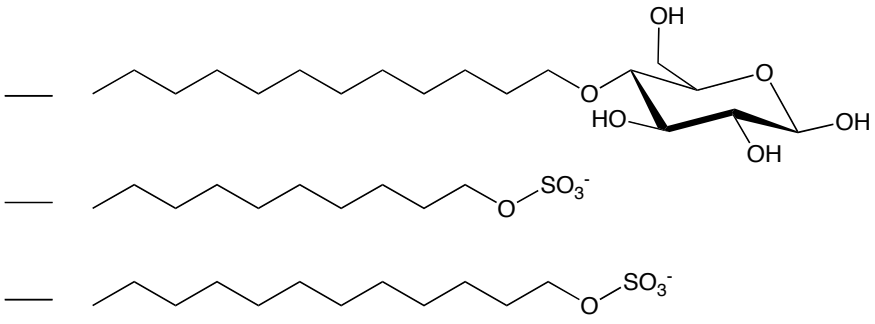
Chem 391 – Exam #1 **Name**_____
October 4, 2006

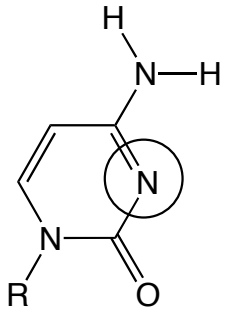
The exam period is 9 AM to 10:20 AM. This is a closed book/notes exam. You may only use a calculator and a pencil. Note that there are **5 pages & 8 questions** on this exam. R = 0.001987 $^{kcal}/_{mol\ K}$. Unless stated otherwise, T is 298 K.

1. (10 points) I was recently surprised to learn that fish living at 1.9°C do not need hemoglobin in their blood because O_2 is sufficiently soluble at those temperatures to support life. Briefly explain the thermodynamic issues (enthalpic and entropic) associated with the dissolution of O_2 in water from the gas phase and how they cause O_2 to be more soluble at low temperature.

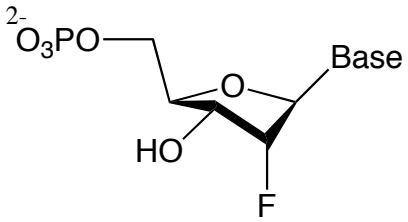
2. (10 pts) Three detergent molecules are shown below. Rank them in terms of their predicted critical micelle concentrations. (1 = lowest cmc, 3= highest cmc) and briefly provide a rationale.



3. (10 pts) I have drawn the conjugate base of cytosine below (this is why it's called a base after all). The circled nitrogen is where cytosine gets protonated. Under normal circumstances the pK_a of the conjugate acid of cytosine is 4.0. Draw the Watson-Crick base pair of cytosine with guanine and describe how that interaction affects the pK_a of the conjugate acid of cytosine. (R=ribose)



4. (8 pts) Nucleotides of 2'-deoxy-2'-fluororibose prefer the 3'-endo sugar conformation, as shown below.



a. Will polymers of these nucleotides be more likely to adopt the A or B conformation? Explain in one or two sentences, with a drawing if you like.

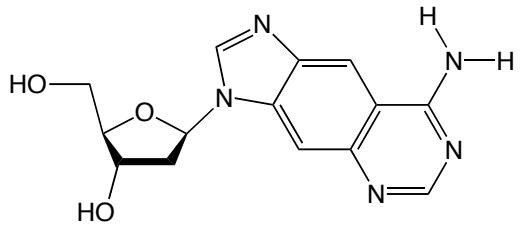
b. Are these polymers likely to be more or less stable than RNA to hydrolysis? Provide a mechanistic scheme (i.e. show what happens in hydrolysis) to support your answer.

5. (10 pts) Let's say you have a 16-residue peptide. You have know the chemical shift of each proton on each α carbon in the 16 residue stretch. Describe an NMR experiment that would allow you to demonstrate that the 16 residues form two strands of anti-parallel β sheet. What would you expect to observe in this spectrum?

6. (12 pts) Suggest a six residue peptide sequence that could form an amphipathic β-strand. Please use three letter code **and** draw the structure of this peptide.

7. (20 pts) The following deoxynucleoside (called xA) has been designed to participate in a Watson-Crick base pair with thymine.

a. Draw thymine in a base pair with xA in the space below.



xA

The following thermodynamic data were collected on the **formation** of duplexes containing xA and T (xDNA) or with A in place of xA (DNA).

Table 1. Thermodynamic Parameters for DNA and xDNA

sequence	T_m (°C) at 5 μM	ΔG_{310K} (kcal/mol)	ΔH (kcal/mol)	ΔS (cal/(mol·K))
xDNA	54.9 ± 0.5	−9.5 ± 0.2	−37.0 ± 3.6	−88.7 ± 10.9
DNA	20.1 ± 0.5	−3.7 ± 0.3	−68.1 ± 5.2	−207.8 ± 17.6

b. Briefly suggest an explanation for the enthalpic data shown above.

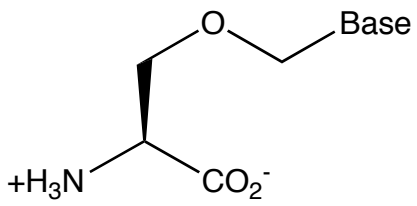
c. Briefly suggest an explanation for the entropic data shown above.

d. When xA is placed in a duplex opposite G or C, the following differences in free energy of duplex formation are observed, relative to the free energy of duplex formation obtained with T:

Base	**ΔΔG (kcal/mol)**
G	+2.6
C	+2.7

Roughly how much **more** or **less** stable are these duplexes relative to the one with T, expressed as a ratio of their equilibrium constants. (One sig fig is fine here).

8. (20 pts) α-Peptide nucleic acids are hybrid polymers built from α-amino acids with the four standard nucleic acid bases on the side chain:



Let's say we build an octapeptide nucleic acid with the base sequence GGAATTCC. Describe (briefly!) two experiments that you could perform to determine whether this sequence forms an α-helix or a helical duplex (a la DNA) in solution.

Experiment #1:

Experiment #2: