2006 Analytical Cumulative Exam Crib, Saturday March 4

Part I

a) Compute the average and unbiased variance for the three values, {13, 17, 12}. Write out both equations in symbolic form. Then use the equations to compute the parameters. Do all math by hand showing explicitly all terms in the equation. That is, do all the addition, subtraction, squaring and division by hand.

$$\bar{x} = \frac{1}{N}\sum_{i=1}^{N} x_i \qquad \bar{x} = \frac{13+17+12}{3} = \frac{42}{3} = 14$$

$$s^2 = \frac{1}{N-1}\sum_{i=1}^{N}(x_i - \bar{x})^2 = \frac{(13-14)^2 + (17-14)^2 + (12-14)^2}{2} = \frac{1+9+4}{2} = 7$$

b) What are degrees of freedom, and how do they come into play with the answer to part (a)?

The degrees of freedom represent the number of independent pieces of information from a measured set of values. For N measurements there are N degrees of freedom, each degree of freedom corresponding to one of the original values. When an average is computed from a set of values, one degree of freedom is lost since any N-1 values and the average can be used to compute the Nth value. In the equation for the mean, the degrees of freedom is N since the computation only involves the data. In the equation for variance division is by N - 1 since the average is used in the computation, thus one of the deviations provides no independent information.

c) Further demonstrate your understanding of degrees of freedom by considering the variance of the fit for a quadratic least-squares. If there are N data points that were fit, how many degrees of freedom are used in the equation for the variance? Why?

The equation for the variance of the fit for a quadratic least-squares is given by,

$$s^2 = \frac{1}{N-3}\sum_{i=1}^{N}\left(y_i - a_0 - a_1 x_i - a_2 x_i^2\right)^2$$

where (x_i, y_i) are the N measured pairs of values, and a_0, a_1 and a_2 are the computed least-squares coefficients. Since the computation involves three parameters computed from the data, the degrees of freedom are reduced by 3.

Part II

d) Consider the equation, $z = ax + by$, where x and y are random variables and a and b are constants. Express the mean and variance of z in terms of the mean and variance of x and y.

$$\mu_z = a\mu_x + b\mu_y$$
$$\sigma_z^2 = a^2\sigma_x^2 + b^2\sigma_y^2$$

e) Use the information in part (d) to derive the variance of the arithmetic average, $\overline{x}$, where x has the standard deviation σ.

$$\overline{x} = \frac{1}{N}\sum_{i=1}^{N} x_i = \frac{x_1}{N} + \frac{x^2}{N} + \cdots + \frac{x_N}{N}$$
$$\sigma_{\overline{x}}^2 = \left(\frac{1}{N}\right)^2 \sigma^2 + \left(\frac{1}{N}\right)^2 \sigma^2 + \cdots + \left(\frac{1}{N}\right)^2 \sigma^2 = \frac{N}{N^2}\sigma^2 = \frac{\sigma^2}{N}$$

f) Consider the equation, $z = x^2$, where x is a random variable. Use your knowledge of expectation value calculus to show that the mean of z is biased. What is the bias?

$$\mu_z = \int_z zh(z)dz = \int_x x^2 f(x)dx$$
$$\text{since} \quad \sigma_x^2 = \int_x x^2 f(x)dx - \mu_x^2$$
$$\text{then} \quad \mu_z = \mu_x^2 + \sigma_x^2$$

g) Use the results of (d-f) to determine the mean of the biased variance (uses the number of values instead of the degrees of freedom). The result should provide a factor that converts the biased variance into the unbiased variance.

The biased variance can be written as a constant, $(1/N)$, times a sum of squared terms, minus a second random variable squared, $\overline{x}^2$.

$$s^2 = \frac{1}{N}\left(x_1^2 + x_2^2 + \cdots + x_N^2\right) - \overline{x}^2$$

The expectation value of the variance can be determined in the same manner as the derivation for (f). The only difference is that $\overline{x}$ is not a constant and has the following expectation value,

$$\mu_{\overline{x}^2} = \mu^2 + \sigma_{\overline{x}}^2 = \mu^2 + \frac{\sigma^2}{N}$$

where (e) is used to convert the variance of the average into the variance of the random variable.

Propagation of the mean yields the following equation.

$$\mu_{s^2} = \frac{1}{N}\left[\left(\mu_1^2 + \sigma_1^2\right) + \left(\mu_2^2 + \sigma_1^2\right) + \cdots + \left(\mu_N^2 + \sigma_N^2\right)\right] - \left(\mu^2 + \frac{\sigma^2}{N}\right)$$

$$\mu_{s^2} = \frac{N}{N}\left(\mu^2 + \sigma^2\right) - \left(\mu^2 + \frac{\sigma^2}{N}\right) = \frac{N-1}{N}\sigma^2$$

To obtained an unbiased estimate the first equation in this derivation needs to be multiplied by $N/(N\text{-}1)$, yielding the familiar expression for the experimental standard deviation.

Part III

h) Consider the equation used to compute the number of theoretical plates in chromatography,

$$n = 16\left(\frac{t_r}{w}\right)^2$$

where t_r is the retention time and w is the peak width. Assume that the width is computed by a difference between two times, $w = t_2 - t_1$, and that the error for all measured times is the same value, σ_t. Use a Taylor's series linearization to obtain a functional form for the variance in n. For $t_r = 100$ s, $w = 10$ s, and $\sigma_t = 0.1$ s what is σ_n? Which parameter, t_r or w, contributed most to the uncertainty in n. Hint: The math is easier if the value of σ_w is expressed as a function of σ_t and t_1 and t_2 are not substituted into the equation!

First define some terms and compute the partial derivatives.

$$n = 16\left(\frac{t_r}{w}\right)^2 \qquad w = t_2 - t_1$$

$$\sigma_{t_r}^2 = \sigma_t^2 \qquad \sigma_w^2 = 2\sigma_t^2$$

$$\frac{\partial n}{\partial t_r} = 32\frac{t_r}{w^2} \qquad \frac{\partial n}{\partial w} = -32\frac{t_r^2}{w^3}$$

Next propagate the variance according to the rules of a linear Taylor's series approximation.

$$\sigma_n^2 = \left(\frac{\partial n}{\partial t_r}\right)^2 \sigma_{t_r}^2 + \left(\frac{\partial n}{\partial w}\right)^2 \sigma_w^2$$

$$\sigma_n^2 = \left(\frac{32t_r}{w^2}\right)^2 \sigma_t^2 + \left(-\frac{32t_r^2}{w^3}\right)^2 2\sigma_t^2$$

$$\sigma_n^2 = \left(\frac{32t_r}{w^2}\right)^2 \left[1 + 2\left(\frac{t_r}{w}\right)^2\right] \sigma_t^2$$

Finally, substitute into this expression the values $t_r = 100$, $w = 10$ and $\sigma_t = 0.1$.

$$\sigma_n^2 = 32^2 \times [1 + 2 \times 100] \times 0.1^2$$

$$\sigma_n^2 = 2058$$

$$\sigma_n = 45$$

From the above expression it is seen that the error in the width contributed a factor of 200 more to the variance than the retention time.

Biochemistry Cumulative Examination for March 4, 2006 - Outline of Answers

1. The ratio can be worked out starting with $k = e^{-(\text{delta } G/RT)}$.
Anyone giving an absurd answer like 2.7 should retake undergraduate physical chemistry.

2. Specific acid catalysis is typically proportional to $[H^+]$ and involves a rapid preequilibrium protonation, in this case to protonate the basic site in the molecule, namely the carbonyl oxygen; it is not a function of [buffer]. General acid catalysis (specified in this problem as involving acetic acid) can be observed to occur at constant pH, and is a function of [buffer] (more specifically, here, the acid component). Importantly, the catalyst molecule (acetic acid) is part of the transition state.

3. The enolase reaction is of course part of the glycolytic pathway, which you should know. The graphs illustrate a substantial primary deuterium kinetic isotope effect at pH 6-7, indicating a rate-determining removal of the carbon-bound C2 D or H. This is an E1CB mechanism. The PKIE diminishes at high and low pH, consistent at least with a change in the RDS.

4. Carbonic anhydrase catalysis the reversible hydration of carbon dioxide. See Voet & Voet, Chaps. 14 and 15.

5. Acetoacetate (the anion of acetoacetic acid) is one of the ketone body constitutents, and a major metabolite in the pathway involving energy mobilization from fats. The experiment here identifies a critical active site lysine, permits an estimate of its (unusual) pKa, and leads to a very simple mechanism (Voet & Voet, Chap. 15).

Inorganic Chemistry Cumulative Exam Crib

Purdue University

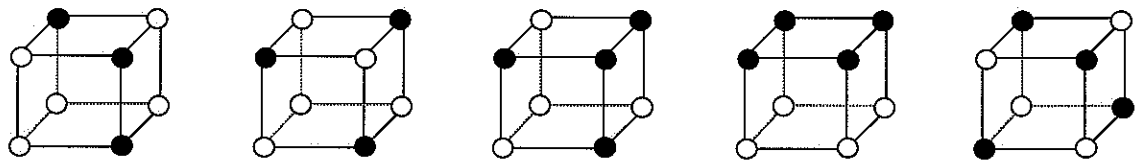
March 4, 2006

Subject: Symmetry, Point Group, Character Table

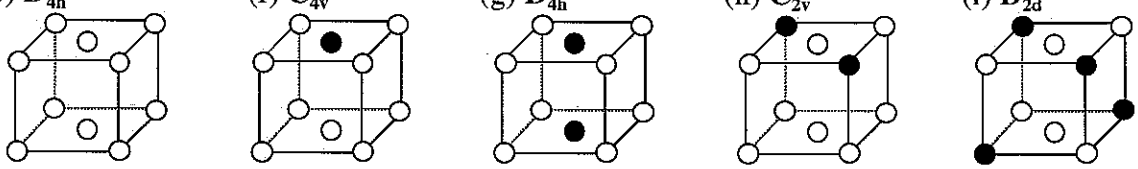
There are 100 possible points in this exam.

1. (30 points) Determine the point groups of the following cubes.

(a) $\mathbf{C_s}$ (b) $\mathbf{C_{3v}}$ (c) $\mathbf{C_{3v}}$ (d) $\mathbf{C_{4v}}$ (e) $\mathbf{T_d}$



(e) $\mathbf{D_{4h}}$ (f) $\mathbf{C_{4v}}$ (g) $\mathbf{D_{4h}}$ (h) $\mathbf{C_{2v}}$ (i) $\mathbf{D_{2d}}$



2. (20 points) A C_{2v} character table is given below. To which irreducible representations do x, y, z, and xy functions belong?

C_{2v}	E	C_2	$\sigma(xz)$	$\sigma(yz)$	
A_1	1	1	1	1	z
A_2	1	1	-1	-1	xy
B_1	1	-1	1	-1	x
B_2	1	-1	-1	1	y

3. (10 points) Explain the meaning of "group" in the term, "point group".

<u>A collection of symmetry elements</u> that belong to a particular molecule compose a <u>mathematical group</u>.

4. (10 points) Identify subgroups of D_{4h}.

D_4, C_{4h}, C_4, S_4, C_{4v}, D_{2h}, D_2, C_2, C_{2v}, C_{2h}, C_i, C_s, C_1

5. (10 points) Determine whether each of the following point groups is centrosymmetric or noncentrosymmetric.

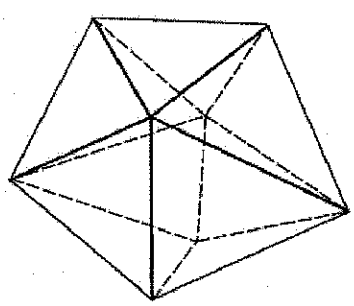
(a) C_{2h} **(Centrosymmetric)**
(b) C_{3h} **(Noncentrosymmetric)**
(c) C_{4v} **(Noncentrosymmetric)**
(d) T_d **(Noncentrosymmetric)**

6. (10 points) What group is obtained by adding a center of inversion, *i*, to C_3?

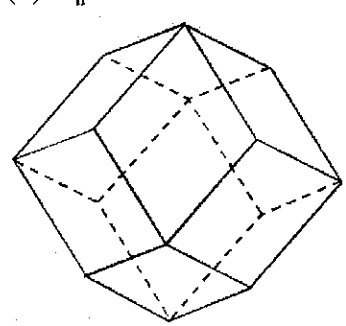
S_6

7. (10 points) To what point group does each of these dodecahedra belong?

(a) **C_{2v}**



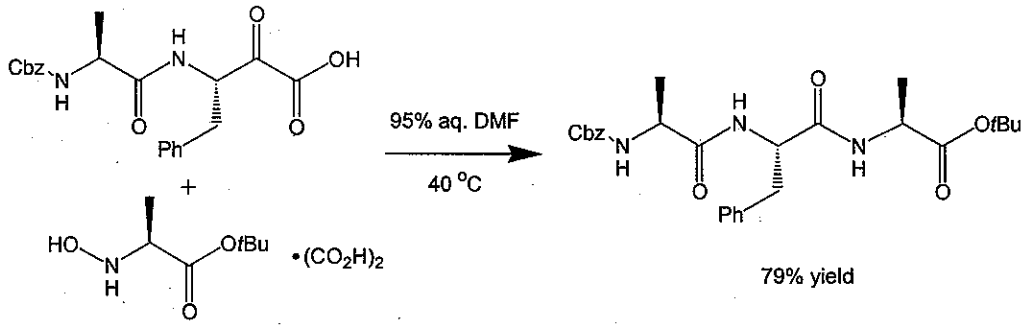
(b) **O_h**



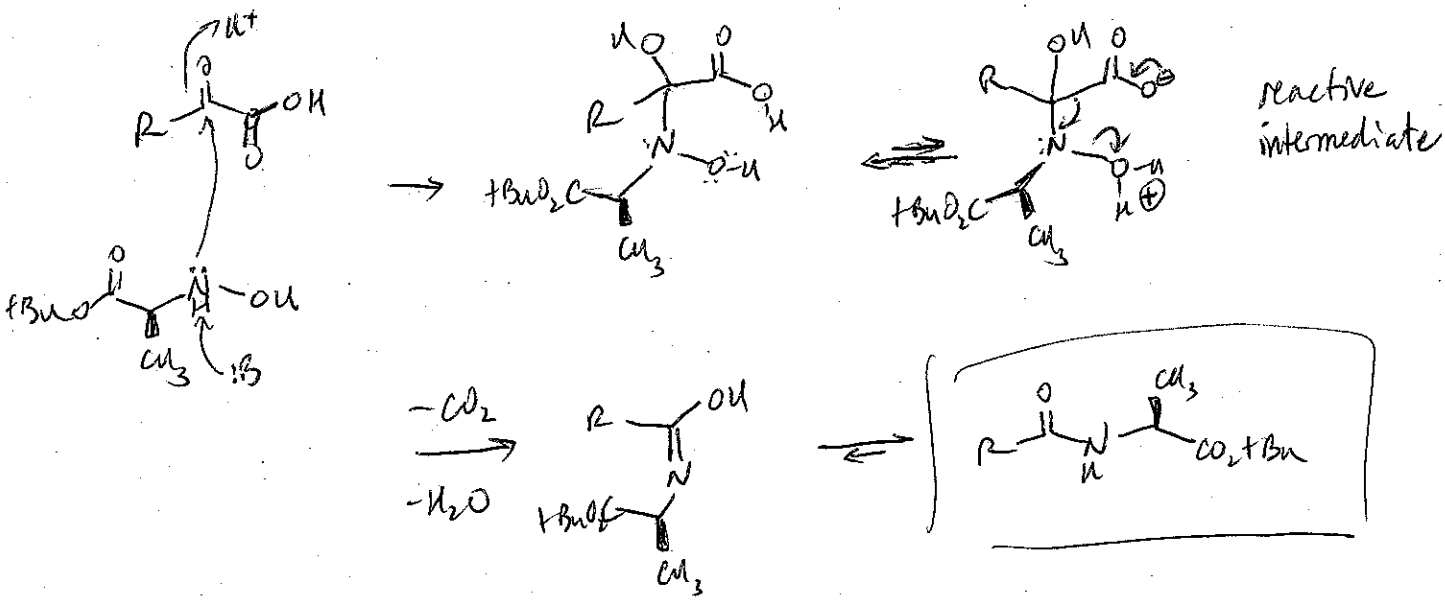
CRIB

Organic Cumulative Exam March 4, 2006

1. (25 pts.) Bode and co-workers have recently developed a novel way to form peptide linkages from *N*-alkylhydroxylamines and α-ketoacids (*Angew. Chem. Int. Ed.* **2006**, *45*, 1248-52). This coupling reaction is remarkable because it requires no activating agents.

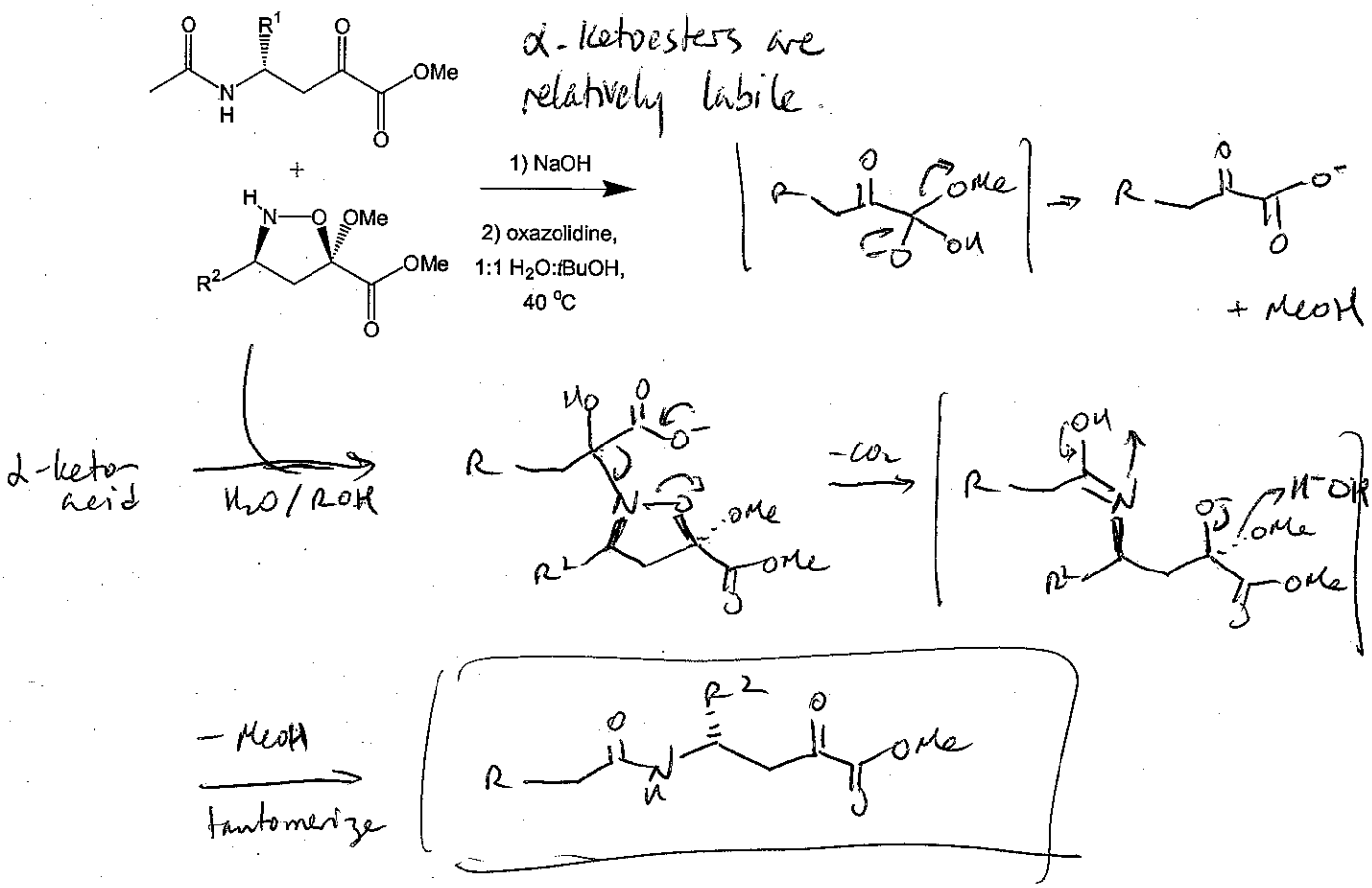


Provide a mechanistic explanation for the reaction above.

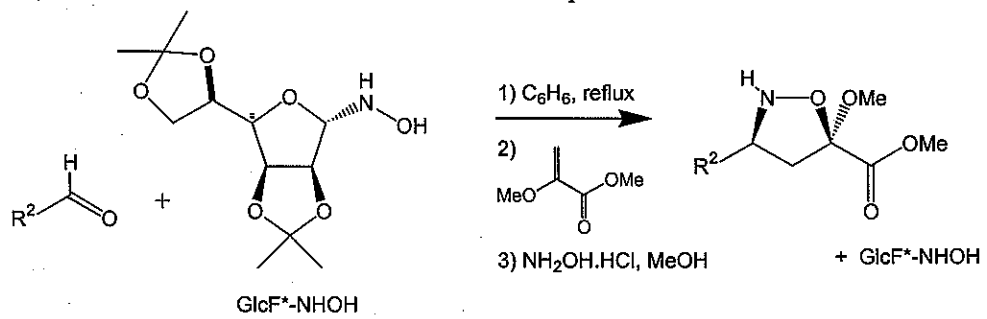


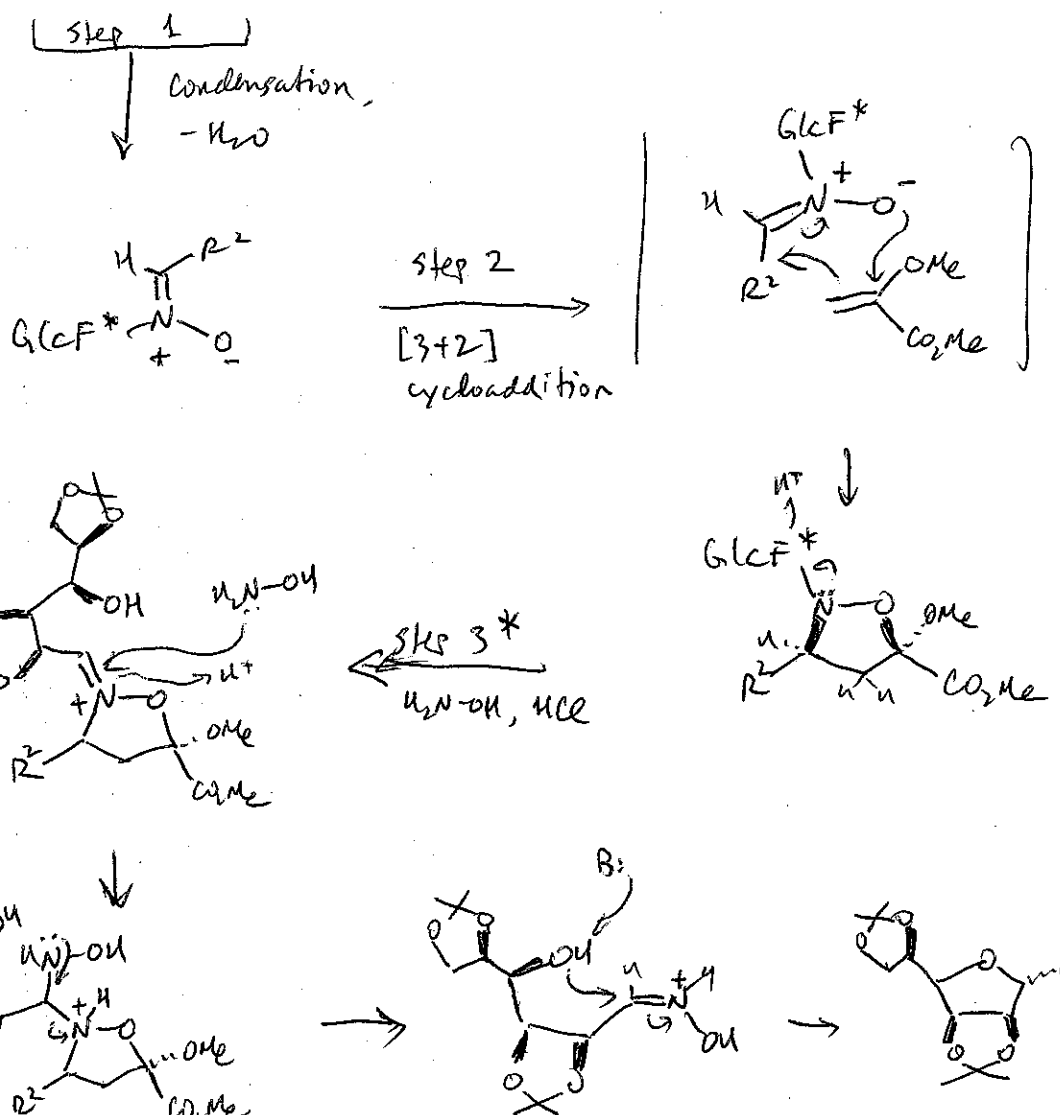
2. (25 pts.) Bode *et al.* apply their decarboxylative coupling reaction toward the reiterative synthesis of β-peptide oligomers, using isoxazolidine acetals as building blocks (*J. Am. Chem. Soc.* **2006**, *128*, 1452-53). The yields of these couplings are reported to be well over 90%.

Draw the structure of the reaction product, supported by a detailed mechanism. (In this reaction, the α-ketoesters is treated with NaOH prior to addition of the isoxazolidine)



3. (25 pts.) The isoxazolidines are prepared *via* a chiral nitrone intermediate, which react with an enol pyruvate and are treated with NH_2OH under acidic conditions for recovery of the chiral auxiliary (GlcF*). Provide the mechanism for this reaction sequence.





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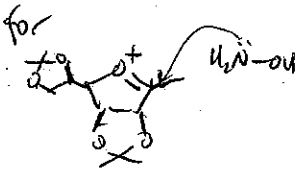
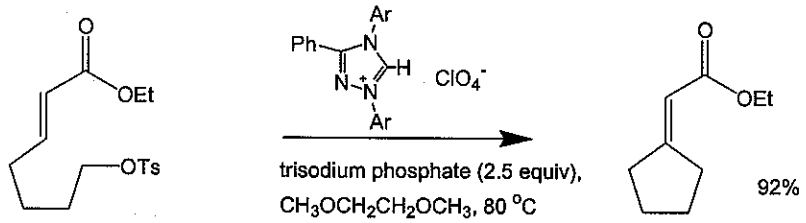
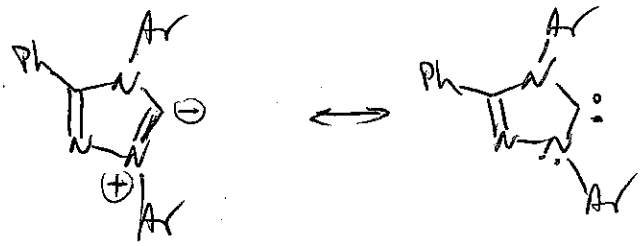


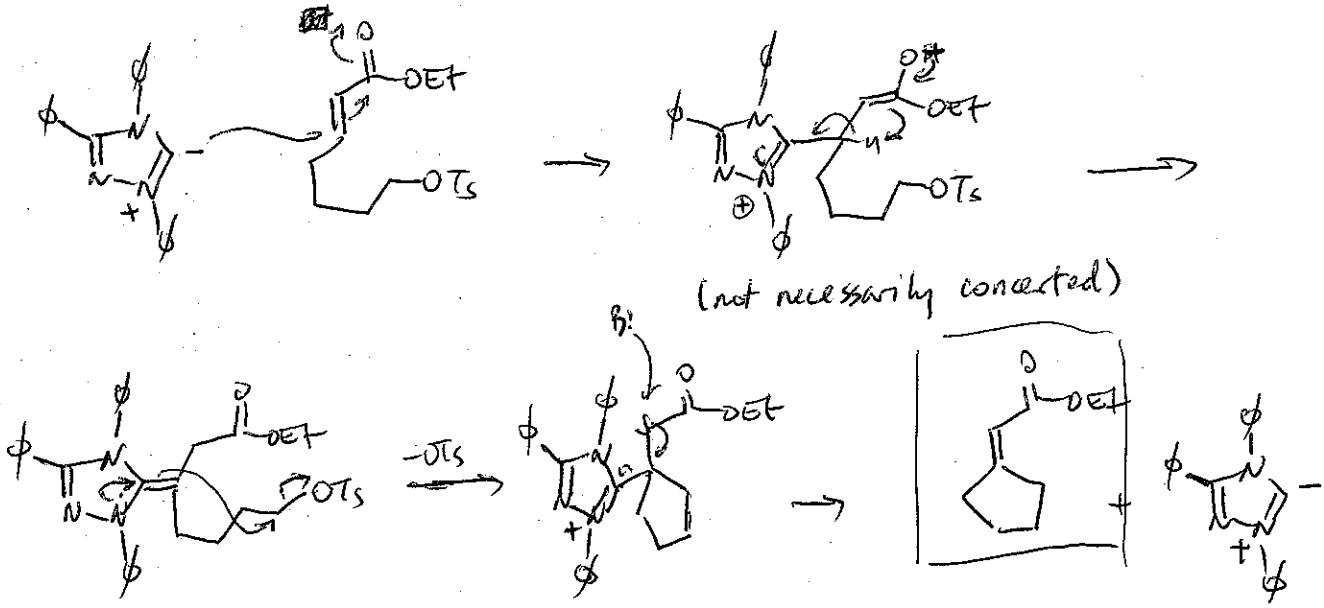
4. Fu and coworkers report a method for generating a nucleophilic carbene catalyst under basic conditions (*J. Am. Chem. Soc.* **2006**, *128*, 1472-73). They demonstrate its utility for organic synthesis in the "umpolung" (electrophile–nucleophile reversal) reaction below:



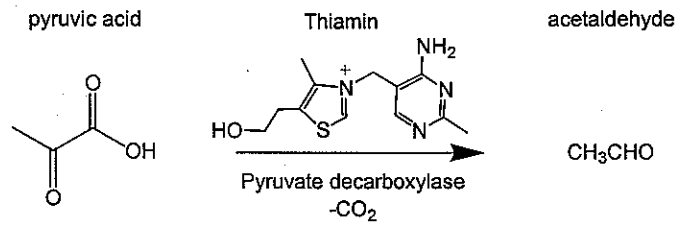
(a) (10 pts.) Draw two resonance structures of the active carbene species (*Note*: molecules similar to the triazolinium salt above are reported to have pK_a's between 14-18).



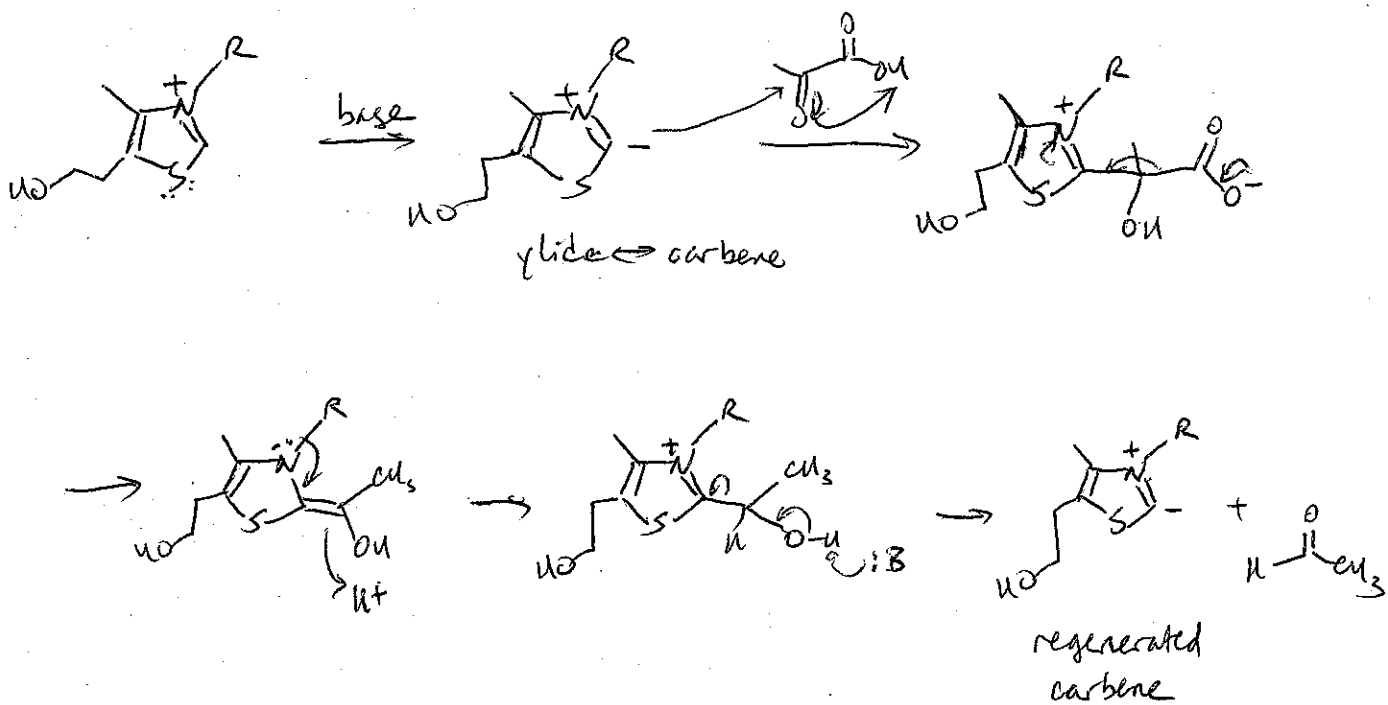
(b) (15 pts.) Provide a mechanistic description of the reaction sequence which regenerates the carbene catalyst. "Ar" = *p*-$MeOC_6H_4$.



5. Extra credit (15 pts.) The catalyst above bears some resemblance to thiamin (vitamin B_1), an enzyme cofactor. Thiamin is the active ingredient in pyruvate decarboxylase, which converts pyruvic acid into acetaldehyde (see below). Thiamin also has a remarkably low pK_a, and can be deprotonated in the environment of an enzyme active site.



Provide the mechanistic details of this classic transformation in enzyme chemistry. (The accepted mechanism was proposed 50 years ago by Ronald Breslow at Columbia University).



No Physical Crib

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