Chemistry 605 (Reich)
SECOND HOUR EXAM
Sat. April 19, 2014

Question/Points

R-13A____/20
R-13B____/15
R-13C____/20
R-13D____/15
R-13E____/20
R-13F____/10
Total _____/100

Distribution from grade list (average: 61.1; count: 26)

Answer Key

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.
Problem R-13A. Assign several of the protons and analyze multiplets of a steroid.

(a) Assign and analyze the following signals (report multiplicity and \( J \) values). Use the steroid numbering on the structure:

\[
\begin{align*}
\delta 3.55 & \quad H^3, \text{tdd, } J = 11, 7, 6 \text{ Hz} \\
\delta 4.55 & \quad H^{15}, \text{ddd, } J = 7, 5, 2 \text{ Hz} \\
\delta 5.40 & \quad H^6, \text{dt, } J = 5, 2 \text{ Hz}
\end{align*}
\]

(b) Assign the 2-proton signal between \( \delta 2.4 \) and \( \delta 2.7 \). Briefly provide a rationale for this assignment. What kind of multiplet is this? \textit{AB of ABX}

Apart from \( H^3, H^{15} \) and \( H^6 \), the \( H^{16} \) protons will be the most downfield. The large \( ^2J \) (19 Hz) also means the protons must be next to the keto group

(c) Analyze this multiplet in a mathematically correct fashion (also show a coupling tree), using the frequencies given. Report coupling constants and chemical shifts. If two solutions are possible present them, and provide a rationale for choosing one of them.

\[
\begin{align*}
c_1 &= 693.8 \quad & \Delta \nu_{\text{ab}} &= 15.3 \quad & c_1 \pm \Delta \nu_{\text{ab}}/2 &= 701.51, 686.15 \\
c_2 &= 690.4 \quad & \Delta \nu_{\text{ab}} &= 21.2 \quad & c_2 \pm \Delta \nu_{\text{ab}}/2 &= 700.95, 679.86
\end{align*}
\]

\[
\begin{array}{c|c|c}
\text{Solution 1} & \text{Solution 2} & \\
\hline
J_{\text{AB}} & 19.1 & 19.1 \\
J_{\text{AX}} & 0.6 & -14.8 \\
J_{\text{BX}} & 6.3 & 21.6 \\
\nu_A & 701.2 & 693.5 \\
\nu_B & 683.0 & 690.7 \\
\nu_{\text{AB}} & 18.2 & 2.9 \\
i_{14}=i_{15} & 0.0074 & 0.47 \\
\delta_A & 2.60 & 2.57 \\
\delta_B & 2.53 & 2.56 \\
\end{array}
\]

Solution 1 is correct - can't have a negative \(^3J\), as in Sol 2. Also the Sol. 2 couplings are unreasonably large
Problem R-13A
270 MHz $^1$H NMR Spectrum in CDCl$_3$
Source: Ieva Reich (3/27)

The spectrum shows the chemical shifts and multiplicity of the protons in the compound. The peaks are labeled with their corresponding protons and their assignments are provided with their respective coupling constants. The spectrum is presented with a scale for ppm and Hz.
Problem R-13B. Compound R-13B is a disubstituted naphthalene. Spectra of just the aromatic region are provided in two different mixtures of CDCl₃ and C₆D₆. From an analysis of the spectra, determine the positions of substitution. The substituents are:

(a) Draw a possible structure, and label it with chemical shifts. Use the top spectrum for this, please.

There are two patterns of 1,2,4-hydrogens

(b) Is another substitution pattern consistent with the spectra? Explain.

There is no way to determine the relative position of the substituents on the two rings with the information at hand.
**Problem R-13C.** You are given the structure of a pentose thiol triacetate and asked to determine the relative stereochemistry and conformation from the 270 MHz $^1$H NMR spectrum presented on the next page.

(a) Analyze the sets of signals and show coupling constants in the standard format. When you have completed the analysis, assign the individual protons (e.g., H$_{5a}$). Use the numbering system given on the structure in part (b).

$$\delta$$ 3.75 \hspace{1cm} dd, J = 12, 9 Hz

This must be H$_{5a}$ from the chemical shift - coupled gem and ax-ax. Thus H$_4$ must be axial.

$$\delta$$ 4.05 \hspace{1cm} ddd, J = 11.5, 4.5, 1 Hz

This must be H$_{5e}$ - coupled gem and eq-ax. There is also a W-coupling to the equatorial H$_3$.

$$\delta$$ 4.95 \hspace{1cm} dd, 8, 2.5 - H$_2$

br d, 8 - H$_1$

This is an AB pattern, one half is coupled to an X proton by ca 2.5 Hz, the other half is broadened. These must be the H$_1$ and H$_2$ protons, the H$_1$ is broadened by exchange of the SH (which is a broad singlet at $\delta$ 2.17). The 8 Hz coupling between H$_1$ and H$_2$ means both protons are axial. The small coupling (2.5 Hz) of H$_2$ to H$_3$ means H$_3$ is equatorial.

$$\delta$$ 5.07 \hspace{1cm} ddd, J = 8.5, 4.5, 3

This is the proton at H$_4$, coupled to the axial proton at C$_5$ (9 Hz) and to the eq protons at C$_5$ and C$_3$. Thus H$_3$ must be equatorial.

$$\delta$$ 5.55 \hspace{1cm} td, 2.5, 1

This is the equatorial H$_3$ proton, coupled twice eq-ax (2.5 Hz) to H$_4$ and H$_2$. There is a small W coupling to H$_{5e}$.

(b) Determine the stereochemistry of **R-05K**. Place the appropriate substituents in each of the boxes on the structure below.

(c) Briefly describe how you made the assignment at C-4.

H$_{5a}$ and H$_{5e}$ can be assigned from their chemical shifts (most upfield of the ring protons) and coupling patterns. H$_{5a}$ shows, in addition to the 12 Hz gem coupling, a 9 Hz vicinal coupling, which means H$_4$ must be axial. H$_4$ can be assigned from the three couplings, two of which are to the H$_5$ protons.
Problem R-13C (C<sub>11</sub>H<sub>16</sub>O<sub>7</sub>S)
270 MHz <sup>1</sup>H NMR spectrum in CDCl<sub>3</sub>
(Source: Paul Savage/Gellman 11/32)

![NMR spectrum and molecular structure](image)

Curphy-Morrison:
- SH: 1.3
- O-Alkyl: 2.10
- O-Ac: 3.45
Problem R-13D. This problem requires you to interpret the partial 500 MHz $^1$H NMR spectrum of a 1,2-dimethylpiperidine deuterated 94% on the N-methyl group (source: F. A. L. Anet J. Am. Chem. Soc. 1989, 111, 3429).

Identify all of the peaks in both the top and bottom spectra. Briefly explain the pattern, extract all coupling constants and determine exact chemical shifts, and report them in the standard format (e.g., $\delta$ 3.44, t, $^1J_{xy}$ = 3.5 Hz).

- The signals we are looking at are the N-CH$_3$ protons ($\delta$ 2.17) and the N-CH$_2$-D protons (2.11-2.17).
- In the deuterium decoupled spectrum the singlet at $\delta$ 2.17 is N-CH$_3$.
- In D-decoupled the AB quartet centered at $\delta$ 2.14 is the N-CH$_2$-D group. The CH$_2$ group is diastereotopic (there is an asymmetric center at C-2) and so forms an AB quartet.

\[ ^2J_{AB} = 11.7 \text{ Hz}, \quad \delta_A = 2.15, \quad \delta_B = 2.13 \]

- Normal spectrum: each peak of the AB quartet is split into a 1:1:1 triplet by coupling to D. $^2J_{HD} = 1.7$ Hz.
Problem R-13E \((\text{C}_{18}\text{H}_{25}\text{O}_{2}\text{PSi})\). In this problem you are given the structure of a phosphorus compound and asked to interpret parts of the NMR spectrum. For each multiplet or set of multiplets report the pattern in the standard format: \(\delta\) 0.00, triplet of pentets, \(^{1}J_{XY} = 0.0\) Hz. You may use first order analysis.

(a) Assign and interpret the three signals centered at \(\delta\) -0.05.

\[
\text{Me}_3\text{Si signal}
\]

The two small peaks are \(^{29}\text{Si}\) satellites 

\[\text{J}_\text{H-Si} = 7\text{Hz}\]

(b) Assign and interpret the multiplet at \(\delta\) 0.75. Draw and label a coupling tree.

This is the P-CH\(_2\)-SiMe\(_3\) group - the protons are diastereotopic (P is an asymmetric center), so this is an ABX pattern \(X = ^{31}\text{P}\)

\[
\begin{align*}
J_{AB} &= 14\text{ Hz} (^{2}J_{HH}) \\
\delta_{A} &= 0.73 \\
J_{AX} &= 16\text{ Hz} (^{2}J_{H-P}) \\
\delta_{B} &= 0.78 \\
J_{BX} &= 18\text{ Hz} (^{2}J_{H-P})
\end{align*}
\]

(this is "AMX" treatment which always corresponds to Solution1, not a proper ABX analysis, so if this happens to be a Solution 2 situation, then the J's would be very wrong - they do look OK though, and so Solution 1 is probably fine)

(c) Assign and interpret the multiplets at \(\delta\) 3.7 - 4.2. Draw and label a coupling tree.

\[
\text{ABM}_3\text{X}
\]

Each pattern is a doublet of pentets, \(J = 10, 7\) Hz for the diastereotopic O-CH\(_2\)-CH\(_3\) group. The pentet arises because \(^{3}J_{HH}\) to the CH\(_3\) group and \(^{3}J_{HP}\) are nearly the same

\[
\begin{align*}
^{3}J_{HH} &= 7\text{ Hz} \\
^{3}J_{HP} &= 7\text{ Hz} \\
^{2}J_{HH} &= 10\text{ Hz}
\end{align*}
\]

We know the 10 Hz coupling is the gem \(J_{HH}\) because of the size, and leaning effects.

(d) Assign and interpret the multiplet at \(\delta\) 8.2.

This must be the proton ortho to the phosphonate group - approximately a ddd, \(J = 12, 6, 2\) Hz. There are some second-order effects, so couplings are suspect

\[
\begin{align*}
^{3}J_{HH} &= 8\text{ Hz (ortho coupling)} \\
^{4}J_{HH} &= 2\text{ Hz (meta coupling)} \\
^{3}J_{HP} &= 12\text{ Hz (ortho }^{31}\text{P coupling)}
\end{align*}
\]
Problem R-13E (C₁₈H₂₅O₂PSi)
300.1 MHz ¹H NMR Spectrum in CDCl₃.
Source: Olaf Daugulis/Vedejs 08/24

OEt
PO
SiMe₃

Benzene Shifts

O
0.48
0.16
0.24

O
Ph

OMe

PO
OMe

O

CH₃

ddd, J = 12, 6, 2 Hz
³JHH = 8 Hz (ortho coupling)
⁴JHH = 2 Hz (meta coupling)
³JHP = 12 Hz (ortho ³¹P coupling)
Problem R-13F. Here are the two parts of quiz 217 we didn't get to finish during my first lecture. Put your analysis ($\delta$, J, multiplicity) in the space provide, and suggest some possible structures from the quiz answer sheet.

Below are proton multiplets in different molecules. Analyze the pattern and extract the coupling constants. From the chemical shift given, what kind of protons are these likely to be? What part structures are suggested by this pattern? Find one or more molecules on the "NMR Quiz Answers" sheet that fit the chemical shift and coupling pattern.

(b) Integration: 2H

These are two aromatic protons ($H_A$ and $H_B$), coupled to each other with $J = 8$ Hz (ortho). The upfield proton $H_B$ has a second ortho coupling to $H_C$. Both protons are meta-coupled also, $H_A$ to $H_C$, and $H_B$ to $H_D$

(c) Integration: 2H

Coupling constants are consistent for those in a five-membered ring. They don't fit very well for chair cyclohexane