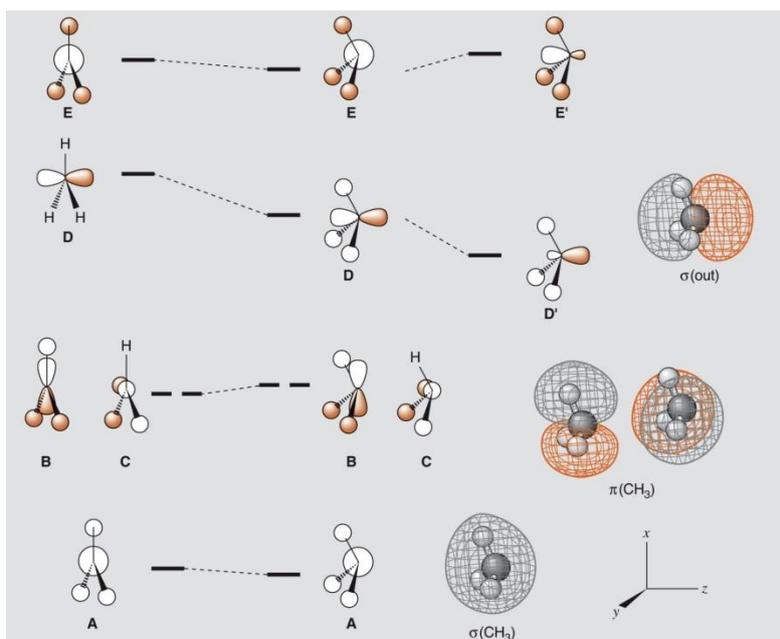


**Exam Physical Organic Chemistry (6KM17)**  
**Monday October 27, 2014 13.30–16.30 h**

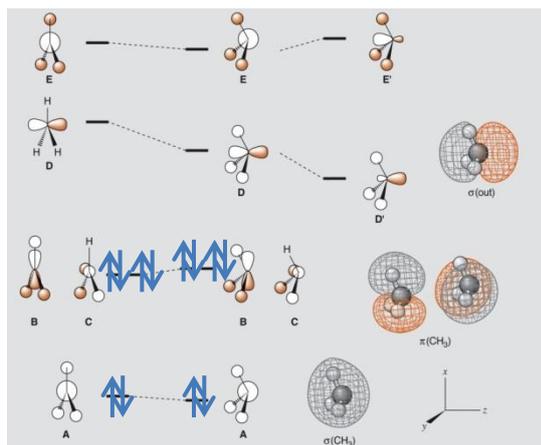
**This exam consists of 4 questions (100 points). Explain your answers clearly.**

**1 Bonding and Stability.**

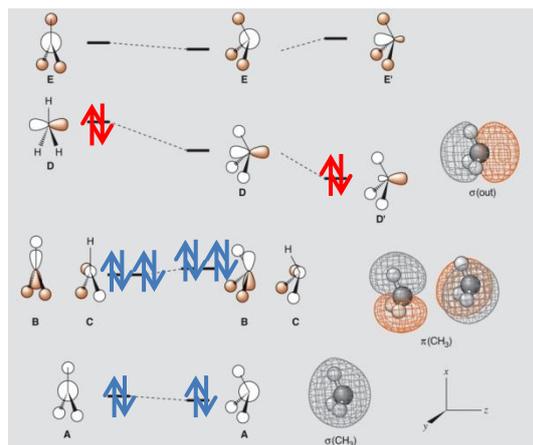
*Below, a Walsh diagram is shown for converting the CH<sub>3</sub> fragment from a planar to a pyramidal geometry.*



a) Using this diagram and the labels (A,B,C,..) for the orbitals, explain why the methyl cation is planar, while the methyl anion is pyramidal. 5 pt



Methyl Cation: 6 valence electrons



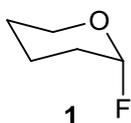
Methyl Anion: 8 valence electrons

In the methyl cation there are 6 valence electrons that fill the orbitals A, B, and C. These orbitals change little in energy upon pyramidalization, hence there is no stabilization of the pyramidal form. In the anion, the orbital D is filled. The energy of this orbital is lowered by pyramidalization, and the orbital is further stabilized by mixing with orbital E.

b) How does the electronegativity of F influence the energy levels of the Walsh diagram above for  $\text{CF}_3$ ? Use these changes to explain why the weak preference of the  $\text{CH}_3$  radical for a planar geometry becomes a strong preference for a pyramidal geometry in the  $\text{CF}_3$  radical. 5 pt

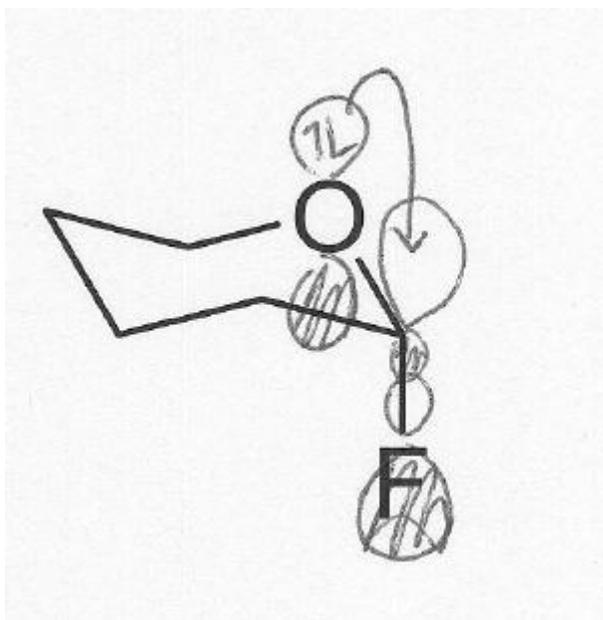
In the methyl radical, the D orbital is singly occupied. Pyramidalization stabilizes this orbital but single occupation does not lead to enough energy difference to favor the pyramidal form. There is no additional stabilization in the planar  $\text{CF}_3$  radical because the orbital coefficients of the F 2s orbitals are zero (that is why no electron clouds are drawn around the hydrogen atoms in planar **D**). In the pyramidal form stabilization is large in the  $\text{CF}_3$  radical, because the electronegative F atoms lower the energy of all orbitals to which they contribute.

*In molecule 1, there is a preference for a conformation with an axial fluorine atom due to the anomeric effect.*

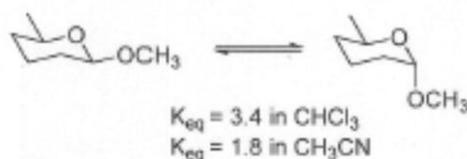


c) Which orbitals interact to stabilize this conformation? Draw these orbitals in the molecule. 5 pt

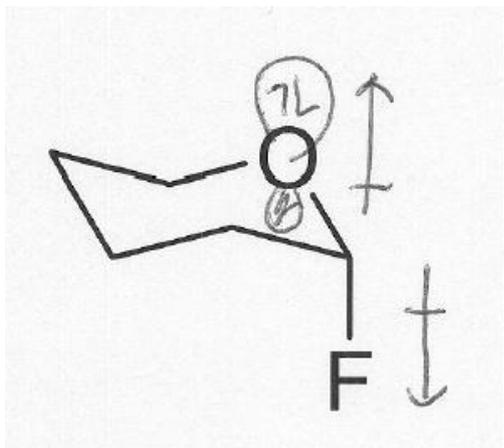
The orbital of one of the free electron pairs on oxygen interacts with the antibonding  $s^*$  orbital of the C-F bond.



*It has been observed that the anomeric effect is weaker in solvents with a higher polarity. This solvent dependence does not agree with the origin discussed in the lectures. In fact there is another proposed origin for the anomeric effect that is consistent with this observation.*



d) In the structure of **1**, consider the lone pair in the axial position on the oxygen atom. Draw a dipole arrow for the lone pair and a dipole arrow for the C-F bond in the two chair conformations of the molecule. 4 pt

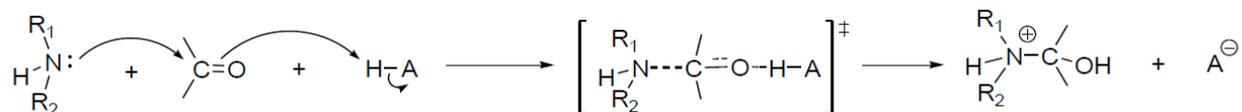


e) Explain using these dipoles why the anomeric effect would be more pronounced in lower polarity solvents. 6 pt

In the axial orientation the dipoles cancel to give no or a small net dipole. Polar solvents can stabilize net dipoles better than apolar solvents. In nonpolar solvents the axial preference is therefore accentuated

## 2 Reaction mechanisms

*The addition of amines to carbonyl compounds, in the presence of acid, is often a concerted process, as shown below.*



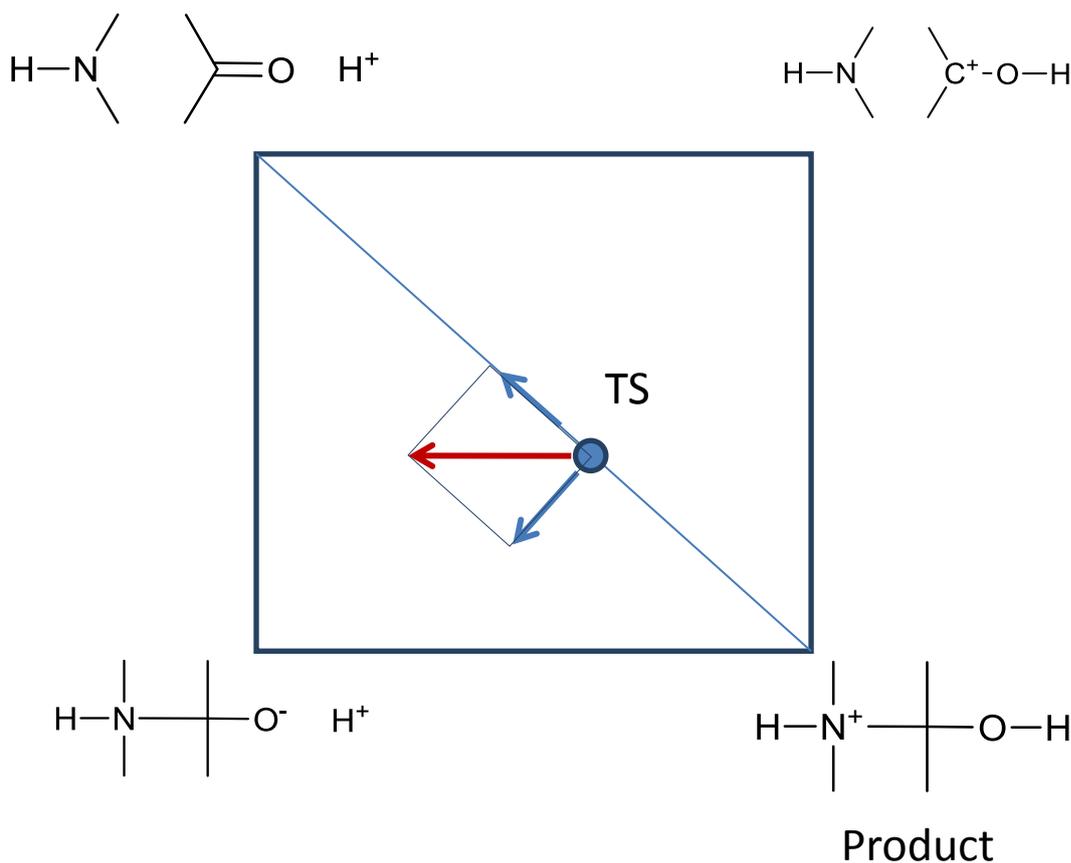
a) Construct a More O'Ferrall – Jencks diagram for the process, clearly indicating the nature and structure of the species at each of the corners. 13 pt

Then demonstrate the following:

b) How would the character of the TS change upon increase of the strength of the nucleophile? 6 pt

c) How would the character of the TS change upon increase of the strength of the acid? 6 pt

Starting material

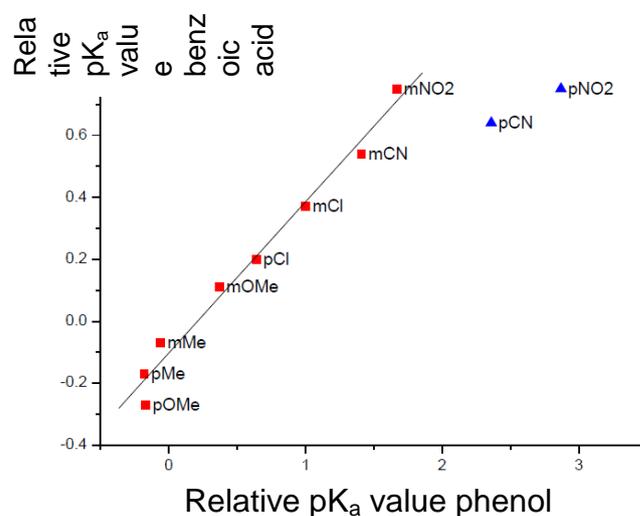


a) The plot shows the starting material in the upper left corner, the product in the lower right corner. The other corners show full formation of the C-N bond in the intermediate (bottom left) and full protonation of the carbonyl oxygen atom in the intermediate. The transition state (TS) is shown as a dot on the reaction coordinate. b) If the nucleophile gets stronger, the TS will move in the direction of the bottom left corner, perpendicular to the reaction coordinate. Simultaneously, due to the Hammond effect, the structure of the transition state will move towards the starting material along the reaction coordinate. The combined effect on the transition state is indicated by the red arrow.

c) If the acid gets stronger, a similar picture can be drawn with the blue arrows to the top right and the top left.

### 3 Linear Free energy relationships

In the plot below, a series of acidity constants for differently substituted benzoic acids is correlated to the pK<sub>a</sub> value of the corresponding phenol.



a) Explain why it makes sense that the relative pK<sub>a</sub> of the benzoic acids are linearly related to the pK<sub>a</sub> of most of the phenols (datapoints in red). Why does it make sense that the slope of the plot is not equal to 1? 5 pt

The plot indicates that as the phenol becomes more acidic, the benzoic acid does so as well. This makes sense because in both deprotonation reactions, a negative charge is developed on the molecule. Stabilization of the negative charge by substituents will in both cases make the molecule more acidic.

The slope is not 1 but approximately 0.5. This means that the stabilization of the phenolate by the substituent is larger than the stabilization of the benzoate by the same substituent. This makes sense because the charge of the phenolate is closer to the phenyl ring than the charge on the benzoate.

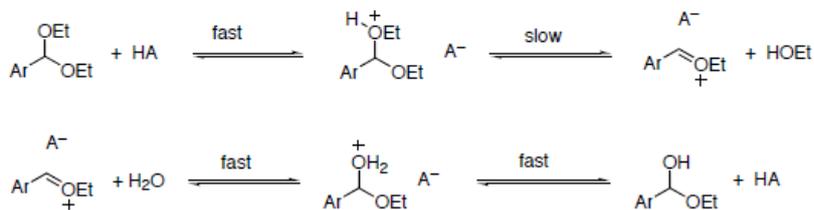
b) Why does the linearity fail for the two datapoints in blue? 4 pt

The p-cyano and the p-nitro group are able to stabilize charge by resonance. However, the negative charge on the carboxylate group cannot be delocalized by resonance. Therefore their effect on the pK<sub>a</sub> of the phenol is larger than on the benzoic acid.

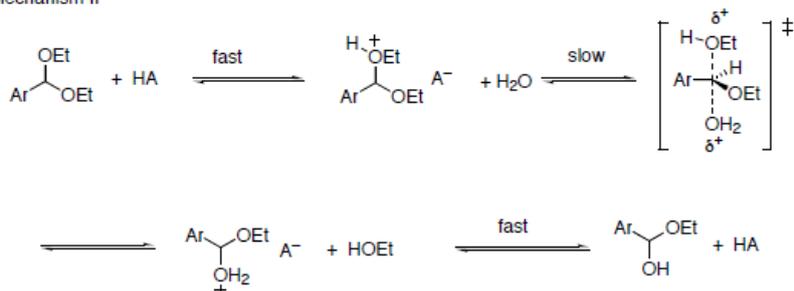
*Two possible mechanisms for the hydrolysis of an benzaldehyde acetal to a hemiacetal under acidic conditions are shown below:*



Mechanism I



Mechanism II



- c) positive  $\Delta S^\ddagger$  values are found for this reaction. What do these values suggest about the transition state? Which mechanism is more consistent with these  $\Delta S^\ddagger$  values? (4 pt)

Positive values indicate a loose transition state with translational or conformational freedom. This is more consistent with mechanism 1

*In an effort to distinguish between the two mechanisms, the rate for hydrolysis of a series of meta and para substituted benzaldehyde acetals were measured. A plot of  $\log(k_{rel})$  vs. the Hammett parameter  $\sigma$  is shown below.*

- d) Explain how the Hammett parameter  $\sigma$  is defined. 4 pt

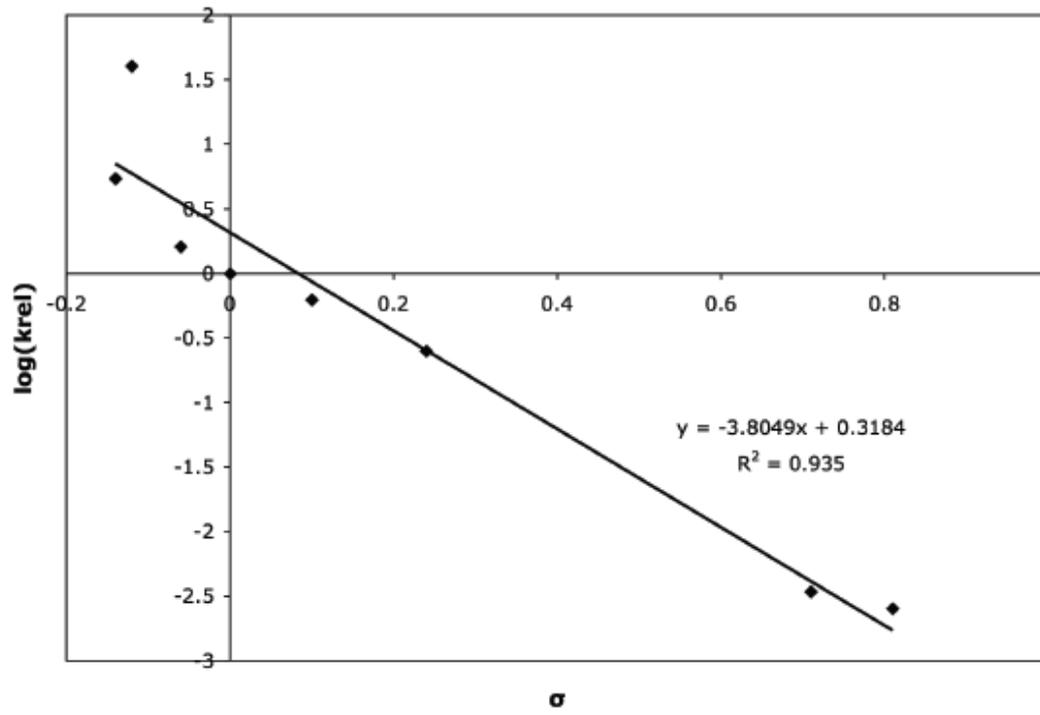
The  $\sigma$  parameter is defined as the pKa of a substituted benzoic acid relative to benzoic acid itself.

- e) The plot has one datapoint at the origin. Which substituents on benzaldehyde does this datapoint represent? 3 pt

Y= H and X=H

- f) Based on the Hammett plot, which mechanism seems more likely? Explain the specific information that leads you to this conclusion. 5 pt

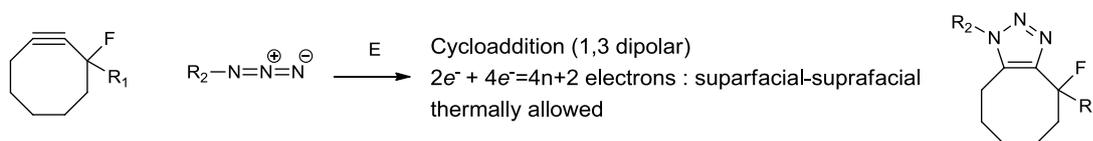
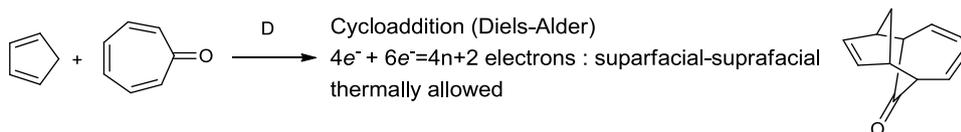
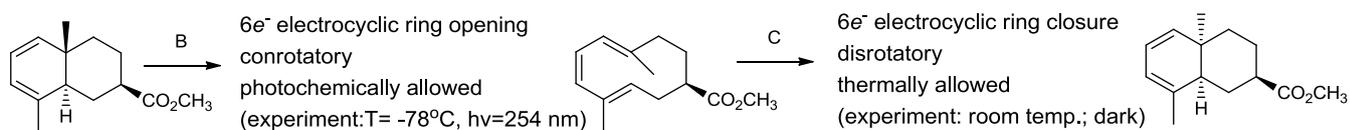
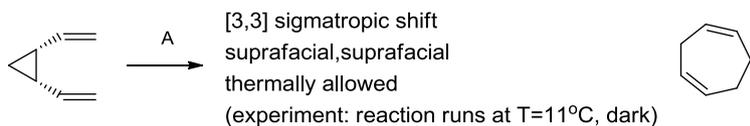
The plot has a large negative slope, which means that the reaction develops significant positive charge in the transition state. In mechanism I, the transition state will have much charge on the carbon atom, since it is similar in structure to the intermediate. Mechanism I is favored.



## 4 Orbital Controlled Reactions (25 pt)

For each of the five reaction steps (A-E) shown below, indicate:

- the type of pericyclic reaction (1 point each)
- the appropriate stereochemical course of the reaction (conrotatory/disrotatory/suprafacial/antarafacial) (2 points)
- the appropriate reaction conditions (heat or light) (2 points)



**SUCCESS!**