Chemistry 605 (Reich)

SECOND HOUR EXAM

Thur. April 12, 2012

Question/Points

R-11H_____/30

R-11J,K_____/15

R-11L,M_____/30

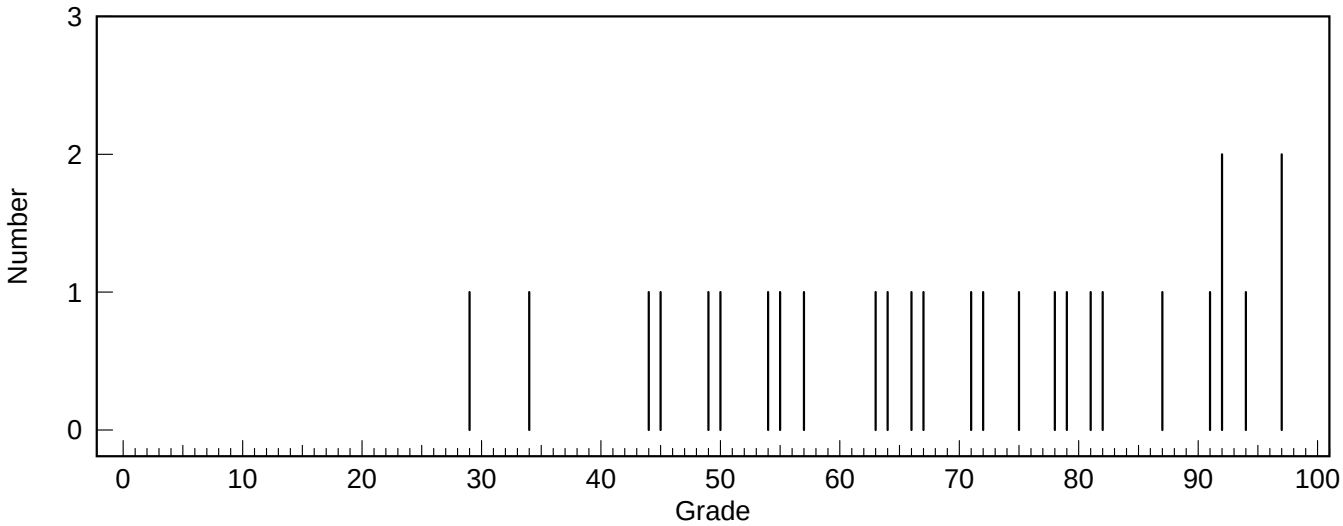
R-11N_____/17

R-11O_____/8

Total _____/100

Hi	97 (2)
Average	69
Median	71
AB	78
BC	50
CD	40

Distribution from grade list (average: 69.1; count: 27)



Name_____

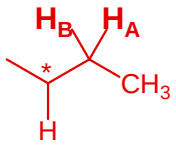
If you place answers anywhere else except in the spaces provided, (e.g. on the spectra or on extra pages) clearly indicate this on the answer sheets.

30

Problem R-11H ($C_{12}H_{16}O_3$). You are provided the ^1H and ^{13}C NMR spectra of a compound. Interpret the spectra, and determine the structure or structures. Note that the signal at δ 6.5 disappeared when D_2O was added.

2 (a) DBE 5

(b) Analyze the multiplets below. Identify the patterns (e.g., ABXYZ - underline the observed nuclei). If they are first order, report them in the standard format (δ 0.00, dqt, J = 0.0, 0.0, 0.0, 2H). Provide part structure(s) defined by these protons.

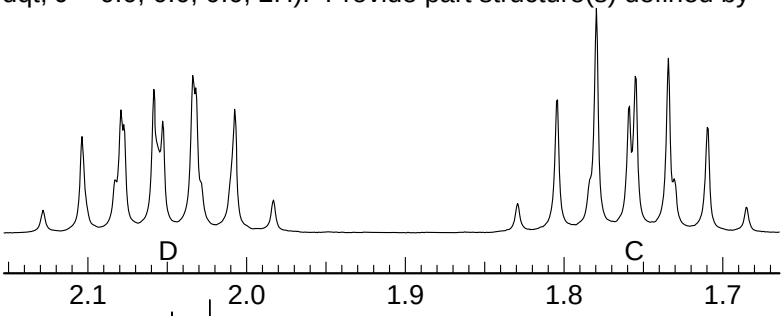


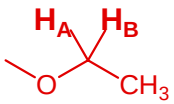
ABM$_3$Y

5 δ 2.05, d quintets, J = 13.4, 7.5

δ 1.75, d quintets, J = 13.5, 7.5

δ 1.7-2.1



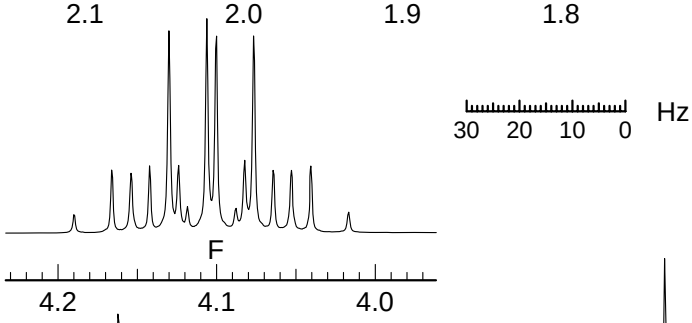


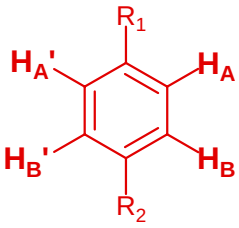
ABX$_3$

5 δ 4.13, dq, J = 11, 7

δ 4.08, dq, J = 11, 7

δ 3.9-4.1



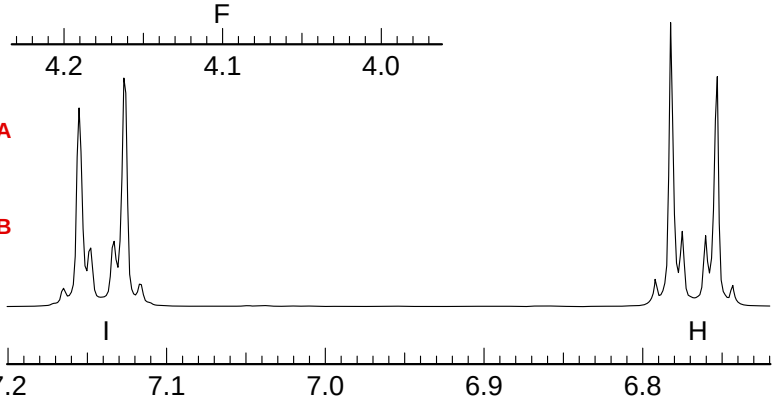


R_1, R_2 must be electron donating

AA'XX' (or AA'BB')

5

δ 6.7-7.2



(c) Identify at least 3 signals in the ^{13}C NMR spectrum which provide significant structural information, and describe the part structures obtained from them.

δ 175.2 - This is an ester carbonyl carbon

δ 155.1 - This is likely an sp^2 carbon (aromatic) bearing an electronegative group C-O

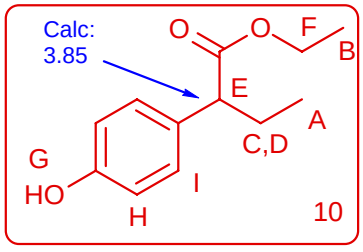
3 δ 60.9 - sp^3 carbon, probably a CH_2-O group

δ 52.7 - sp^3 CH

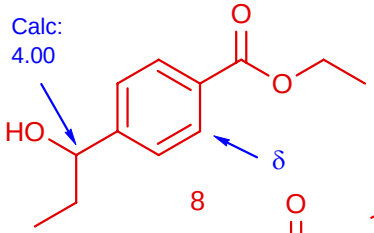
There arealso two CH_3 carbons (neither one on O) and an aliphatic CH (52.7) , also probably not on O

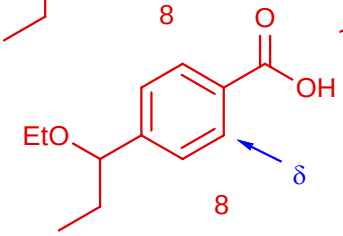
(d) Draw the structure of **R-11H** below. If more than one structure fits the data, draw them, but circle your best choice.

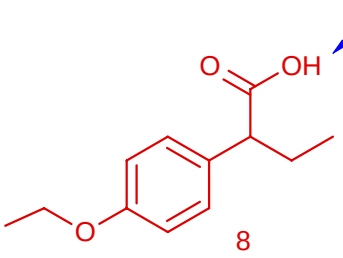
10

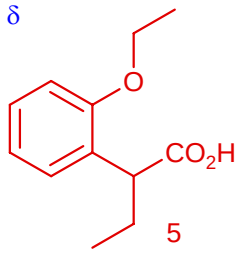


3 or 4 other structures at 2-3 points





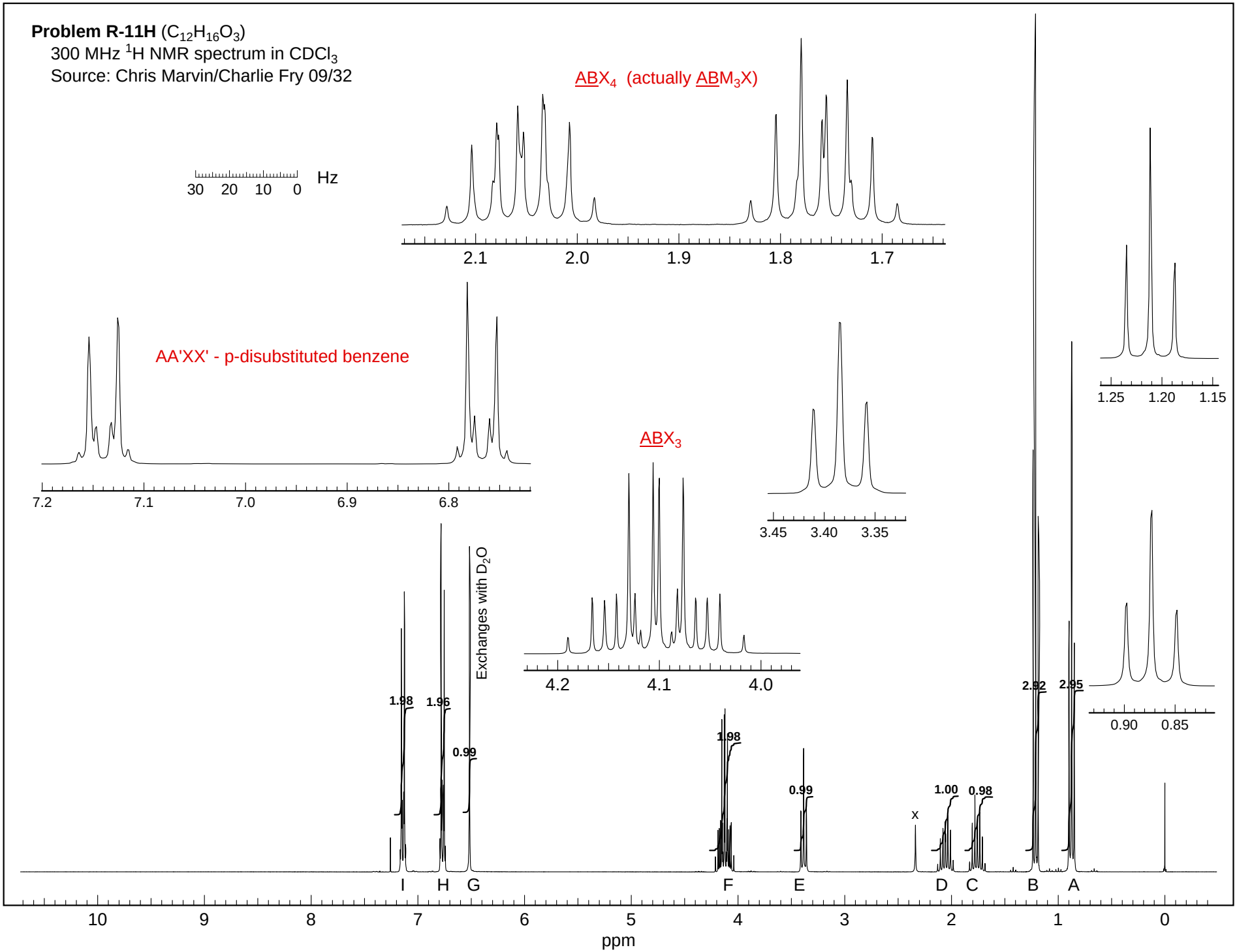




Problem R-11H ($C_{12}H_{16}O_3$)

300 MHz ^{1}H NMR spectrum in $CDCl_3$

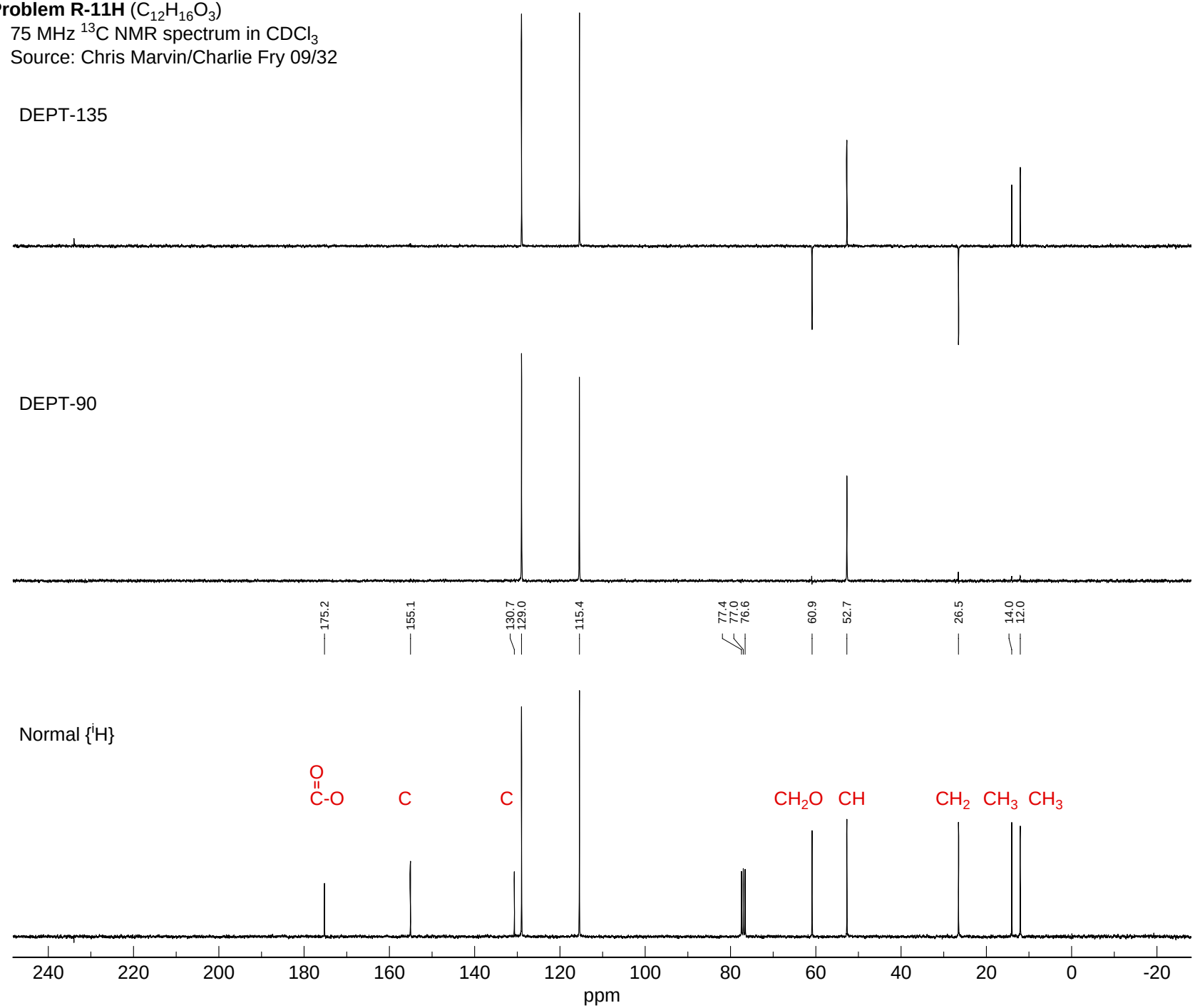
Source: Chris Marvin/Charlie Fry 09/32



Problem R-11H ($C_{12}H_{16}O_3$)

75 MHz ^{13}C NMR spectrum in $CDCl_3$

Source: Chris Marvin/Charlie Fry 09/32



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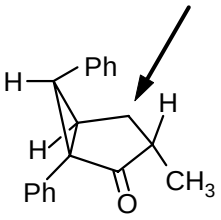
Problem R-11J and K ($C_{19}H_{18}O$). You are given 200 MHz ^{1}H NMR spectra of two **stereoisomers** of a compound which differ at one stereocenter only (i. e., **1** and **2**, or **6** and **8**), the possibilities are **1** to **8** below. Your task is to make both a structural and a stereochemical assignment. Explain the basis of your assignment below, taking care to clearly identify the signals you are using.

10

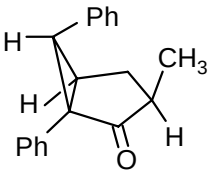
(a) What spectral features allow you to distinguish the two structural types (**1** to **4** versus **5** to **8**)?

Each spectrum has an isolated AB pattern at 2.7 and 3.1, and an ABMX3 pattern, which is as expected for the compounds **5** - **8**. In compounds **1** - **4** the coupling pattern would be more complicated, since one of the cyclopropane protons would be coupled to the CH_2.

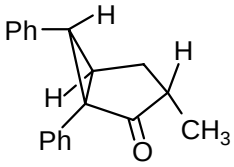
2



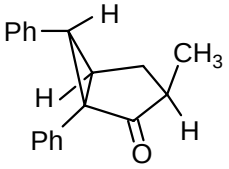
1 2



2 2



3 1



4 1

(b) What spectral features allow you to distinguish the pair of isomers? Write the spectrum number (**R-11J** or **R-11K**) in the appropriate blank.

The AB coupling of the cyclopropane protons is identical in both, so stereochemistry has to be the same (both cis). The other coupling constants are quite similar, and do not provide much insight. However, there are some large chemical shift differences - in **G** the Me doublet is unusually upfield (δ 0.2), and the CHMe multiplet normal (δ 2.5), whereas in **H** the methyl is normal (δ 0.9) , and the multiplet unusually upfield (δ 1.2). This can only be explained by large anisotropy effects of the phenyl group in compounds **5** and **6**.

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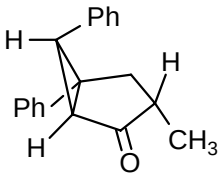
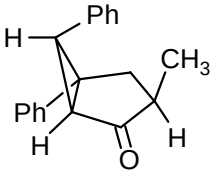
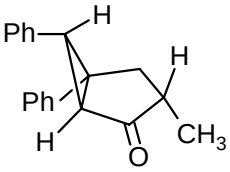


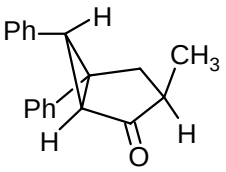
5 R-11K 5



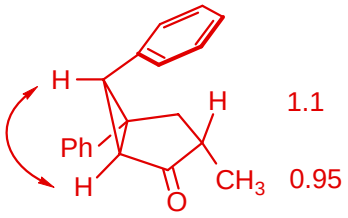
6 R-11J 5



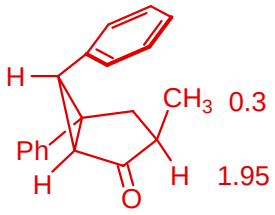
7 2



8 2



5 (R-11K)



6 (R-11J)

Endo protons are both upfield

Normal

The relatively large vicinal coupling of the two cyclopropane protons (10 Hz) shows a cis relationship between them.

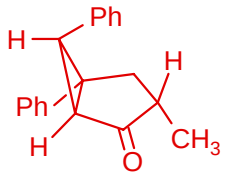
(c) Just to show you understand the spectra, give just the chemical shifts of the two protons at the CH_2 group (marked with an arrow in **1**).

R-11J 2.0, 2.7

2

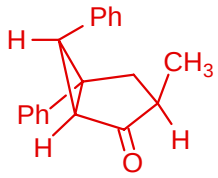
R-11K 2.0, 2.7

Problem R-11J ($C_{19}H_{18}O$)
200 MHz ^{1}H NMR Spectrum in $CDCl_3$
(Source: Drew Weber/Zimmerman 11/18)



R-11K

Problem R-11K ($C_{19}H_{18}O$)
200 MHz ^{1}H NMR Spectrum in $CDCl_3$
(Source: Drew Weber/Zimmerman 11/18)



R-11J

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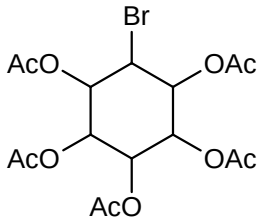
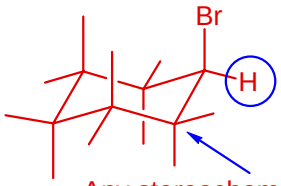
Problem R-11L and R-11M. From the 270 MHz ^{1}H NMR spectra of two stereoisomeric bromo pentaacetoxy cyclohexanes assign stereochemistry and conformation ("interpret" means give δ, *J* and multiplicity).



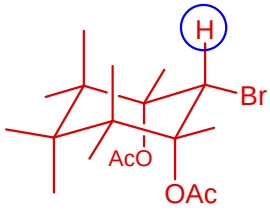
(a) Interpret the signal at δ 4.5 in **R-11L**. Suggest possible part structures. Circle the proton at δ 4.5

4

δ 4.5, t, J = 4 Hz - the chemical shift suggests a CHBr proton, the small couplings must be ee or ae:



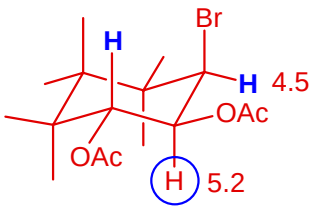
Any stereochem here



Less likely, but possible

(b) Interpret the signal at δ 5.2 in **R-11L**. Suggest possible part structures. Circle the proton at δ 5.2.

4



δ 5.2, dd, J = 10, 4

- must be an axial proton (10 Hz J) with one neighboring eq and one ax
- probably coupled to 4.5 proton (the one at 5.7 has a smaller J, and leaning suggests it is coupled to the t at 5.59)

(c) Identify other significant multiplets in the expansion (δ 5.3 - 5.8) on the right (**R-11L**), draw coupling trees, and identify part structures. HINT: these are all first order

6

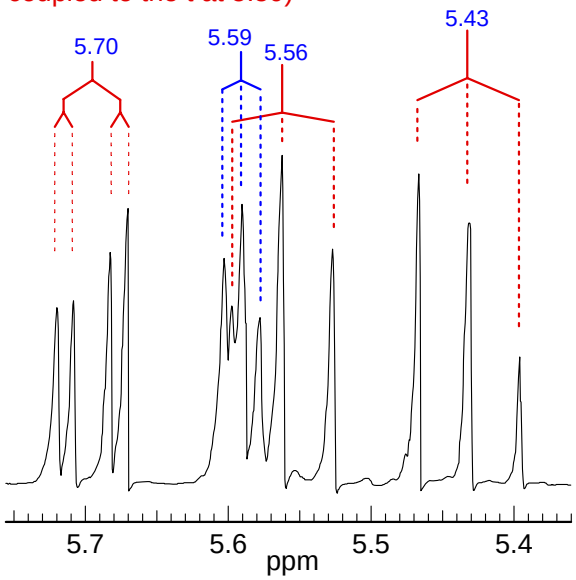
δ 5.43, t (J = 10), axial proton, axial on both sides

δ 5.56, t (J = 10), axial proton, axial on both sides

δ 5.59, t (J = 3.5), equatorial proton

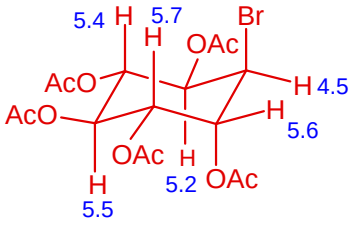
δ 5.70, dd (J = 10, 2.5), axial on one side, equatorial on other

5.43 and 5.56 are coupled to each other - hence adjacent



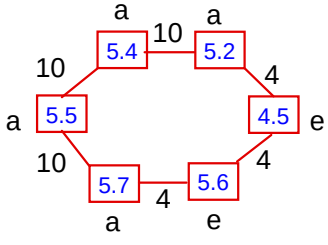
(d) Complete the structure for **R-11L** below by placing bromo and acetoxy groups with the appropriate stereochemistry on the structure.

4



R-11L

The two adjacent triplets (5.43 and 5.56) means that there must be four adjacent axial hydrogents. The other two protons must be equatorial (triplets with J <4 Hz)

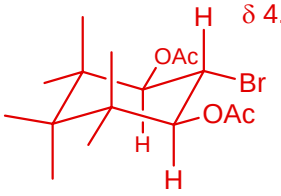


(e) What do the signals at δ 2 tell you about the structure of **R-11M** (compare them to the δ 2 signals of **R-11L**).

3 The CH_3-C(=O) signals are in a 2:2:1 ratio, so there is likely a symmetry element in the molecule (there are 5 different ones in R-11L)

(f) Assign and interpret the signal at δ 4.0 in **R-11M**. Suggest possible part structures.

3



From the shift, this must the CHBr proton. The 10 Hz triplet means the proton is axial, and so are both flanking protons

(g) Analyze the rest of the NMR spectrum of **R-11M**. Point out significant features of the spectrum which can be used to assign stereochemistry. HINT: there are some second-order effects in the multiplet δ 5.1 - 5.5.

δ 5.15, t (J = 9 Hz)

δ 5.35, probably a dd J = 8, 9 Hz)

3 It looks as if all protons are of the axial type, although there is a bit of a mess at δ 5.3, proably some second order effects (or an impurity?). Can't be due to one equatorial proton, because that will cause 2 other protons to have one small coupling.

(h) Complete the structure of **R-11M** below by placing bromo and acetoxy groups with the appropriate stereochemistry on the structure.

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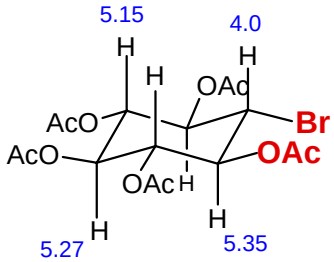


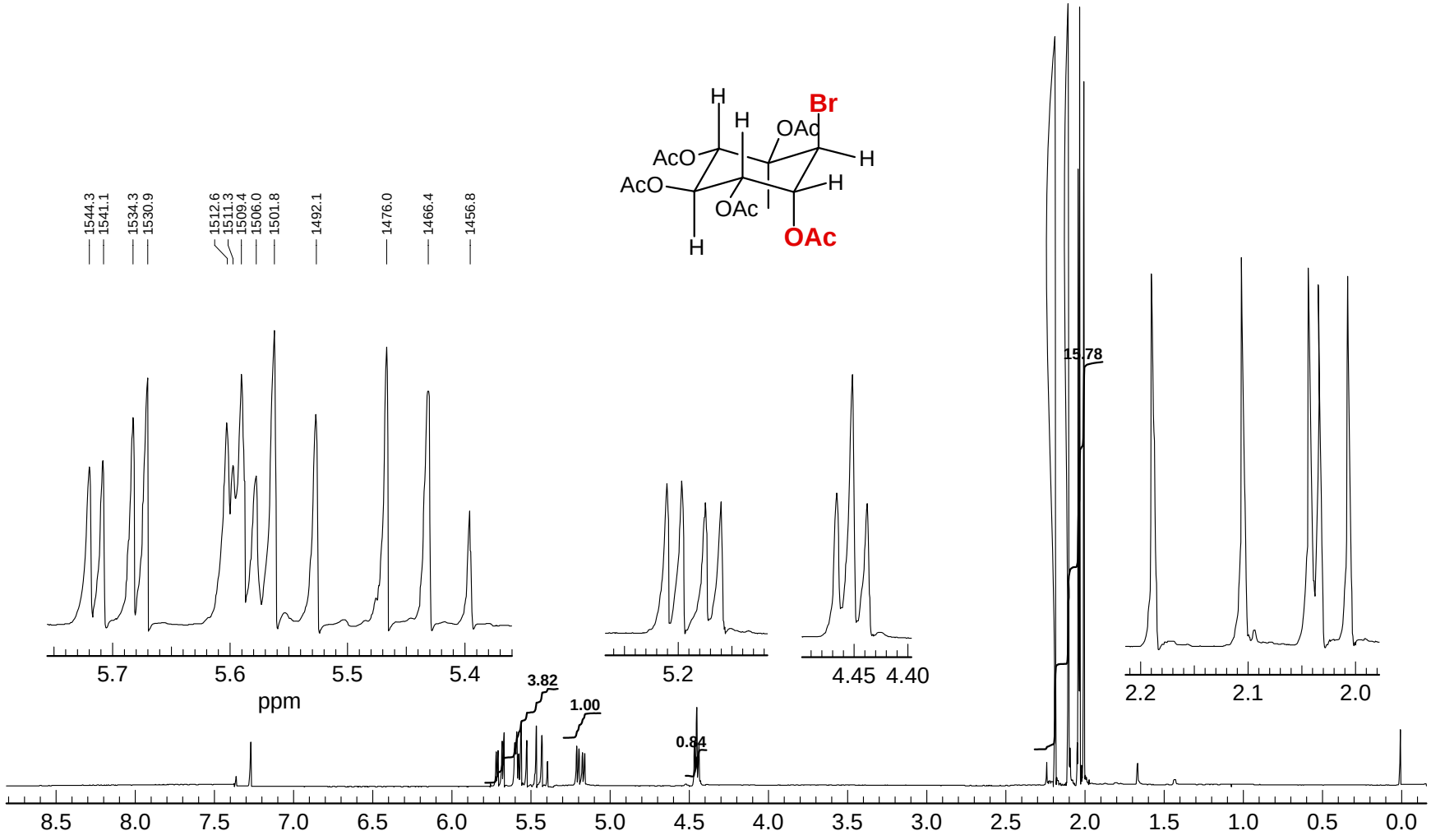
R-11M

This has a plane of symmetry, so there are only 4 kinds of CH protons and 3 kinds of acetate Me

Problem R-11L ($C_{16}H_{21}BrO_{10}$)

270 MHz ^{1}H NMR Spectrum in $CDCl_3$

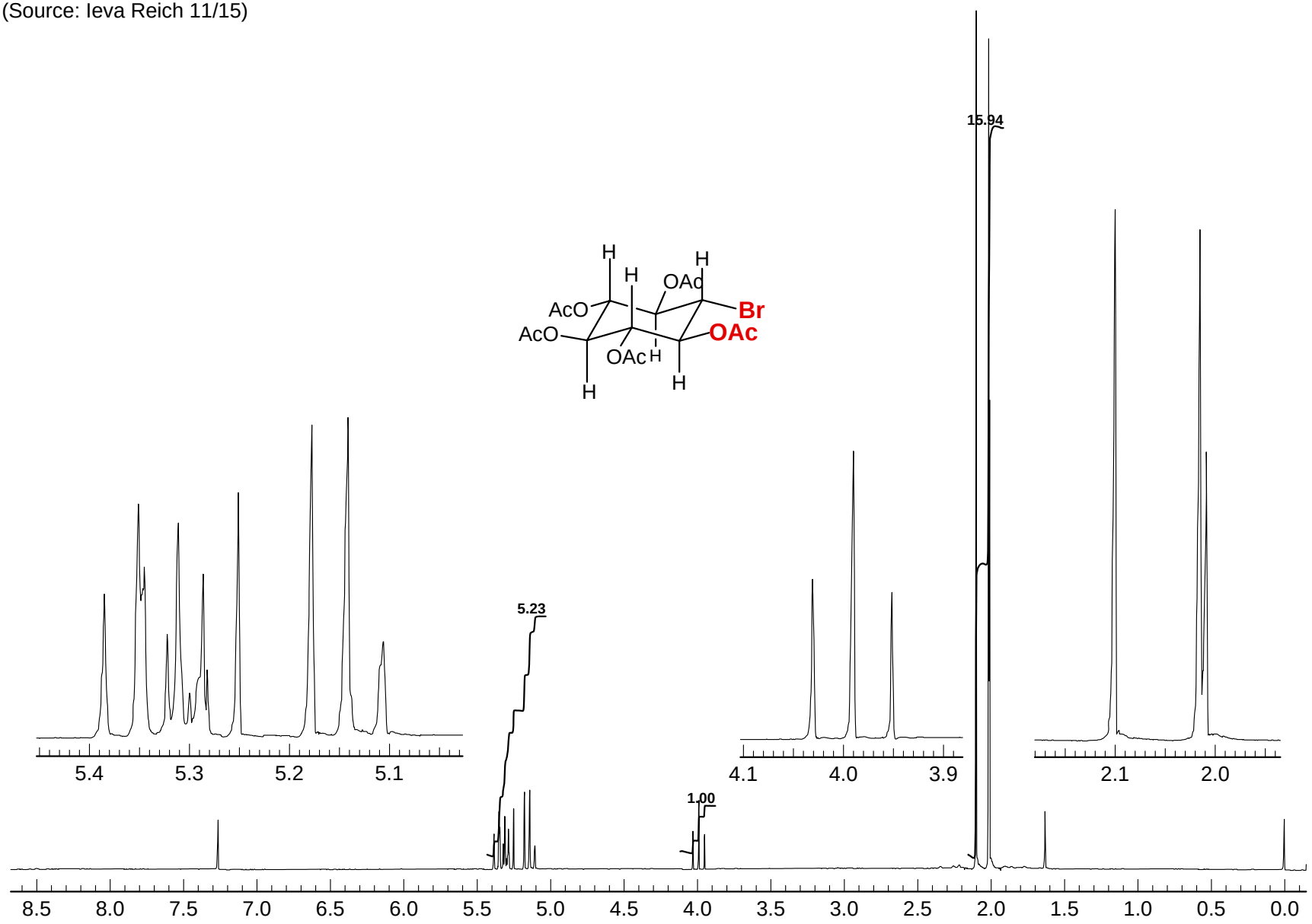
(Source: Ieva Reich 11/15)



Problem R-11M ($C_{16}H_{21}BrO_{10}$)

270 MHz ^{1}H NMR Spectrum in $CDCl_3$

(Source: Ieva Reich 11/15)



17

Problem R-11N ($C_9H_{16}ClN$). In this problem you are required to determine the position of a Cl substituent in a 1-aza-bicyclo[2.2.2]heptane from the ^1H NMR spectra. You are given the ^1H NMR spectra of the compound and the 7,7-dideuterated analog.

(a) Analyze the coupling system of **R-11N** and report your results below. For each position either give the multiplicity, *J* and δ values, or enter Cl if that is where you think it is. NOTES: 1 .You may use first order analysis - there are no significant second order effects. 2. There are no effects detectable due to coupling between H and D.

2x δ 3.1, ddd, J = 13, 10, 4.5

2n δ 2.6, dddd, J = 10, 9, 7, 3

3x δ 1.3, ddd, J = 12, 10, 6

3n δ 1.7, dddd, J = 10, 9, 5, 2

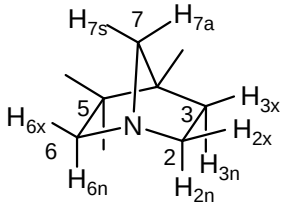
10

6x Cl 3

6n δ 4.6, d, J = 2

7s δ 2.95, dt, J = 10, 2

7a δ 2.15, dd, J = 10,2



One proton replaced by Cl

(b) Briefly describe how you decided on the location of the chlorine

The four protons at C-2 and C-3 are all coupled to each other (and the endo protons are coupled to 7s), if the Cl was on one of these they would be much simpler.

3

The proton at δ 4.6 has to be the CHCl proton. It is coupled only to one of the C-7 protons (7a). So the Cl must be in the exo position

There is also the absence of a W-coupling between H_{2x} and H_{6x}, which would be expected to be significant in any other isomer

(c) Briefly describe specifically how you distinguished proton(s) at 2 from those at 3.

2

Simple chemical shift argument - α to N is downfield. Couplings are nearly the same

(d) Briefly describe how you distinguished the x and n signals at carbons 2 and 3

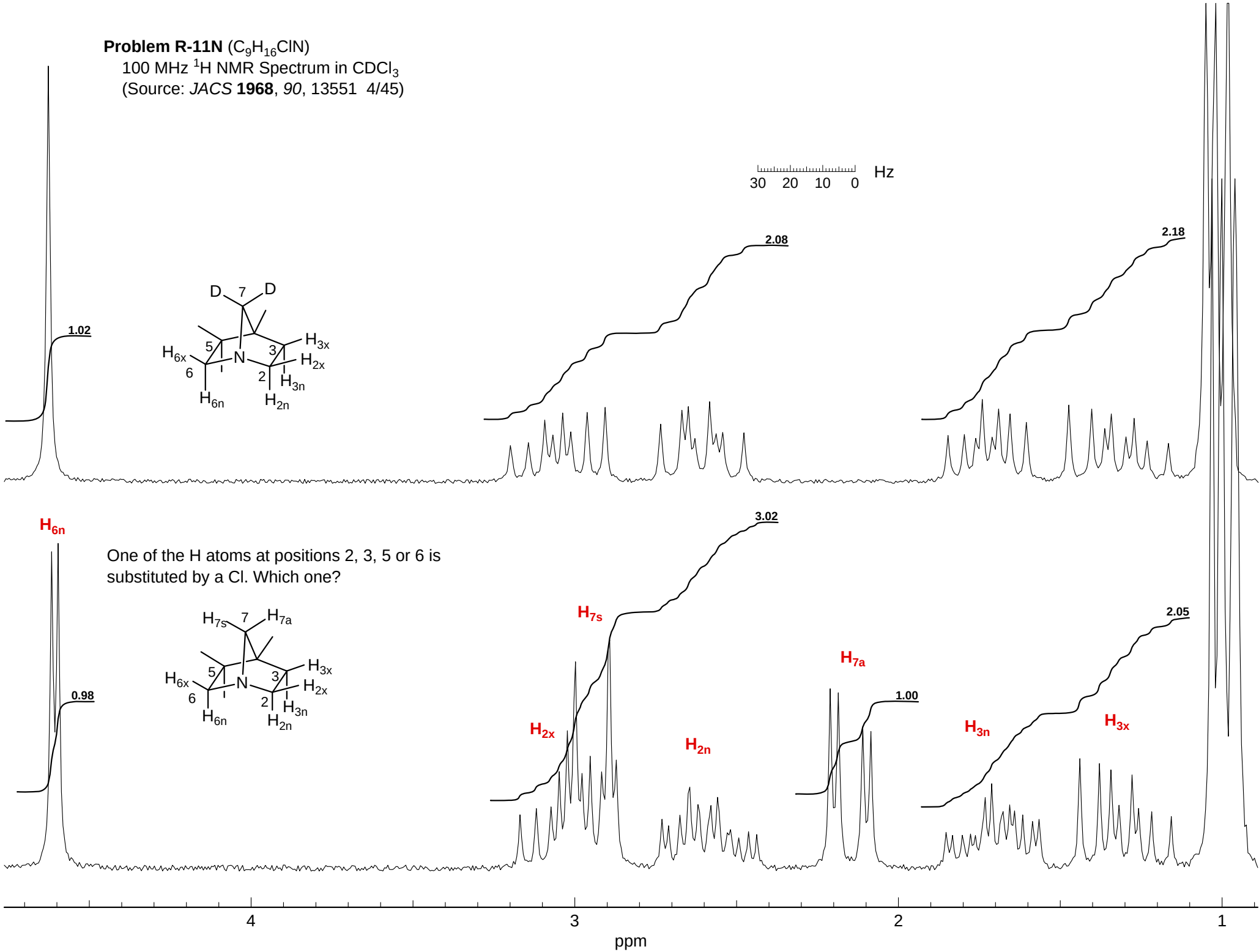
2

Only the endo (2n, 3n) can have a long range W-coupling to the C-7 protons - that coupling disappears in the D compound

Problem R-11N ($C_9H_{16}ClN$)

100 MHz ^{1}H NMR Spectrum in $CDCl_3$

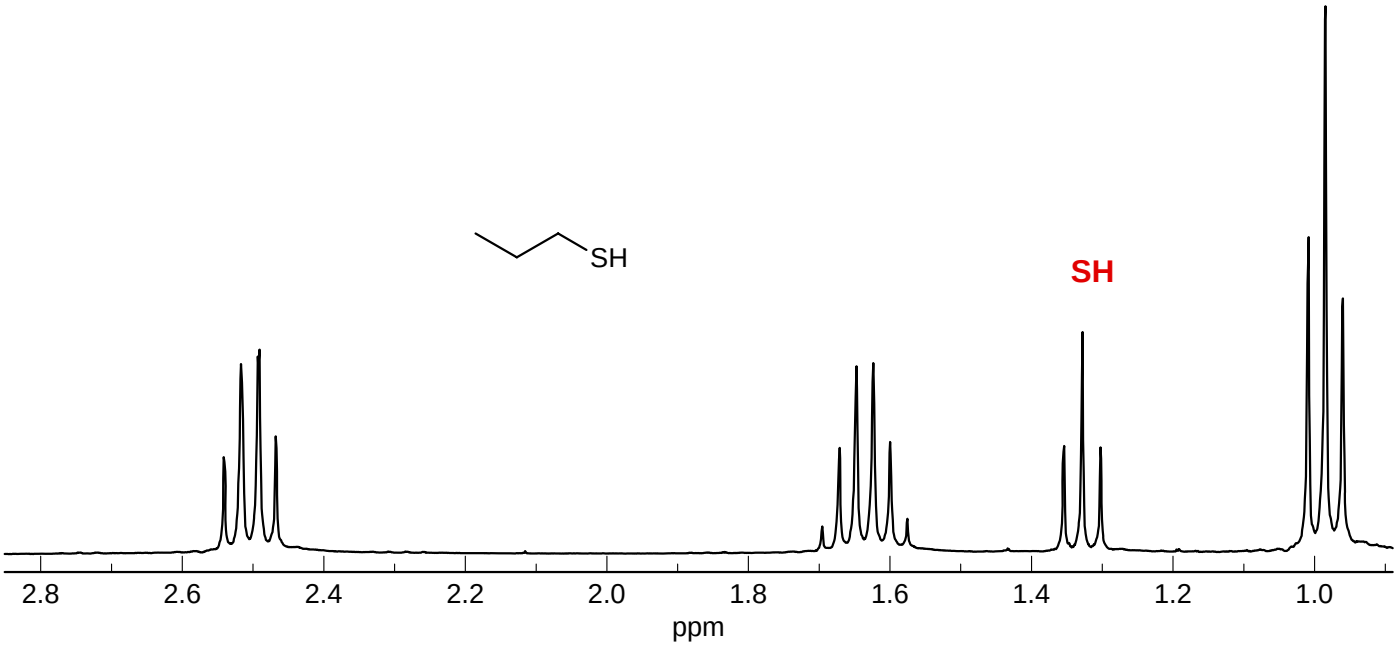
(Source: *JACS* **1968**, *90*, 13551 4/45)



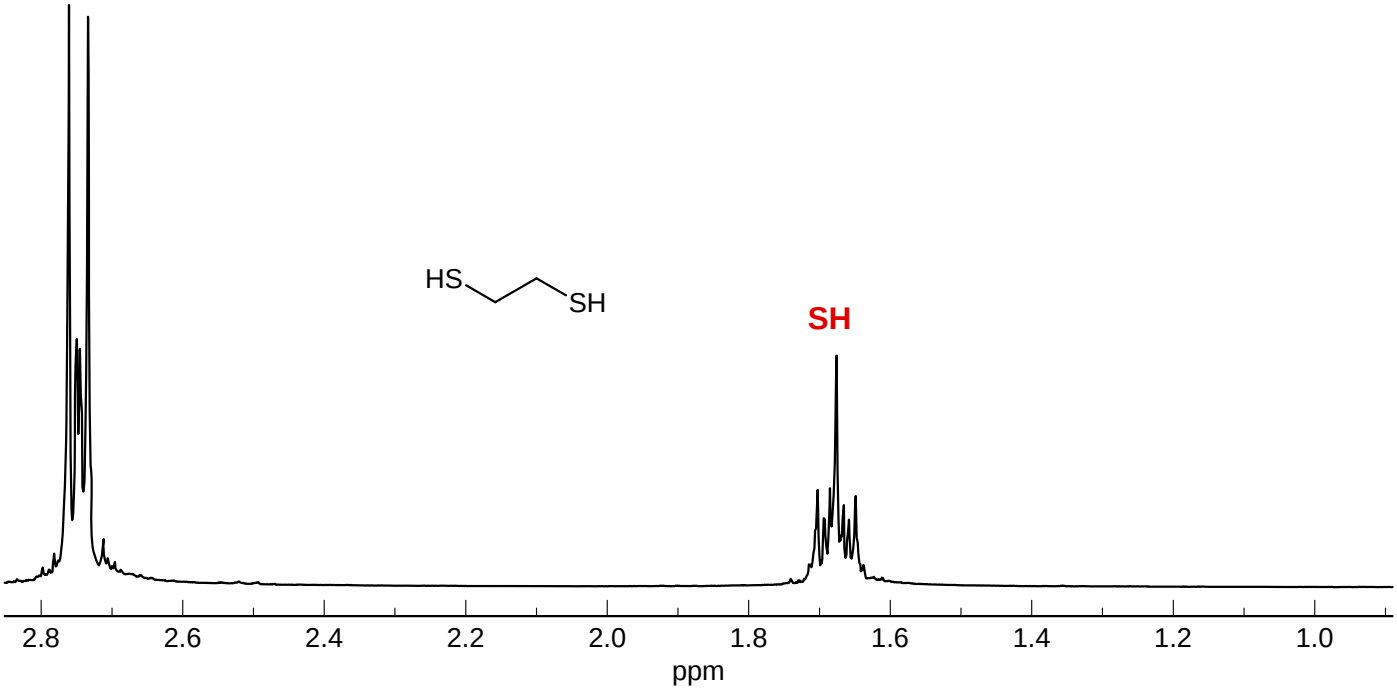
8

Problem R-11O. Identify the SH protons in the two 300 MHz ^{1}H NMR spectra ($CDCl_3$) below, and explain the difference in their appearance (Source: Aldrich NMR Library).

2



2



In the top spectrum the SH proton is coupled to the CH_2 protons, which are well separated from their other coupling partner, the second CH_2 group. So the SH proton is a simple triplet.

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The spin system is AA'BB'B''B''' - so decidely second order. Specifically, the B protons (CH_2CH_2) are stongly coupled, so the A protons (SH) are second order - an example of virtual coupling.