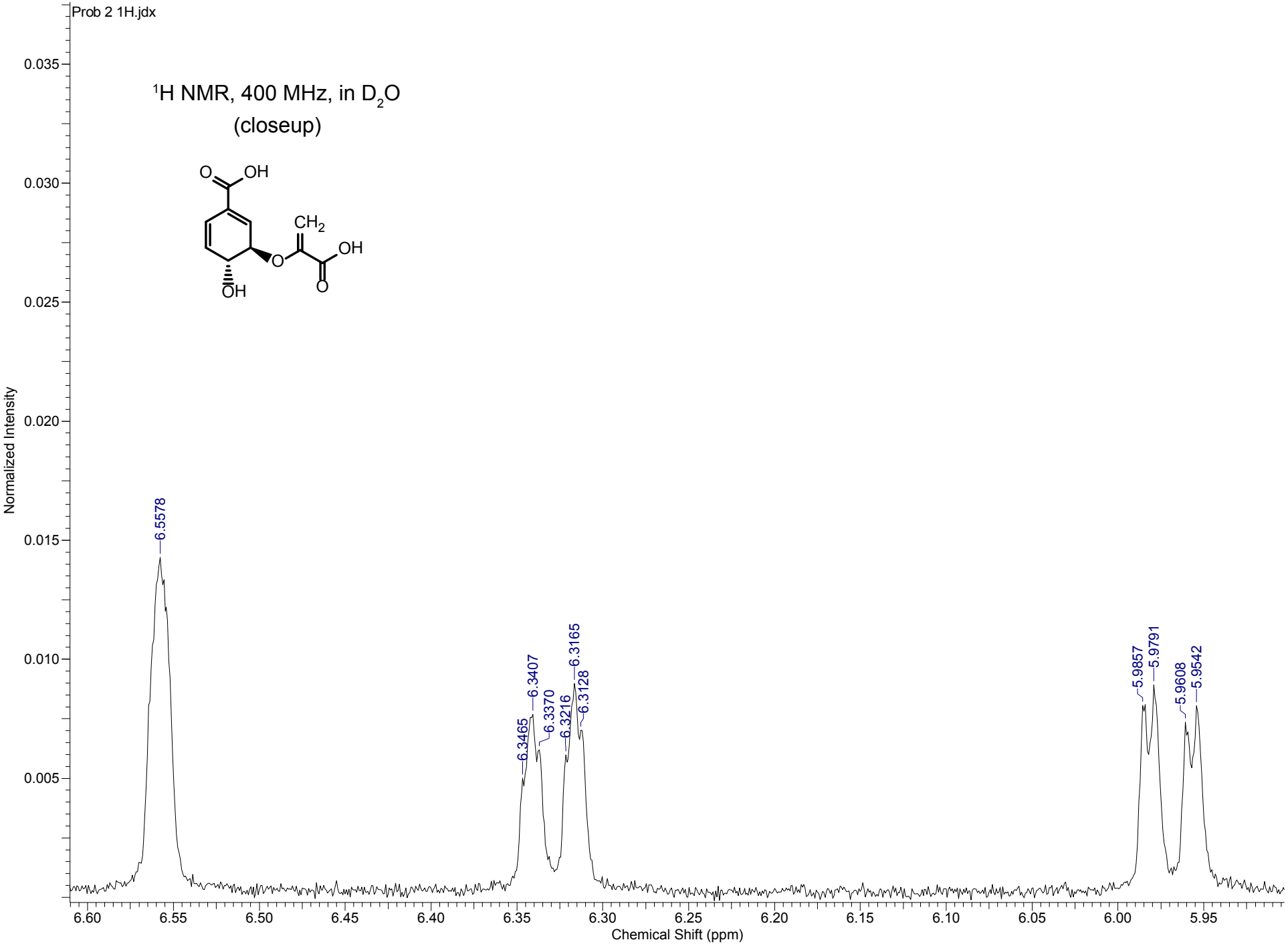
a. Assign each resonance in the ^{1}H NMR spectrum to a specific proton in the structure of chorismic acid. Also identify the multiplicity of each resonance, and calculate corresponding coupling constants.

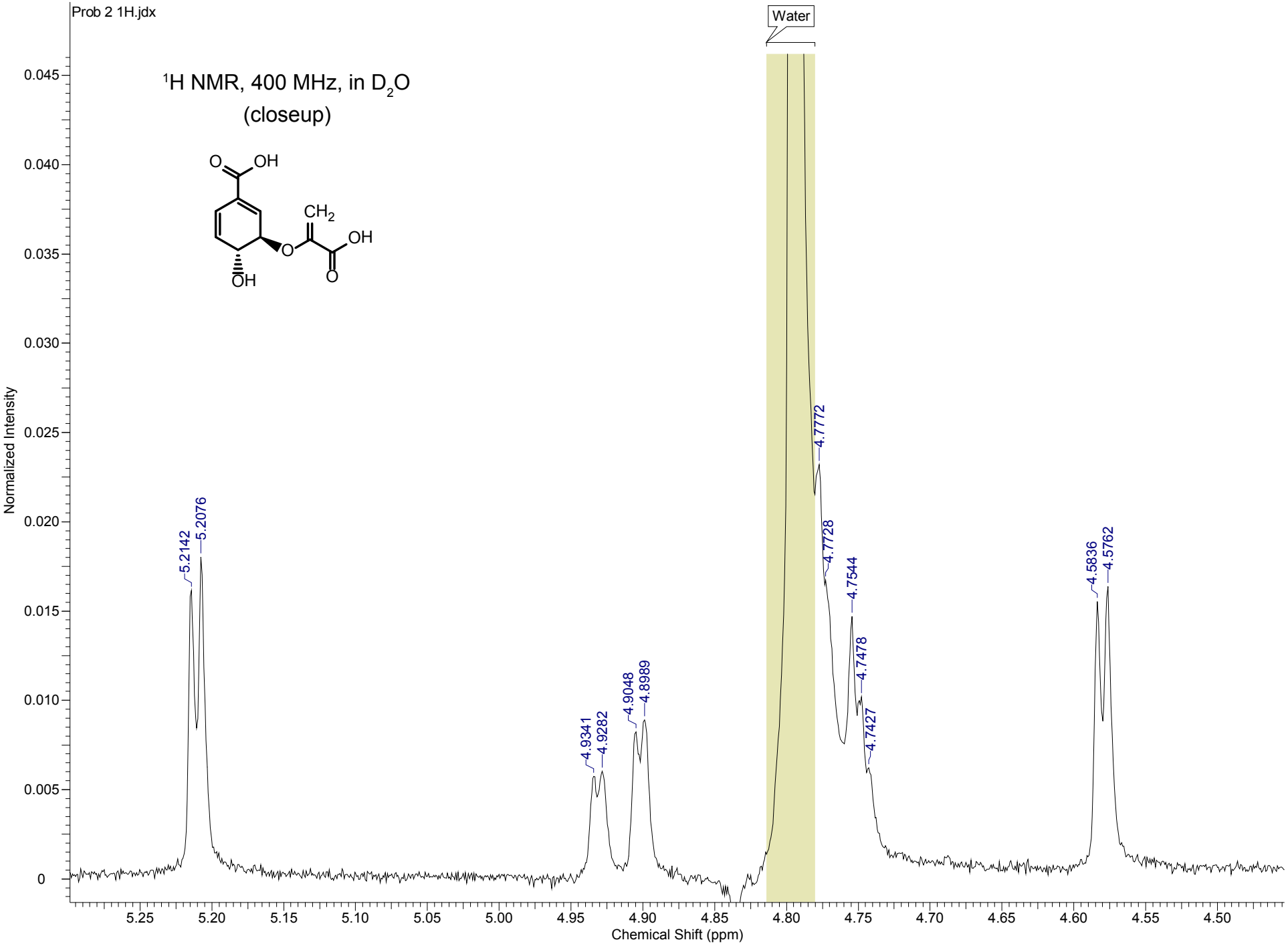
b. Based on the coupling constants you calculated, which protons are coupled to which in chorismic acid? Why are some adjacent protons not coupled or only weakly coupled? How might the geometry of chorismic acid affect this?

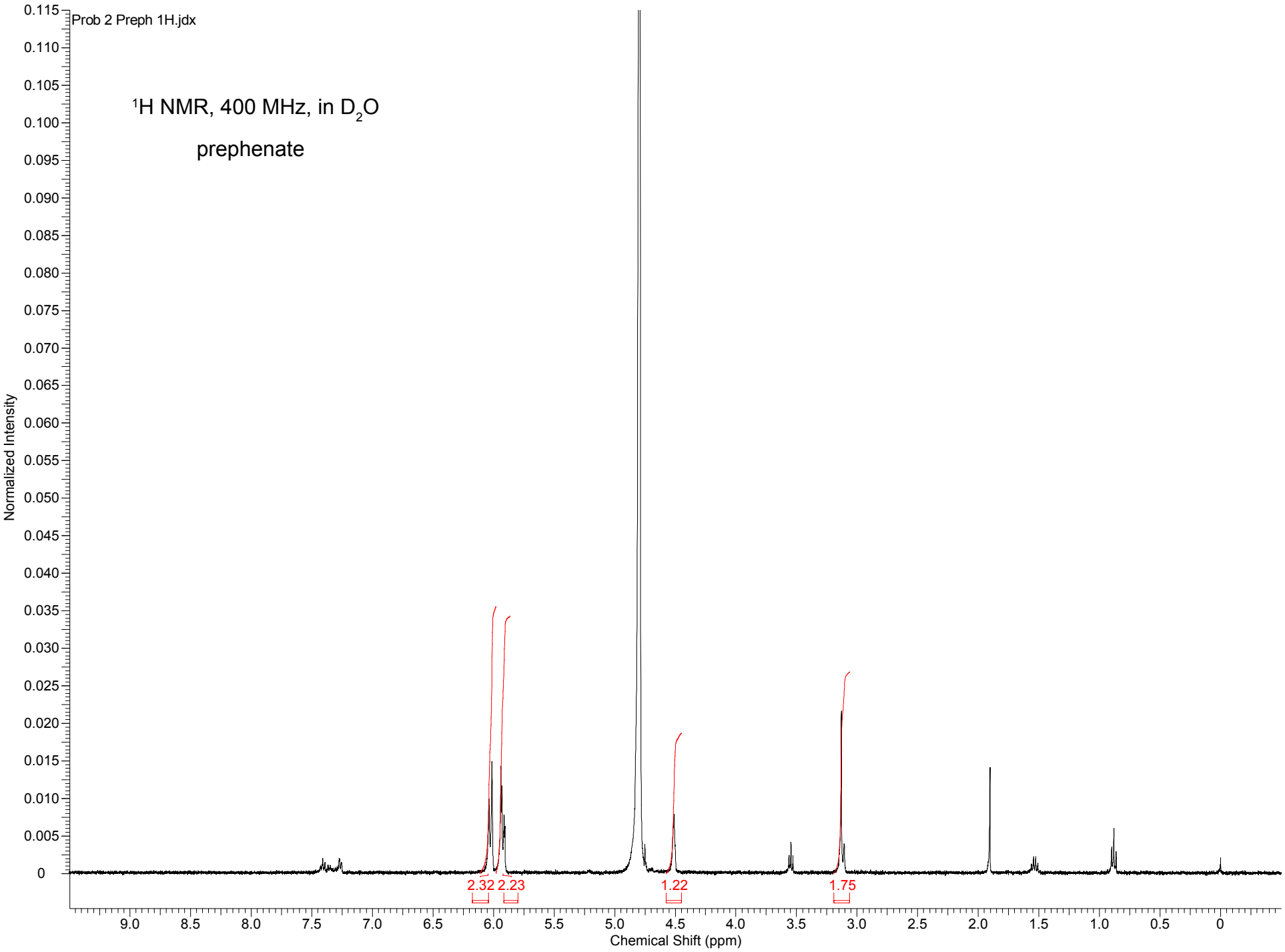
Chorismic acid undergoes either thermal or enzyme-catalyzed Claisen rearrangement to form prephenate. The 400 MHz ^{1}H NMR spectrum of that product is also given on the subsequent three pages.

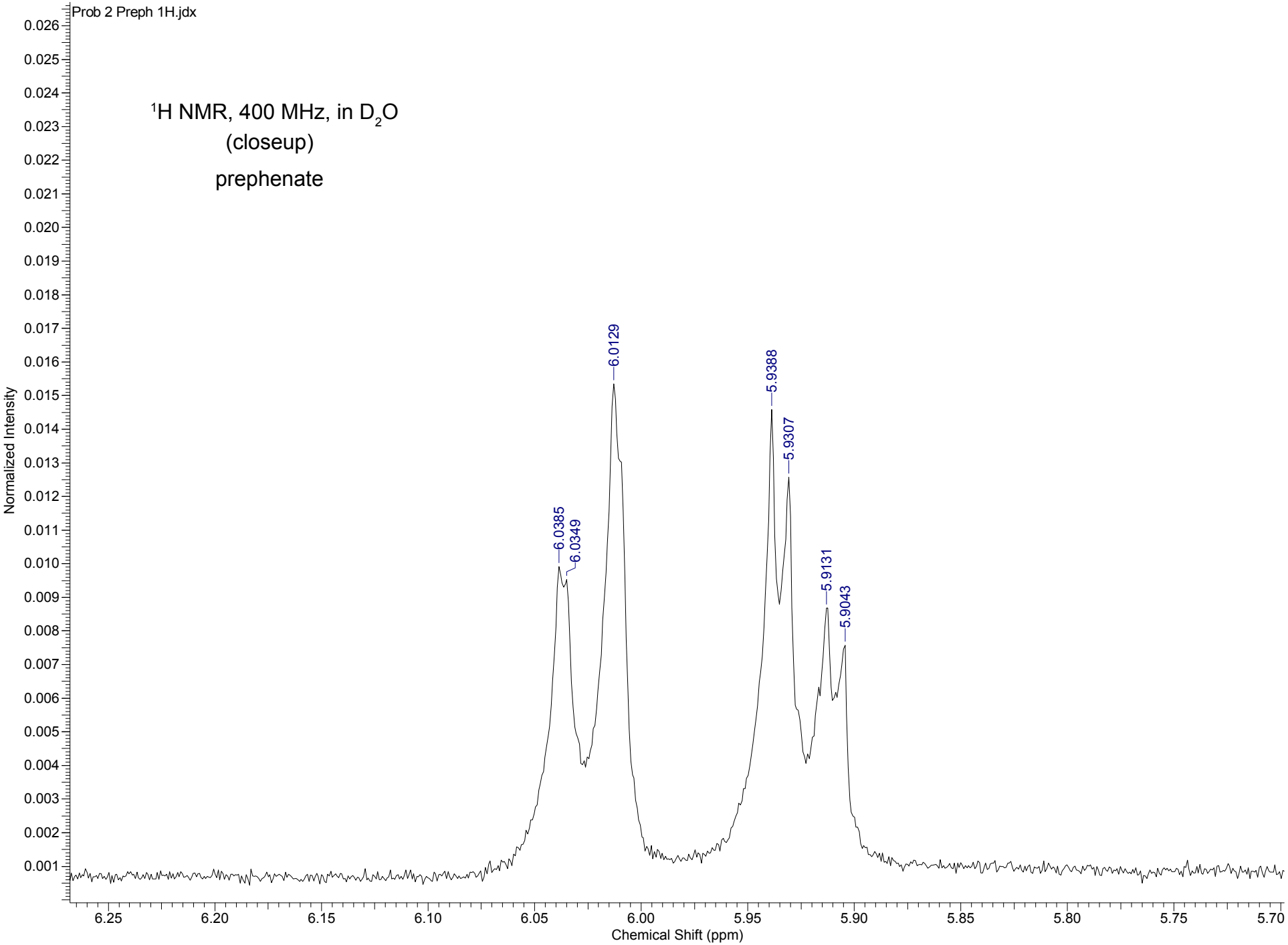
c. Assign each resonance in the ^{1}H NMR spectrum of prephenate to a specific proton in the structure of chorismic acid. Also identify the multiplicity of each resonance, and calculate corresponding coupling constants.

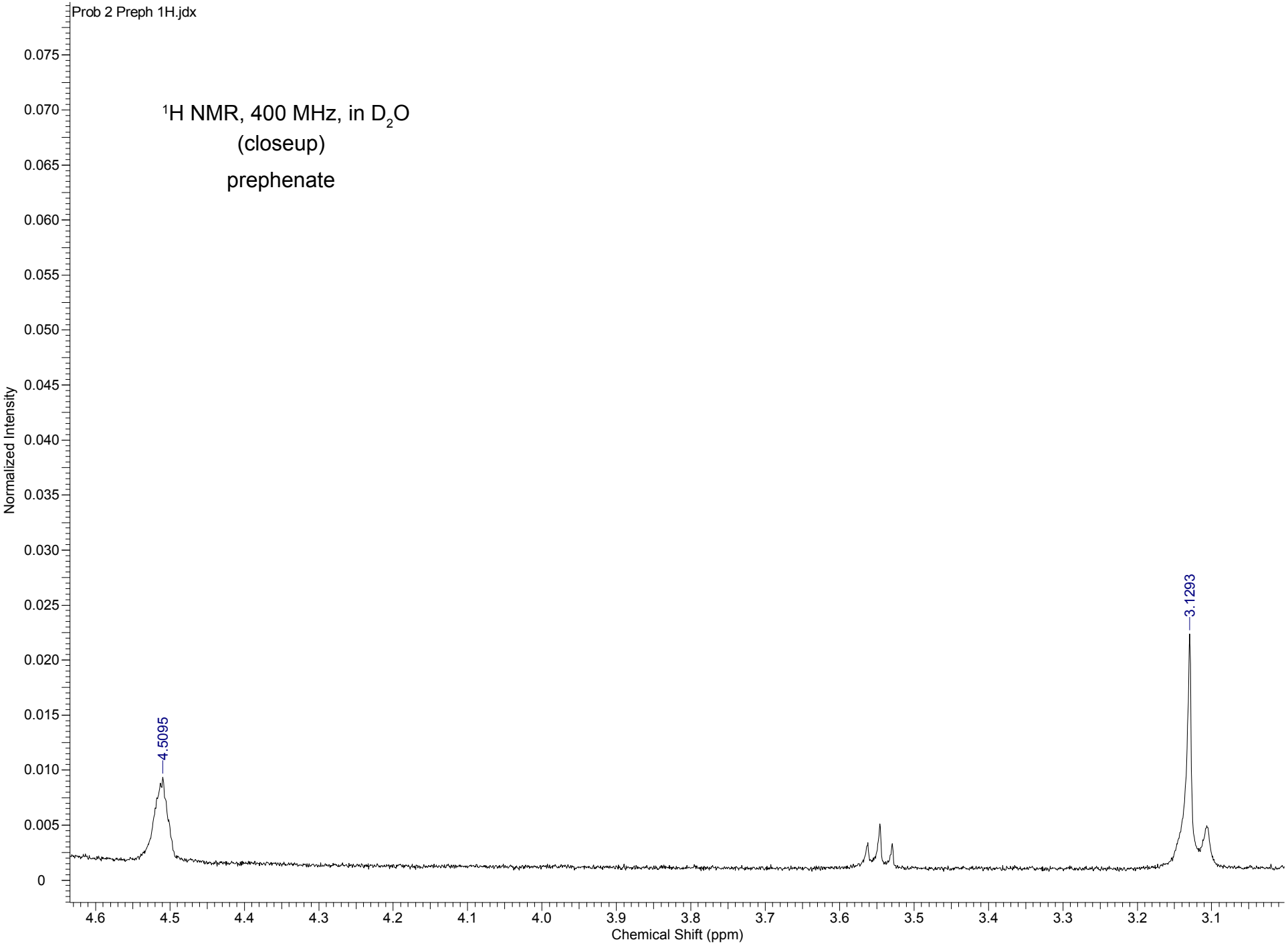

Prob 2 1H.jdx
^{1}H NMR, 400 MHz, in D_2O
O
OH
CH2
OH
O
O
OH
Normalized Intensity
0.060
0.055
0.050
0.045
0.040
0.035
0.030
0.025
0.020
0.015
0.010
0.005
0
1.00
1.04
1.04
1.01
0.94
1.07
9.0
8.5
8.0
7.5
7.0
6.5
6.0
5.5
5.0
4.5
4.0
3.5
3.0
2.5
2.0
1.5
1.0
0.5
0
Chemical Shift (ppm)


Prob 2 1H.jdx
^{1}H NMR, 400 MHz, in D_2O
(closeup)
O
OH
CH2
OH
O
O
OH
Normalized Intensity
0.035
0.030
0.025
0.020
0.015
0.010
0.005
6.5578
6.3465
6.3407
6.3370
6.3216
6.3165
6.3128
5.9857
5.9791
5.9608
5.9542
6.60
6.55
6.50
6.45
6.40
6.35
6.30
6.25
6.20
6.15
6.10
6.05
6.00
5.95
Chemical Shift (ppm)

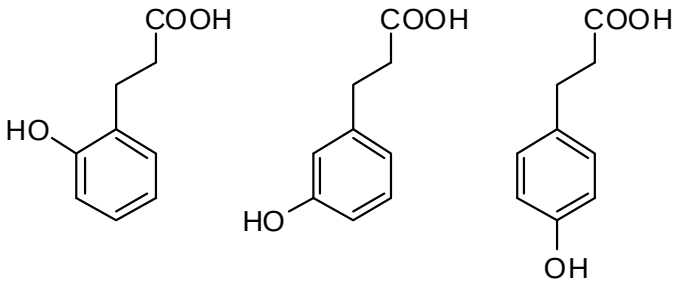

Prob 2 1H.jdx
^{1}H NMR, 400 MHz, in D_2O
(closeup)
Water
Normalized Intensity
Chemical Shift (ppm)
5.2142
5.2076
4.9341
4.9282
4.9048
4.8989
4.7772
4.7728
4.7544
4.7478
4.7427
4.5836
4.5762

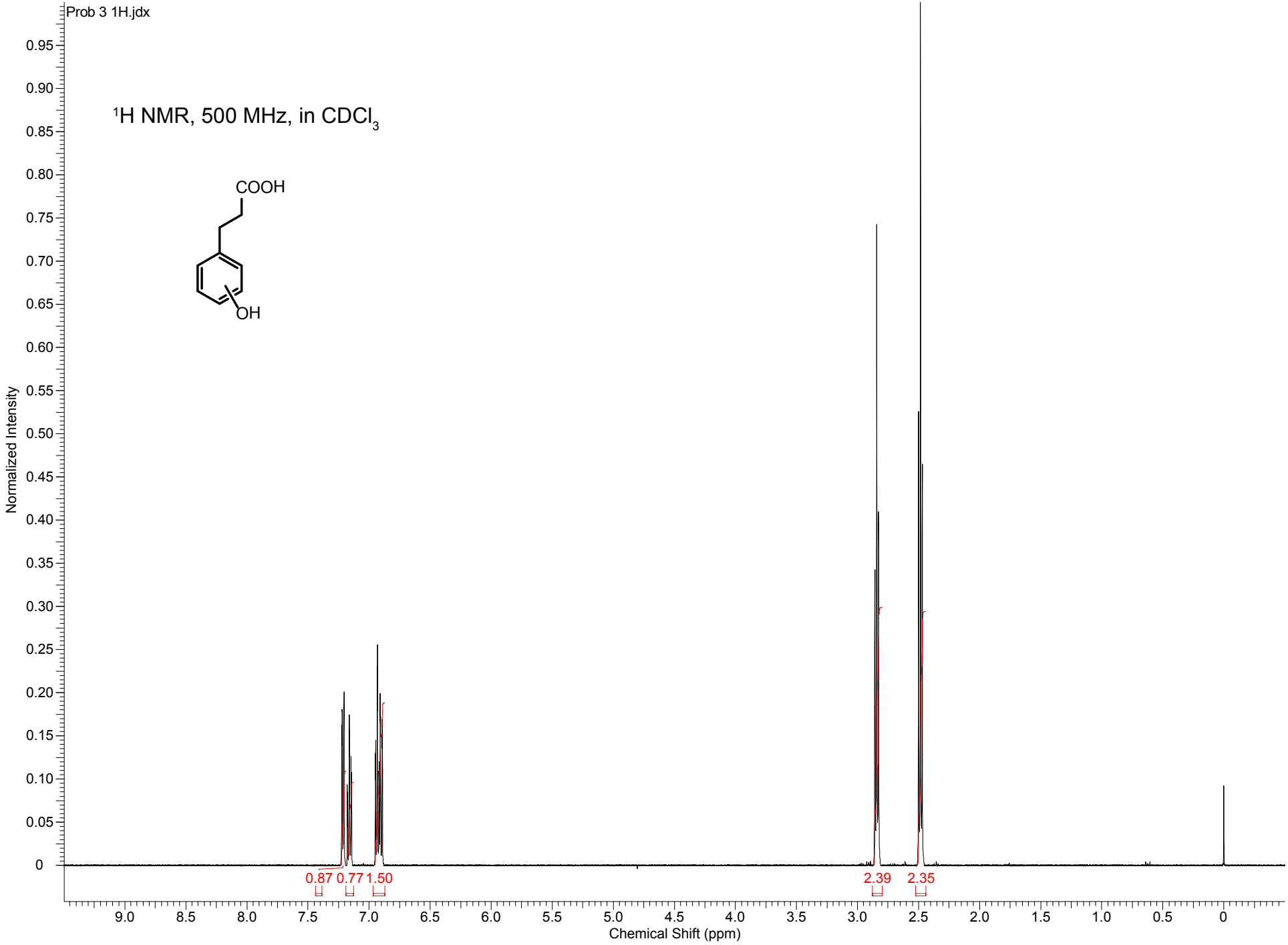

Prob 2 Preph 1H.jdx
^{1}H NMR, 400 MHz, in D_2O
prephenate
Normalized Intensity
Chemical Shift (ppm)
2.32
2.23
1.22
1.75

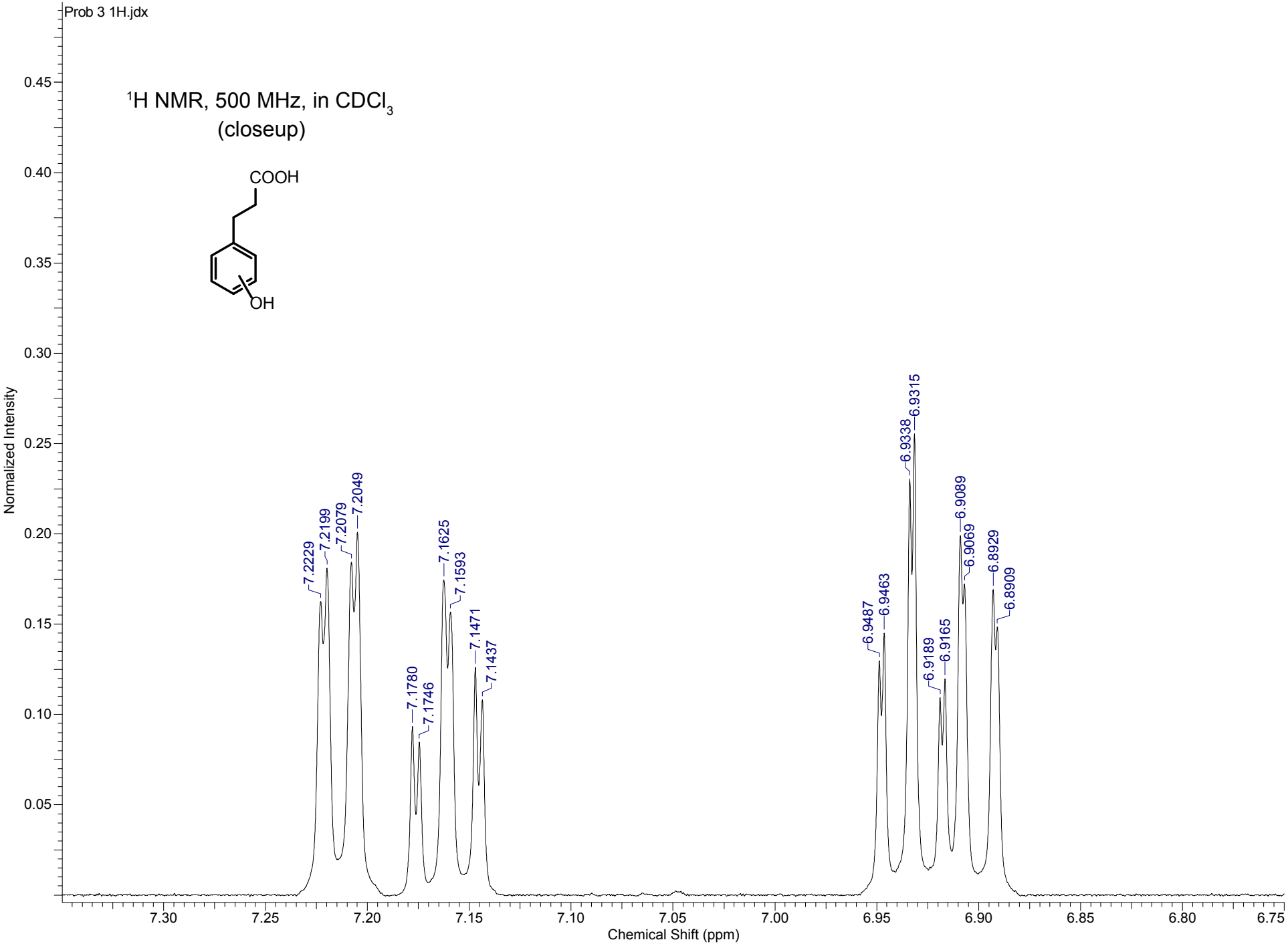

Prob 2 Preph 1H.jdx
^{1}H NMR, 400 MHz, in D_2O
(closeup)
prephenate
Normalized Intensity
Chemical Shift (ppm)
6.0385
6.0349
6.0129
5.9388
5.9307
5.9131
5.9043

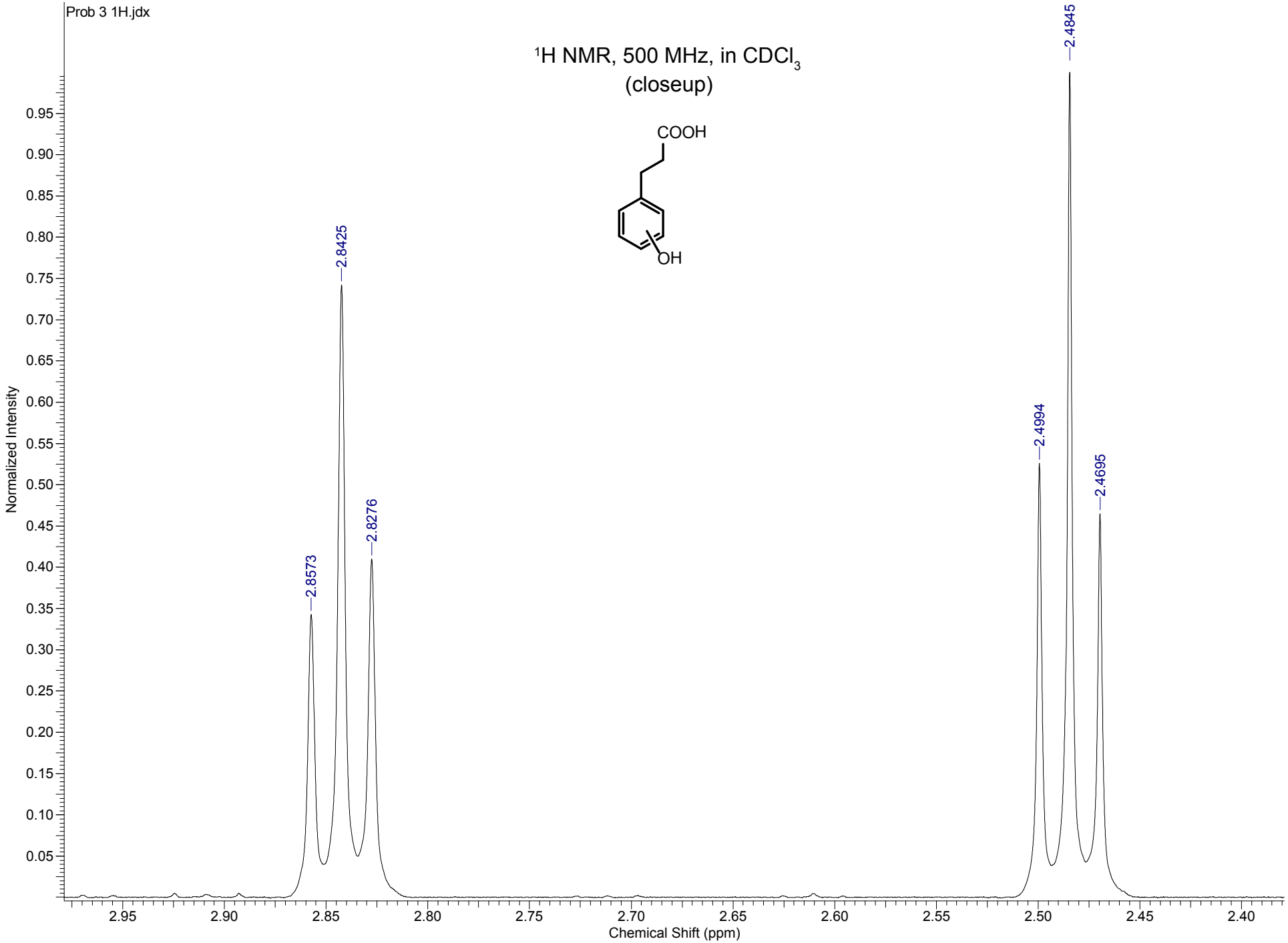

Prob 2 Preph 1H.jdx
^{1}H NMR, 400 MHz, in D_2O
(closeup)
prephenate
Normalized Intensity
0.075
0.070
0.065
0.060
0.055
0.050
0.045
0.040
0.035
0.030
0.025
0.020
0.015
0.010
0.005
0
4.5095
3.1293
4.6
4.5
4.4
4.3
4.2
4.1
4.0
3.9
3.8
3.7
3.6
3.5
3.4
3.3
3.2
3.1
Chemical Shift (ppm)

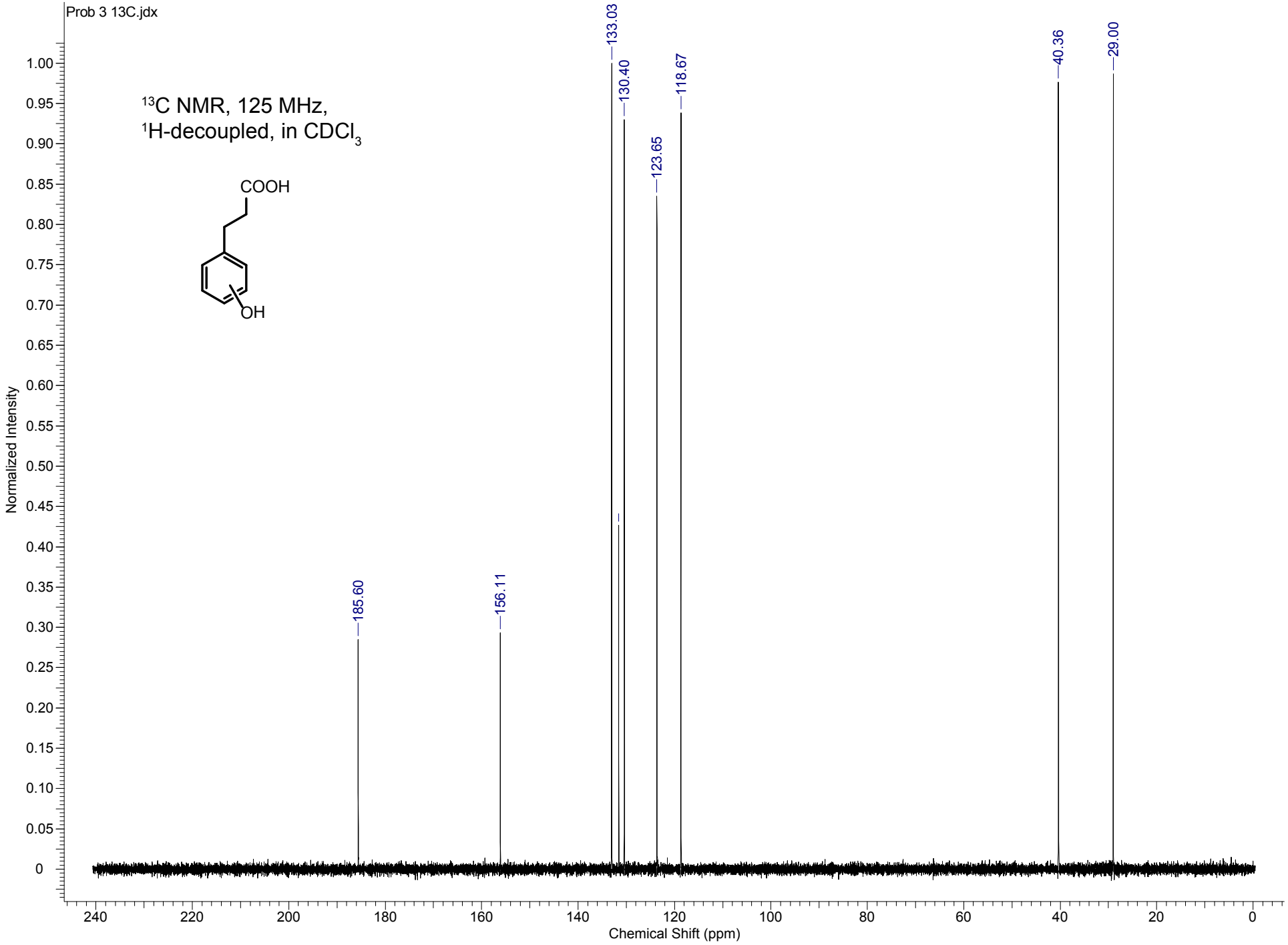
3. The 500 MHz ^{1}H NMR spectrum (taken in $CDCl_3$, with a TMS standard) on the next pages corresponds to a (hydroxy-phenyl)propionic acid. Which one? As best you can, assign each of the resonances in the spectra to a specific atom in the structure of the acid you chose. Also identify the multiplicity of each resonance in the ^{1}H spectrum, and calculate corresponding coupling constants.

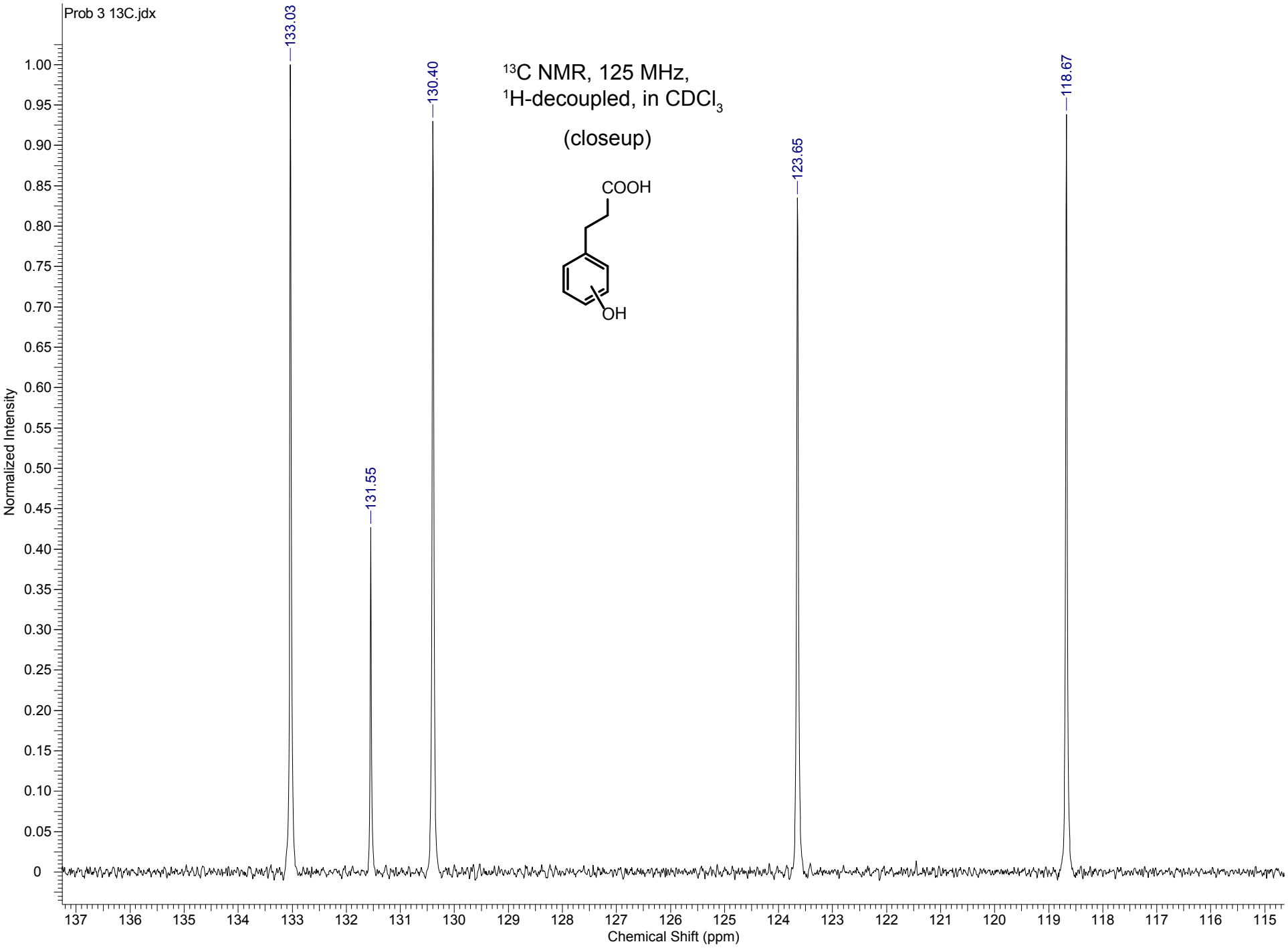



Prob 3 1H.jdx
^{1}H NMR, 500 MHz, in $CDCl_3$
COOH
OH
Normalized Intensity
Chemical Shift (ppm)
0.87
0.77
1.50
2.39
2.35

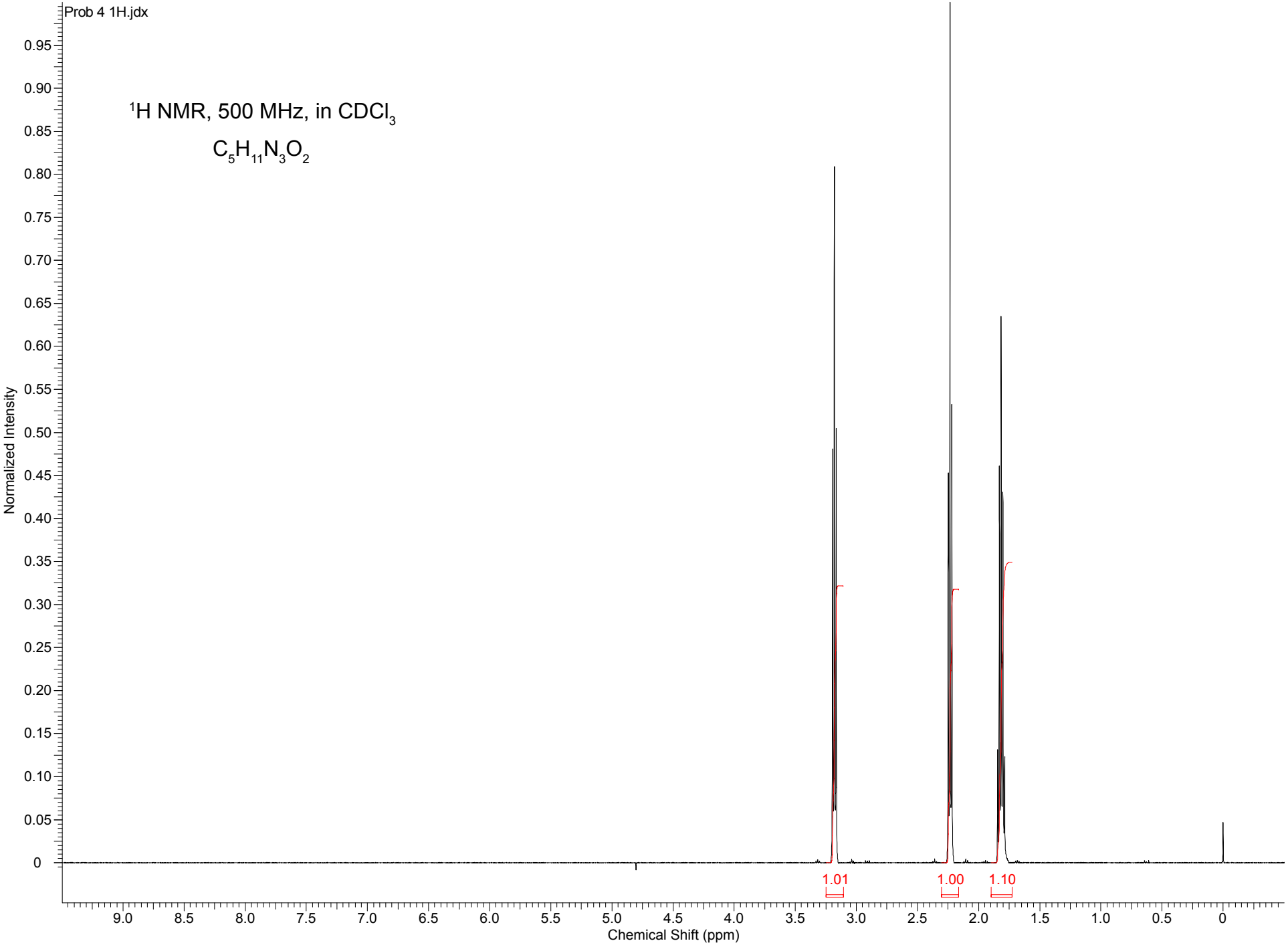

Prob 3 1H.jdx
^{1}H NMR, 500 MHz, in $CDCl_3$
(closeup)
COOH
OH
Normalized Intensity
0.45
0.40
0.35
0.30
0.25
0.20
0.15
0.10
0.05
7.2229
7.2199
7.2079
7.2049
7.1780
7.1746
7.1625
7.1593
7.1471
7.1437
6.9487
6.9463
6.9338
6.9315
6.9189
6.9165
6.9089
6.9069
6.8929
6.8909
7.30
7.25
7.20
7.15
7.10
7.05
7.00
6.95
6.90
6.85
6.80
6.75
Chemical Shift (ppm)

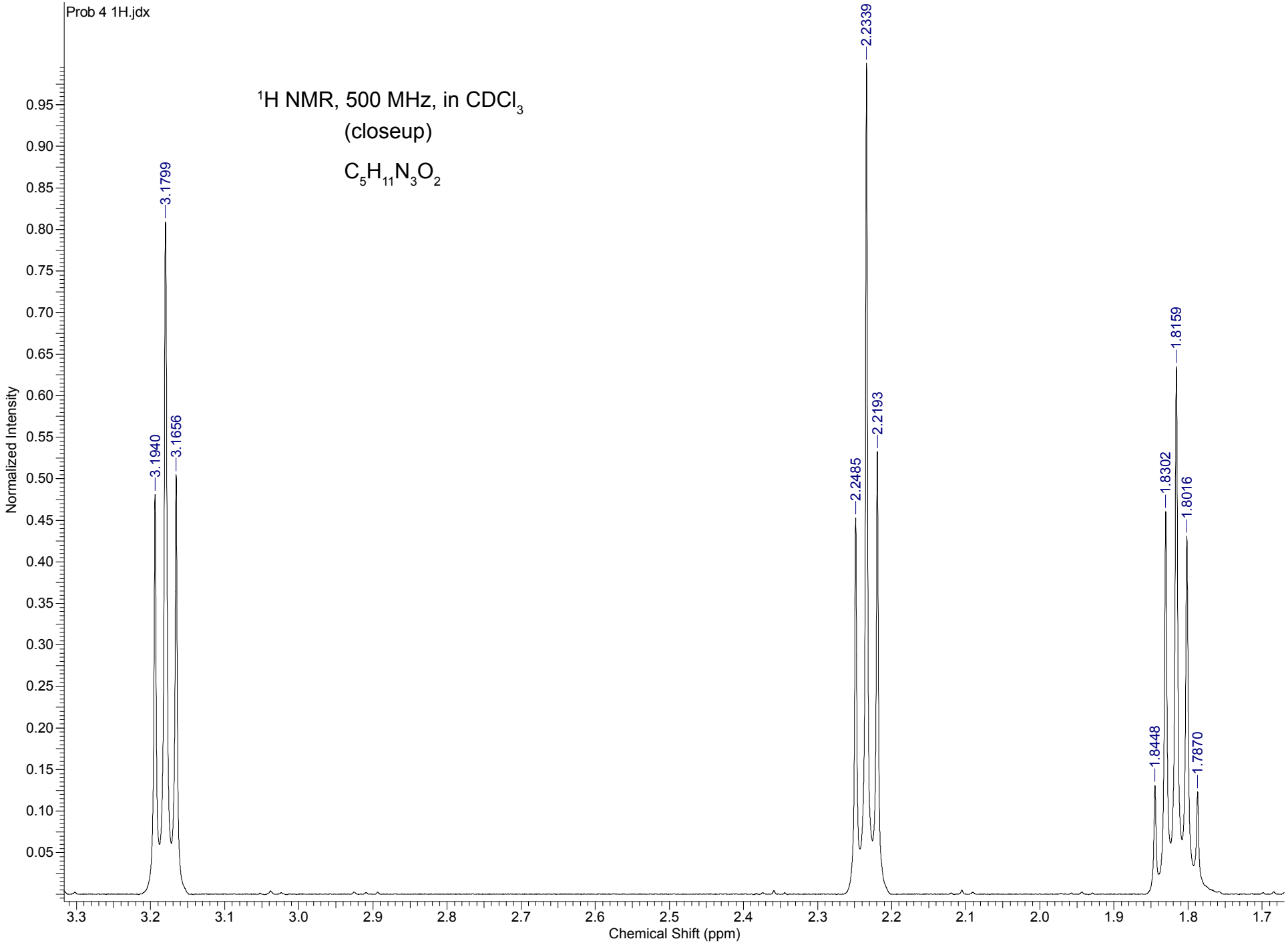

Prob 3 1H.jdx
^{1}H NMR, 500 MHz, in $CDCl_3$
(closeup)
COOH
OH
2.8573
2.8425
2.8276
2.4994
2.4845
2.4695
Normalized Intensity
Chemical Shift (ppm)

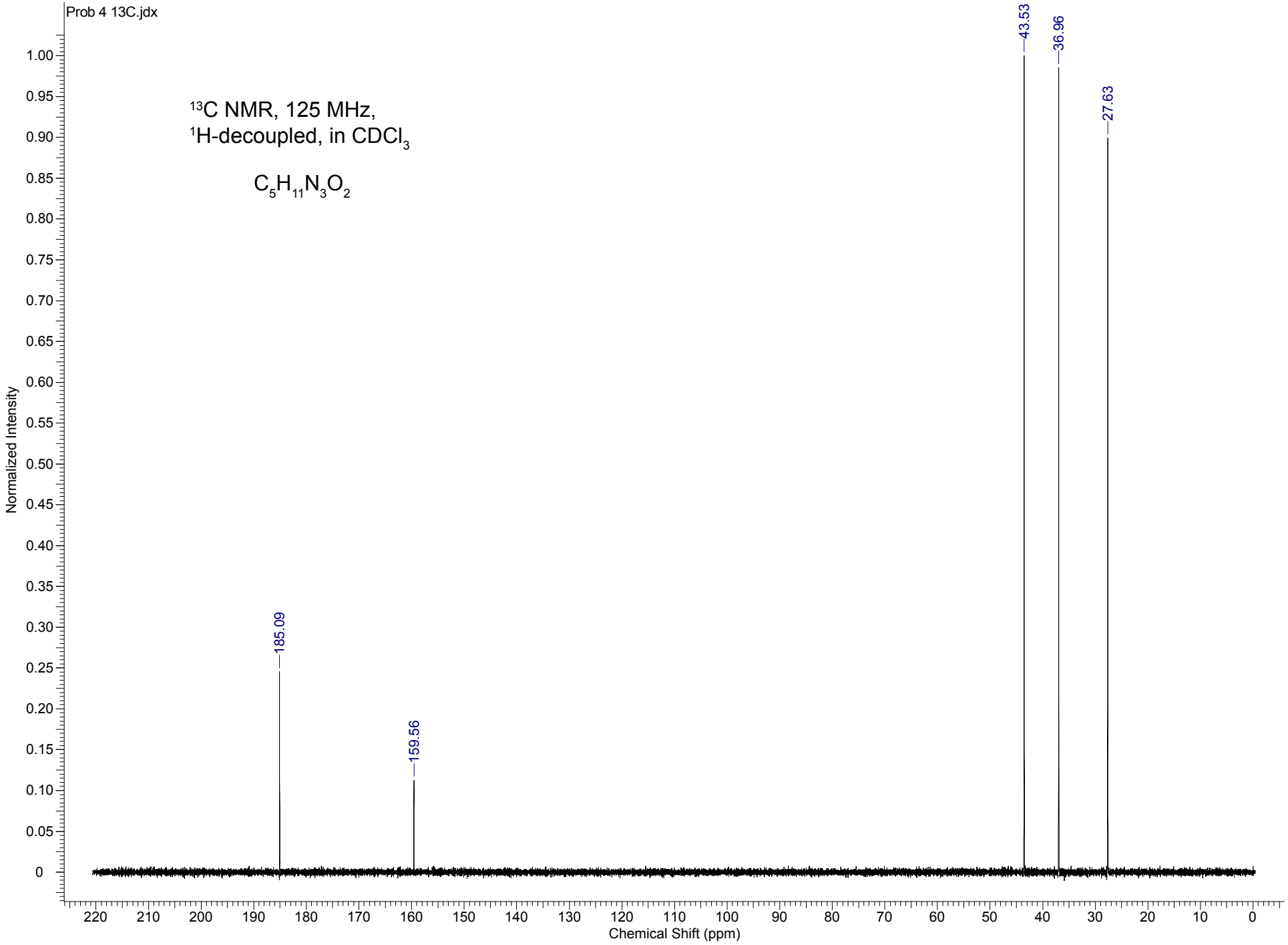

Prob 3 13C.jdx
^{13}C NMR, 125 MHz,
^{1}H-decoupled, in $CDCl_3$
COOH
OH
133.03
130.40
123.65
118.67
40.36
29.00
185.60
156.11
Normalized Intensity
Chemical Shift (ppm)


Prob 3 13C.jdx
133.03
130.40
131.55
123.65
118.67
^{13}C NMR, 125 MHz,
^{1}H-decoupled, in $CDCl_3$
(closeup)
COOH
OH
Normalized Intensity
Chemical Shift (ppm)

4. The 500 MHz ^{1}H and 125 MHz, ^{1}H-decoupled ^{13}C NMR spectra on the next pages were taken of a small molecule isolated from cell culture and identified (by high resolution mass spectrometry) to have chemical formula $C_5H_{11}N_3O_2$. What is the structure of this molecule?


Prob 4 1H.jdx
^{1}H NMR, 500 MHz, in $CDCl_3$
$C_5H_{11}N_3O_2$
Normalized Intensity
Chemical Shift (ppm)
1.01
1.00
1.10


Prob 4 1H.jdx
^{1}H NMR, 500 MHz, in $CDCl_3$
(closeup)
$C_5H_{11}N_3O_2$
Normalized Intensity
Chemical Shift (ppm)
3.1940
3.1799
3.1656
2.2485
2.2339
2.2193
1.8448
1.8302
1.8159
1.8016
1.7870


Prob 4 13C.jdx
^{13}C NMR, 125 MHz,
^{1}H-decoupled, in $CDCl_3$
$C_5H_{11}N_3O_2$
43.53
36.96
27.63
185.09
159.56
Normalized Intensity
Chemical Shift (ppm)